present analysis of upper limb function in non-ambulant paediatric DMD patients seen at Great Ormond Street Hospital, London UK, from October 2019 to date. We analysed functional status by measuring Performance of Upper Limb Module for DMD 2.0 (PUL) and Egen Klassifikation Scale Version 2 (EK) on average every 6 months. We compared progression in PUL and EK scales in patients on GC treatment vs those not on GC treatment. We also analysed progression to key disease milestones such as ability to perform hand-to-mouth function and eat independently. We included in the study 84 patients who performed at least one PUL assessments (median=3; range 1-6 assessments/patients) for a total of 237 assessments. In the same population we also performed 237 EK scale assessments. Average age at first PUL assessment was 13.4 years, and median age at time of loss of ambulation (LOA) was 10.1 years (range 6.6-16 years). At first assessment, 30 patients (35%) were on daily GC (prednisolone or deflazacort), 40 on intermittent or alternate day regimen (48%) and 14 not on CG (17%). We observed linear correlation between PUL score and age at LOA and time from LoA, and between EK and PUL scale ($p<0.001$). Longitudinal analysis (available for 62 patients) showed an annual decrease in PUL score of 2.7 units/year for the whole cohort, with no difference between GC treated and untreated patients. In summary, this study helps to better understand course of the non-ambulant phase of this disease and support clinical practice and care for patients. However, further analysis is needed to better clarify role and effect of various factors on the PUL slope and important key milestones.

http://dx.doi.org/10.1016/j.nmd.2023.07.083

P149

Delayed pulmonary progression in Golodirsen-treated patients with Duchenne muscular dystrophy vs mutation-matched external controls

J. Iff [1], E. Tuttle [2], Y. Liu [2], F. Wei [2], N. Done [2], L. Servais [3,4], A. Seferian [5], V. Straub [6], M. Guglieri [6], E. Mercuri [7,8], F. Muntoni [9,10]

[1] *Sarepta Therapeutics Inc, Cambridge, USA;* [2] *Analysis Group, Inc., Boston, USA;* [3] *Div Child Neurology, Centre de Références des Maladies Neuromusculaires, Dept Paediatrics, Univ Hosp Liège & University of Liège, Belgium;* [4] *MDUK Oxford Neuromuscular Centre & NIHR Oxford Biomedical Research Centre, University of Oxford, UK;* [5] *Assistance Publique Hôpitaux de Paris, Sorbonne Université, Institut de Myologie, AFM-Téléthon, Essais Cliniques I-Motion Enfants, Hôpital Armand Trousseau, Paris, France;* [6] *John Walton Muscular Dystrophy Research Centre, Translational & Clinical Research Institute, Newcastle University and Newcastle Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK;* [7] *Paediatric Neurology Unit, Università Cattolica del Sacro Cuore Roma, Rome, Italy;* [8] *Nemo Clinical Centre, Fondazione Policlinico Universitario A Gemelli IRCCS, Rome, Italy;* [9] *Dubowitz Neuromuscular Centre, Univ College London, Gt Ormond Street Inst Child Health, London, UK;* [10] *Nat Inst Health Research Gt Ormond St Hosp Biomedical Research Centre, London, UK*

Pulmonary decline in Duchenne muscular dystrophy (DMD) increases the risk of hospitalization, morbidity, and mortality. Golodirsen is FDA approved for the treatment of DMD in boys with mutations amenable to exon 53 and has been shown in Study 4053-101 (NCT02310906) to have functional benefits in a declining population of patients with DMD vs mutation-matched external controls (EC). This post hoc analysis compared longitudinal trajectories of percent predicted forced vital capacity (FVC%p) and projected time to cough-assist and nighttime ventilation in patients with DMD receiving golodirsen vs mutation-matched EC. Golodirsen-treated patients from Study 4053-101 and the open-label extension 4045-302 (NCT03532542) were required to have ≥2 FVC%p assessments at age ≥10 y at baseline. Mutation-matched EC were from CINRG-DNHS (NCT00468832), PRO-DMD-01 (NCT01753804), and Study 4658-301 (NCT02255552) and at baseline were age ≤12y. A linear mixed-effects model adjusting for baseline age and FVC%p was used to analyze FVC%p. Time to cough-assist (FVC%p ≤60) and nighttime ventilation (FVC%p ≤50) was predicted using a linear extrapolation of the model-estimated decline in FVC%p (from average FVC%p readings observed). At baseline, golodirsen-treated (n=20) and EC (n=17) were well-balanced for age and FVC%p; mean (SD) follow-up was 3.6 (1.8) and 2.4 (1.3) y, respectively. Results from the adjusted model indicated an attenuation of 3.8 percentage points in the annual rate of FVC%p decline for golodirsen-treated patients vs mutation-matched EC (2.9% vs. 6.7%; $P<0.01$). A previously published analysis of eteplirsen vs mutation-matched EC demonstrated similar rates of FVC%p decline. The estimated delay in time to reach cough-assist and in time to reach nighttime ventilation for golodirsen-treated patients vs EC was 5.6 (~14 vs 19) and 7.5 (~16 vs 23) y, respectively. In conclusion, golodirsen treatment was associated with significant attenuation of pulmonary decline based on FVC%p.

http://dx.doi.org/10.1016/j.nmd.2023.07.084

P150

Factors affecting the measurement variability of SV95C in ambulant patients with Duchenne muscular dystrophy

