O.06. Rapamycin prevents experimental scleroderma tous chronic graft-versus-host disease in mice

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Background
The most widely used mice model of chronic graft-versus-host disease (cGvHD) is an MHC-matched bone marrow transplantation model of sclerodermatous cGvHD. A limitation of that model is that mortality is relatively low, making difficult to study the impact of potentially therapeutic compounds.

Aims
To develop a more severe model of cGVHD and to assess the impact of rapamycin administration in that model.

Results
Lethally irradiated Balb/C mice were injected with 10x10^6 bone marrow cells and 70x10^6 splenocytes from B10.D2 donor mice. Twenty-one days later, all mice developed cGvHD. For the severe model, donor B10.D2 mice were injected with 0.5x10^6 splenocytes from Balb/C twenty-one days before transplantation. All mice from the severe model (n=8) died a median of 32 days while 3 of 7 mice in the classical model survived beyond day 52. Mean survival was decreased in the severe model compared to the classical model (p=0.0185). Recipient mice in the severe group experienced higher weight loss, hair loss and skin fibrosis. Numbers of T lymphocytes (p=0.0032) and CD4+ T cells (p=0.0018) per microliter of blood at day 21 were lower in the severe model. Moreover, number of regulatory T cells (Tregs) was decreased in the severe model (p=0.0151). We then investigated whether rapamycin administration could prevent GVHD in the severe model. All (n=8) mice treated with PBS (placebo) died a median of 32 days after transplantation, while 6 of 8 mice given 1mg/kg/day i.p. rapamycin survived beyond day 52 (p=0.0012). Number of Tregs/µl was higher at day 21 in rapamycin-treated mice than in PBS-treated mice (p=0.0796). Moreover, number of naïve CD4+T (p= 0.0089) and effector memory T cells (EMT) (p= 0.0125) were higher in rapamycin mice. Finally, proliferation of EMT (assessed by flow cytometry using Ki-67) was higher in PBS than in rapamycin mice (p=0.0474).

Conclusion
We have developed a mice model of severe cGVHD. Interestingly, rapamycin prevented death from cGVHD in that model, perhaps through in vivo expansion of Treg.

O.07. Retrospective analysis on the impact of iron chelation therapy on survival and leukemia progression in transfusion dependent MDS patients in Belgium

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Background/methodology
While appropriate iron chelation can prolong survival in patients with thalassemia major, this remains highly debated in MDS. This study aims to investigate the potential effect of iron chelation treatment (ICT) on overall and leukemia free survival and to examine treatment modalities, transfusion needs and chelation practices in transfusion dependent MDS patients. Follow-up data was collected from 186 patients, previously identified in a Belgian cross-sectional study performed in 2008 (Delforge et al., 2011).

Results
Of the patients, 38% were still alive and 4% lost to follow-up. AML progression was reported for 18% of patients. At the time of diagnosis, 68% of patients were classified as low-intermediate1 IPSS score, 9% with intermediate2-high IPSS score, whereas no IPSS score was available for 23%. ICT was started on average 3.6 yrs after diagnosis and 1.4 years after the first RBC transfusion. At initiation of ICT, the mean serum ferritin was 2302±2607 µg/L. 40% never received ICT. Median survival for low-intermediate1 IPSS patients was 87 months. Patients within this group, who received ICT had a longer median survival than non-chelated patients (123 vs. 37 months; p<0.001). Moreover, the intensity of ICT was associated with outcome: patients having received more intense ICT had a longer survival than patients receiving Desferal bolus injections (126 vs. 52 months; p:0.001), whereas no significant survival difference was observed between Desferal bolus injections vs. no ICT (52 vs. 37 months; p:0.322). Similar differences were observed for AML-free survival. In Cox Proportional Hazard models the use and intensity of ICT appeared to be the most prominent factors impacting survival, followed by calculated "transfusion intensity".

Summary/conclusion
Although we cannot exclude a patient selection bias, this study confirms, in an independent fashion, the previous findings of the GFM (Rose et al., 2010) and of the Dusseldorf registry (Fox et al., 2010): patients who received ICT have a better outcome. Prospective randomised trials remain necessary to confirm the benefit of ICT.

O.08. Quantitative and qualitative analysis of metabolic response at interim FDG pet-scan is highly predictive of outcome in diffuse large B-cell lymphoma (DLBCL)

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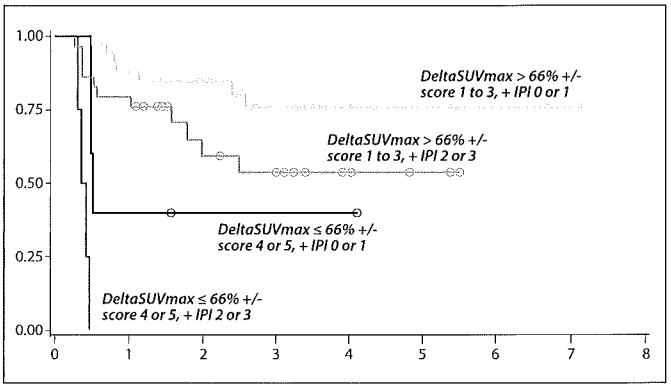
We investigated whether mid-treatment metabolic response had prognostic value in 74 DLBCL pts (median 60y; 47M/27F; IPI: low/low-int 50%, high-int/high 50%) treated upfront with anthracyclin-containing regimens. Qualitative analysis was done using Deauville's criteria, and quantitative analysis by comparing baseline and interim metabolic activity (ΔSUV(max)). Survivals are at two years. Deauville's score was 1 in 34%, 2 in 23%, 3 in 15%, 4 in 18%, and 5 in 10%. Median ΔSUV(max) was 85%. 18% had a ΔSUV(max) ≤ 66%, a highly discriminating threshold. Outcome in pts with Deauville's score of 1 to 3 ("negative") was better than in pts with score 4 or 5 ("positive") in EFS (79% vs 36%, P<.0001), PFS (83% vs 47%, P.0006), and OS (91% vs 58%, P.0003). Pts with a ΔSUV(max) > 66% or ≤ 66% also had different EFS (73% vs 41%, P.009), PFS (78% vs 50%, P.02), and OS (88% vs 56%, P.008). Pts with a positive qualitative pet and a ΔSUV(max) ≤ 66% had an OS of 20%. Pts (n=33) combining aaIPI 0 or 1, and negative pet by any criteria showed excellent outcome (EFS: 85%, PFS: 88%, OS: 94%).

Figure 1. EFS according to results of interim pet with aaIPI.



Deauville's and ΔSUV(max) response independently predicted for EFS (HR 4.3; HR 4.3), PFS (HR 3.2; HR 3.5), and OS (HR 3.6; HR 4.2, respectively). IPI did not retained independent prognostic value. Combination of a favourable IPI (0, 1) and a negative interim pet by any criteria yielded a negative predictive value (PV) of 96%, while positive PV remained poor (50%). In this retrospective study, analysis of metabolic response at mid-treatment, using adapted criteria, was