survival was 35 months (95% CI: 22 – 43 months). There were no dose limiting toxicities. Grade 3 toxicities were similar to those observed with high dose melphalan alone. The dose of bortezomib administered after melphalan was safely escalated to 1.3 mg/m^2. FA/BRCA pathway gene expression was evaluated with quantitative RT-PCR (i) at baseline, (ii) after 1 dose of bortezomib, and (iii) after the 2 pre-transplant cycles of bortezomib in 17 patients (15 had transplants). After the first dose of bortezomib, there was a statistically significant decreased expression of FANCD1 ($P = 0.072$) and FANCF ($P = 0.0458$) as well as a suggestion of decreased expression of 4 other FA/BRCA genes. We conclude that bortezomib can be safely combined with high dose melphalan and with no added toxicity. The combination of bortezomib and melphalan conditioning warrants further evaluation with a phase 2 study design in a broader myeloma population.

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PROLIFERATIVE CAPACITY AND CELLULAR COMPOSITION OF APHERESIS PRODUCTS COLLECTED FROM PATIENTS MOBILIZED SEQUENTIALLY WITH NEUPOGEN THEN NEUPOGEN PLUS PLERIXAFOR

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Background: Mobilization with Neupogen plus Plerixafor versus Neupogen alone yields a product with more CD34$^+$ stem cells, thus reducing the overall time and cost for stem cell collections. Since the mechanism of action is different for these two mobilizing agents, we determined whether or not there are differences in the proliferative potential and cellular composition of the apheresis products collected after mobilization.

Methods: We compared apheresis products from patients mobilized with both stem cell regimens sequentially (Neupogen only, then Neupogen plus Plerixafor). Stem cells (CD45/34) were enumerated prior to cryopreservation by flow cytometry. The proliferative capacity of thawed apheresis products was evaluated using a HALO assay (Hemogenix), which utilizes luminescence to measure the proliferative capacity of cells by quantifying ATP concentrations. The cellular composition of the thawed samples was evaluated by flow cytometry for various lineage markers and T-cell differentiation markers.

Results: The proliferative capacity of apheresis products collected after mobilization with Neupogen was lower compared to products collected after Neupogen plus Plerixafor mobilization ($p < 0.05$). This correlates with the CD34 content in the products, which tends to be lower in products mobilized with Neupogen (0.25±0.18%) versus Neupogen plus Plerixafor (0.35±0.27%), but the difference is not significant ($p = 0.23$). However, ATP levels calculated per stem cell were similar ($P = 0.34$, $n = 15$ patients) between products mobilized with the two regimens. Phenotypic analyses of the products from 3 patients each mobilized with both regimens were performed. T-helper cells (CD4) were higher (32% vs. 24%, $P = 0.02$) in the apheresis products mobilized with Neupogen only versus Neupogen plus Plerixafor. There were no other significant differences in phenotypic markers, however, there was a trend toward a lower percentage of lin1^{dim}HLA-DR$^+$CD11c$^+$ dendritic cells ($p = 0.08$) in the apheresis products mobilized with Neupogen versus Neupogen plus Plerixafor. Evaluation of additional samples will determine if this trend is significant.

Conclusion: Although the mechanisms of action of Neupogen and Plerixafor are different, the proliferative capacity of the stem cells generated after treatment with Neupogen alone versus Neupogen plus Plerixafor is similar. However, the cellular composition of the products is different and may affect the quality of the stem cell graft.

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INITIAL MOBILIZATION OF AUTOLOGOUS PERIPHERAL BLOOD STEM CELLS WITH GRANULOCYTE COLONY-STIMULATING FACTOR AND PLERIXAFOR IN PATIENTS WITH MULTIPLE MYELOMA: A PROSPECTIVE COMPARISON IN LENALIDOMIDE- AND NON-LENALIDOMIDE-TREATED PATIENTS

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Background: The use of lenalidomide (LEN) in patients (pts) with multiple myeloma (MM) is associated with impaired mobilization and collection of autologous peripheral blood stem cells (PBSCs) after granulocyte colony-stimulating factor (G-CSF) or chemotherapy plus G-CSF. The combination of G-CSF and plerixafor (PLX; Mozobil®) is an evolving strategy for PBSC mobilization, but effects of LEN exposure on mobilization with G-CSF and PLX have not been extensively evaluated. This single-center prospective study compared results of initial PBSC mobilization with G-CSF and PLX in MM pts whose primary therapy did or did not include LEN.

