per the Armand classification. Overall and progression-free survival were compared between the overall risk groups (low, intermediate, high and very high).

Results: Median age (range) was 49.4 (19-73.8) years. 139 (43%) patients received matched sibling grafts, 120 (37%) from matched unrelated donors and 63 (20%) from unrelated one HLA-antigen/allele mismatched donors. AML was the most common diagnosis (40%); 31% of all patients were in CR1. HCT-CI scores were 0 (13%), 1-2 (32%) and 3 or greater (55%). 42% of patients had a Karnofsky performance status of 100%. 89% of patients were targeted to a busulfan AUC of 5300 mM*min. GVHD prophylaxis consisted of tacrolimus and methotrexate in 77% of patients. Disease risk by CIBMTR classification was Early 42%, Intermediate 34%, and Advanced 24%. Disease, stage, and overall risk groups, according to the criteria set forth by Armand, et al. as well as the corresponding overall (OS) and progression free survivals (PFS) are shown in the table:

Table

Disease risk	Stage risk	% of patients	Overall risk	OS @ 3 yrs	PFS @ 3 yrs
Low	Low	11%	Low	46%	47%
Low	High	4%	Intermediate	45%	38%
Intermediate	Low	45%			
Intermediate	High	15%	High	39%	34%
High	Low	18%			
High	High	7%	Very High	33%	29%
P value				0.34	0.08

Conclusion: Our outcomes were different in the Low and Very High risk groups reported by Armand, et al. This may be accounted for by a different distribution of diseases or stages within each overall risk category. Variations in other confounding factors also likely contribute to the disparate results. Further analyses of these differences will need to be done to evaluate the validity of this disease risk index in our patients.

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The Cure of HIV with Hematopoietic Cell Transplantation

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Hematopoietic cell transplantation (HCT) has produced the only known cure of HIV infection in a patient. The patient had AML and HIV infection and was transplanted in 2007 using peripheral blood stem cells from an adult *CCR5*-delta32/delta32 donor. The patient, now known as "The Berlin Patient", does not require antiretroviral drug therapy and, in the analysis of peripheral blood cells and numerous tissue samples, no proviral DNA can be detected. However, this successful HCT has not been repeated because the frequency of *CCR5*-delta32/delta32 is less than 1% in Caucasians and much less in other ethnic groups, and patients in need of an HCT generally have only a few potential donors. Moreover, a very close HLA match between donor and patient is required when an adult donor is used. In marked contrast, cord blood HCT requires a significantly less stringent HLA match between donor and patient making it much more feasible to find an appropriate unit for an HIV infected patient. We have tested more than 18,000 cord blood samples from our cord blood bank and collaborating cord blood banks, and have identified 121 cryopreserved *CCR5*-delta 32/delta32 units that are available for HCT. An adequate cord blood cell dose need be only 1 x 10(7) TNC/kg if a combined haploidentical/cord blood transplant is performed. Projections of HLA match rates for an inventory of 300 homozygous units indicates a probability of finding an adequately matched cord blood unit with an adequate cell dose 82.1% of the time for Caucasian adults and for 85.6% for Caucasian pediatric patients. For adult African-Americans, Mexican-Americans and Chinese-Americans the potential HLA match rates are 31.6%, 48.9% and 13.9%, respectively.

Conclusion: Patients who have an indication for an HCT for a hematologic malignancy or other disorder, and who are infected with HIV should be considered for transplantation with a *CCR5*-delta32/delta32 cord blood unit.

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Can Intravesical Instillation of Recombinant Activated Factor VII (rFVIIa) and Aminocaproic Acid (AA) Stop Bleeding in Hemorrhagic Cystitis?

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Hemorrhagic cystitis (HC) is a serious complication of hematopoietic stem cell transplant (HSCT) caused by toxic effects of the conditioning regimen and/or viral reactivation. Treatment of HC is supportive and most interventions result in only transient hemostasis. rFVIIa is a potent procoagulant and is FDA approved for use in patients with Hemophilia. Intravenous rFVIIa has been used off-label to establish hemostasis in multiple conditions. Intravenous rFVIIa in patients with HC has been shown to briefly stop the bleeding. We successfully used intravesical installation of rFVIIa to stop bleeding in patients with post-transplant HC. Pediatric patients with post-transplant HC were treated with intravesical rFVIIa. The bladder was irrigated by normal saline (NS) until clear outflow was achieved; then rFVIIa (~ 50mcg/kg) was instilled in 50-100 ml of NS and dwelled for 1-2 hours. The intravesical instillation of rFVIIa resulted in hemostasis, however it took several days for the bleeding to completely stop. To enhance hemostasis, we instilled 4 gm of AA in 50-100 ml of NS immediately after the rFVIIa was drained and dwelled AA for 1-2 hours. The addition of AA lead to effective hemostasis and development of intravesical clot. Intravesical instillation and dwelling of rFVIIa followed by instillation and dwelling of AA safely and effectively stops HC post HSCT. Based on this experience we are developing a standardized protocol to treat post-transplant HC in the early stages of its development.

