examination of 2 patients revealed PCR positivity with a 3 or 4-log increases of normalized BCR-ABL amount and subsequent hematologic relapse, which occurred 2 and 4 months later, respectively. Although our data should be interpreted cautiously, the presence of chronic GVHD may reduce the risk of relapse in Ph+ ALL. Real-time quantitative RT-PCR appears to be a useful test for BCR-ABL transcript monitoring.

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ALLOGRAFTING WITH FLUDARABINE AND ATG AFTER FAILED ENGRAFTMENT OF AUTOLOGOUS PERIPHERAL BLOOD STEM CELLS

Bayer, R.; Focazio, B.; John, V.; Loscalzo, J.; Buchbinder, A. North Shore University Hospital, Manhasset, NY.

High-dose myeloablative regimens with autologous stem cell transplantation have been pursued as a consolidation strategy in first remission AML patients. We report two patients with AML who received autologous stem cell transplants in first CR. Both patients received similar regimens and failed to engraft their autologous blood stem cells. Both were then given Fludarabine and ATG with subsequent engraftment of cells from an HLA matched sibling. Patient A.S. is a 32 y.o male diagnosed with AML, FAB subtype M2, with normal cytogenetics who received induction chemotherapy with Ara-C 100mg/m2 x7 days, Daunorubicin 40mg/m2 x3 and VP16 40mg/m2 x3. His intensification/mobilization included Ara-C 2gm/m2 x8 and VP16 10mg/kg x4. The regimen used for autologous stem cell transplant was Busulfan p.o. 1mg/kg x16 doses and VP16 60mg/kg x1. He received 15.6 x 10 E6 CD34 cells/kg bodyweight. On day 52 there was no sign of engraftment. He was then given Fludarabine 30mg/m2 x4 doses and ATG 15mg/kg x6 doses. Peripheral blood stem cells, 4.2 x 10 E6 CD34 cells/kg, were given from his HLA matched brother. Engraftment was noted on Day 12 post transplant. He had no signs of GVHD. He is now 100% donor, confirmed by variable number tandem repeats (VNTR). Patient R.S. is a 46 y.o male who was diagnosed with AML, FAB subtype M2, with normal cytogenetics. His induction chemotherapy consisted of Ara-C 100mg/m2 x7 days and Daunorubicin 30mg/m2 x3 days. This was followed by an intensification/mobilization regimen of Ara-C 2gm/m2 x8 doses and VP16 10mg/kg x4 doses. He received Busulfan IV 0.8mg/kg x16 doses and VP16 60mg/kg x1 dose as a regimen for his autologous stem cell transplant. He received 11 x 10 E6 CD34 cells/kg bodyweight. On day 36 there was no engraftment. He was then given Fludarabine 30mg/m2 x4 doses and ATG 15mg/kg x6 doses. He was given peripheral blood stem cells, 2.1 x 10 E6 CD34 cells, from his HLA matched brother. Engraftment was noted on Day 7 post transplant. The patient developed Grade I GVHD which responded to treatment with Prednisone. He is presently 98% donor confirmed by VNTR. We conclude that Fludarabine and Antithymocyte globulin is a safe and effective regimen for allografting after failed engraftment of autologous peripheral blood stem cells in patients with AML.

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THE CD4 PEPTIDE ANALOGUE 802-2 INHIBITS PROLIFERATION OF BOTH TH1 AND TH2 CELLS IN RESPONSE TO ALLOGENEIC STIMULATION

Zhu, Z.; Mookerjee, B.; Korngold, R.; Flomenberg, N. Thomas Jefferson University School of Medicine, Philadelphia, PA.