Patients and Methods: Of 23 consecutive pts, 17 had received a median of 5 (range 2-12) 21-day cycles of LEN; 6 had not received LEN. All pts received G-CSF (10 μg/kg/day sq × 4 days) and PLX (0.24 mg/kg sq on the evening of 4th day of G-CSF), with first apheresis (3 × blood volume) at a median of 16.6 (range 15.3-17.5) hr after PLX injection. Pts who collected $< 6 \times 10^6$/kg CD34+ cells with first apheresis received both G-CSF and PLX that evening and underwent a second day of apheresis. Mobilization failure was defined as total collection of < 2 x10^6/kg CD34+ cells; optimal collection was defined as $\geq 6 \times 10^6$/kg CD34+ cells.

Results: All 17 LEN-treated pts collected $\geq 2 \times 10^6$/kg CD34+ cells (median 7.22×10^6/kg; range $2.32\text{-}17.11 \times 10^6$/kg) with a median of 2 (range 1-3) aphereses. Eleven pts (64.7%) collected $\geq 6 \times 10^6$/ kg CD34+ cells, 8 with 1 apheresis. Five of 8 pts who received ≤ 4 cycles of LEN collected $\geq 6 \times 10^6$/ kg CD34+ cells with 1 apheresis, compared with 3 of 9 pts who received > 4 cycles ($P = 0.35$). All 6 pts without LEN collected $\geq 6 \times 10^6$/kg CD34+ cells (median 13.67×10^6/kg; range $6.56\text{-}22.66 \times 10^6$/kg) with a median of 1 (range 1-2) apheresis. The LEN group had lower median day 1 peripheral blood CD34+ cell levels (75.83 vs. 135.00/μL; $P = 0.052$), day 1 apheresis yields (4.96 vs. 13.67×10^6/kg CD34+ cells; $P = 0.030$) and total apheresis yields (7.22 vs. 13.67×10^6/kg CD34+ cells; $P = 0.024$) than the non-LEN group.

Conclusions: Initial mobilization with G-CSF and PLX is effective in LEN-treated MM pts, with a trend to more robust day 1 PBSC collections after ≤ 4 cycles of LEN. In this prospective comparison, however, the outcomes in LEN-treated pts were inferior to those in pts without LEN exposure. Additional studies are needed to delineate the influence of LEN on mobilization of PBSCs with G-CSF and PLX.

Table 1. Outcomes of Autologous PBSC Mobilization with G-CSF and Plerixafor in Multiple Myeloma Patients Previously Treated with or without Lenalidomide (LEN)

	LEN-treated				
	All (n=17)	≤4 cycles (n=8)	>4 cycles (n=9)	No LEN (n=6)	P*
Day 1 CD34+ cells/μL, median (range)	75.83 (12.46-167.37)	73.57 (12.46-167.37)	50.68 (26.24-163.08)	135.00 (52.56-222.84)	0.052**
Day 1 CD34+ cell yield (x 10^6/kg), median (range)	4.96 (1.43-17.11)	6.87 (1.43-17.11)	4.14 (2.26-14.19)	13.67 (4.16-22.66)	0.030**
Total CD34+ cell yield (x 10^6/kg), median (range)	7.22 (2.32-17.11)	6.87 (2.32-17.11)	6.20 (4.15-14.19)	13.67 (6.56-22.66)	0.024**
CD34+ cell yield ≥6 × 10^6/kg, no. of patients (%)					
Day 1	8 (47.1)	5 (62.5)	3 (33.3)	5 (83.3)	0.18†
All days	11 (64.7)	5 (62.5)	6 (66.7)	6 (100)	0.14†

*All LEN-treated patients vs. no LEN;
**2-sided Mann-Whitney U test;
†2-sided Fisher exact test