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UTILIZING PERIPHERAL BLOOD CD34 COUNT AS A PREDICTOR FOR THE NEED FOR PLERIXAFOR IN AUTOLOGOUS STEM CELL MOBILIZATION – SINGLE INSTITUTION EXPERIENCE

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Background: Mobilization and collection of sufficient autologous hematopoietic stem cells (AHSC) is crucial for success of autologous stem cell transplantation. Moncada et al. reported 14% of patients receiving chemotherapy and GCSF for AHSC donation fail to mobilize enough AHSC for transplant (*Transfusion 43:495ff, 2003*). Plerixafor + GCSF resulted in 3-fold higher rate of patients achieving the targeted CD34 count in fewer AHSC collections (DiPersio et al. *Blood 110:601ff, 2007*). Plerixafor use in all patients is unnecessary and unlikely cost-effective. At UIHC (chemo-mobilized patients were excluded from this analysis), all patients undergoing AHSC collection receive GCSF daily for 5 d prior to leukapheresis. Peripheral blood CD34 (PBCD34) count on the morning of day 4 is obtained. If the PBCD34 ≤ 8/μL, plerixafor is administered that evening followed by GCSF the next morning (P+G), however if the PBCD34 count is > 8, AHSC collection proceeds without plerixafor (G). The goal of this study is to evaluate our current practice in utilizing PBCD34 as a predictor of the need for plerixafor.
Methods/Results: We retrospectively reviewed data on patients mobilized at UIHC for AHSC collections following the implementation of the previous algorithm between Jan 2009 & Aug 2010. 78 patients were analyzed: 32 in the P+G group and 46 in the G group. Patients' characteristics are displayed in Table 1. Almost all patients in the P+G group (30/32) had undetectable PBCD34 on d 4 (2 patients had PBCD34 of 3 and 8/μL), compared to a median of 24/[sup]μ[/sup]L (mean 31.5, SD 17.95) in the G group ($p < 0.0001$). All patients reached their targets in ≤ 3 collections. No mobilization failures occurred. There was no significant difference in the number of collections ($p = 0.32$) or in the final product CD34 counts between the two groups ($p = 0.15$) (P+G mean $8.2*10^6$ +/-5.0, G mean $6.6*10^6$ +/-5.5). More than 2/3 of the patients in P+G group (n = 22, 68.8%) reached their CD34 target on first day of collection compared to 56.5% (n = 26) from G group ($p = 0.14$). (P+G mean $7.3*10^6$ +/-5.6, G mean $5.4*10^6$ +/-5.6). In the P+G group 5 patients needed 2 collections and 5 patients needed 3 collections to reach their target compared to 14 and 6 in the G group respectively.
Conclusion: Despite unmeasurably low PBCD34 count in the peripheral blood the day prior to AHSC collection, plerixafor permitted these patients to collect at least as well as patients with > 8 cells/μL, usually in a single session.

Table 1. Patients' Characteristics

	P+G group (n=32)	G group (n=46)	p-value
Age (Median, Mean, SD)	60, 55.8, 13.7	56, 51.6, 13.2	0.18
Gender (Male:Female)	14:18	26:20	0.27
Diagnosis:			
Multiple Myeloma (42%)	15	18	0.64
Hodgkin Lymphooma (18%)	4	10	0.37
Non Hodgkin Lymphoma (40%)	13	18	1
Prior Therapy:			0.88
Chemotherapy only	26	38	
Chemotherapy and Radiation	6	8	
Number of prior chemotherapy cycles (Median, Mean, SD)	8.5, 8.6, 4.1	9, 7.8, 3.2	0.68
Target CD34 count in the final product of collection (Median, Mean, SD)	3, 4, 1.55	3, 4, 1.45	0.72

