fungal infections, 3 hematuria of viral etiology (BKV/ADV), and 1 each of ADV, CMV, RSV, Parainfluenza, HSV, or Mycobacterium infections.

Conclusion: RI AlloSCT based on BFA conditioning is feasible and tolerable in C&A, and results in prompt achievement of durable mixed donor chimerism and excellent OS.

236

DRIED BLOOD SPOT ANALYSIS: AN EASY AND RELIABLE TOOL TO MONITOR THE BIOCHEMICAL EFFECT OF HEMATOPOIETIC STEM CELL TRANSPLANTATION IN HURLER SYNDROME PATIENTS IN A MULTI-CENTER INTERNATIONAL SETTING

Aldenhoven, M.[1], de Koning, T.J.[2], Verheijen, F.W.[3], Prinsen, B.H.[4], Wijburg, F.A.[5], van der Ploeg, A.T.[6], de Sain – van der Velden M.G.M.[4], Boelens, J.J.[1] [1] University Medical Center Utrecht, Netherlands; [2] University Medical Center Utrecht, Netherlands; [3] Erasmus University, Rotterdam, Netherlands; [4] University Medical Center Utrecht, Netherlands; [5] Academic Medical Center Amsterdam, Amsterdam, Netherlands; [6] Erasmus University, Rotterdam, Netherlands

Hurler syndrome (HS), the most severe phenotype in the spectrum of MPS I, is caused by a severe deficiency of the lysosomal enzyme alpha-L-iduronidase (IDUA). At present, hematopoietic stem cell transplantation (HSCT) is the only treatment able to prevent disease progression in the central nervous system and therefore considered the treatment of choice in HS patients. Since IDUA enzyme levels after HSCT have been suggested to influence the prognosis of HS patients, monitoring these levels after HSCT remains highly important. The current standard for biochemical monitoring after HSCT is the leukocyte IDUA enzyme level. There is however a high inter-laboratory variability concerning the analysis of leukocyte IDUA, which makes enzyme level comparison between centers very difficult. The use of dried blood spot (DBS) for enzyme analysis has already been demonstrated to be an easier and less expensive method. Furthermore, this method requires only a minimal amount of blood and makes worldwide shipment feasible. DBS analysis would therefore be more suitable for use in large-scale international studies.

From 13 HS patients receiving HSCT, 35 paired whole blood and DBS samples were analyzed on leukocyte and DBS IDUA levels, respectively. In order to correct for potential interfering factors, simultaneous assay of the alpha-Galactosidase-A (AGA) level was performed in the DBS samples and an IDUA-AGA-ratio was calculated. A strong correlation was demonstrated between the DBS IDUA-AGA-ratio and the leukocyte IDUA levels ($r^2 = 0{,}875$, $p < 0{,}001$). This linear correlation was applicable to all enzyme levels, including the levels measured early after HSCT as well as heterozygous levels due to mixed chimerism or the use of a carrier donor. These results demonstrate that the DBS method is reliable to monitor the biochemical effect of HSCT in HS patients. This method is therefore a useful alternative to the conventional leukocyte assay during the follow-up of HS patients after HSCT as well as during large-scale international studies. In the future, the DBS method might be extended towards monitoring the biochemical effect of HSCT or any future therapy (eg gene therapy) on other lysosomal storage disorders.

237

TOTAL LYMPHOID IRRADIATION FOR THE TREATMENT OF REFRACTORY BRONCHIOLITIS OBLITERANS FOLLOWING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

Lewis, J.A.[1], Jenrette, J.M.[2], Watkins, J.M.[2], Kraveka, J.M.[1], Hudspeth, M.P.[1] [1] Medical University of South Carolina, Charleston, SC; [2] Medical University of South Carolina, Charleston, SC

