stop or significantly reduce steroids. With a median follow-up of 31 months (3-45) 27 patients are alive and 7 patients died: 4 due to GVHD progression and 2 for infections; 17 patients are in continue response at last follow-up, without additional treatments. The RR observed in this second trial, in a larger series of patients with steroid-refractory cGVHD seems slightly inferior, compared to the RR observed in the first trial, probably due to the more stringent response criteria used. Moreover the higher median age and the different kind of patients could have influenced these results: the previous study included only patients with skin fibrotic cGVHD and pediatric patients. However the stable response observed after 12 months and the promising outcome (Figure 1: OS; Figure 2: EFS), in this very hard to treat set of patients, suggest that Imatinib is a valuable option in patients with steroid-refractory or steroid-dependent cGVHD.

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O320
Circulating B-cell activating factor level predicts likelihood of chronic GvHD flare and probability of successful steroid taper during extracorporeal photopheresis therapy
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Introduction: Extracorporeal photopheresis (ECP) is an important second line therapeutic intervention in steroid refractory chronic GVHD (cGVHD) with recognised efficacy as a steroid sparing agent. Few reliable biomarkers predicting ECP response exist. B-cell activating factor (BAFF) has described roles in immature B-cell survival. Elevated BAFF levels reportedly correlate with cGVHD activity and excess BAFF may contribute to cGVHD maintenance. We report that BAFF level following 6 months of ECP therapy predicts the likelihood of disease flare and capacity for successful steroid taper.

Methods: We retrospectively evaluated 28 adult patients undergoing ECP for steroid-refractory, resistant or intolerant cGVHD. ECP was performed using the Therakos XT™ or Cellex™ devices. ECP treatment schedule was 2-weekly dual treatments for an initial 3 months, then monthly paired treatments until at least 12 months. 24/28 patients were receiving steroids at start of ECP. Skin disease response was assessed using the Modified Rodnan skin scoring system. Extracutaneous organ cGVHD response was assessed by reduction in symptoms as defined by NIH criteria. Disease flare was defined as significant symptomatic increase of, or reappearance of, GVHD in affected organ(s). Initiation of steroid or other immunosuppressives during treatment was also regarded as loss of disease control. Successful uninterrupted steroid taper was defined as the capacity for dose reduction without steroid re-escalation between 3 and 18 months of ECP. Soluble BAFF in patient sera was measured prior to ECP, and at 3, 6, 9 and 12 months of ECP using commercially available enzyme-linked immunosorbent assay.

Results: All patients with serum BAFF levels above 4 ng/ml following 6 months of ECP therapy (n=15) experienced a loss of disease control as evidenced by GVHD flare between 3 and 18 months of ECP. This resulted in re-escalation of steroid dose in 13/15 patients (87%) and steroid introduction in 1 patient. Loss of GVHD control was significantly less common amongst patients with BAFF levels below 4 ng/ml at 6 months of ECP; 6/13 patients experienced disease flare between 6 & 18 months (P=0.001, Fishers exact) resulting in steroid or cyclosporine re-escalation in 5/13 patients (P=0.002) whilst steroid taper without escalation was possible in 7/11 patients (P=0.001).

Conclusions: Our data supports further prospective studies to assess the potential prognostic value of early BAFF measurement in ECP therapy for cGVHD.
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 (32 days versus 37 days; p=0.0185). Recipient mice in the severe group experienced higher weight loss, hair loss and skin fibrosis. Numbers of T lymphocytes (231 ± 151.4 versus 951 ± 532.8; p=0.0032) and CD4+ T cells (63.25 ± 41.93 versus 135.0 ± 14.39; p=0.0018) per microliter of blood at day 21 were lower in the severe group than in the classical model. Moreover, number of naïve CD4+ T cells (0.004 ± 0.192 versus 0.25 ± 0.185; p=0.0089) and effector memory T cells (EMT) (30.6743 ± 180 versus 67.33 ± 7.881; 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 (45.26%±4.084 versus 31.90%±2.003; p=0.0474).

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

### Stem Cell Source and Donor

#### O322

**Different effect of HLA disparity on transplant outcomes after single unit cord blood transplantation between paediatric and adult patients with leukaemia**


Recent advances in unrelated cord blood transplantation (UCBT) has provided increased chances for patients with hematological malignancies to receive hematopoietic stem cell transplantation (HSCT).

