failure with capillary leak syndrome, and 2 had renal failure. Ten patients had disease resistance or relapse after transplant, and all have expired. Overall survival to date is 42% (48% for sibling transplants and 35% for UD) with a range of follow-up from 283 to 1366 days (median 535 days). Acute GVHD grade III or IV was seen in only 3 patients. After day 100, 27% had extensive GVHD. The best results were seen in AML or CLL in CR or early relapse with chemosensitive disease, no AML patient in full blown relapse survived. This regimen is well tolerated and offers a suitable platform for reduced intensity allogeneic stem cell transplantation. The benefit(s) of ECP require further testing in the context of improved radiation therapy, TBI versus TLI (total lymphoid irradiation).

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NON-MYELOABLATIVE ALLOGENEIC TRANSPLANTATION WITH ALEMTUZUMAB, FLUDARABINE AND CYCLOPHOSPHAMIDE USING 3-6/6 HLA MATCHED DONORS

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To broaden the proportion of patients able to undergo allogeneic therapy, we have investigated the use of 3-6/6 HLA matched family member donors in combination with donor T cell depletion in a non-myeloablative preparative regimen. **Methods:** Seventy five matched and 63 mismatched patients received fludarabine 30 mg/m^2 IV qd $\times$ 4, cyclophosphamide 500 mg/m^2 IV qd $\times$ 4, and alemtuzumab 20 mg IV qd $\times$ 5 followed by infusion of donor stem cells. In those with a matched donor, no other GVHD prophylaxis was used. In those with a 3-5/6 HLA matched donor, mycophenolate 1000 mg po BID was given to the first 35 and cyclosporine was added to the subsequent 28 for 6-8 weeks following transplantation. **Results:** Patient diagnoses included lymphoma/myeloma n = 36, leukemia/MDS n = 63, myelofibrosis/aplasia n = 10, metastatic solid tumors n = 29. The median age was 48 (17-70) with a median follow up of approximately 20 months. Engraftment occurred in 100% of matched recipients and 92% of mismatched patients. Eight percent had secondary graft failure as well. Forty six patients with a matched donor and 23 with a mismatched donor also had a DLI (range 10^5-10^7 CD3+ cells/kg). Grade III-IV acute GVHD occurred in only 7/75 (7%) in the matched setting and 8/63 (13%) of patients. Four percent of matched and 15% of the mismatched patients developed chronic GVHD and CMV reactivation was common. One hundred day treatment related mortality for both groups was <10%. Combining both matched and mismatched patients, only 12% entered in remission, though 76% attained a CR. The most common cause of death remained progressive disease (42%) and GVHD (8%). Despite the high risk nature of this group, 21 had aplastic anemia/myelofibrosis or leukemia in first or second CR and no other available donor other than their mismatched family member. This group had an encouraging 50% 3 year median survival. Phenotypic, spectratype and TRECs analysis reveals robust recovery by 6 months following transplantation from peripheral expansion of residual transplanted T cells **Conclusions:** The results demonstrate reasonable tolerance and reliable engraftment using T cell depleted, 3-6/6 HLA matched family member donors in a non-myeloablative setting with low treatment related mortality and severe GVHD. The future challenge will to be to develop strategies to improve immune recovery to enhance immune-mediated graft-versus-tumor effect and to minimize the risk of infections.

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THE RELATIONSHIP OF DAY 30 AND DAY 100 DONOR CHIMERISM TO CLINICAL OUTCOMES FOLLOWING REDUCED-INTENSITY ALLOGENEIC TRANSPLANTATION FOR HEMATOLOGIC MALIGNANCIES

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Background: We analyzed chimerism in unfractionated blood samples of 94 patients enrolled in a prospective phase II trial of allogeneic transplantation for hematologic malignancies. The aim was to determine the relationship between chimerism and clinical outcomes. **Methods:** All patients received fludarabine, melphalan, alemtuzumab, post-transplant tacrolimus and peripheral blood stem cells from related or unrelated donors. PCR-based analysis of ten polymorphic loci (VNTR) was performed on donor and recipient unfractionated bone marrow aspirates and/or peripheral blood samples prior to and on approximately day 30 and day 100 after transplantation. The percentage of donor chimerism and the change in chimerism between the two time points were examined for effect on relapse, acute graft vs. host disease, chronic graft vs. host disease, death, and time to these events. **Results:** A total of 39/94 (42%) relapsed and 47/94 (50%) have died with a median follow up of 14 months (range: 1-40 months). Of the 94 patients, 22 had acute GVHD with a severity grading of between II and IV and 15 experienced chronic GVHD. 86 (91%) of 94 patients had samples collected for day 30, and 66 (70%) had samples collected for day 100. The mean chimerism on day 30 samples was 93% donor (95% CI: 90-97%). There was no significant relationship between the day 30 chimerism and acute GVHD, chronic GVHD, relapse, death, or time to these events. The mean chimerism for the 66 subjects with available day 100 samples was 88% (95% CI: 83-92%). There was also no relationship found between the day 100 chimerism or its change from the day 30 and chronic GVHD, relapse, death, or time to these events **Conclusions:** A fludarabine, melphalan and alemtuzumab conditioning regimen results in rapid attainment of high rates of donor chimerism. The percentage of donor chimerism in unfractionated cell populations did not correlate with clinical outcomes in this study. Analysis of T-cell subsets may be more predictive and is currently being evaluated.

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PRIOR INVASIVE FUNGAL INFECTION DOES NOT PRECLUDE SUCCESSFUL ALLOGENEIC TRANSPLANTATION

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Prior invasive mold infection has historically been considered a contra-indication for allogeneic stem cell transplantation because of the high risk of fungal reactivation, and the limited efficacy and high toxicity of amphotericin-based drugs. Newer antifungal agents with broad antifungal coverage and an excellent safety and tolerability profile have dramatically altered the management and outcome of fungal infections. Here we present a series of 22 consecutive patients with hematologic malignancy and prior invasive fungal infection that underwent T-cell depleted allogeneic stem cell transplantation at the University of Chicago Hospitals between 2002 and 2005. Fifteen patients had AML, three had ALL, two had large cell lymphoma and one each had CLL or MDS. Their median age was 52 (range 23-68). Eleven patients had HLA-identical sibling donors, ten had unrelated or mismatched related donors, and one had a syngeneic donor. Seventeen patients participated in a prospective study of fludarabine-melphalan-alemtuzumab conditioning (*J Clin Oncol* 2005;23:5728). Six patients received various other conditioning regimens containing alemtuzumab. Post-transplant GVHD prophylaxis was tacrolimus in all patients. All had suffered probable or proven invasive aspergillus infection prior to transplant, involving the lungs in twenty, and the sinuses in two. All had received intensive antifungal treatment prior to transplant. They continued such treatment during transplant and for a prolonged period after transplant. Twenty of the 22 patients engrafted. Nine died; three from relapse and one each from sepsis, cardiac arrest, veno-occlusive disease, fungal pneumonia, PTLD, and multi-organ failure. Three patients experienced recurrent fungal infection, with one death. Thirteen patients remain alive with a median follow-up for survivors of 284 days (range 274-1124). We conclude that in the modern antibiotic era, prior invasive fungal infection should not preclude the use of stem cell transplantation as treatment for hematologic malignancy.