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Lower Dose of Antithymocyte Globulin (ATG) Decreases Infection Rate without Increasing Graft-Vs-Host Disease (GVHD) and Relapse in Patients Undergoing Reduced-Intensity (RIC) Allogeneic Hematopoeitic Stem Cell Transplant (HSCT)

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Background: Various doses of ATG have been utilized in RIC allogeneic transplantation targeting T cell depletion, with the goal of decreasing the incidence and severity of both acute and chronic GVHD. This is an update to the previously published data where we showed that lower ATG dose resulted in improved non-relapse mortality and infection rate without compromising control of GVHD.
Methods: We retrospectively analyzed 136 consecutive patients who received RIC HSCT between 2006 and 2010. Following October 2007, ATG dosing was lowered from 7.5 mg/kg (R-ATG) to 6 mg/kg (r-ATG). Progression-free (PFS) and overall survival (OS) were analyzed using the log-rank test. Cumulative incidences of GVHD were analyzed using Gray's test, accounting for competing risks.
Results: Thirty-nine patients received R-ATG and 97 received r-ATG. There were no significant differences in age, gender, KPS, degree of HLA match, prior autografts, donor/recipient CMV status, and CD34 cell dose between the two groups ($P >$ .15). More patients were transplanted with r-ATG than R-ATG for CLL and fewer with AML/MDS/NHL/HD/other histologies ($P = .02$). Time to platelet engraftment as well as donor-cell chimerism at days +30, +90, +180 were not significantly different between the groups, but time to neutrophil engraftment was shorter with R-ATG ($P = .001$). Proportions of aGVHD II-IV were 52% and 41% ($P = .34$) in r-ATG and R-ATG respectively and proportions of cGVHD were 40% and 53% ($P = .23$). Further, no significant differences in the cumulative incidence of GVHD were observed (Figure 1). The R-ATG group experienced more episodes of bacterial infections than the r-ATG cohort (54% vs. 8%; $P < .0001$). No differences in PFS ($P = .69$) or OS ($P = .95$) were observed between the cohorts.
Conclusion: r-ATG did not result in an increase incidence of acute or chronic GVHD. No PFS or OS differences were observed between the cohorts; however, R-ATG resulted in a higher proportion of bacterial infections.

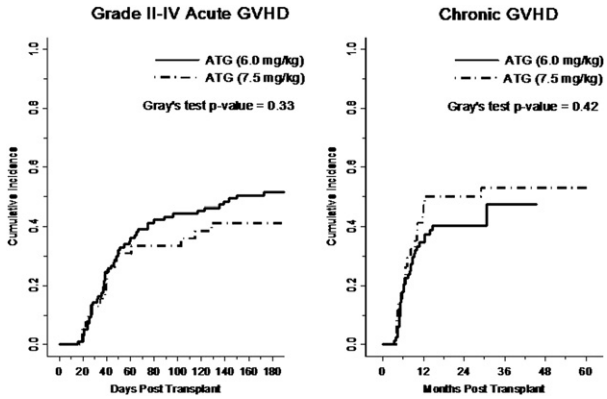

Figure 1. Acute and chronic GVHD

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Soluble Aminopeptidase N (CD13) Is a Diagnostic Biomarker of Late-Onset Chronic Graft Vs. Host Disease in Adults

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Background: Chronic graft vs. host disease (cGVHD) is a major cause of morbidity and mortality after allogeneic HSCT. As an insidious onset and heterogeneous presentation renders this disease difficult to diagnose, there is a need for validated diagnostic biomarkers. Previously, soluble aminopeptidase N (CD13) was identified in a pediatric study as a biomarker for early onset cGVHD (diagnosed 3-9 months post transplant). Aminopeptidase N is a protease involved in immunoregulation on several levels; functions include attraction of T cells, antigen presentation, facilitation of adhesion and phagocytosis. Although it is integrated in the membrane of several cell types it can also be cleaved into soluble aminopeptidase N. In this study, we tested the potential plasma biomarker soluble aminopeptidase N in an adult population of late onset cGVHD patients using both a targeted method (enzymatic assay) as well as a non-targeted approach (proteomics).
Methods: Samples used in this study were frozen, EDTA-treated plasma samples derived from a single institution participating in the Chronic GVHD Consortium and consisted of 17 cases and 21 time-matched controls, all from adult patients. Cases were within 1 month of diagnosis of late-onset cGVHD (onset >9 months post transplant). Time posttransplant for cases vs. controls was 12 (9.2-26.8) vs. 11.9 (5.3-13.5) months, respectively. Other potential clinical variables included age at sample collection, gender, graft source, donor type, conditioning intensity, prior acute grade II-IV GVHD, and months from sample collection. Aminopeptidase N activity was determined by cleavage of L-leucine-p-nitroaniline; quantitative proteomic analyses were done with iTRAQ.
Results and Conclusions: Plasma from cGVHD patients had significantly higher mean levels of aminopeptidase N enzyme activity than did plasma from control patients (0.30 vs. 0.18 mU/ml, respectively $P = .0008$). Proteomic analyses using the same samples revealed that this difference was not restricted to activity; aminopeptidase N showed the most significant difference in protein levels corresponding to presence or absence of cGVHD of all the proteins identified. Relative amounts of soluble aminopeptidase N were 1.44 vs. 0.9, in cases and controls, respectively ($P = .0042$). This study supports soluble aminopeptidase N as a potential diagnostic biomarker in adult GVHD. These results will be validated in a larger population which also includes early onset cGVHD.

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Long-Term Survival After Allogeneic Haematopoietic Cell Transplantation for Acute Myeloid Leukemia. Comparable Results From Myeloablative and Non-Myeloablative Conditioning in Young and Elderly Patients

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Nonmyeloablative (NM) conditioning in allogeneic transplantation is increasingly used in patients aged over 50 years with acute myeloid leukemia (AML). In this single-center retrospective study, we report the results of NM and myeloablative (MA) conditioning in 207 consecutive AML