Engagement of CD4 and the T cell receptor (TCR)-CD3 complex generates signals which lead, in part, to the activation of helper T (Th) cells. Activated Th cells contribute to graft-versus-host disease (GVHD) arising from allogeneic MHC class II and minor histocompatibility antigenic differences. The 802-2 synthetic cyclic heptapeptide, designed and confirmed by NMR spectroscopy to mimic the D1-CC' loop of CD4, inhibits Th cell activation in human and murine systems. Since Th1 cells appear to be more important in the pathogenesis of acute GVHD than their Th2 counterparts, the efficacy of 802-2 in modulating allogeneic responses of both Th1 and Th2 cells was therefore tested. Primary polarization of Th cells was performed by stimulating purified CD4+ cells from healthy donors with irradiated EBV transformed B cells (EBV-B) obtained from unrelated, HLA mismatched donors in the presence of Th1 (IL-2 + IL-12) or Th2 (IL-2 + IL-4) polarizing cytokines. After similar restimulation on days 3 and 6, cells were subsequently propagated in the presence irradiated autologous mononuclear cells through weekly allogeneic restimulation and biweekly cytokine supplementation. Th1 and Th2 cells from 3-4 week old cultures were harvested and stimulated with irradiated EBV-B in the presence of IL-2 with and without 802-2 peptide. The presence of 802-2 (200μM) reduced the proliferation of both Th1 and Th2 cells to near background levels. Delaying exposure to 802-2 by more than 72 hours after allogeneic stimulation substantially reduced or eliminated its ability to inhibit proliferation. While murine Th cells, activated in vivo, in the presence of 802-2 appear to undergo apoptosis, it has not been possible to similarly demonstrate apoptosis of human Th cells activated in vitro in the presence of 802-2. The lack of inhibitory effects of 802-2 when added at later time points after allostimulation rules out a non-specific inhibition of cellular proliferation or toxicity. We hypothesize that 802-2 inhibits multimerization of the CD4/MHC class-II/antigen/TCR complex during allostimulation. The resultant spatial disruption of the associated signaling molecules leads to abrogation of the signals for cell proliferation and may render the Th cells anergic, as occurs in other situations where lymphocytes receive partial or disordered activation signals.

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ADDING MYCOPHENOLATE MOFETIL (MMF) AND ATGAM TO CYCLOSPORIN DECREASES SEVERE GVHD AND TRANSPLANT-RELATED MORTALITY (TRM) AFTER NON-MYELOABLATIVE ALLOGENEIC PBSC TRANSPLANTATION (MINI-PBSCT)

Schwarer, A.P.; Spencer, A.; Kapuscinski, M.; Muirhead, J. Bone Marrow Transplantation, Alfred Hospital, Melbourne, VIC, Australia.

INTRODUCTION: Mini-PBSCT can provide cure for some older or less fit patients with hematological malignancies not eligible for standard PBSCT. Mini-PBSCT uses lower doses of conditioning chemotherapy and/or radiotherapy to improve the safety of allogeneic PBSCT and relies on the graft-versus-tumor (GVT) effect for cure. **METHODS:** We treated 31 patients, not eligible for standard PBSCT, with mini-PBSCT: median age 51 (29-63) yrs; 20 male, 11 female; 25 advanced disease (6 AML)CR1, 5 NHL, 4 myeloma, 2 MDS, 2 HD, 2 mycosis fungoides, and 1 each of CML-BC, Waldenstom's macroglobulinemia, myelofibrosis, T-PLL) and 6 early disease (2 AML-CR1, 2 CLL, 1 CML, 1 LG-NHL). All patients received fludarabine (25 mg/m^2 x5) and melphalan 140 mg/m^2 prior to undergoing HLA-matched (22 sibling, 1 cousin, 8 unrelated) donor mini-PBSCT. The first 12 patients received CSA 3 mg/m^2/day IVI alone as GVHD prophylaxis in an attempt to not excessively inhibit a potential GVT effect. An unacceptably high incidence of severe acute GVHD and TRM occurred with a low relapse rate. Therefore, we modified the protocol to include ATGAM 15 mg/kg from day -4 to +5 and MMF 15 mg/m^2 from day 0 to +27 for all subsequent patients (n=19). **RESULTS:** Although more patients in CSA/ATGAM/MMF cohort than CSA alone cohort underwent mini-PBSCT with unrelated donors (42% vs 0%) the incidence of severe acute and extensive chronic GVHD was less, 100 day TRM was less (see Table) and overall TRM was less (26% vs 42%; p=0.38) in CSA/ATGAM/MMF cohort. To date, the relapse rate was similar in both cohorts although the follow-up of survivors was shorter in CSA/ATGAM/MMF cohort - 504 (19-634) days vs 942 (865-1089) days. **CHIMERISM:** T cell and myeloid chimerism using VNTR polymorphism analysis was assessed in CSA/ATGAM/MMF cohort but not the earlier CSA alone cohort. Of 14 evaluable patients 13 showed sustained >90-95% donor chimerism by 1 month post mini-PBSCT. The remaining patient achieved <50% donor chimerism which was managed by ceasing MMF; >90% donor chimerism rapidly developed accompanied by the onset of severe acute GVHD. No graft rejection was noted in either cohort. **CONCLUSION:** The combination of CSA/ATGAM/MMF appears to be effective GVHD prophylaxis for older, less fit patients with advanced disease undergoing mini-PBSCT.