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CD34+ CELLS FROM POOR MOBILIZERS ARE QUALITATIVELY EQUIVALENT TO CD34+ CELLS FROM GOOD MOBILIZERS

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Marrow damage from chemo- and radiation therapy can lead to poor CD34+ cell mobilization. Such therapies have also been suggested to affect quality of CD34+ cells. We tested the hypothesis that CD34+ cells from low mobilizers are qualitatively inferior to CD34+ cells from high mobilizers.

CD34+ cell quality was defined by proportion of primitive CD34+ cell subsets (CD34+CD38-, CD34+HLA-DR- and CD34+ in G0 stage of cell cycle), the proportion of CD34+ cells that express CXCR4 and CD26 homing proteins and days to neutrophil and platelet engraftments post transplant. CD34+ cell content and CD34 subsets analyses were performed using flow cytometry. Cell cycle analysis was performed using simultaneous staining of DNA (Hoechst) and RNA (Pyronin Y) to distinguish CD34+ cells in G0, G1 and S/M phases of cell cycle.

We evaluated the CD34+ cell quantity and quality of 139 autologous filgrastim mobilized HPC products collected between 2004 and 2007. The median patient age was 58 years and 60% were males. Patients were diagnosed with plasma cell dyscrasia, or non-Hodgkin's lymphoma. The median CD34+ cell/kg was 4.9×10^6 and median time to neutrophil and platelet engraftment was 12 and 18 days respectively.

Patients were grouped into low, moderate and high mobilizers if their total CD34+ cell collection was $\leq 3 \times 10^6$/kg, $> 3 \times 10^6$/kg and $< 5 \times 10^6$/kg, and $\geq 5 \times 10^6$/Kg respectively. The median number of primitive stem cells increases with increasing CD34+ cell numbers and this association was statistically significant ($p = 0.001$). However, when the ratios of the primitive CD34 subsets to total CD34+ cell counts were compared among the mobilization groups, the ratios were not significantly different. Co-expression of neither CD26 nor CXCR4 homing proteins with CD34 antigen correlated with CD34+ cell mobilization.

Table 1. CD34+ cell subsets and mobilization capacity

	Mobilization (median $\times 10^6$/Kg)			
CD34+ subsets	Low	Moderate	High	p value
N	33	70	36	
CD34+	3	4.6	6.6	<0.001
CD34+CD38-	1.2	2.6	3.8	<0.001
CD34+HLA-DR-	1.1	1.6	2	0.001
CD34+CD26+	0	0	0	0.88
CD34+CXCR4+	0	0	0	0.55
CD34+G0 stage	1.5	3.3	4.6	<0.001
	CD34+ subsets/CD34+ ratio			
CD34+CD38-	0.52	0.55	0.53	0.41
CD34+HLA-DR-	0.30	0.35	0.27	0.84
CD34+G0 stage	0.71	0.75	0.64	0.58

Evaluation of days to neutrophil engraftment among the mobilization groups did not show a statistically significant difference ($p = 0.1$). However, days to platelet engraftment among the mobilization groups was statistically significantly different ($p = 0.05$). This finding may not be clinically significant.

In summary, the proportion of primitive CD34+ cells in HPC products and days to neutrophil engraftment were not influenced by CD34+ cell mobilization capacity. The quality of CD34+ cells from low mobilizers was comparable to CD34+ cells from high mobilizers. Prior therapies may affect the quantity but not the quality of CD34+ cells.

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CYCLOPHOSPHAMIDE (CY)/G-CSF CANNOT COMPLETELY OVERCOME IMID-INDUCED IMPAIRMENT OF PERIPHERAL BLOOD STEM CELL (PBSC) MOBILIZATION (MOB) IN PATIENTS WITH MULTIPLE MYELOMA (MM)

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Novel agents are routinely used as induction therapy for MM, but there is concern about their impact on PBSC Mob. Some studies suggest that CY/G-CSF Mob may overcome suppressive effects of lenalidomide on PBSC Mob, however an optimal mobilization strategy for this population remains controversial.

