are higher after NMT while TRM is higher after HDT; and 4) long term remissions suggest that NMT is associated with an important graft vs lymphoma effect.

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STABLE LONG TERM ENGRAFTMENT AND AMELIORATION OF CLINICAL PHENOTYPE FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANTATION FROM A MATCHED SIBLING DONOR FOR SICKLE CELL DISEASE USING A REDUCED INTENSITY CONDITIONING REGIMEN

Krishnamurti, L.[1]; Wu, C.[2]; Baker, S.[3]; Yeager, A.M.[4]; Wagner, J.E.[3] 1. Children's Hospital of Pittsburgh, Pittsburgh, PA; 2. Dana Farber Cancer Institute, Boston, MD; 3. University of Minnesota, Minneapolis, MN; 4. University of Pittsburgh Medical Center, Pittsburgh, PA.

Hematopoietic stem cell transplantation (HCT) from sibling donors has been demonstrated to cure hemoglobinopathies such as sickle cell disease (SCD) and Thalassemia. Concerns about high regimen related toxicity (RRT) have prevented the use of HCT in older patients, those with advanced organ damage or those without a HLA matched related donor. Also, potential for late sequelae such as chronic graft-versus-host disease (GVHD) and infertility have limited the acceptance of this treatment even by eligible patients. HCT following a reduced intensity conditioning (RIC) regimen has the potential for reducing toxicity and potentially making this curative therapy more acceptable and applicable to this group of patients. We initiated a pilot study to evaluate the safety and efficacy of HCT following a RIC regimen for patients with high risk hemoglobinopathies. We report stable long term engraftment with amelioration of clinical phenotype in the first three patients with SCD receiving HCT (unmodified bone marrow) from a matched sibling donor, on this study. The conditioning regimen consisted of Busulfan 2 mg/kg orally q 12 hr × 2 days (0.8 mg/kg IV q 6 hr × 2 days for patient #3), Fludarabine 35 mg/m^2/dose IV daily × 5 days, antithymocyte globulin 30 mg/kg/dose IV daily × 5 days and total lymphoid irradiation administered as a single fraction of 500 cGy with shielding of the liver, lungs, heart, and gonads. Prophylaxis for GVHD consisted of cyclosporine A and Mycophenolate mofetil. Clinical characteristics of the patients and outcomes are summarized in Table 1. The preparative regimen was well tolerated with no serious infections or mucositis in any patient. Nadir of absolute neutrophil count was 140–200 × 10^9/L. Nadir of platelet count was 25–40 × 10^9/L. Transfusion requirements were modest (3 PRBC and 3–5 platelet transfusions). All patients are off immunosuppressive medications. Recovery of splenic function was observed except in patient #2 had who had prior splenectomy. No patient has had any recurrence of previous sickle cell related symptoms such as stroke, pain crisis, priapism or acute chest syndrome. End-organ changes are stable in all patients. Lineage-specific chimerism analysis (patient #3) suggest predominance of donor erythropoiesis. These findings indicate that HCT for sickle cell disease following a RIC regimen is well tolerated and can lead to stable long term engraftment with amelioration of clinical phenotype and stabilization of end- organ damage.

Clinical Characteristics of Patients With Sickle Cell Disease Undergoing HCT From a Matched Sibling Donor Following a Reduced Intensity Conditioning Regimen

PIN; Indication for HCT, Age (Years)	Follow-up (Years)	Organ Toxicity	Duration of ANC <500 (Days)	GVHD Acute/ Chronic	Engraftment % Donor (Bone Marrow) d + 30	Engraftment % Donor (Bone Marrow) d + 100	Engraftment % Donor (Bone Marrow) d + 365
1. Stroke, allosensitization 8 yrs.	4	None	7	Nil	89	100	100
2. Repeated ACS, 8 yrs.	3	None	8	Grade II Skin	75	81	81
3. Repeated ACS, 6 yrs.	1	None	9	Nil	75	85	81

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INTRAVENOUS BUSULFAN DOSED FOUR TIMES DAILY OR ONCE DAILY AS PART OF THE STANDARD BUCY PREPARATIVE REGIMEN FOR ALLOGENEIC STEM CELL TRANSPLANTATION

Shaughnessy, P.J.; Bachier, C.; Alexander, L.; Bowen, B.; LeMaistre, C.F. Texas Transplant Institute, San Antonio, TX.

