from day +1 until neutrophil engraftment. GVAX was initiated between day +8 to +10 if there was adequate hematologic recovery and no grade II-IV acute GvHD. GVAX was administered and ID/SC qwk × 3 doses, then q2wks × 3 doses. Taper of tacrolimus began after vaccine completion. Ten patients (6 URD, 4 MRD) were administered and ID/SC qwk × 3 doses, then q2wks × 3 doses. Taper of tacrolimus began after vaccine completion. One of 10 patients were able to start vaccination post transplant. Reasons for failure to initiate vaccination included: death before day +10 (1); acute GvHD (2); insufficient count recovery (3). Among those who received GVAX, there was no GvHD or toxicity attributable to vaccination. Focal infiltrates of lymphocytes were observed in skin biopsies of the vaccination sites. Two of four vaccinated patients are alive: 1 in CR, and 1 in relapse 5 and 6 months post transplant, respectively. Overall, 7 of 10 patients have relapsed, 6 before day +100. Although results are preliminary and the high incidence of early relapse has hindered our ability to initiate vaccination, GVAX appears to be safe for patients with MDS/AML after NSt. Further cytoreduction prior to NSt is necessary for disease control and improve feasibility of GVAX vaccination in this very high-risk population.

43 TREATMENT OF PATIENTS (PTS) WITH CHRONIC MYELOID LEUKEMIA (CML) AND IMATINIB FAILURE AFTER DEVELOPING BCR-ABL KINASE MUTATIONS WITH ALLOGENIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (ASCT)

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ASCT is curative for many pts with CML, and may be effective after imatinib failure. Resistance to imatinib is most often associated with point mutations in the Bcr-Abl kinase domain. The outcome of pts with Bcr-Abl kinase mutations after ASCT is not known. We assessed the outcome of ASCT in 9 pts with CML (chronic phase [CP] = 3, accelerated phase [AP] = 3, blast phase [BP] n = 3) harboring 8 different protein kinase mutations. P-loop mutations were detected in 4 (44%) pts; T315I mutation was detected in 2 pts (one AP and one CP). Seven male and 2 female pts, median age of 44 years (range, 26-63 years), received their ASCT between June 2003 and July 2005. At the time of ASCT, one pt was in major molecular remission (MMR) (BP, Q252H), mutations were detected in 4 (44%) pts; T315I mutation was (chronic phase [CP] = 3, accelerated phase [AP] = 3, blast phase [BP] n = 3) harboring 8 different protein kinase mutations. P-loop mutations were detected in 4 (44%) pts; T315I mutation was detected in 2 pts (one AP and one CP). Seven male and 2 female pts, median age of 44 years (range, 26-63 years), received their ASCT between June 2003 and July 2005. At the time of ASCT, one pt was in major molecular remission (MMR) (BP, Q252H), one was in major cytogenetic response (CP, T315I), and 2 were in complete hematologic response (2 BP, Y253H and E281A). Preparative regimen was busulfan + cyclophosphamide in 7 and fludarabine + cyclophosphamide in 2 pts. Donor was fully matched related in 4 (44%) and unrelated in 5 (56%) pts. Source of stem cells was peripheral blood and bone marrow in 7 and 2 pts, respectively. Graft-versus-host disease (GVHD) prophylaxis consisted of tacrolimus and mini methotrexate. All patients engrafted; there was no treatment-related mortality. Chimerism studies at day 30 and 100 post ASCT were available in 7 pts and were 100% of donor type. Eight pts achieved a complete molecular remission (CMR); one pt with a T315I mutation achieved a MMR. Two (22%) pts (Q252H [BP] and T315I [AP]) relapsed after a median of 7 months; one of them (T315I) died of disease progression. All the remaining 7 pts were CMR for a median of 13 months (range, 3-20+ months). We conclude that ASCT remains an important salvage option for pts who develop resistance to imatinib through Bcr-Abl mutations. Early introduction of such strategy may result in better outcome.

