had worse engraftment compared to congenic wildtype mice. In conclusion, both, vacating of HSC niche space, and the effects of host regulatory cells, that are activated during the TLI procedure appear critical to permit donor HSC engraftment post-TLI/ATG. The dynamics of engraftment after TLI/ATG are unique. Further studies to define the exact roles of host Tregs and NKT cells in engraftment after TLI/ATG and other conditioning modalities are underway.

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IMMUNE RECONSTITUTION AND CLINICAL OUTCOME AFTER HSCT INFUSION FOR SEVERE COMBINED IMMUNODEFICIENCY IN NEWCASTLE

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Background: Hematopoietic stem cell transplantation (HSCT) is the treatment of choice for severe combined immunodeficiency (SCID). There remains debate on whether to pre-condition with chemotherapy prior to infusion of stem cells. We aimed to determine the long-term progress of classic SCID patients who had undergone HSCT infusion at our centre, with respect to clinical outcome and immune comparing outcome based on transplant at <3 or >3 months of age, and molecular diagnosis.

Methods: A retrospective case notes review of patients undergoing a first HSCT infusion for classic SCID from 01/1995 to 02/2011, surviving > 2 months. Patients with previous HSCT were excluded. Parameters analyzed included clinical outcome, chimerism, lymphocyte subsets including recent thymic emigrants, specific antibody levels and Ig replacement. Statistical analysis was performed using c^2 (Fisher exact test) and nonparametric wilcoxon rank sum. A 2-sided p value < 0.05 was considered significant.

Results: Twenty seven of 100 patients with SCID treated fulfilled the study criteria; 10 had ADA deficiency, 7 had T-B-NK+ phenotype, 8 had CgC/JAK3 SCID, and 2 had other forms of SCID. 12 were transplanted < 3 months of age, median age at HSCT was 3 months (range 0-8 months). Twenty had infection at diagnosis, all > 3 months. Eleven had MSD, 1 MMSD, 5 MFD, 3 MMFD, 6 MUD, 1 MMUD. Twenty received GvHD prophylaxis. Median follow up was 80 months (2-187). Seven developed grade II-IV GvHD, 3 grade III. Five were re-transplanted, 2 received boost infusion for poor engraftment (1 CgC, 1 T-B-NK+), 3 received a conditioned HSCT (3 T-B-NK+). TRM was 11% (1 ADA, 2 T-B-NK+). Neurological and autoimmune complications were more common in the ADA and T-B-NK+ groups. Recent thymic emigrants were most commonly present in the CgC/JAK3 and ADA groups, and absent from the T-B-NK+ group. The ADA group had the most complete donor chimerism including myeloid chimerism, T-B-NK+ SCID only achieved donor T cell chimerism. Most ADA patients discontinued IVIG, compared to none with T-B-NK+ SCID.

Conclusion: HSCT infusion is an effective treatment for SCID. Best results are obtained if transplanted < 3 months of age. Establishment of donor B cell chimerism may require additional therapies to achieve engraftment within the stem cell niche in all but ADA SCID.

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DECITABINE IN COMBINATION WITH DONOR LYMPHOCYTE INFUSION AS SALVAGE THERAPY FOR RELAPSED AML POST-ALLOGENEIC STEM CELL TRANSPLANTATION

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Prognosis is extremely poor for AML patients who relapse after allogeneic stem cell transplantation. Donor Lymphocyte infusions (DLI) can be used to salvage these patients with complete response rates reported to be 10-15% with an associated 40-60% chance of developing clinically significant GVHD. The mechanism by which DLI results in clinical responses is thought to be a T-cell mediated process. Data suggest that DLI normalizes the T-cell receptor repertoire and expands the anti-leukemic cell population. Hypomethylating agents, which appear to foster the graft versus leukemia phenomenon, were combined with DLI in attempt to enhance the graft versus leukemia effect.

We report ten AML patients who received Decitabine +/- Etoposide with incremental DLI as salvage after relapse from allogeneic stem cell transplantation during the years 2007-2010. These patients were between the ages of 26- 73 years. Six patients had de novo AML. Three patients were transformed from MDS, and one from essential thrombocythemia. Eight patients had reduced intensity conditioning regimens. Two patients received a fully ablative preparative regimen. Average time to progression post transplant was 17 months.

Patients received Decitabine at 20mg/m^2 for 5 - 10 days, some in combination with Etoposide for 3-5days for disease control. Patients received 1-4 courses of treatment approximately every 28 days with DLI between days 14-21. Two patients who progressed while receiving Decitabine/Etoposide received Clofarabine at 20-52mg/m^2 for 5 days, with subsequent DLI. Cell dose ranged from 1.27 to 31.7 CD3+ cells / kg. Two patients received a mobilized DLI.

