the incidences of grade2-4 aGVHD (35.9% vs 31.6%, p = 0.18) and cGVHD (29.3% vs 30.5%, p = 0.67). However, the liver involvement of aGVHD was higher in recipients with HCV (13.9% vs 23.9%, p = 0.031), while there was no differences in liver involvement of cGVHD (37.3% vs 45%, p = 0.33) and VOD (10.7% vs 17.3%, p = 0.17). Furthermore, the recipients with HCV had significantly higher non-relapse mortality (NRM; 25.9% vs 38.0% at 2 year, p<0.01) and poor overall survival (OS; 51.4% vs 41.1% at 2 year, p<0.01). Multivariate analysis revealed that HCV sero-positivity remained significant as a risk factor for NRM (HR 1.60, p<0.01) and OS (HR 1.34, p = 0.016) after adjusting with gender, age, disease, and donor source. Proportions of patients who died due to hepatic failure (4.9% vs 14.3%) and bacterial infection (9.4% vs 18.2%) were significantly higher in recipients with HCV than in those without HCV.

Conclusion: HCV sero-positivity was identified as a risk factor for poor survival in HSCT. In addition, we should carefully manage not only liver dysfunction but also bacterial infection in HCV positive patients.

336

DEPLETION OF HOST DENDRITIC CELLS DURING THE EFFECTOR PHASE OF GVHD ENHANCES ACUTE GVHD AND MORTALITY

Jordán Garrote, A.-L.[1,2], Brede, C.[1,2], Riedel, S.S.[1,2], Bäuerlein, C.A.[1,2], Ritz, M.[1], Mattenheimer, K.[1], Kiesel, C.[1], von Krosigk, V.[1], Chopra, M.[1], Einsele, H.[1], Negrin, R.[3], Mottok, A.[4], Garbi, N.[5], Lutz, M.B.[6], Beilhack, A.[1] [1] Wuerzburg University Medical School, Germany; [2] Graduate School of Life Sciences Wuerzburg, Germany; [3] Division of Blood and Marrow Transplantation, Stanford University; [4] Institute of Pathology, University of Wuerzburg, Germany; [5] Institutes of Molecular Medicine andExperimental Immunology, Bonn, Germany; [6] Institute of Virology and Immunology, University of Wuerzburg, Germany

After allogeneic stem cell transplantation remaining recipient dendritic cells (DCs) in secondary lymphoid organs are essential to initiate acute graft-versus-host disease (aGVHD). Yet, to which extend mucosal DCs in peripheral tissues contribute to augment, maintain or even down-modulate aGVHD remains elusive. Therefore, we investigated the function of host DCs during the effector phase of intestinal aGVHD. Until day 8 after transplantation (H-2q FVB/N into H-2b C57BL/6, 9Gy) we detected predominantly persisting host DCs but only few donor DCs by immunofluorescence microscopy. Histopathological analysis revealed high numbers of host DC - donor T cell contacts in the intestinal mucosa during the aGVHD effector phase. Time kinetics experiments established that these dominating population of $CD11c^+CD11b^+$ intestinal DCs arose from radiation-resistant host-type monocytes that were attracted to areas of inflammation and differentiated into DCs. At sites of T cell contact DCs engaged costimulatory molecules such as CD80. To address the role of this interaction we induced aGVHD in transgenic C57Bl/6-DOG mice that express the diphtheria toxin (DTx) receptor in DCs under the control of the CD11c promoter and subsequently applied DTx intraperitoneally to eliminate host type DCs. Immunofluorescence microscopy and FACS analysis proved efficient host DC depletion in the intestinal tract (>90%). DC depleted DOG recipients presented considerably higher GVHD scores and reduced survival than aGVHD controls that did not receive DTx (n = 25/group). Additional controls were used in order to rule out possible cytotoxic effects of the DTx: WT mice, syngeneic controls and bone marrow controls sensitive to the toxin, were not affected by the administration of DTx. Subsequently we excluded a possible reduction of FoxP3+ regulatory T cells in the intestinal tract from DTx and non-DTx treated mice. Inflammatory cytokines such as IFN-γ and TNF did not differ in the serum of DTx and non-DTx treated mice on day 6 after allo-HCT, ruling out a possible cytokine storm effect due to the DC killing. However, elevated levels of the inflammatory cytokine CCL2 in DTx treated DOG mice indicate that DC depletion enhances signals to recruit precursors in order to refill the mucosal DC-compartment. Our study provides evidence for a likely underappreciated function of DCs during later stages of aGVHD and provides evidence for a protective role of remaining host DCs from monocytic origin during aGVHD.