44 IN VIVO BIOLUMINESCENCE IMAGING OF ACUTE PROMYELOCYTIC LEUKEMIA CELL TRAFFICKING AND MOBILIZATION BY AMD3100

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Novel approaches have been developed to mobilize hematopoietic stem cells (HSC) for patients undergoing autologous and allo transplantation. These strategies may provide insights into improved HSC collection and enhanced egress of leukemic cells and thus sensitivity to anti-leukemia therapy. CXCR4/SDF-1 axis regulates the trafficking of normal HSC to and from the bone marrow (BM). AMD3100 (AMD) specifically and reversibly blocks SDF-1 binding to CXCR4, and is a promising mobilizing agent currently in clinical development. We utilized a mouse model of acute promyelocytic leukemia in which the PML–RARα transgene was knocked into a single allele of the murine cathespin G locus. We transduced banked leukemia cells with a dual function reporter gene that encodes a click beetle red (CBR) luciferase, a bioluminescence imaging (BLI) optical reporter gene, and EGFp for ex vivo cell sorting (CBR/EGFP). We isolated EGFp+ cells using a MoFlo cell sorter, and passaging them in secondary syngeneic recipients that developed rapidly fatal acute leukemia. Upon intravenous (iv) injection of 108 APL cells into syngeneic recipients, APL rapidly migrated to the BM, with increased BLI signal in the femurs, spine, ribs, and skull, at 4 days after injection, followed by spleen infiltration and by death due to leukostasis by 14-16 days. To our knowledge, this represents the only mouse leukemia model in which leukemia cells home preferentially to the BM in a manner that is similar to what is seen in human AML. AMD (5 mg/kg) at the time of APL infusion or bid on days 0-7, had no impact on the engraftment of either normal HSC or the PML. We observed rapid mobilization of the APL cells when AMD was administered 11 days after APL injection. 40% of mice that received AMD on day +11 died 2 to 4 hours after AMD injection as a result of the rapid and massive mobilization of blasts. Interestingly, CXCR4 expression in mobilized tumor cells decreased from 31 ± 3% before AMD administration to 19 ± 6%, and 7.8 ± 0.6% after 2 and 12 hours (FACS; P <.001). AMD + AraC (200 mg/kg) on day +11 prolonged the overall survival of mice, compared with mice treated only with AraC. In summary, we developed a mouse model to study the APL cell trafficking, and we have shown leukemia cell mobilize from the BM into PB after AMD administration. In these preliminary results we observed that AMD may sensitize APL cells to AraC. We propose that CXCR4/SDF-1 is a key regulator for leukemia migration and homing to the BM.

LYMPHOMA/MULTIPLE MYELOMA

45 POSITIVE POSSITON EMISSION TOMOGRAPHY (PET) PRE-AUTOLOGOUS STEM CELL TRANSPLANTATION (ASCT) IN NON-HODGKIN LYMPHOMA (NHL) DOES NOT PRECLUDE SUCCESSFUL OUTCOME

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PET has become an important imaging modality for lymphoma, and has been reported to be of prognostic significance prior to ASCT for NHL. Methods: To assess the prognostic value of PET prior to ASCT in NHL, PET pre and post ASCT was prospectively obtained in all NHL patients. From May 2003 to December 2004, 100 patients underwent ASCT for NHL. PET was considered positive if it had abnormal FDG uptake; CT was positive if it had areas of lymphadenopathy as defined by the international response criteria. Results: Median age was 58 (range 17-74); 69% were male. Patients had received chemotherapy before ASCT (range 1-9). At relapse, prior to ASCT, the median IPI was 2 (range 1-5); 31% of patients were stage I or II; 69% were stage III or IV. Histology included DLBCL, 50, transformed NHL 15, mantle cell NHL 11, low-grade NHL 8, T-cell NHL 6, primary CNS NHL 5, and high grade NHL 5. At ASCT, 43 patients were in CR, 49 in PR, 3 in unrelapsed remission, and 8 in resistant disease. The conditioning regimen was BEAM in 89; Zevalin/BEAM in 10. Pre-ASCT PET was not obtained in 8