Six out of ten patients regained full chimerism. One patient who relapsed with extra medullary disease never lost his graft. Seven out of ten patients achieved a complete remission. Only one patient developed Grade 2 GVHD of the skin. Overall survival in these patients after relapse from allogeneic transplantation was 10.8 months.

The combination of Decitabine and DLI is a well tolerated outpatient therapeutic option for patients with relapsed AML post allogeneic stem cell transplantation. The majority of patients regained full chimerism and achieved complete remission with little or no GVHD.

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IS THE USE OF 9/10 HLA UNRELATED DONORS STILL ACCEPTABLE IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR HEMATOLOGICAL MALIGNANCIES? COMPARISON WITH TRANSPLANTS FROM 10/10 HLA UNRELATED DONORS AND SIBLINGS

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To evaluate the outcome of allo-HSCT from 9/10 HLA mismatched unrelated donors compared to those from 10/10 HLA identical unrelated donors and siblings; we retrospectively studied the outcome of 213 patients who received allo-HSCT for different hematological malignancies, 121 (57%) from HLA identical siblings, 63 (29%) from 10/10 HLA identical unrelated donors and 29 (14%) from 9/10 HLA mismatched unrelated donors between 2006 and 2011 at our institution. The different patient characteristics and figures will be provided in the future during the presentation. After HSCT, engraftment was significantly lower in the 9/10 HLA group (90%) than in the 10/10 HLA group (95%) than in the sibling group (99%), (p = 0.03); the cumulative incidence of acute GVHD> = 2 at 3 months was 32% (23-41), 20% (15-26) and 27% (23-32) respectively; the cumulative incidence of extensive chronic GVHD at one year was 21% (13-30), 9% (5-13) and 17% (14-21) for the 3 groups respectively. After a median follow-up of 8 months (0-54) in the 9/10 HLA group, 10 months (0-60) in the 10/10 HLA group and 18 months in the siblings group, the median OS was 10 months (5-21), 18 months (11-NR) and 60 months (31-NR) respectively with a 2-years probability of 19% (8-44), 43% (31-59) and 63% (54-74) respectively. There was a higher but not significant relapse incidence at one year in the 9/10 HLA group compared to other groups while the TRM was significantly higher with a cumulative incidence at 1 year of 45% (35-55) vs. 33% (27-39) for 10/10 and 12%(9-15) for siblings, (p<0.001). In multivariate analysis, OS was negatively affected by unrelated donors [9/10 HR = 5 (2.7-10), p = 0.0001; 10/10 HR = 2 (1.2-4), p = 0.01], female donors [HR = 2 (1.4-4), p = 0.03] and disease status < CR1 or <chronic phase 1 [HR = 3 (1.4-6), p = 0.003]; while the TRM was negatively affected by

unrelated donors [9/10 HR = 9 (4-20), p<0.001; 10/10 HR = 4 (1.2-10), p = 0.03], female donors [HR = 3 (1.2-7); p = 0.01] and ABO minor incompatibility [HR = 2.5 (1.2-5), p = 0.01]. We showed that allo-HSCT from 9/10 HLA mismatched unrelated donors have a significantly worse OS than those from matched unrelated donors and siblings; this was mainly due to an increased TRM in this group. Patients in first CR or CP could benefit the more from matched or 9/10 unrelated allo-HSCT while the use of transplants from 9/10 HLA unrelated donors in patients not in CR1 should be limited to clinical trials.

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OUTCOMES OF ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PATIENTS WITH ACUTE MYELOID LEUKEMIA IN THIRD REMISSION

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Introduction: A small minority of patients (pts) with Acute Myeloid Leukemia (AML) achieve complete remission (CR3) after a second relapse. The role of allogeneic HCT (allo-HCT) for such patients is unclear. Here we present the outcomes of CR3 AML patients treated at the M D Anderson Cancer Center.
Methods: We conducted a retrospective analysis of prospectively collected data on all AML pts (n = 33) who received their allo-HCT in ≥ CR3 between 11/2/1990- 7/1/2009.
Results: Median age was 40 years (range, 19-67) and 46% were female. CR3 pts comprised 2.7% of all pts with AML treated at the same time period in our institution (n = 1227). 3/33 had secondary AML (2 with prior myelodysplastic syndrome and one with previous myeloproliferative disorder). Cytogenetics risk categories were low in 24%, intermediate in 30%, high in 21% and unknown in 25%. Pts had a median of 4 chemotherapy lines prior to transplant. Donor was matched unrelated in 48%, matched related in 24%, mismatched related in 15% and mismatched unrelated 9%. Graft source was peripheral blood (52%), marrow (39%) or umbilical cord blood (9%). Ten pts had prior allo-HCT. Conditioning regimen was of reduced intensity in 60% and myeloablative in 40% of pts. and 84% of pts received Tacrolimus/Methotrexate +/- Pentostatin for graft- versus-host disease (GVHD) prophylaxis. 97% of the pts engrafted. Cumulative incidence rate of grade II-IV acute GVHD was 26% and of chronic GVHD was 27%. Overall survival was 19% (95 % CI: 7-34%) and progression-free survival (PFS) was 12% (95% CI: 3-26%)[Figure below]. Relapse rate was 29%, and cumulative incidence of non relapse mortality (NRM) was 46%. Less NRM was seen among pts who had allo-HCT after year 2002, year in which molecular class I HLA typing was incorporated (32% vs. 64%; p = 0.9); improved PFS was also observed after 2002 (22% vs. 0% before 2002, p = 0.5). Prior allo-HCT was not a risk factor for adverse outcomes with PFS of 20% with prior HCT vs. 7% for pts without prior allo-HCT (p = 0.7) and NRM rates were comparable (20% vs. 58%; p = 0.3). Seven pts are alive, with a median follow-up of 11.3 months. Causes of death (n = 26) were relapse (n = 7), infections (n = 8), GVHD (n = 5), other (n = 3), and unknown (n = 3).
Conclusions: Pts in CR3 may benefit from allo-HCT, but should be considered for investigational approaches given high non-relapse and relapse mortality.

