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ALLOGENEIC STEM CELL TRANSPLANTATION FOR T-CELL LYMPHOMA

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Introduction: Results of conventional and even high-dose chemotherapy with ASCT for T-cell lymphomas are poor when compared with their aggressive B-cell counterparts. We analyzed the results of allogeneic stem cell transplantation in 23 patients with T-cell lymphoma at our Institution.

Patients and Methods: Gender: 15 males and 8 females with a median age of 43 years (19 to 65) underwent allogeneic HCT at Mount Sinai Medical Center between 5/2000 and 8/2009. The different histologic subtypes were: 8 PTCL, 6 hepatosplenic T-cell lymphoma, 4 angioimmunoblastic T-cell lymphoma, 2 CTCL, 1 NK-T cell lymphoma, 1 ATLL, 1 anaplastic T-cell lymphoma. Donor sources included 15 PBSC, 7 BM and 1 CB. Donor types were: 13 related and 10 unrelated. Conditioning regimens used were: NST (Flu/TBI200/ATG) 9 pts, RIC (Flu/Mel) 7pts, (Flu/Cy/Campath) 1 pt. and MA (TBI 1,200/Cy) in 6 pts. Six patients had prior ASCT. The rest received allografting as primary modality.

Results: Eight patients are alive in CR at a median of 637 days post-transplant (149-1729). Four of the six patients who underwent prior ASCT achieved CR after allogeneic HCT. Six patients died of progressive disease after allogeneic HCT. Nine patients died from complications of GVHD and/or infection.

Conclusions: Allogeneic stem cell transplantation results in disease-free survival in a fraction of patients with T-cell lymphoma. Some patients 4/6 achieved CR after allogeneic HCT even after progression post ASCTx. This observation supports the existence of clinically-relevant graft versus T-cell lymphoma allo-responses. Whether this effect exists for all histologic sub-types of T-cell lymphomas as well as the optimal timing and conditioning for allografting for this disease are issues that deserve prospective studies.

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REDUCED INTENSITY CONDITIONING (RIC) REGIMEN BASED ON FLUDARABINE (FLU) FOR PATIENTS TREATED WITH ALLO-SCT FOR SEVERE APLASTIC ANEMIA (SAA)

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Allo-SCT is the treatment of choice for patients with SAA. Reduced intensity Conditioning (RIC) has been used in the past to ensure adequate engraftment and reduce mortality related to the procedure. Here we report a retrospective analysis of our experience using a fludarabine based RIC in patients with SAA.

Since 2006, 12 patients (1 Fanconi Anemia, 11 adquired SAA), mean 38 years (13-60), 10 males, 2 females, have been treated with HLA identical related RIC allo-SCT. Conditioning regimen consisted of Flu (30 mg/m^2/day $\times$ 4 days), Cyclophosphamide (Cy 10 mg/kg/day $\times$ 4 days) and horse antithymocyte globuline (ATG 2 mg/Kg/day $\times$ 4 days). GVHD prophylaxis consisted in Ciclosporine and metrotexate for 4 patients, cyclosporine and MMF for 4 patients and cyclosporine alone in 4 patients. All grafts were obtained from peripheral blood stem cells. All, but 1 patient, were considered high risk because of more than 20 transfusions before transplantation, co-morbidities (morbid obesity, renal dysfunction, hepatic toxicity), age (3 patients were over 50) or previous transplant (2 patients had previous secondary graft failure after conditioning containing Campath). Mean time from diagnosis to transplantation was 21.1 months (4.1-118.7).

One 13 year old patient, with history of multiple infections expired before stem cell infusion due to severe sepsis. 11 patients engrafted, average at 11 days (range 9-16) for neutrophils and 11 days (range 8-14) for platelets. Transfusion and antibiotic support required was minimal. None of the patients developed mucositis, diarrhea or required parenteral nutrition. Acute GVHD was seen in 2 of evaluable patients; both of them grade IV gastrointestinal disease, one required ATG treatment due to corticoid refractory disease. Chronic GVDH was seen in 1 patient who developed a nephrotic syndrome.

At a mean follow-up of 15 months (range 1-42), 11 patients are alive and in remission of SAA.

This experience suggests that Flu based RIC protocol allows rapid and sustained engraftment with minimal early toxicity even in high-risk patients.

Multicenter prospective clinical trials with longer follow-up are warranted to confirm our observation.

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REDUCED INTENSITY ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION CAN ACHIEVE BOTH DISEASE CONTROL AND VERY GOOD OUTCOMES IN ELDERLY (>60) PATIENTS WITH HEMATOLOGIC MALIGNANCIES

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With the rapidly escalating numbers of healthy, elderly patients with hematologic malignancies, defining optimal therapy for this patient group is necessary to improve control of the underlying disease without excess morbidity. The graft vs. malignancy effects associated with allogeneic hematopoietic stem cell transplantation (HSCT) may offer disease control with acceptable toxicity. A standard approach to healthy, elderly patients with high-risk hematologic malignancies involves reduced intensity conditioning followed by allogeneic HSCT. We report the outcomes of 75 patients, age 60 to 74, treated with this approach from 2001 through May 2009.

Conditioning regimens included Fludarabine/TBI (15); TBI alone (3); Fludarabine/Melphalan (10); and Busulfan/Fludarabine/TBI (47). Most patients had AML/MDS (53), with the rest comprising NHL (10), CLL (6), CML (3), ALL (2), and plasma cell disorder (1). Disease control was achieved prior to transplant in a majority of patients (50 patients in CR, 25 not in CR or untreated). Donors included matched unrelated (41) matched related (26), and mismatched unrelated (8).

Currently, the outcomes in this high-risk cohort include 47% of patients are alive. In analyzing cause of death, recurrence accounted for 38% deaths, with additional deaths from infection (23%), GVHD (21%), organ failure (15%) and graft failure (1 patient, 3%). Acute GVHD was seen in 64% of patients, with grade 3-4 present in 19% of patients. Of the 65 patients evaluable for chronic GVHD, 85% had cGVHD, with the majority having extensive cGVHD. Of particular note, in the 25 patients not in CR at the time of transplant, 60% were in CR at the last disease status evaluation.

Outcomes despite aggressive non-transplant treatments in older patients with hematologic malignancies remain dismal. Two year survival rates for AML are below 30% due to the high rate of disease relapse and complications. Alternative treatment options are necessary and increasingly, allogeneic HSCT appears favorable. In this report, we show very good outcomes in this elderly, high-risk patient population not dissimilar to younger patients undergoing reduced intensity transplantation. While relapse remains a large cause of death in our cohort, it is encouraging to see that 60% of patients not in CR were able to achieve complete remission in the post-transplant setting. The goal will be to continue to optimize this treatment approach with improvements in supportive care and disease control.

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MIXED AUTOLOGOUS AND ALLOGENEIC TRANSPLANTATION, A NEW MODEL TO ESTABLISH STABLE MIXED CHEIMRSIM

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Graft versus tumor (GVT) effect after allogeneic bone marrow transplantation (BMT) for hematological malignancies has a potent