M. Rogers [1,2], S. Motola [1], D. Eggenspieler [1], M. Poleur [3], G. Parinello [1], D. Lozeve [1], A. Danon [3], L. Szabo [4], K. Aragon-Gawińska [5], A. Potulska-Chromik [5], N. Butoianu [6], C. Anghelescu [6], Mirea [7], D. Osredkar [8], E. Vrščaj [8], J. Haberlova [9], S. Kodsy [10], A. Salah [10], P. Strijbos [11], L. Servais [2,3]

[1] *Sysnav Technologies, Vernon, France;* [2] *Specialised Translational Research Oxford Neuromuscular Group, Dept Paediatrics, University of Oxford, UK;* [3] *Centre de Référence Liégeois des Maladies Neuromusculaires, Centre Hospitalier Régional de la Citadelle, Liege, Belgium;* [4] *Semmelweis University 2nd Dept of Paediatrics, Budapest, Hungary;* [5] *Warsaw Med Univ Hosp, Dept of Neurology, Warsaw, Poland;* [6] *Paediatric Neurology Clinic, Clinical Hosp Psychiatry, Bucharest, Romania;* [7] *Nat Clin Hosp for Children Neurorehabilitation, Bucharest, Romania;* [8] *University Children's Hospital, Dept for Paediatric Neurology, Ljubljana, Slovenia;* [9] *Fakultni nemocnice v Motole, state contributory organization, Prague, Czech Republic;* [10] *Galaa Military Medical Complex, Cairo, Egypt;* [11] *F. Hoffmann-La Roche Ltd, Basel, Switzerland*

Stride Velocity at the 95th Centile (SV95C) is a novel clinical outcome measure that is captured during normal daily living using wearable technology and represents the maximum ambulatory ability of a patient. SV95C is qualified by the European Medicines agency (EMA) for use as a secondary endpoint in pivotal studies in DMD, and is an important real-world functional endpoint complementary to the traditional in-clinic assessments such as the North Star Ambulatory Assessment scale and the Six Meter Walk Test. The Context of Use of SV95C as defined by EMA states that SV95C should be measured for at least 50h during normal daily living to yield an outcome variability that would render SV95C suitable for regulatory decision-making. Considering the increasing use of SV95C in drug development for DMD, it is critical to understand the most common drivers of endpoint variability. Using data from ActiLiège-NEXT, a prospective natural history study in ambulant patients with DMD designed to longitudinally characterise functional disease progression using multiple outcome measures, we evaluated the impact of the time of day, the day of the week as well as seasonal changes on the measurement variability of SV95C in ambulant patients with DMD. Specifically, SV95C will be computed for morning only (8am-12pm) and afternoon recording periods (2pm-6pm) and compared. A similar sensitivity analysis will be done for SV95C computed on weekdays (Monday-Friday) and weekend (Saturday-Sunday). The seasonal impact on the compliance and SV95C will be conducted on longitudinal data and adjusted by the geographical location of the patients, restricting to countries where the maximal temperature difference over the year exceeds 15° and maximal temperature does not exceed 30°C. This data provides important context to the factors that impact the measurement variability of SV95C and will be useful to inform clinical trial design in DMD, when using SV95C as an outcome measure of efficacy.

http://dx.doi.org/10.1016/j.nmd.2023.07.085

P151

Serum adipokines in Duchenne muscular dystrophy: relationships to BMI, corticosteroids, and muscle fat fraction

A. Barnard [1], N. Ikelaar [2], H. Kan [2], E. Niks [2], K. Vandenborne [1], G. Walter [1], P. Spitali [1]

[1] *University Of Florida, Gainesville, USA;* [2] *Leiden University Medical Center, Leiden, Netherlands*

Duchenne muscular dystrophy (DMD) is a progressive neuromuscular disorder hallmarked by muscle degeneration, replacement by fat, and weakness. Corticosteroids slow disease progression, but they also cause metabolic disruptions such as significant weight gain. For this preliminary study, we evaluated levels of serum adipokines, or factors released by adipose tissue, in a large cohort of individuals with DMD. 309 serum samples were collected from 94 participants with DMD (longitudinal samples) and 14 controls (one time point) enrolled in the ImagingDMD natural history study. Large-scale serum proteomics were conducted using the SomaScan platform. Targeted analysis was performed on 11 adipokines including leptin, adiponectin, resistin, visfatin, chemerin, omentin, ghrelin, obestatin, apelin, retinol binding protein (RBP), and vaspin. Levels were evaluated in relation to diagnosis, corticosteroid use, body mass index (BMI), and soleus muscle fat fraction, which was determined by magnetic resonance spectroscopy. Correcting for multiple comparisons, leptin, resistin, ghrelin, omentin, apelin, RBP, and vaspin levels were different in control and DMD serum, while RBP differed between serum from corticosteroid treated (n=268) and untreated individuals with DMD (n=14). BMI was strongly correlated with leptin (r=0.79) and weakly correlated with resistin, omentin, ghrelin, apelin, and RBP. When taking BMI into account, soleus muscle fat fraction was independently correlated with leptin ($p<0.0001$), adiponectin ($p<0.0001$), omentin ($p=0.0003$), and ghrelin levels ($p=0.0011$). Overall, 8 of 11 adipokines were altered in DMD, and 7 were correlated