Bronchiolitis obliterans (BO) is one of the most challenging late noninfectious complications of allogeneic hematopoietic stem cell transplantation (HSCT). BO is associated with a progressive decline of pulmonary function secondary to air flow obstruction and overall survival of only 13% at 5 years. Treatment strategies mirror that of chronic GVHD consisting of systemic corticosteroids and augmentation or re-institution of immunosuppressive therapy. Response is poor with a 3-year mortality rate of 65% when BO accompanies cGVHD. Total lymphoid irradiation (TLI) has been used with some success for the treatment of BO following lung transplantation but has not been reported in the treatment of BO following allo-HSCT. We present two pediatric patients who received TLI for refractory BO after unrelated peripheral blood stem cell transplant (PBSCT). The diagnosis of BO was made by an irreversible obstructive pattern on pulmonary function testing, CT scans with bilateral air trapping, and absence of infection. BO progressed despite aggressive therapy with corticosteroids, tacrolimus, mycophenolate mofetil, and etanercept. Patient 1 is a 15 year-old who underwent a 9/10 (one C allele mismatch) PBSCT in 2005 for secondary AML with TLI initiated at 30 months after PBSCT. Patient 2 is a 9 year-old who had a 10/10 PBSCT in 2006 for relapsed ALL with TLI initiated at 26 months after PBSCT. Patients received a total of 80 cGy of irradiation delivered in two 8 cGy fractions per week for a total of 10 fractions. Treatment was well tolerated with grade 1 thrombocytopenia in patient 1 and grade 2 anemia and grade 3 thrombocytopenia in patient 2 per CTCAE v 3.0. Patient 1 had no further decline in FEV1 with improvement in FEV1/FVC and FEF 25%-75% at 6 months after TLI but died at 11 months post TLI due to multiple infections. Patient 2 had a dramatic increase in FEV1, FEV1/FVC, and FEF 25%-75% that remains sustained at 10 months post TLI. These results strongly suggest that TLI is a useful modality in the treatment of refractory BO following allo-HSCT and should be evaluated in future studies.

Table 1. Pulmonary Function Tests Before and After Total Lymphoid Irradiation (TLI)

	Patient #1 TLI at 30 months			Patient #2 TLI at 26 months		
Time after PBSCT	FEV1 % predicted	FEV1/ FVC	FEF 25% - 75% % predicted	FEV1 % predicted	FEV1/ FVC	FEF 25% - 75% % predicted
12 months	75%	92%	93%	96%	100%	118%
18 months	71%	89%	92%	93%	96%	119%
23 months	62%	80%	55%	70%	94%	102%
26 months	46%	73%	27%	54%	88%	48%
30 months	47%	67%	27%	78%	93%	101%
36 months	48%	77%	37%	95%	99%	124%

Abbreviations: PBSCT (peripheral blood stem cell transplant)

238

TREATMENT OF PEDIATRIC HIGH-RISK MALIGNANCIES USING NON-MYELOABLATIVE (NM) HEMATOPOIETIC CELL TRANSPLANTATION (HCT): A MULTI-INSTITUTIONAL EXPERIENCE

Thakar, M.S.[1], Storer, B.[1], Storb, R.[1], Shizuru, J.[2], Niederwieser, D.[3], Pulsipher, M.[4], Sahebi, F.[5], Sorror, M.[1], Chen, Y.[1], Georges, G.[1], Maloney, D.[1], Woolfrey, A.[1], Sandmaier, B.M.[1] [1] Fred Hutchinson Cancer Research Center/University of Washington, Seattle, WA; [2] Stanford University Medical Center, Palo Alto, CA; [3] University of Leipzig, Leipzig, Germany; [4] University of Utah Medical Center, Salt Lake City, UT; [5] City of Hope National Medical Center, Duarte, CA

Compared to older adults, the role of NM-HCT to cure pediatric malignancies is not well-established and has typically been reserved for high-risk patients (pts). We conducted a retrospective multi-center analysis of all pts who were <22 yrs old with hematological malignancies treated on protocol to determine factors associated with outcome after NM-HCT. Between Jan 2001-July 2008, 26 pts with a median age of 17.9 (5.1-21.9) yrs were treated for ALL (CR1,n = 1;CR2,n = 3;CR3,n = 5), AML (CR2,n = 5; CR4,n = 1; PR, n = 1), Hodgkin lymphoma (CR1,n = 1; CR3, n = 2; PR,n = 2;Ref,n = 1), MDS (n = 2), or NHL (CR3, n = 1; Rel, n = 1). NM-HCT was chosen for concern of increased regimen-related toxicity due to comorbidities alone (n = 11) or prior