

decreases overall survival. Several risk factors for graft failure have been reported, such as reduced intensity conditioning, HLA-mismatch, T-cell depleted grafts etc. However, in the early post-transplant period following myeloablative conditioning there is a lack of tools for early detection of patients at risk for subsequent graft failure. For this purpose, we retrospectively evaluated all patients who after myeloablative conditioning received peripheral blood cells (PBSC) at our centre during 1995 to 2007 (n = 219). The indications for transplantation were: AML (43%), ALL (23%), CML (17%), myelodysplastic syndrome (6%), lymphoma (5%), metabolic disorders (4%), and multiple myeloma (2%). Graft failure was defined as absolute neutrophil count (ANC)  $<0.5 \times 10^9/L$  or less than 5% donor cell chimerism. Moreover, primary graft failure was set to day 28 post-transplant, and patients who died prior to that day were excluded from further analyses. Three patients experienced graft failure within 100 days post-transplant (2 primary and 1 secondary graft failure), which means that the incidence of graft failure was 1.4%. In univariate analysis, there was a tendency that the total nucleated cell dose was associated with primary graft failure (P = 0.06). In contrast, when analyzing risk factors for graft failure within 100 days post-transplant the total nucleated cell dose seemed to be unimportant (P = 0.17). Interestingly, in subanalyses the risk of graft failure within 100 days post-transplant was markedly increased in those patients who still had an ANC less than  $0.2 \times 10^9/L$  at day 16 post-transplant (OR = 30, P < 0.01). In conclusion, we suggest that in patients with less than  $0.2 \times 10^9/L$  in ANC 16 days post-transplant one must consider interventions to avoid subsequent graft failure. For this purpose, strategies such as administration of hematopoietic growth factors (e.g. G-CSF) or donor lymphocyte infusions need further evaluation.

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#### **IN-VIVO T-CELL DEPLETION USING THYMOGLOBULIN (THYMO) ALLOWS SUCCESSFUL ALLOGENEIC STEM CELL TRANSPLANTATION (ALLO-SCT) FROM MISMATCHED, UNRELATED DONORS (MM-URD): POTENTIAL INFLUENCE OF GRAFT SOURCE ON OUTCOME**

Slack, J.L.<sup>1</sup>, Leis, J.F.<sup>1</sup>, Reeder, C.B.<sup>1</sup>, Mikhael, J.R.<sup>1</sup>, Tiedemann, R.E.<sup>1</sup>, Stewart, A.K.<sup>1</sup>, Betcher, J.A.<sup>1</sup>, Higgins, M.S.<sup>1</sup>, Peterson, M.E.<sup>1</sup>, Gillette-Kent, G.<sup>1</sup>, Tromp, L.R.<sup>1</sup>, Salzburg, D.B.<sup>2</sup>, Dial, K.L.<sup>2</sup>, Hospodar, K.L.<sup>2</sup>, Jallo, C.H.<sup>2</sup>, Adams, R.H.<sup>2</sup> <sup>1</sup>Mayo Clinic, Phoenix, AZ; <sup>2</sup>Phoenix Children's Hospital, Phoenix, AZ

Historically, allo-SCT using MM-URD has been associated with poor outcomes, due primarily to high rates of GVHD. Decreasing the rate of GVHD, without increasing relapse, should lead to better outcomes and wider use of this life-saving procedure. Between 6/1/05 and 9/30/09, 88 patients (pts) received a first allo-SCT from an unrelated adult volunteer donor at Mayo Clinic Arizona/Phoenix Children's Hospital. This report focuses on the subset of 69 pts transplanted for malignancy who received at least one dose of Thymo (dose range 2.5-10 mg/kg, dependent on degree of HLA mismatch) as part of their GVHD prophylactic regimen (19 excluded, 9 with non-malignant disease, 10 who did not receive Thymo due to MD preference). Forty-two pts were HLA-identical (10/10) with their unrelated donor by high resolution typing, while 27 were mismatched at one or more loci as follows: 1 allele mismatch (7); 1 antigen (Ag) mismatch (11); 2 allele mismatch (2); 1 Ag and 1 allele mismatch (5); and 2 Ag mismatch (2). The median age was 37 (0.5-75). Conditioning was ablative in 48, reduced intensity in 21; graft source was PBSC in 47, marrow in 22. In addition to Thymo, all pts received a calcineurin inhibitor (or sirolimus) plus methotrexate or MMF for GVHD prophylaxis. The outcomes are shown in the Table. The estimated 2-yr overall survival (OS) did not differ between the matched (61.1%) and mismatched pts (60.5%). The rates of aGVHD grades II-IV (48.6% matched vs. 39.9% mismatched) and relapse (28.6% matched vs. 17.5% mismatched) also were not significantly different. Pts who received mismatched marrow grafts had relatively poor outcomes (2 yr OS 21.9%) due to increased relapse and higher than expected NRM, which did not appear to be explained by higher disease risk. By design, these pts received relatively high doses of Thymo (7.5-10 mg/kg), and such high doses may have led to excessive T-cell depletion of marrow grafts, abrogating the graft vs. malignancy