337

CLINICAL PRACTICE GUIDELINE FOR THE TREATMENT OF BK-VIRUS INDUCED HEMORRHAGIC CYSTITIS IN THE POST-ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANT SETTING

Morrison, D.[1], Kochuparambil, T.[2], DeRemer, D.[2], Kota, V.[2], Jillella, A.[2], Awan, F.[2] [1] Georgia Institute of Technology, Atlanta, GA; [2] Georgia Health Sciences University, Augusta, GA

Introduction: BK-virus induced hemorrhagic cystitis (HC) frequently affects patients undergoing allogeneic hematopoietic stem cell transplant (allo-HSCT) and results in significant morbidity and mortality. There are no existing guidelines to dictate clinical practice. We present our institutional data and recommend a clinical practice guideline that could potentially improve the outcomes of patients with BK-virus infections.

Methods: Our retrospective analysis included 75 consecutive patients who underwent allo-HSCT from 2001-2011. Data was collected on patients with PCR proven BK-viuria under existing IRB approved protocols.

Results: 12% of all patients developed PCR proven HC. The median age of patients at transplant was 37-yrs. 66% had AML or ALL and the median number of prior therapies was 3. 33% had a MUD transplant while 66% received RIC conditioning and 33% received ATG. The mean CD34+ cell dose was $4.8x10^6$/kg and the CD3+ cell dose was $8.6x10^{11}$/kg. The median time of onset of HC was 44-days and lasted for an average of 53-days. 33% patients were neutropenic at the onset of HC and the mean absolute neutrophil count was 4300/ul. Most common symptoms were dysuria in 66%, bladder spasms in 44% and urinary retention in 22%. All patients had received GVHD prophylaxis with methotrexate and tacrolimus and 77% were on concurrent steroids and mycophenolate. 88% of patients had concurrent acute GVHD at the time of HC. 88% had CMV and 11% had EBV viremia at the time of HC. 44% developed BK-viremia while 55% had BK-virus induced nephropathy defined as an increase of serum creatinine >1.5. Management approach was tiered into prophylaxis, symptomatic relief and anti-viral therapy. All patients received ciprofloxacin and 88% received IVIg. No single therapy component including reduced immunosuppression, cidofovir and leflunomide was independently identified as a more efficacious option (p>0.05), but of the patients who received cidofovir, 75% had resolution of symptoms and were able to clear the BK-viuria.

Conclusion: Our analysis suggests that BK-virus induced HC is the result of multifaceted host and donor interactions and the concurrent use of immune altering therapies. We have also developed a multitiered approach that includes prophylactic intervention for patients undergoing T-cell depleting regimens; symptomatic management; and antiviral therapy in select subsets of patients to uniformly manage our patients in an effort to improve clinical outcomes.

338

IN-VIVO MODEL OF HUMAN ALLOGENEIC STEM CELL REJECTION IN NSG MICE

Mahmud, D.[1], Nicolini, B.[2], Mahmud, N.[1], Patel, P.[1], Arpinati, M.[2], Rondelli, D.[1] [1] University of Illinois Hospital and Health Science System, Chicago, IL; [2] University of Bologna, Bologna, Italy

T cell alloreactivity against human CD34+ cells was tested for the first time in-vivo in a NOD/SCID γ-null (NSG) mouse model. Human allogeneic blood CD3+ T cells were co-transplanted with allogeneic cord blood CD34+ cells (2×10^5/mouse) in sublethally irradiated mice at high (50:1, 10:1, 5:1) or low (2:1, 1:1, or 0.5:1) CD3:CD34 cell ratio. Control mice received CD34+ cells alone. At 6 weeks post transplant, marrow and spleen cells were harvested and analyzed by flow cytometry. Independently of high or low CD3:CD34 cell ratio of the graft, all the mice showed a reduced overall number of huCD45+ cells in the marrow (p = 0.0001) compared to control. Stem cell graft failure was documented by detecting only the engraftment of human T cells and no myeloid or B cells in the marrow and spleen of mice at every T cell:CD34 ratio tested. HuCD45+ T cells included CD4+ and CD8+ cells at normal ratio and a low number of CD56+ cells. Failure to engraftment of CD34+ cells was also confirmed by FISH analysis in animals

