Feasibility of Low Dose Azacitidine Post T Cell Depleted Allogeneic Hematopoietic Stem Cell Transplants in Patients with Myeloid Malignancies At High Risk for Relapse
Ron Tamar1, Doris Ponce2, Ann A. Jakubowski2, Sergio A. Giralt1, James Young2, Hugo Castro-Malaspina2, Lori DeCook2, Nicci Johnson2, Minral Patnai2, Mark Litzow2, William Hogan4, Luis Portra6, Sherman Holtan4, 5, 6 Blood and Marrow Transplant, Mayo Clinic, Rochester, MN; 2 Mayo Clinic Arizona; 3 Division of Transfusion Medicine, Mayo Clinic, Rochester, MN; 4 Mayo Clinic, Rochester, MN; 5 Hematology, Mayo Clinic, Rochester, MN; 6 Oregon Health & Science University

Background: Post transplant relapse remains a main cause of transplant failure and mortality in patients with myelodysplastic syndrome (MDS) and acute myelogenous leukemia (AML). Azacitidine, a hypomethylating agent, has been reported to reduce post transplant relapse in these patients after unmodified allogeneic hematopoietic stem cell transplantation (HSCT). There have been no reports of azacitidine use in patients undergoing T cell depleted (TCD) HSCT.

Patients: Nine patients; 4 with high risk MDS, 1 with AML evolved from MDS, 2 with therapy-related AML and 2 with de-novo AML, who had undergone TCD HSCT, were treated with azacitidine post transplant. The dose of azacitidine, as determined in a phase 1 study, was 32mg/m2 subcutaneously daily for 5 days monthly. All patients had been conditioned with a myeloablative regimen of busulphan, melphalan, fludarabine and rabbit ATG and had received a peripheral blood stem cell graft from a matched or mismatched related or unrelated donor.

Results: Seven patients were treated in complete remission as a prophylactic measure, one patient was treated in relapse and one patient received, in addition to azacitidine, a dose of DUJ (0.5x10^6 CD3 cells/kg) for increasing host chimerism and a new cytogenetic abnormality. Treatment began at a median of 117 days post transplant (range 80-333) and patients received a median of 3 cycles (range 1-7). At a median of 8 months follow-up, 7 patients were alive and 2 had died; one of pulmonary failure, possibly secondary to busulphan and the other patient of relapsed disease. In one patient, treatment was discontinued after development of an EBV-LPD while receiving budesonide for upper GI GvHD, and in another patient therapy was discontinued because of severe pancytopenia secondary to adenovirus infection. A third patient had treatment interruption after developing dyspnea secondary to heart failure and chronic obstructive lung disease. The patient with relapsed disease had persistent pancytopenia throughout the treatment. In the 8 remaining patients, there were 4 with grade 1 anemia and/or thrombocytopenia. Only one of the 8 patients required G-CSF and azacitidine dose reduction (20%). However, this patient’s neutrophils were noted to decrease prior to initiation of Azacitidine, possibly related to treatment of an EBV-LPD with Rituxan. Two patients had grade I skin GvHD and one patient had grade 1 upper GI GvHD. Therapy with azacitidine did not worsen the severity of GvHD.

Conclusions: This review shows that timely administration of low dose azacitidine is feasible after TCD transplant in patients with MDS and AML. The most common toxicity related to azacitidine, myelosuppression, has been reported only in patients who had concomitant viral infections. A phase II trial will be conducted to assess the efficacy of post transplant azacitidine after TCD transplant.

Allograft Leukocyte Content and Post-Allogeneic Hematopoietic Cell Transplant Lymphopenia and Monocytopenia
Mary Thoma1, Jennifer Gleff1, Eappen K. Jacob3, Tanya Hunekte2, Lori DeCook2, Nicci Johnson2, Minral Patnai2, Mark Litzow2, William Hogan4, Luis Portra6, Sherman Holtan4, 5, 6 Blood and Marrow Transplant, Mayo Clinic, Rochester, MN; 2 Mayo Clinic Arizona; 3 Division of Transfusion Medicine, Mayo Clinic, Rochester, MN; 4 Mayo Clinic, Rochester, MN; 5 Hematology, Mayo Clinic, Rochester, MN; 6 Oregon Health & Science University

Background: We have previously shown that lymphocyte and monocyte recovery by 2-3 months post-allogeneic hematopoietic (HCT) is associated with improved survival in recipients of both myeloablative and reduced intensity conditioning. Here, we test the hypothesis that the allograft lymphocyte and monocyte content correlates with recovery of those hematologic parameters prior to and at day +100.

Methods: We pooled the hematologic recovery data, including absolute lymphocyte and monocyte counts (ALC and AMC, respectively) at day +15, +30, +60, and +100, and outcomes data from our original cohorts of allogeneic HCT recipients undergoing myeloablative or reduced intensity (fludarabine/melphalan). We included only those with peripheral blood stem cell allografts and excluded those with incomplete data regarding allograft leukocyte subset content. 216 consecutive patients from 2000-2010 were included in the analysis.

Results: Neither allograft lymphocyte, monocyte, granulocyte, nor CD34+ content correlated with hematologic recovery parameters or overall survival in this cohort when cell doses were analyzed as continuous variables or divided in quartiles. No overall prognostic or optimal pattern of allograft cellular content as determined by unsupervised hierarchical clustering could be identified. With this pooled data, prognostic factors for overall survival based on multivariate analysis included severity of chronic GVHD (P < .001), development of post-transplant relapse (P = .001), day +60 AMC > 0.3 x 10^9 cells/L (P = .0015), and day +100 ALC > 0.3 x 10^9 cells/L (P < .001).

Conclusions: We conclude that, unlike in the autologous HCT setting, post-allogeneic HCT lymphopenia and monocytopenia appear to be related to complications and treatment-related factors, and not related to allograft leukocyte content.

Survival After Second Allogeneic Transplant Is Improved in Recipients by Using the Original Donor
Waseem Touma1, Mark A. Schroeder2, Ningying Wu3, Keith Stockerl-Goldstein2, Peter Westervelt2, John F. DiPersio2, Ravi Vij2, Bone Marrow Transplantation hospitalist, Internal Medicine, Washington University School of Medicine, St. Louis, MO; 2 Bone Marrow Transplantation & Leukemia Section, Division of Oncology, Washington University School of Medicine, St. Louis, MO; 3 Biostatistics, Washington University School of Medicine, St. Louis, MO

Relapse remains a major problem after allogeneic stem cell transplant (alloHST). There are limited data on the outcomes after second alloHST. We conducted a single institution retrospective review of 39 subjects who have