Dyskeratosis Congenita (DC): A Review of 12 Patients

The median age at transplantation was 16.5 years (range 3 to 27). Two pts had the non classical forms of disease (Revesz syndrome and severe aplastic anemia with evidence of short telomeres). Five pts received bone marrow from their HLA matched siblings and were conditioned with Cyclophosphamide (CY) 200mg/Kg. Seven pts were transplanted from unrelated donors (URD): 6 BM (match 10/10: 4pts and 9/10: 2pts) and 1 CB (5/6). Conditioning Regimen for the URD BMT was CY30-60mg/Kg + Fludarabine 125mg/m² + rabbitATG5mg/Kg and CB Busulfan 12mg/Kg + Fludarabine 125mg/m² + rATG5mg/Kg. Graft versus host disease (GVHD) prophylaxis: methotrexate and cyclosporine for all patients, except for the one who received CBU. Median of TNC: BM: 3.97 x 10⁸/Kg. CBU:

Hematopoietic Stem Cell Transplantation (HSCT) for Dyskeratosis Congenita (DC)

Graft versus host disease (GVHD) prophylaxis: methotrexate and cyclosporine for all patients, except for the one who received CBU. Median of TNC: BM: 3.97 x 10⁸/Kg. CBU: 6.5 x 10⁷/Kg. All pts survived more than 28 days and were available for engraftment. All but one pt had stable hematological engraftment. Chimerism was complete in 7 patients and mixed in the other 5 patients. Mucositis was the only toxicity observed (grade II in 5 pts and grade III in 2 pts). GVHD was observed only among unrelated transplants. Two pts developed grade II acute GVHD and both progressed to chronic GVHD (limited). The probability of survival in 2 year was 50%. Two deaths were related to the procedure (SOS and adenovirus sepsis). Four pts died between 1 and 10 years after transplant because of progression of underlying disease. Six patients (4 recipients of an URD) are alive between 6 months and 11 months after transplant with a median follow up of 1.6 years.

Conclusions: Regimen related toxicity was very low and an appropriate engraftment was achieved. Late mortality was consequent to the progression of underlying disease. Long term follow up is essential in order to detect late complications related to the transplant procedure or the underlying disease.

Conclusions:

- Adults with histiocytic disorders, primarily HLH, have survival rates after allogeneic SCT similar to those seen in the pediatric literature. Inclusion of alemtuzumab prior to or in concert with conditioning is common in adults. Allogeneic SCT regimens for HLH merit prospective studies in adults as well as children. We encourage participation in the BMT-CTN 1204 study, a phase II study of reduced-intensity conditioning for children and adults with hemophagocytic syndromes or selected primary immune deficiencies preceded by alemtuzumab therapy.

Recipient T-Cell Repertoire Diversity after Double Umbilical Cord Transplantation Correlates with Non-Relapse Mortality and Survival

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Complications of allogeneic stem cell transplant, such as infection, relapse and GvHD, are linked to failure of balanced immune reconstitution. Early quantification of immunologic

Histiocytic disorders are rare but often fatal illnesses. Within these, familial and secondary hemophagocytic lymphohistiocytic disorders (HLH) are primarily diagnosed in childhood, and there have been few large analyses of outcomes in adults with HLH. The widely-accepted HLH-94 treatment regimen consisting of dexamethasone, etoposide and cyclosporine therapy followed by allogeneic stem cell transplantation (SCT) has been employed primarily in children. In the largest series to date of 113 children under 15 years of age, a 3 year survival rate of 55% overall and 62% for those receiving allogeneic SCT was seen (Henter. Blood 2002; 100:2367-2372). In light of the highly proinflammatory cytokine environment that characterizes HLH, alemtuzumab for profound lymphocyte depletion in concert with conditioning for pediatric SCT is becoming increasingly common, with an impact on rates of acute GvHD and mixed chimerism reported. (Marsh. Blood 2010;116:5824-5831; Marsh. Pediatr Blood Cancer 2013;60:101-109). To assess current practices and outcomes in adults, we performed a retrospective review using the CIBMTR database of all subjects over 18 years of age receiving allogeneic SCT for histiocytic conditions between 2001 and 2012.

Results: 47 subjects were identified, 16 of whom were transplanted in 2011 or 2012. Median age was 25 (18-67). Underlying diagnoses were familial HLH (47%), secondary HLH (32%), malignant histiocytosis (15%), and histiocytic disorders not otherwise specified (6%). 31 subjects (66%) received transplants from unrelated donors. 26 subjects (55%) received PBSCs. The remaining subjects received bone marrow, except for one who received umbilical cord blood. 26 subjects (56%) received myeloablative conditioning, primarily cytoxan-TBI-based or cytoxan and busulfan. 21 subjects underwent reduced-intensity or non-myeloablative conditioning with fludarabine-based regimens. 18 subjects (38%) underwent conditioning in combination with alemtuzumab. Kaplan-Meier survival rate estimates for the entire cohort were 93% at 100 days (95% CI, 71-93), 60% at one year (95% CI, 45-75) and 57% at 2 years (95% CI, 40-72).

Conclusions: Adults with histiocytic disorders, primarily HLH, have survival rates after allogeneic SCT similar to those seen in the pediatric literature. Inclusion of alemtuzumab prior to or in concert with conditioning is common in adults. Allogeneic SCT regimens for HLH merit prospective studies in adults as well as children. We encourage participation in the BMT-CTN 1204 study, a phase II study of reduced-intensity conditioning for children and adults with hemophagocytic syndromes or selected primary immune deficiencies preceded by alemtuzumab therapy.

Outcomes after Allogeneic Stem Cell Transplantation in Adults for Histiocytic Disorders Including Hemophagocytic Lymphohistiocytosis

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Complications of allogeneic stem cell transplant, such as infection, relapse and GvHD, are linked to failure of balanced immune reconstitution. Early quantification of immunologic