Intravenous busulfan (IVBu) (Busulfex® ESP Pharma) is now regularly substituted for oral busulfan as part of the standard busulfan and cyclophosphamide (BuCy) preparative regimen for allogeneic stem cell transplantation (ASCT). Oral busulfan was originally dosed 4 times daily, which led to the current accepted dosing schedule for IVBu. Pharmacokinetics (PK) and busulfan clearance allow for once daily dosing now that IVBu is available. We performed a retrospective review of 36 consecutive patients who received the BuCy preparative regimen with IVBu prior to ASCT. Twenty-one males and 15 females with a median age of 46 years (23–64) were treated for AML (n=15), ALL (n=1), CML (n=8), MDS (n=8), NHL (n=2), and multiple myeloma (n=2). IVBu was dosed 0.8 mg/kg 4 times daily for 16 doses (n=16) or 3.2 mg/kg once daily for 4 doses (n=20) on days −7 to −4, and cyclophosphamide was dosed 60 mg/kg once daily for two doses on days −3 and −2. IVBu was dosed by ideal or adjusted ideal body weight and no PK studies were done. Bone marrow (n=6) or peripheral blood (n=30) stem cells were infused on day 0 from HLA matched siblings (n=26) or unrelated donors (n=9), and one partially matched unrelated donor. Engraftment occurred in 34 patients (pts) (94%). Two pts who failed to engraft had bone marrow grafts with low numbers of total mononuclear cells infused. Regimen related toxicity (RRT) included mild VOD in 2 pts (5%) that self resolved, with one pt receiving IVBu 4 times daily and the other once daily. There was no seizure activity or non-infectious interstitial pneumonitis attributed to RRT in any patient. Other RRT were not significantly different between the patients who received 4 times daily or once daily IVBu. Day 100 mortality was 17%, and at a median follow up of 12 months (1–54) 17 pts (47%) survive. Five of 16 pts (31%) survive who received 4 times daily IVBu, and 12 of 20 pts (60%) survive who received once daily IVBu, however, most patients who received once daily IVBu were treated more recently. Three patients received once daily IVBu as outpatients. In conclusion, this small retrospective single institution study revealed IVBu dosed once daily by ideal or adjusted ideal body weight appeared to have similar RRT, engraftment, and survival compared to 4 times daily IVBu when used as part of the BuCy preparative regimen for ASCT.

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HIGH RELAPSE RATE FOLLOWING ALEMTUZAMAB USE IN ALLOGENEIC TRANSPLANTS FOR MYELOID HEMATOLOGIC MALIGNANCIES

Shea, T.C.[1]; Serody, J.[1]; Gabriel, D.[1]; Comeauu, T.[1]; Morris, D.[2]; Irons, R.[1]; Harvey, D.[3]; Sharf, A.[1]; Krasnov, C.[1]; Dunphy, C.[4]; Banderenko, N.[4]; Brecher, M.[4] 1. Department of Medicine, Bone Marrow and Stem Cell Transplant Program; 2. Department of Radiation Oncology; 3. Department of Pharmacy; 4. Department of Pathology and Laboratory Medicine, UNC Hospitals, Lineberger Comprehensive Cancer Center and School of Medicine, Chapel Hill, NC.

Chakravarti (Blood, '02, p 1071) and others have described the use of alemtuzamab in vivo for control of graft vs host disease in allotransplantation. Control of GVHD has been good, but high relapse rates and infectious complications have been reported. We describe 47 pts, 16 women and 31 men, median age 49, and median f/u 11 months who underwent matched related (31) or unrelated (16) bone marrow (8), blood stem cell (38), or both (1), transplants for hematologic malignancies. All AML pts had high-risk disease defined as beyond CR1 (11), CR1 with high risk cytogenetics (5), AML with dysplasia (12), or failed prior autolograft (1). Three had >10% marrow blasts at time of transplant. All other pts had multiply recurrent disease. All pts received Alemtuzamab at 20 mg/d × 5 (17), 30 mg/d × 3 (25) or lower doses (5) between days −8 through −4, followed by tacrolimus. Conditioning regimens included 12.8 mg/kg IV busulfan, (27), 6.4 mg/kg IV busulfan (9), melphalan 140 mg/m^2 (6), or Cy/TBI (1). All non-TBI patients received 30 mg/m^2/d × 5 of fludarabine. Median recovery of ANC