We report here PBSC collection outcomes of 107 consecutive MM patients, who uniformly underwent Mob with CY (1.5mg/m^2) and G-CSF (10μg/kg/day). 44 patients received older induction therapies, while 63 received novel agents (including; lenalidomide- (n = 13), bortezomib- (n = 15) and IMiD- (n = 49) containing regimens). Mob parameters including, peak peripheral blood (PB) CD34+ count, CD34+ cell yield on day1, total CD34+ cell yield, and number of apheresis sessions were analyzed relative to induction regimens. Mobilization failure was defined as failure to collect $\geq 2 \times 10^6$ cells/Kg body weight.

The median patient age was 57yrs. The median number of prior therapies was one, while 29% received prior radiation. Compared to older regimens, patients receiving novel inductions had lower peak PB CD34+ count (70/uL vs. 47/uL; $p = 0.003$), however total CD34+ cell yield (7.6×10^6 vs. 6.4×10^6; $p = 0.07$), CD34+ dose collected on day 1 (3.9×10^6 vs 3.1×10^6 $p = 0.20$) and total number of apheresis sessions (2.6 vs 2.2 $p = 0.068$) were not significantly different. Lenalidomide containing regimens when compared to all other regimens (n = 94) revealed a lower peak PB CD34+ count (34/uL vs 59/uL; $p = 0.03$) and higher total number of apheresis sessions (3.3 vs 2.3; $p = 0.001$). Total CD34+ yield (6.8×10^6 vs 7.1×10^6 $p = 0.78$) and CD34+ cells collected on day 1 (2.6×10^6 vs 3.7×10^6; $p = 0.24$) were not significantly different. IMiDs as a class when compared to non-IMiD regimens showed significantly lower peak PB CD34+ count (45/uL vs 66/uL; $p = 0.004$) and higher number of apheresis sessions (2.7 vs 2.2; $p = 0.004$). Total CD34+ yield (7.6×10^6 vs 6.7×10^6 $p = 0.21$) and dose collected on day 1 (3.5×10^6 vs 3.6×10^6; $p = 0.91$) were not significantly different. A total of 6 patients failed mobilization, including 3 who received lenalidomide.

In conclusion our limited retrospective study shows that CY/G-CSF Mob partially overcomes suppressive effects of lenalidomide on PBSC mobilization by requiring increased number of apheresis sessions. Our data also suggest that impairment of PBSC Mob might be a class-effect of IMiDs, and not merely restricted to lenalidomide, at least in the context of CY/G-CSF Mob.

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THE EFFECT OF BODY MASS INDEX ON PATIENT MORTALITY AFTER AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Elevated body mass index (BMI) is associated with lifelong risk of medical morbidity and has been implicated as a risk factor for mortality after hematopoietic stem cell transplantation HSCT. Previous publications suggest various thresholds for increased mortality. The Center for International Bone Marrow Transplant Research (CIBMTR) threshold for considering obesity a significant comorbidity is a BMI greater than 35. A recent publication using CIBMR data suggested a BMI of 30 was a significant threshold for morbidity and mortality.

Objective: To further investigate the association of BMI with excess mortality in a single center analysis, we undertook a survey of 232 consecutive autologous HSCT (aHSCT) patients with myeloma and non-Hodgkin's lymphoma.

Patients and Methods: These 232 adult patients studied received their aHSCT at UAB between November 2006 and September 2010. Height and weight were obtained during the final evaluation and consent visit just prior to initiation of preparative therapy, excluding 10 patients with missing one or the other of these variables. Myeloma patients received melphalan 200mg/ M2 (reduced to 140mg/M2 for age greater than 70 or creatinine clearance < 40mL/min). Non-Hodgkin's lymphoma (NHL) patients received intravenous busulfan targeted to a total exposure of 16000μM*min, cyclophosphamide (5gm/M2) and etoposide (1800 mg/M2). Based upon the reviewed literature, we defined obesity using three BMI cohorts: non-obese < 35kg/M2, obese = 35-39kg/M2, morbidly obese