from 2000-2011. Patients included in the analysis all achieved CR1 or PR1 by CIBMTR definition prior to transplant. Patients who received tandem transplants, allogeneic transplants, or who were transplanted on clinical protocol were excluded. Disease status prior to transplant and disease status 100 days after transplant was recorded for both patients younger than 65 and 65 years of age and older.

Data from transplants of 117 patients were analyzed. 32 patients (27%) were age 65 and older, and 85 patients (73%) were younger than age 65. Prior to transplant, 20/32 patients (63%) age 65 and above were in CR or VGPR compared to 23/85 (27%) of patients younger than age 65. At 100-day restaging after transplant, 25/32 patients (78%) age 65 and above achieved a CR or VGPR compared to 44/85 patients (52%) younger than 65. There was one transplant-related death in each age group corresponding to a transplant-related mortality of 3% and 1% in the older and younger age groups, respectively. Two patients who were both younger than age 65 had evidence of progressive disease at 100-day restaging.

Based on our single-institution analysis, multiple myeloma patients age 65 and above have experienced similar outcomes compared to younger patients with respect to transplant-related mortality and disease status 100-days after transplant. Specifically both age groups experienced a consolidative benefit to high-dose therapy followed by autologous SCT. Prospective studies evaluating the impact of age on transplant outcome should be performed for further investigation.

Table 1. Characteristics of Myeloma Patients Transplanted at Temple from 2000-2011

Number of Patients	117
Median Age	58
Range of Ages	40-77
Age 65 and greater	32
Younger than Age 65	85
Number of Males	70
Number of Females	47
IgG Subtype	62
IgA Subtype	24
Free Kappa Light Chain	16
Free Lambda Light Chain	11
Other (IgD, Oligoclonal, Non-secretory)	4
Median Time from diagnosis to BMT	11.5 months
Median CD34 dose	5.56E + 06 cell dose/kg

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SUCCESSFUL STEM CELL MOBILIZATION AND ENGRAFTMENT IN HEAVILY PRETREATED MULTIPLE MYELOMA PATIENTS WITH PRIOR HIGH DOSE MELPHALAN AND AUTOLOGOUS STEM CELL TRANSPLANTATION

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Salvage second autologous transplantation for patients with relapsed multiple myeloma (MM) after prior autologous transplantation has shown to be beneficial in particular if the first remission is longer than 12-18 months. In addition second salvage autologous transplant may be used in the contest of progressive refractory myeloma for temporarily disease control or for hematopoietic reconstitution after prior extensive therapy. Customarily, patients with multiple myeloma who received prior alkylating agents or autologous transplantation with high dose Melphalan are considered non transplant candidate because of the deleterious effects on stem cell collection. Plerixafor is a chemokine receptor -4- antagonist which is approved by FDA for use in combination with G-CSF for mobilization of CD34+ stem cells in patients with NHL and multiple myeloma. We have explored the feasibility of Plerixafor and G-CSF in stem cell collection for second salvage autologous transplantation in 4 consecutive patients with multiple myeloma who underwent prior extensive therapy including prior autologous transplantation with Melphalan-200. Patient characteristics, chemotherapy used and interval between first and second salvage transplant are shown in Table 1. All Patients received GCSF at dose of 10 mcg/KG for 4 days in AM, Plerixafor on the evening of the 4th night and subsequent nights prior to apheresis at a dose of 0.24 mg/kg. The number of apheresis procedures were 2 in two patients and 3 in two patients. The number of CD34 + cells collected were 4.25, 3.06, 3.63, 3.78 million cells/Kg. All the patients engrafted successfully after the second transplant. Neutrophils engraftement were at day 10, 12, 12 and 11 while platelet engraftment were at day 10, 15, 32 and 19 respectivlely for the four patients.

Our Data shows the feasibility of stem cell collection in heavily pretreated MM patients including high dose Melphalan and autologous stem cell transplantation. Prospective studies are needed to confirm such feasibility. Such approach may have future clinical application in eliminating minimal residual disease after the first autologous transplant when used in MM patients with planned upfront tandem autologous transplant.