effect and leading to increased infectious mortality. In contrast, pts receiving mismatched PBSC grafts (who received similar doses of Thymo), had good outcomes (2 yr OS 91.5%) and low relapse rates (2 yr rel 0%). We conclude that 1) using PBSC as graft source and in vivo T-cell depletion, mismatched unrelated SCT can be safely performed with excellent outcomes in adult and pediatric pts with hematologic malignancy; and 2) modification of the Thymo dose will be necessary to achieve similar success using marrow grafts.

#### **Outcomes by Match Grade and Graft Type**

Match Grade	Graft	N	2 Yr OS	2 Yr Rel	aGVHD II-IV	aGVHD III-IV
Matched	Either	42	61.1%	28.6%	48.6%	8.3%
Matched	PBSC	30	57.3%	30.4%	46.2%	8.1%
Matched	Marrow	12	68.2%	25.4%	53.9%	8.8%
Mismatched	Either	27	60.5%	17.5%	39.9%	14.6%
Mismatched	PBSC	17	91.5%	0.0%	41.8%	16.3%
Mismatched	Marrow	10	21.9%	50.5%	37.1%	12.2%

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#### **PERIPHERAL BLOOD CHIMERISM CAN REPLACE MARROW CHIMERISM ANALYSES FOLLOWING ADULT ALLOGENEIC STEM CELL TRANSPLANT**

Rauwerdink, C.A.<sup>1</sup>, Tsongalis, G.T.<sup>2</sup>, Hill, J.M.<sup>1</sup>, Meehan, K.R.<sup>1</sup> <sup>1</sup>Dartmouth Hitchcock Medical Center, Dartmouth Medical School, and the Norris Cotton Cancer Center, Lebanon, NH; <sup>2</sup>Dartmouth Hitchcock Medical Center, Dartmouth Medical School, and the Norris Cotton Cancer Center, Lebanon, NH

Chimerism defines the amount of donor versus recipient hematopoiesis following allogeneic stem cell transplant (SCT). PCR-based analyses of short tandem repeats (STRs) are commonly used and are accurate and applicable to allogeneic transplant recipients. These analyses are performed on peripheral blood and marrow aspirates, but it is not known if it is necessary to analyze both. We performed a retrospective analysis of 42 consecutive adult allogeneic SCT recipients at our institution with available chimerism studies. PCR and capillary electrophoresis of microsatellite loci were performed at 30, 60, and 90 days after SCT on both unfractionated blood and unfractionated marrow aspirate. Full donor chimerism (FDC) was defined as 95% or greater donor chimerism. PCR analyses of STRs for chimerism performed on unfractionated blood did not differ from results obtained on unfractionated marrow aspirate at 30, 60, or 90 days post transplant (P < 0.0001). Peripheral blood PCR-based chimerism analyses provide similar information as marrow aspirate analyses. Using peripheral blood alone saves the expense of an additional analysis on marrow aspirate and prevents an uncomfortable procedure. These findings provide unique results suggesting larger studies in the adult population are needed to further delineate the role of chimerism analyses following allogeneic SCT.

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#### **T-CELL DEPLETED ALLOGRAFTS FROM UNRELATED DONORS CONFER A LOW RISK OF RELAPSE ON PATIENTS WITH HEMATOLOGIC MALIGNANCIES**

Jakubowski, A.A.<sup>1</sup>, Small, T.<sup>2</sup>, Barker, J.N.<sup>1</sup>, Boulad, F.<sup>2</sup>, Castro-Malaspina, H.R.<sup>1</sup>, Hsu, K.C.<sup>1</sup>, Kernan, N.<sup>2</sup>, Koebne, G.<sup>1</sup>, Perales, M.-A.<sup>1</sup>, Prockop, S.<sup>2</sup>, Scaradavou, A.<sup>2</sup>, van den Brink, M.R.M.<sup>1</sup>, Young, J.W.<sup>1</sup>, O'Reilly, R.J.<sup>2</sup>, Papadopoulos, E.B.<sup>1</sup> <sup>1</sup>Medicine; <sup>2</sup>Memorial Sloan-Kettering Cancer Center, New York, NY

**Introduction:** Allogeneic hematopoietic stem cell transplantation (HSCT) is a curative treatment option for an expanding spectrum of patients (pts) with a greater variety of diseases and graft sources, cytoreductive regimens, cellular therapies, and supportive care.