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COMPARISON OF OUTCOMES AFTER TRANSPLANTATION OF UNRELATED DONOR UMBILICAL CORD BLOOD VERSUS MATCHED SIBLING BONE MARROW FOR PEDIATRIC PATIENTS WITH LEUKEMIA AND MYELODYSPLASTIC SYNDROMES

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Are unrelated Umbilical Cord Blood (U-UCB) source of stem cells equivalent to matched sibling bone marrow (MS-BM) for treatment of pediatric patients with leukemia and myelodysplastic syndromes (MDS)? To address this question, we retrospectively studied the outcomes of 110 children that received a Hematopoietic Stem Cell Transplant (HSCT) at Children's Memorial Hospital between 1992 and 2003 for treatment of leukemia or MDS. Patients underwent a uniform conditioning regimen and similar graft-vs.-host disease (GVHD) prophylaxis followed by HSCT with either U-UCB or MS-BM. Patients receiving other regimens or stem cell sources were excluded from this analysis. The conditioning regimen was comprised of fractionated total body irradiation (fTBI, 150 cGy × 8 = 1200 cGy), etoposide (1000 mg/m^2) and cyclophosphamide (60 mg/kg/d ×3d) for both stem cell sources. GVHD prophylaxis was comprised of CsA (3 mg/kg/d), methotrexate (15 mg/m^2 day +1 and 10 mg/m^2 days +3 and +6) and (for UCB recipients) equine ATG (20 mg/kg days +1, +3, +5 and +7).

These results for HSCT in pediatric leukemia and MDS patients suggest that relapse free survival and overall survival are similar between these two groups and the only difference is time to engraftment (slower in U-UCB). Thus, pediatric leukemia patients previously considered HSCT candidates only if MS-BM was available should be considered candidates for HSCT if an U-UCB unit of adequate size can be identified.

Table.

Stem Cell Source	Matched Sibling BM	Unrelated UCB	*P* Value
Male/female (number, percent)	34 (64%), 19 (36%)	31 (54%), 26 (46%)	0.34
Age at HSCT(years), (median, range)	9.2 (0.5, 23.0)	7.1 (0.7-20.7)	0.47
ALL, AML, other	35 (66%), 14 (26%), 4 (8%)	23 (40%), 17 (30%), 17 (30%)	0.004
Caucasian, Hispanic, African American, Asian (number, percent)	34 (65%), 11 (21%), 3 (6%), 4 (8%)	25 (44%), 14 (25%), 13 (23%), 5 (9%)	0.04
15, 30, 45, 60 day ANC Engraftment	42%, 79%, 86%, 92%	4%, 48%, 91%, 95%	0.001
15, 30, 45, 60 day Platelet Engraftment	13%, 60%, 77%, 85%	2%, 20%, 44%, 64%	0.007
100 Days Survival (number, percent)	43 (81%)	44 (77%)	0.65
Chronic GVHD (number, percent)	4/41 (10%)	8/44 (18%)	0.35
Relapse (number, percent)	12 (23%)	8 (14%)	0.32
1, 2, 3 Year Relapse-free Survival	63%, 57%, 54%	61%, 53%, 53%	0.97
1, 2, 3 Year Overall Survival	65%, 58%, 58%	57%, 50%, 50%	0.56

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ALLOGENEIC HSCT WITH REDUCED INTENSITY CONDITIONING REGIMENS IN HIGH RISK PATIENTS WITH MYELOFIBROSIS

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Idiopathic Myelofibrosis (IM) is a rare chronic myeloproliferative disorder without curative treatment. The main therapeutic option remains transfusion support. For patients with high risk Lille scores (Hb < 10g; WBC <4,000 or >30,000) the median survival is less than 2 years. Fully ablative allogeneic conditioning results in a 25% peritransplant mortality, with few long term DFS in this typically elderly group. We report on 20 patients, median age 54 yrs (range:27-68), who received a non-myeloablative allogeneic HSC transplantation from HLA-matched related (n = 18) or unrelated (n = 1), or 1Ag-mismatched related donor (n = 1). Marked splenomegaly was present in 15 pts, in the remaining 5, 3 were splenectomized. Eighteen of 20 pts had grade III/IV marrow fibrosis and 9 pts were RBC and 3 PLT transfusion-dependent. Reduced intensity conditioning (RIC) regimens included low doses TBI (200 cGy) and Fludara (n = 5), Fludara/Melphalan (n = 6), Thiotepa/EDX (n = 8) and Thiotepa/Fludara (n = 1). Engraftment of ANC >500 and Plt >20K occurred within days 12-18 and 16-77, respectively, in all pts. Chimerism analysis on d30 showed >90% donor cells in 18/20, while the remaining 2 (70% and 56%) achieved 100% after DLI. Acute GVHD grade II-IV was observed in 5 patients and chronic GVHD in 8 of 16 evaluable pts. Day 100 TRM was 0%. Eighteen of 20 pts (90%) are alive at 18 months median follow-up. Two deaths were due to aGVHD and aGVHD + aspergillosis (post DLI). Marrow fibrosis was reduced to grade 1 in the majority of the patients. CBC also improved after transplant since median values of Hb and Plt pre- and post-Tx are: 8.1 g/dL (range: 6.2-10.7) vs 10.0 g/dL (range: 8.1-15.5), and 70 × 10^9/L (range: 8-278) vs 110 × 10^9/L (range: 17-340), respectively. Splenomegaly was dramatically reduced in all patients. Allogeneic HSC transplantation with RIC regimens can be safely performed in IM patients, with 1) low TRM 2) eradication of marrow fibrosis and massive organomegaly and 3) restoration of more normal hematopoiesis. These provocative outcomes will prompt randomized trials in IM, including allogeneic transplantation for patients with a matched donor.

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EFFECT OF COMORBIDITIES ON ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANT OUTCOMES IN AML/MDS PATIENTS IN FIRST COMPLETE REMISSION

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Introduction: Comorbidities can have significant impact on both survival and treatment selection in several types of malignancies. However, little attention has been paid in the literature to assess the effect of comorbidity on transplant outcomes in hematologic malignancies. We studied the impact of comorbidities on outcomes of allogeneic hematopoietic stem cell transplant (HSCT) in acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS) patients in 1st complete remission (CR). **Methods:** Seventy-eight patients with AML or MDS who received a matched or partially mismatched bone marrow, peripheral blood or cord blood transplant from a related or unrelated donor between January 1990 and December 2001 at the University of Texas MD Anderson Cancer Center were retrospectively reviewed. Data on demographics, comorbid conditions, and transplant outcomes were collected from the Blood and Marrow Transplantation database, patient charts and institutional electronic clinical information retrieval system. Charlson Comorbidity Index (CCI) was used to score comorbid conditions and CCI score was calculated for each