PEDIATRIC DISORDERS

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A TREOSULPHAN BASED REDUCED TOXICITY CONDITIONING PROTOCOL FOR THALASSAEMIA MAJOR

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We present data comparing two conditioning protocols for beta thalassaemia major in patients treated in our unit from 2005 to 2011. Twenty children aged between 2 and 9 years were treated using oral busulphan 16 mg/kg/day with cyclophosphamide 200 mg/kg/day were assigned to group one. Twenty children aged between 1 and 14 years were treated using thiotepa 8 mg/kg, treosulphan 42 gm/m2 and fludarabine 160 mg/m2 were assigned to group two. Data was analysed retrospectively for Lucarelli class, mucositis, blood product requirement, need for parenteral nutrition, engraftment and transplant related mortality. Group one had 4 class I, 10 class II and 6 class III patients between age groups 1 to 14 years. Mucositis was grade two and above in 11 children and they needed partial parenteral

Table 1.

Patient #	AGE	Induction pre 1st Transplant	Mobilization Regimen	First Transplant Type	Maintenance/Relapse treatment	Re-Induction	Interval between transplants (Years)
1	46	VAD X4 then Thalidomide for 1 year	Cytoxan/G-CSF	Single	Thalidomid then Lenalidomide maintenance	RVD × 3	8.57
2	66	VAD X4	Cytoxan/G-CSF	Planned Tandem	Dex/Thal followed by Bro/Doxil	MPV-Rituximab	4.77
3	56	Thal/Dex then Bro/Dex then MP	Cytoxan/G-CSF	Single	Dex/Thal then RVD×3 then VD-PACE	MPV-Rituximab ×2	4.43
4	67	Lenalidomide/Dex × 4	G-CSF	Single	Lenalidomide maintennace for 15 months	RVD × 4, VD-PACE ×2	1.75

X indicates number of cycles; RVD, lenalidomide, Bortezomib, Dex.; Thal, Thalidomide; MPV, Melphalan, Prednisone , Bortezomib; PACE, Cisplatin, Doxorubicin, Cytoxan, Etoposide; Bro, Brotezomib.

nutrition. Red cell requirement was < 4 units in 9 children and > 4 units in 11 children. Platelet support was required < 5 in 5 children and > 5 in 15 children. Two of the eighteen children did not engraft and 4 children had graft versus host disease and 1 child died on day 10 due to acute cardiomyopathy. Two children had mild sinusoidal obstruction syndrome. Group two had 9 class I, 3 class II and 8 class III patients between age groups 1 to 13 years. Mucositis was grade two and above in 5 children and they needed partial parenteral nutrition. Less than 4 units of red cells were required in 15 children and > 4 units in 5 children. Platelet support was required on less than occasions in 10 children and > 5 in 10 children. All of the eighteen children engrafted and 2 children had graft versus host disease. There was no mortality and two children had early graft rejection before day 100. No child had sinusoidal obstruction syndrome.

We conclude that this treosulphan based regimen is well tolerated and results in durable engraftment even in Class III thalassaemia major children with no major toxicity or mortality.

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PULMONARY ARTERYOPATHY AND PULMONARY HYPERTENSION FOLLOWING TANDEM AUTOLOGOUS TRANSPLANTS IN PEDIATRIC PATIENTS WITH CNS TUMORS

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Introduction: Young children with central nervous system (CNS) tumors are frequently being treated with tandem cycles of high dose chemotherapy followed by autologous stem-cell transplants in an attempt to avoid cranial irradiation. The most common combinations of chemotherapy used is carboplatinum and thiotepa. Though, multiple side effects were documented, pulmonary arteriopathy leading to pulmonary hypertension (PH) was not previously documented in patients treated for primary CNS disease. We herein report PH as a complication post autologous transplantation using carboplatinum and thiotepa as conditioning therapy.

Methods: A retrospective evaluation of all pediatric patients diagnosed with primary CNS tumors between 2001-2010 who were scheduled to be treated with 3 cycles of high dose chemotherapy with carboplatinum (17mg/kd/day for 2 days) and thiotepa (10mg/kg/day for 2 days) followed by autologous stem-cell transplants was conducted. The primary objective was to evaluate the incidence of PH in this population and patients' outcome following the development of PH.

Results: 14 patients were scheduled to received 3 cycles of autologous transplantation. The median age was 28 months (range 3-41months). Patients' diagnoses were: atypical teratoid rhabdoid tumor – 8 patients, medulloblastoma- 4 patients and primitive neuroectodermal tumor- 2 patients. Three patients developed biopsy confirmed pulmonary arteriopathy. The two patients that developed echocardiographic evidence of PH after the third cycle of high dose therapy succumbed to right heart failure, while one patient who's PH was detected after the second cycle didn't receive the third cycle and survived this complication. The overall survival (OS) of the 14 patients was 0.48 +/- 0.15 at a median of 14.32 months (range 4.99-68.21 months). Death from progression was 0.43 +/- 0.16 and non-relapsed mortality was 0.15 +/- 0.10. The 2 patients who died from PH represented the only non-relapsed mortality in our cohort.