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IMPROVING AUTOLOGOUS TRANSPLANT OUTCOMES IN THE ELDERLY

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Introduction: High dose chemotherapy and autologous stem cell transplant (HD-SCT) improve disease free (DFS) and overall survival (OS) and can be curative in various hematologic malignancies. HD-SCT is also associated with significant morbidity and hence is not routinely offered to elderly patients.
Methods: In this study we describe our experience in patients aged 70 years or above who underwent HD-SCT between 2000 and 2010. Data was collected from retrospective review of our transplant registry and medical records and was analyzed utilizing SPSS v13.
Results: Twenty patients aged 70 years or above underwent HD-SCT for a variety of hematologic malignancies (10 patients with Multiple Myeloma, 9 with Non-Hodgkin Lymphoma and 1 with Hodgkin Lymphoma). Median age of the patients was 71 years (range 70-76). All patients had a good performance status (median ECOG PS was 1, range 0-1) at the time of transplant. 80% of the patients were males and 60% were in a complete remission at the time of transplant. Conditioning was with BEAM for NHL and HL patients (20% required dose adjustment due to co-morbid conditions) and Melphalan for MM patients (20% received 140mg/m2 due to renal function). The mean CD34 cells collected was $7.5x10^6$ cells/kg and the number infused was $5.54 x10^6$ cells/kg. All patients engrafted and the median number of days for neutrophil engraftment was 10 and for platelets was 12. Overall the transplant process was well tolerated with mucositis being the most common complication seen in 40% of the patients (grades 1-3). Other complications included diarrhea (10% grade 1-2 and 20% grade 3-4), febrile neutropenia (20% grade 3-4), sepsis (15% grade 3-4) and atrial fibrillation (10% grade 1-2). The estimated 5-year overall survival is 56.7% and 5-year progression free survival is 55.4%. There were no deaths during the immediate transplant process.
Conclusions: Our data suggests that in a well-selected elderly population older than 70 years HD-SCT appears to be a well tolerated therapeutic option. We therefore recommend that age should not be utilized as sole exclusion criteria for patients undergoing HD-SCT for their various hematologic malignancies.

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BORTEZOMIB FOLLOWED BY A PHASE I STUDY OF BORTEZOMIB IN COMBINATION WITH HIGH-DOSE MELPHALAN AS A PREPARATIVE REGIMEN FOR HEMATOPOIETIC CELL TRANSPLANTS IN PATIENTS WITH PRIMARY REFRACTORY MULTIPLE MYELOMA OR PLASMA CELL LEUKEMIA

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Preclinical and non-transplant clinical data indicates synergism between melphalan and bortezomib with enhanced melphalan-induced DNA damage via bortezomib-mediated down regulation of Fanconi anemia (FA)/BRCA DNA repair pathway. We designed a trial to examine the sequencing of high dose melphalan (100 mg/m^2/day × 2 days), immediately followed by one dose of bortezomib (0.7, 1.0, or 1.3 mg/m^2 on a phase I study design) and tandem autologous transplants. Thirty patients with primary refractory multiple myeloma or plasma cell leukemia were treated between 05/2005 and 02/2009. The patients received 2 cycles of preconditioning bortezomib (1. 3 mg/m^2) and proceeded with transplants. The median age was 54.5 years (range, 36 – 70 years). The median beta 2-microglobulin was 4.35 mg/L (range: 1.8-11.4); albumin was 3.7 g/dL (range: 3.1-4.9). Preconditioning bortezomib resulted in 1 complete response (CR), 1 very good partial response (VGPR), 9 partial response (PR), 13 stable disease (SD), 3 progressive disease (PD) and 3 patients were not evaluable. The overall response rate (ORR) was 36%. A total of 25 patients proceeded with transplants. By 90 days, we documented 5 CR, 6 VGPR, 10 PR and 1 SD post tandem transplants. The ORR increased to 84% at the peak of best response with 9 CR, 3 VGPR, and 9 PR. With a median follow-up of 24.5 months (range, 3 – 62 months), the median progression-free survival from the first dose of bortezomib was 15 months (95% CI: 11 – 20 months) and the median overall