We have investigated the effect of HLA disparity of unrelated cord blood on HSCT outcome in children and in adults separately. 498 children aged 15 years or younger (HLA-A, -B low resolution and -DRB1 high resolution matched, n=82, one locus mismatched, n=222, two loci mismatched, n=158, three loci mismatched, n=36) (median age, 5 years) and 1,880 adult patients (HLA matched, n=71, one locus mismatched, n=309, two loci mismatched, n=1,025, three loci mismatched, n=475) whose age was 16 years or older (median age, 49 years) at the time of transplant were analyzed. Subjects were recipients of single unit UCB as first HSCT with leukemia. Median infused total nucleated cell number was 5.30 x 10^7/kg in children and 2.52 x 10^7/kg in adults (p<0.001).

With adjusted analyses, in children, HLA two-antigen mismatched UCBT showed significantly increased risk of overall mortality (relative risk [RR]=1.61, P=0.042) and transplant-related mortality (RR=3.55, P=0.005) compared to HLA matched. Risk of relapse did not differ significantly. Risk of mortality increased according to the number of mismatched loci (p for trend, 0.043 and 0.002 for overall mortality and TRM). Risk of relapse was not different among HLA disparity groups in children. Risk of grade 2 to 4 acute GVHD was increased in one- (RR=2.18, P=0.003) and two- (RR=2.51, P=0.001) loci mismatched in children. Two-loci mismatched was associated with higher risk of grade 3 to 4 acute GVHD in children (RR=2.45, P=0.041).

In Adults, the risk of mortality did not increase with the number of mismatched loci (RR=0.98, P=0.924 for one-locus mismatched, RR=0.88, P=0.423 for two-loci mismatched, and RR=0.95, P=0.746 for three-loci mismatched for overall mortality). In adults, risk of relapse was significantly decreased in two-loci mismatched (RR=0.67, P=0.029). Risk of TRM, grade 2 to 4 or grade 3 to 4 acute GVHD did not differ among HLA disparity groups in adults.

Effect of HLA disparity on transplant outcomes were different between children and adults. In children, increased number of mismatched HLA loci correlated with increased risk of mortality. In adults, there was no increase in mortality with increase in the number of mismatched HLA loci.

#### O323

**Co-infusion of haematopoietic progenitors from a HLA non-identical adult donor is a most efficient strategy for cord blood transplants early neutrophil recovery, engraftment and survival in adults with haematological malignancies**


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Late engraftment is a risk factor for CBT in adults. To overcome this limitation in 1999 we developed the “dual transplant” method (1): co-infusion of only one CB unit and highly T-depleted mobilized CD34+ (HP) cells from an adult third party donor (TPD), haploidentical or not. Here we report data from 98 adults (61/37 M/F) median weight 70 Kg (42-111) transplanted in 3 Spanish centers to treat high risk hematological malignancies (HM). Indications: Acute Leukemia (AL) 85 (43 AML, 32 ALL), other 13.

Transplant products cellularity and HLA compatibility data shown in Table 1; 105 CB units were used as a 2nd unit was required for 7 patients: 2 rejections; 4 graft failures due to lack of viable HP: 1 relapse.

Conditioning: For 49: 10 Gy fractionated TBI, Fludarabine 60 mg/m, CTX 120 mg/kg and ATG; other 49 received Busulfan 3,2 x2-3 mg/kg instead of TBI.

Post-Tx treatment: G-CSF, Prednisone 1 mg/Kg 8-14 days and CsA till full CB chimerism.

Engraftment data shown in Table 1. The TPD did not take in 8 cases: 1 due to very early CB engraftment; 6 seemingly due to recipient allo sensitization against TPD (mother or husband). Other 6 who had engraftment failure/rejection of the initial CBt had sustained TPD graft until the take of a second CBT, given after 33-94 days preceded by a 2nd conditioning (Fludarabina+ATGz 2 Gy TBI or Thioteplus+Fludarbin+ATG).

MORB-mortality and survival data on incidence of TRM, relapses and GVHD are shown in Table 1. In no case were TPD cells involved in aGVHD lesions. Most common infections were CMV (72 episodes), declining after 3-4 months with 6 deaths. Other 2 deaths were due to toxoplasmosis and 1 each to EBV-PTLS, leishmaniasis and scedosporium prolificans infection (related to long pre-tx neutropenia).

Conclusions: Time to neutrophil recovery after dual transplants is consistently shorter than reported for other approaches (ex-vivo expansion, double CBT, intrabone infusion), resulting in low risk of early infections. This and the favorable data on aGVHD and relapses (i.e. GVT) contribute to less hospital days, what together with the procedure relative low cost translates into favorable costs/results ratio. The procedure may allow selection of CBT units prioritizing HLA compatibility to cell content and use of a fraction of CBT