Conclusions: Pulmonary hypertension is a major complication following high dose chemotherapy and autologous transplantation with a high likelihood of mortality despite PH directed therapy. Echocardiographic evaluation of the right ventricle and screening specifically for PH should be included after each cycle of high dose chemotherapy in pediatric CNS tumor population. Consideration for longer interval between cycles should be done to allow proper follow-up between cycles.

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OUTCOMES OF HAEMATOPOIETIC STEM CELL TRANSPLANTATION FOR INHERITED METABOLIC DISORDERS: A REPORT FROM ANZCHOG AND ABMTRR

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We report a retrospective analysis of 53 haematopoietic stem cell transplants for inherited metabolic disorders performed at Australia and New Zealand Children's Haematology Oncology Group (ANZCHOG) transplant centres between 1992 and 2008. The most common indications for transplant were Hurler syndrome (47%), adrenoleukodystrophy (ALD) (28%) and metachromatic leukodystrophy (17%). The median age of patients was 2 years (0-15). 11 (32%) patients received marrow from matched siblings, 1 from an HLA-identical parent. The remaining 66% received grafts from unrelated donors, with 22 (42%) using single UCB, 13 BM or PBSC (23%) and one double UCB transplant. 55% of patients received Busulphan and Cyclophosphamide as their conditioning regimen, and 34% received Bu/Cy + Other (Melphalan or Fludarabine). 54% had in-vivo T cell depletion using ATG or Campath, and 15% had ex-vivo T cell depletion. Median time to neutrophil and platelet engraftment was 16 and 35 days respectively, with a cumulative incidence (CI) at day +42 of 94% and 73% respectively. There were 3 graft failures, all engrafted after a second URD, and are alive at 10, 5 and 3 years post transplant. The CI of aGVHD grade II-IV and III-IV at day +100 was 39% and 14% respectively. 17% of patients had cGVHD at 1 year post transplant. Transplant related mortality (TRM) was 12% at day +100, and 19% at 1 year post transplant. Overall 5 year survival (OS) was 78% for the cohort, with 73% for ALD and 83% for Hurler syndrome. There were no late deaths reported for the cohort, with median follow up of 4 years. Neither age, year of transplant, donor source, or HLA match impacted OS. In contrast, the development of interstitial pneumonitis was the only significant variable associated with an increase in TRM and decrease in OS. This is keeping with previously reported literature for this patient cohort[1]. In summary, we report excellent OS in a large cohort of patients transplanted for a range of metabolic disorders.

1. Orchard PJ, Milla C, Braulin E et al. "Pre-transplant risk factors affecting outcome in Hurler syndrome" *Bone marrow transplant.* (2010) 45: 1239-1246.

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CHEMOTHERAPY-ONLY PREPARATIVE REGIMEN FOR ALTERNATIVE DONOR HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR PATIENTS WITH FANCONI ANEMIA

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Background: A significant number of patients with Fanconi anemia (FA) who survive hematopoietic stem cell transplantation (HSCT), develop solid tumors. The relative contributions of total body irradiation (TBI) and chronic graft vs. host disease (GvHD) to the development of tumors are unknown. Our study aims to examine whether non-TBI based preparative regimen improves alternative donor HSCT outcome in FA. Here we report results of our interim analysis after first 17 patients.

Methods: Seventeen patients were enrolled in this phase II multicenter protocol between June 2009 and October 2011. See Table 1 for patient and donor characteristics. Preparative regimen included: Busulfan 0.8-1.0 mg/Kg/dose Q 12H x 4 doses (D-7&-6), Cyclophosphamide 10 mg/Kg/day, Fludarabine 35 mg/m2/day and Rabbit ATG 2.5 mg/Kg/day x 4 days (D-5 to D-2).GvHD prophylaxis was cyclosporine starting D-2. Filgrastim was used starting D+1. Busulfan doses were adjusted to keep the steady state concentration low in most cases. All grafts were T-cell depleted using the CliniMacs CD34 columns (Miltenyi). Cell doses of the grafts were: 4.9 -42.7 x 10^6 CD34 cells/Kg and 2.24- 49.90 x 10^3 CD3 cells/Kg.