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BROAD EXPRESSION OF A MINOR HISTOCOMPATIBILITY ANTIGEN RESULTS IN IMPAIRED ANTITUMOR IMMUNITY THAT CANNOT BE OVERCOME WITH DENDRITIC CELL VACCINATION

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Although allogeneic transplant remains a potent immunotherapy for high-risk hematopoetic malignancies, relapse is the main cause of treatment failure. We, and others, have shown that alloreactivity associated with minor histocompatibility antigen (miHA) mismatch reduces quantitative responses to vaccines targeting tumor-specific antigens. The effect of miHA mismatch on the antitumor response when the tumor also expresses the miHA has not been well-studied, and could provide important insight into the biology of the graft-versus-tumor effect. We therefore utilized a murine allotransplant system in which donors and recipients were mismatched at the clinically relevant male miHA HY, followed by DLI with HY-specific T cells and challenge with an HY-expressing tumor. Professional HY antigen presentation was provided at the time of DLI using an activated male dendritic cell (DC) vaccine. Recipients were monitored for clinical GVHD and antitumor responses measured by tumor-free and overall survival. Further analysis of HY specific T-cells in secondary lymphoid organs was performed by flow cytometry using congenic markers. When HY is expressed only on the tumor, following syngeneic transplant of female (HY-naive) T-cell depleted marrow into female recipients, there is 100% tumor-free survival following HY-specific DLI and male vaccination. However, when HY is expressed in all nonhematopoetic tissues, following transplantation of female marrow into male recipients, there is approximately 20% tumor-free survival regardless of whether an activated male DC vaccine is given. Interestingly, expression of HY in both the nonhematopoetic and hematopoetic (when male marrow is transplanted into female recipients) compartments produces a robust expansion of HY-specific T-cells, suggesting that the impaired antitumor immunity is due to dysfunction, rather than clonal deletion. Indeed, nearly 100% of HY-specific T-cells from secondary lymphoid organs express high levels of PD-1 in the allogeneic transplant setting, compared to low levels in syngeneic recipients and no expression in lymphocytes reconstituted independently of the DLI. Studies are underway to functionally characterize these exhausted alloreactive T cells and and identify targets for therapeutic blockade to restore the effectiveness of antitumor vaccination in the allotransplant setting while minimizing GVHD.

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THE IMPACT OF HCV SERO-POSITIVITY OF RECIPIENTS ON CLINICAL OUTCOMES FOLLOWING ALLOGENEIC HSCT IN JAPAN

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Background: It is estimated that over 2,000,000 people suffer from hepatitis C virus (HCV) infection in Japan. Therefore, HCV infection is one of major liver diseases. In hematopoietic stem cell transplantation (HSCT), HCV infections of recipients might induce a transient liver dysfunction, and an increasing risk of veno-occlusive disease (VOD), although these are controversial. In addition, the genotypes of HCV in Japan are considered different from those in Western countries. Therefore, we have assessed the impact of HCV sero-positivity of recipients on clinical outcomes in Japan.
Patients: The population was based on TRUMP data confirmed in 2010. The eligible population included the all recipients who received an initial allogeneic HSCT since 2006 and whose data about age, gender, HCV sero-positivity of recipients and status of survival at last observation were available.
Results: We identified 136 and 7720 recipients with and without HCV, respectively. Although more recipients with HCV tended to be male (p = 0.054) and to receive female to male HSCT (p = 0.081), there were no differences in other background. The recovery of more than 5x10^10/L platelet was significantly later in recipients with HCV (38 vs 47 days, p = 0.013), while there was no significant difference in neutrophil engraftment. There were no differences between groups without and with HCV in