There were 22 males, 18 females, ages 7 mo – 18.7 yrs, median 5.5 years. Stem cell sources for the msibs were marrow for 7 and PBSC for 11. Conditioning regimen was fTBI based in 25, busulfan based in 15–of those, 5 were reduced intensity. Graft-versus-host disease prophylaxis included cyclosporin A and either methotrexate (n = 35) or mycophenolate (n = 5). Disease status at time of HSCT was CR1 in 23, 11 were in CR2 and 6 had evidence of residual AML (~5% by morphology or [+] cytogenetics).

The median time to reach an ANC > 500/μl was 18 days (29 days for UCB vs 12 after m/PBSC). An unsupported Plt Ct > 20,000/μl was achieved in 36 pts at a median of 21 days (49 for UCB vs 13 after m/PBSC). 4 UCB pts failed to engraft with donor hematopoiesis. 14 pts developed Gr II-IV acute GVHD, 8 of the 35 pts surviving more than 100 days developed chronic GVHD (2 limited, 6 extensive). 9 UCB and 5 m/PBSC pts developed acute GVHD. 7 m/PBSC patients but only 1 UCB patient developed chronic GVHD.

Overall survival (OS) rates 3 years post HSCT were similar when comparing UCB recipients (63%) versus combined matched m/PBSC donors (78%), respectively. This result is despite the higher proportion of CR2 and PR patients in the UCB cohort (64 vs 17%). OS of patients in CR1 and CR2 at the time of HSCT are 87 % and 43 % respectively.

Table 1. HSCT for Pediatric AML-msib v UCB

	All pts, n=40	Matched sibs, n=18	UCB, n=22
Male–Female	22–18	12–6	10–12
Age (yrs, median +/− sd)	5.5 +/− 5.6	11.6 +/− 5.7	3.5 +/− 4.2
Weight (kg, median)	21	38	15
Diagnosis to HSCT (mo, median)	5.1	3.5	6.4
CR1	23	15	8
CR2 or PR	17	3	14
fTBI-VP-CY	25	8	17
Bu4-CY+/−VP	10	6	4
Flu-Bu2 +/− ATG	5	4	1
ANC engraft (days, median)	18	12	29
Platelet engraft (days, median)	21	13	49
Non-engraft	4		4
TRM	5	1	4
Relapse	8	4	4
Overall Survival (%)	69	78	63

Our experience supports continued consideration of allogeneic HSCT for pediatric AML in CR1 utilizing matched sibling donors. The results using unrelated UCB stem cell sources suggest that young AML patients lacking a msib donor should search for an UCB match and consider that option for HSCT in CR1. Methods to enhance engraftment/limit rejection of UCB could potentially further improve the results using UCB stem cells.

291

HIGH DOSE CARBOPLATIN, ETOPOSIDE, MELPHALAN AND AUTOLOGOUS HEMATOPOIETIC STEM CELL RESCUE WITH FOR THE TREATMENT OF RELAPSED PEDIATRIC GERM CELL TUMORS

Villela, N.C., Gouveia, R.V., Macedo, C.R.D.P., Zecchin, V.G., Ginani, V.C., Marconcini, J.F., Felix, O.M.O., Barros, D.P., Alves, L.R., Ibanez, A., Simoes, P.C., Silva, A.G., Petrilli, A.S., Seber, A. Instituto de Oncologia Pediátrica, São Paulo, SP, Brazil

High dose chemotherapy with autologous hematopoietic stem cell transplantation (HSCT) is the treatment of choice for relapsed or refractory germ cell tumors (GCT) but few pediatric patients are included in most reports. Our objective is to describe the institutional experience with autologous HSCT for GCT.