transplanted with sex-mismatch CD34+ and CD3+ cells. Only when mice were transplanted with a very low CD3:CD34 cell ratio (0.1:1) a mix chimerism of huCD45+ CD3+ (21±11%) T cells, CD19+ (44±9%) B cell, CD34+ cells (3±1%), CD33+ myeloid cells (14±1%) and CD14+ monocytes (6±1%) was observed. To investigate whether a single T cell population could cause stem cell rejection, mice were transplanted with selected CD3+CD4+ or CD3+CD8+ T cells and CD34+ cells at 1:1 ratio. Rejection was observed in 100% of mice transplanted with human CD3+CD4+ cells. CD4+ cells in marrow and spleen were mostly CD45RA+. Instead, mice transplanted with human CD3+CD8+ cells showed a mixed chimerism of T, B and myeloid cells both in marrow and spleen. Spleen was larger in recipients of CD4+ than CD8+ cells ($p = 0.005$). Finally, spleen cells obtained from mice transplanted with CD4+ or CD8+ cells were tested in-vitro as responders against irradiated CD34+ cells in mixed leucocyte cultures. Controls included CD4+ or CD8+ cells that were frozen at the time of transplant. Spleen CD4+ cells and both CD4+ and CD8+ control cells proliferated after stimulation with CD34+ cells, whereas spleen CD8+ cells were unresponsive in-vitro. These results show that alloreactive CD4+ T cells serve an important role in stem cell rejection while CD8+ T cells appear to facilitate immune tolerance. Our work also supports the use of NSG mice to analyze the mechanisms of stem cell rejection or graft failure.

339

HEMATOPOIETIC CELL TRANSPLANTATION CO-MORBIDITY INDEX (HCT-CI) TO PREDICT NON RELAPSE MORTALITY (NRM) AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT)

Colella, M.P., Miranda, E.C.M., Aranha, F.J.P., Fernandes-Junior, V.C.A., Medina, S.M., de Souza, C.A., Vigorito, A.C. University of Campinas, Campinas, Sao Paulo, Brazil

In recent decades, several advances were made in the management of patients (pts) who underwent allogeneic hematopoietic stem cell transplantation (HSCT). Tools that could predict TRM, based on pre HSCT characteristics and co-morbidities were always sought. Some of these tools are the modified hematopoietic cell transplantation co-morbidity index (HCT-CI).Our aim was to apply the modified HCT-CI and correlated it with overall survival (OS) and non-relapse mortality (NRM).This analysis include patients who underwent an allogeneic HSCT, for malignant and non malignant hematological diseases, after high or low dose conditioning regimens, from related and unrelated donor, from 1993 to 2010. Each co-morbidity was assigned an integer weight, and the HCT-CI score was the sum of this integer weights. The patients were then assigned to one of the risk groups 0, 1, 2 and 3 or more. Kaplan-Meier was applied for estimation of overall survival. NRM was estimated by cumulative incidence considering primary relapse disease as competing risk.457 pts were analyzed at the beginning. However, 331 (72.4%) were evaluable, 126 (27.6%) were excluded when at least one parameter was missing. 208 (63%) were male with a median age of 36.5 (5-65) years, 249 (75%) pts received high dose (HD) conditioning and 82 (25%) low dose (LD). HCT-CI in HD was: 127 (51%) score 0; 39 (16%) score 1; 19 (7%) 2 and 64 (26%) score ≥ 3; in LD 33 (40%) score 0; 14 (17%) score 1; 8 (10%) score 2 and 27 (33%) score ≥ 3. The median follow up in HD was 22 months (0-201) and 9 (0-203) in LD. The adjusted OS at 10 year for HD conditioning according to the HCT-CI was 55% for score 0, 34% for score 1-2 & 34% for score ≥ 3 and for LD conditioning was 58% for score 0, 53% for score 1-2 & 15% for score ≥ 3 ($p < 0.0001$). The NRM rate in the HD cohort was 32% in the pts with a score 0, 42% for score 1-2 and 53% in the score ≥ 3. In the LD cohort, the NRM was 23% in the pts with a score of 0; 35% for score 1-2 and 54% in the score ≥ 3 ($p = 0.002$). The adjusted OS for conditioning type in patients with cardiac valve disease was associated to a lower OS (29% and 33% $p = 0.002$) whereas mild hepatic involvement was just significant in the HD cohort. The OS and NRM were worse for score ≥ 3 either in HD and LD groups. The heart valve disease emerged as a worse outcome in both conditioning type and mild hepatic involvement only in HD group. The HCT-CI showed to be a valid tool to predict outcome after allogeneic HSCT.

