allogeneic sibling matched bone marrow transplant in autum 2005, after ovarian tissue cryopreservation. The conditioning regimen included IV busulfan (12.8 mg/kg total dose), cyclophosphamide (200 mg/kg total dose) and antilymphocyte globulin. A stable 100% donor chimerism was obtained from D60. An acute grade II GVHD was followed by limited chronic GVHD for 7 months. Clinical menopause with amenorrhea due to premature ovarian failure occurred within the first year post-HSCT. Hormone replacement with oestro-progestogens was started 6 months after HSCT and was maintained until ovarian function restoration. In spring 2008, as the patient had been menopausal for 2.5 years, an orthotopic autotransplantation of ovarian cortex was performed in two consecutive laparoscopic procedures, the first one aiming to induce local angiogenesis. One thawed strip of ovarian cortex was fixed in the ovarian incision, 5 others were deposited in the peritoneal window. Three days later, 3 thawed cortical strips were fixed into the left ovary and one into the peritoneal window. Ovarian function recovery was evaluated by hormonal levels and follicular development was observed by ultrasound.

The patient conceived spontaneously in a natural cycle in autumn 2008, and delivered a healthy child in June 2009. This first case report of pregnancy and delivery after ovarian autograft in a patient treated by HSCT suggests that cryopreservation of ovarian tissue should be offered prior to HSCT not only to women of childbearing age but also to prepubertal patients, as primordial follicles are already present in the post natal ovaries.

Conclusion: Our case series shows that addition of ECP to commonly used regimen for BO results in faster symptomatic improvement in an otherwise debilitating long term complication after allo-SCT. A limitation of this study is a small sample size, short follow-up, however impressive clinical response.

LEUKEMIA

195 IMATINIB MAINTENANCE FOLLOWING ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION (HCT) FOR PATIENTS WITH PHILADELPHIA CHROMOSOME POSITIVE (Ph+) ACUTE LYMPHOBlastic LEUKEMIA (ALL)
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The addition of tyrosine kinase inhibitors (TKIs) to conventional ALL therapy has significantly improved outcome for Ph+ patients, resulting in more patients being able to receive HCT in remission. Maintenance therapy with TKI following HCT may additionally improve outcomes. We performed a retrospective chart review on transplants since 2001 when TKI first became available for use following HCT. From March 2001 through June 2009, 66 patients with median age 37 years (range 15-61) received an allogeneic HCT for Ph+ ALL in CR1 (n = 56) or CR2 (n = 10); 28 patients were in complete molecular remission at time of HCT. Patients received matched related (n = 30) or matched unrelated (n = 27) peripheral blood (n = 35), bone marrow (n = 22), or mismatched cord blood cells (n = 9) following a myeloablative TBI-based (n = 48) or non-TBI-based (n = 18) transplant conditioning regimen. GVHD prophylaxis was tacrolimus-based. All patients received TKI prior to HCT. Patients were eligible to receive TKI maintenance following HCT if they had hematologic recovery defined by an unsupported platelet count >50,000/uL and absolute neutrophil count >1500/uL. Forty-seven percent (n = 31) of patients received TKI in the form of imatinib at median dose 300 mg (range 100-800) initiated at median of 2 months (range 1-12) following HCT. Median duration of imatinib use post HCT was 13 months (range 1-91). The most common reason for treatment discontinuation was physician preference followed by disease progression. Cytopenias and gastrointestinal discomfort were the most common imatinib-related toxicities. With a median follow-up of 4 years among survivors (range 0.1-7.7), 2-year overall survival (OS) and progression-free survival (PFS) were 55% and 50%, respectively. Day 100, 1-year, and 2-year non-relapse mortality (NRM) rates were 11%, 26%, and 28%, respectively. The cumulative incidence of grade 2-4 and 3-4 acute GVHD were 48% and 16%, respectively; the incidence of chronic extensive GVHD was 19%. In univariate analysis, imatinib maintenance led to significantly better OS (HR 0.3, 95% CI 0.1-0.8, p = 0.02) and NRM (HR 0.3, 95%CI 0.1-1.1, p = 0.07). Additionally, age > 40 years and CR2 vs CR1 led to significantly worse OS; molecular remission did not reach statistical significance. Large, multicenter trials in Ph+ ALL are in progress to confirm the benefit of TKI maintenance following HCT.

196 DEVELOPING A MURINE MODEL TO STUDY B CELLS AS APC IN VIVO
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Introduction: As dendritic cells (DC) are effective conductors of adaptive and innate immune responses, they are used as cellular adjuvant for active immunotherapy. Nevertheless, challenges to this
approach have been identified. Recently CD40-activated B cells (CD40-B) have been studied as complementary antigen presenting cells. They can be expanded from small amounts of PB at >95% purity under GMP-like conditions and efficiently prime and expand naive T cells in vitro. Importantly these cells are available at virtually unlimited amounts for high-dose, high-frequency vaccination considered crucial for the control of cancer in vivo.