Results: From November, 2001 to October, 2010, 11 patients with GCT underwent HSCT after conditioning therapy with carboplatin (425 mg/m^2/day x 4 days), etoposide (337.5 mg/m^2/day x 4 days) and melphalan (70 mg/m^2/day x 2 days) - doses for children older than 2 years of age and with normal renal function. Their median age was 12.5 years (2-19)and seven were female. One had primary central nervous system (CNS) tumor, 6 gonadal and 4 extra-gonadal tumors. Most patients had been treated according to the Brazilian GCT Protocol-99 and received TIP – paclitaxel, ifosfamide and cisplatin as second line chemotherapy. One patient was in the first remission of a testicular tumor with trophoblastic component and multiple brain and lung metastases; seven were in second remission; one was in third remission and two had refractory disease with partial response to therapy. All patients had a normal bone marrow aspirate and biopsy prior to stem cell collection. Eight patients had peripheral blood stem cell harvest, one marrow, and one both, for a target cell dose of 5 million CD34 cells/kg. All patients had febrile neutropenia (seven also had positive blood cultures), oral mucositis (all needed IV morphine) and diarrhea. One 3-year-old girl in second remission had a CNS bleeding and died two months after HSCT. Five patients had disease progression or relapse, three of them with advanced diseases. Five patients are alive in complete remission with a median follow up of 6.8 years (2-8 years). In conclusion, GCT is a rare indication of autologous HSCT in pediatrics (11/123 autologous transplants in 10 years). Despite acceptable results in adults with refractory diseases, the best timing for autologous transplantation in pediatrics seems to be second remission. Carboplatin, etoposide and melphalan, the same regimen that has been used for many years for stage 4 neuroblastoma, is associated with considerable toxicity but four of six evaluable patients with GCT in second remission remain tumor-free more than six years after transplant.

292

FLUDARABINE, BUSULFAN, AND ALEMTUZUMAB AS A REDUCED TOXICITY REGIMEN FOR CHILDREN WITH MARROW STEM CELL DEFECTS AND MALIGNANCY IMPROVES ENGRAFTMENT AND GRAFT VERSUS HOST DISEASE WITHOUT DELAYING IMMUNE RECONSTITUTION

Law, J.[1], Cowan, M.J.[1], Dvorak, C.C.[1], Baxter-Lowe, L.A.[3], Musick, L.[2], Hwang, J.[4], Horn, B.[1] [1] University of California San Francisco, San Francisco, CA; [2] University of California San Francisco, San Francisco, CA; [3] University of California San Francisco, San Francisco, CA; [4] University of California San Francisco, San Francisco, CA

For many children with malignancies and MSCD, allogeneic hematopoietic cell transplant (HCT) provides the best chance of cure. However, toxicity of conditioning and graft failure remain challenges. We previously reported that busulfan, fludarabine and rabbit ATG conditioning (total dose = 8mg/kg) resulted in less toxicity but no improvement in engraftment rates. Alemtuzumab has been shown to enhance engraftment and reduce rates of GVHD in myeloablative regimens. Thus, we prospectively evaluated targeted IV busulfan, fludarabine and Alemtuzumab (total dose = 1.5mg/kg) in a Phase II study of children receiving closely matched related or unrelated HCT. Thirty-five children were enrolled: 5 with malignancies and 30 with MSCD. Twelve donors were HLA matched relatives, 16 were fully HLA allele-matched unrelated donors and 7 were 9/10 HLA allele-matched unrelated donors. No patient had more than a Grade 2 reaction to Alemtuzumab. The most common toxicity (n = 15) was Grade 3 mucositis. One patient had Grade 4 mucositis. Only 1 patient developed VOD (Grade 3). 11/15 CMV seropositive patients had reactivation and 3/17 CMV seronegative patients had primary CMV infection. None developed CMV disease. Thirty-one of 34 (88%) evaluable patients achieved durable engraftment. Neutrophil recovery occurred at a median of 16 days (range 10-25). Three patients (2 mismatched at 1 antigen) with MSCD failed to engraft from unrelated donor HCT and underwent subsequent transplants. One is alive and progression free. For those successfully engrafted, the median time to CD4 > 200x10e6cells/L and PHA > 50% was 6 months with a maximum of 9 months. At 1 year post transplant, 18/19 evaluable patients had 87% or more donor chimerism in whole blood, CD14/15+ and CD19+ subsets and 71% or more donor chimerism in the CD3+ subset. One patient had only 55% whole blood donor chimerism at 1 year but ultimately achieved 82%. Six patients developed acute Graft versus Host Disease (GVHD) of Grade 2-4 with only 1 patient progressing to chronic GVHD. Seven patients had disease progression/relapse with 1 dying from disease. Four patients died of Transplant Related Mortality (11%). At a median follow up of 29 months (range 3-74), the EFS was 60+/− SE9% with an Overall Survival of 81+/