340

OUTCOMES OF MANTLE CELL LYMPHOMA AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

Costa, R.[1], Palmer, J.[2], Shen, Y.[2], Paris, T.[2], Popplewell, L.[1], Kogut, N.M.[3], Forman, S.J.[1], Nademanee, A.[1] [1]City of Hope National Medical Center, Duarte, CA; [2]City of Hope National Medical Center, Duarte, CA; [3]Southern California Kaiser Permanente- City of Hope Transplant Program, Los Angeles, CA

Background: Mantle cell lymphoma (MCL) commonly has an aggressive course and short survival with conventional chemotherapy. Allogeneic stem cell transplantation (allo-HSCT) is a potentially curative treatment for a subset of MCL patients.
Methods: We conducted a retrospective analysis including 41 consecutive MCL patients who underwent allo-HSCT. Patients with the blastic variant of MCL; extensive marrow involvement; multiple relapses after conventional chemotherapy; relapse after autologous stem cell transplantation (ASCT); unable to collect stem cells to undergo ASCT were considered eligible for allo-HSCT.
Patients: Median age was 54 years (range: 32-70). Median time from diagnosis to transplant was 18 months (range: 5.4-118). Disease status at allo-HSCT included CR1 (n = 7), induction failure (n = 13), 1st relapse (n = 13); >1st relapse (n = 8). 31 patients (76%) had stage IV disease at diagnosis. Median number of prior regimens was 3 (range: 1-7). 35 patients (85%) had chemosensitive disease. 25 patients received allo-HSCT from a matched sibling and 16 from unrelated donors. Conditioning regimens were fludarabine/melphalan-based (n = 29), or TBI-based (n = 12). Most (80%) received peripheral blood stem cells. 23 (56%) received tacrolimus and sirolimus; 18 received cyclosporine or tacrolimus with methotrexate (n = 12) or cellcept (n = 6) for GVHD prophylaxis.
Results: At a median follow-up of 1.7 years, 59% of the patients were still alive. The estimated 5-year overall and progression free-survival was 51% (95% CI, 31% - 68%) and 30% (95% CI, 14% - 48%), respectively.The 5-year cumulative incidence of relapse and/or progression was 43% (95% CI, 26% - 63%). The incidence of acute and chronic GVHD was 56% and 63%, respectively. The 1-year and 5-year non-relapse related mortality (NRM) was 15 % (95% CI, 7% - 29%) and 27% (95% CI, 15% - 43%). Factors associated with increased risk of death and/or disease relapse/progression were: time from diagnosis to transplant, advanced disease status at transplant and prior ASCT.Patients transplanted after one or more relapse events were at 7.28 times the risk of failure compared to those in first CR1 (95%CI: 0.94 - 56.5; p = 0.06).
Conclusions: These results suggest that long-term disease control is possible after allo-HSCT for a subset of patients with MCL with acceptable toxicity. Allo-SCT during CR1 may offer long-term disease control in patients with blastoid variant or those unable to undergo autologous SCT.

341

ASSESSMENT OF LIVER FIBROSIS BY DIAGNOSTIC VALUE OF TRANSIENT ELASTOGRAPHY (FibroScan) IN THE IN PATIENTS WITH β-THALASSEMIA MAJOR CONSIDERED AS CANDIDATES FOR HEMATOPOIETIC STEM CELL TRANSPLANTATION

Hamidieh, A.A.[1], Poustchi, H.[2], Shazad, B.[1], Jalili, M.[1], Hamdi, A.[1], Behfar, M.[1], Jalali, A.[1], Malekzadeh, R.[2], Ghavamzadeh, A.[1] [1]Tehran University of Medical Sciences, Tehran, Islamic Republic of Iran; [2]Tehran University of Medical Sciences, Tehran, Islamic Republic of Iran

Introduction: Transient elastography (TE) is a valuable non-invasive method to assess liver fibrosis. The present study aimed to evaluate the diagnostic value of TE in the assessment of hepatic fibrosis in patients with β-thalassemia major (TM) who are candidates for hematopoietic stem cell transplantation.
Method: We prospectively assessed the results of TE in 41 β-thalassemia major patients (median age of 7 years; range 2.6-20 years; 65.9% male) who were candidates for hematopoietic stem cell transplantation (HSCT) and compared these results with the histological fibrosis stage from liver biopsies. The diagnostic values were compared by calculating the area under the receiver operating characteristic curves (AUROCs).