Methods and Results: For preclinical in vivo testing using high-dose, repetitive vaccinations with CD40-B we developed a murine system to study their ability to induce immune responses in vivo. mCD40B are generated from murine splenocytes by co-culture with murine CD40-Ligand and addition of IL-4. mCD40B cells could be expanded more than 6-fold within 14 days and >90% purity. mCD40B were used to establish a vaccination model to study induction of tumor- and auto-antigen specific immune responses as well as toxicity of very-high-dose injections (VHID) in B6 mice. To determine long-term toxicity mice were vaccinated twice weekly for 5 weeks using high-doses ($3 \times 10^6$ – $1 \times 10^8$/kg) of mCD40B. This is about 2-3 log higher than currently used in DC vaccinations in humans. Acute toxicity was assessed by vaccinating mice once with VHID ($1 \times 10^6$ – 3.3 $\times 10^8$/kg). There was no difference in survival, weight and clinical appearance compared to control mice. Histopathological assessment did not reveal any pathologic changes. Marine Mixed Lymphocyte Reaction was established to investigate the immune-stimulatory capacity of mCD40B in comparison to mDC through detection of T cell proliferation in vitro. Immune monitoring by intracellular cytokine staining for IFN-g and assessment of in vivo cytoxicity revealed that mCD40B vaccination leads to increased IFN-g production by activated T cells and specific lysis of CFSE-labelled peptide-pulsed target cells.

Conclusion: Based on these findings that mCD40B induce T cell responses in vitro and in vivo we are now developing the optimal mCD40B vaccination algorithm for preventive and therapeutic treatment of B16-Melanoma in B6 mice as a next step towards future clinical application in post transplant donor-lymphocyte-infusion or vaccination.

197 ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (SCT) USING FLUDARABINE/RETOULSAN CONDITIONING REGIMEN COMPARED WITH BUSULFAN-BASED MYELOABLATIVE AND REDUCED-INTENSITY CONDITIONING IN PATIENTS WITH AML AND MDS; RELATIVE (MVA) SURVIVAL DEPENDS ON DISEASE STATUS AT SCT

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Allogeneic SCT with both myeloablative (MAC) and reduced-intensity conditioning (RIC) is effective therapy in AML/MDS. However, the relative merits of each differ in different settings. Fludarabine/retoulsan (FT) has been reported as an effective regimen in AML/MDS with limited toxicity. However, the relative dose intensity and expected outcomes with FT in the different SCT settings, compared with Busulfan (Bu)-based regimens, is not well defined. We analyzed the outcomes of 298 pts with AML/ MDS given SCT from sibling (n = 153) or unrelated (n = 145) donors. Pts meeting standard eligibility criteria for MAC were given iv-BuCy (n = 91). Pts at high risk for MAC were given fludarabine and reduced doses of ivBu (6.4 mg/kg, FB2, n = 91), high dose Bu (FB4, 12.8 mg/kg, n = 63) or tosulfan (30-36 g/m2, n = 63). Non-re- lapse mortality was 17%,18%,18% and 20% with FB2,FB4,FT and BuCy, respectively (p = NS). With a median follow-up of 38 months (1-135), estimated 5-yr overall survival (OS) was 36%,33%,49% and 41%, respectively (p = NS). Multivariate analysis (MVA) defined age > 50 [HR 1.5 (1.2-2.0), p = 0.05], active disease at SCT [HR 2.3 (1.6-3.2), p < 0.001] and unrelated donor [HR 1.5 (1-2.0), p = 0.02] as risk factors for shorter OS. The conditioning regimen was not predictive. When the analysis was limited to pts in remission (n = 126), OS was 51%,43%,58% and 43%, respectively. MVA identified age > 50 as an adverse factor, while SCT using FB2 or FT was associated with longer OS [HR 0.3 (0.2-0.7) p = 0.002]. When the analysis was limited to pts with active disease (n = 172), either chemo-refractory (n = 93) or untreated (n = 79), OS was 12%,25%,32%, and 36%, respectively. MVA identified chemo-refractory disease as the major adverse factor for OS [HR 2.2 (1.5-3.3), p = 0.001], while SCT using BuCy or FT was associated with longer OS [HR 0.7 (0.5-1.0), p = 0.06]. In conclusion, dose intensity is associated with different outcomes in the different settings. In pts in remission, outcome is mostly related to SCT toxicity resulting in an advantage to less intensive regimens, such as FB2, while FT shares this characteristic. In pts with active disease, outcome is dominated by the risk for relapse, leading to advantage of more intensive regimens, such as BuCy. FT shares this characteristic mainly in pts with no true chemo-refractoriness and has an advantage over FB2 in this setting. FT should be considered a reduced toxicity myeloablative conditioning that is feasible in pts ineligible for MAC.