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## Upfront Use of Plerixafor and Granulocyte-Colony Stimulating Factor (G-CSF) for Stem Cell Mobilization in Patients with Multiple Myeloma: Efficacy and Analysis of Risk Factors Associated with Poor Stem Cell Collection Efficiency

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### Abstract

Plerixafor (P), an agent that selectively and reversibly binds to the chemokine receptor CXCR4 has been approved in combination with G-CSF (P+G-CSF) for stem cell (SC) mobilization in patients with multiple myeloma (MM). The goal of this study was to determine the SC collection success rate of P+G-CSF using a *clinically relevant* outcome defined as the ability to collect at least  $5 \times 10^6$  CD34+ cells/kg to allow safely two transplants, and identify risk factors impacting SC mobilization. One hundred and thirty eight patients were mobilized with P+G-CSF upfront following induction. The SC collection success rate was 92.8%. We identified exposure to lenalidomide alone ( $p=0.038$ ), WBC count  $< 4 \times 10^3/\text{mL}$  prior to mobilization ( $p=0.01$ ) and non-African American race ( $p=0.019$ ), as risk factors for low efficiency by multivariate analysis. This study demonstrates that P+G-CSF is highly efficient in MM patients and provides strong support for its upfront use in SC collection for MM patients.

### Keywords

Multiple Myeloma; Plerixafor; Stem Cell; Mobilization; Efficiency; Risk factors

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### Conflict Of Interest

The authors declare no conflict of interest

## INTRODUCTION

The initial treatment for younger patients with symptomatic Multiple Myeloma (MM) most often consists of several phases: An initial induction treatment that involves the administration of a combination of drugs – which in the recent years have included an IMiD (thalidomide or lenalidomide) and/or a proteasome inhibitor (most commonly bortezomib) along with dexamethasone – followed by stem cell (SC) mobilization and collection prior to proceeding to autologous stem cell transplantation (ASCT) for eligible patients(1–3) followed by maintenance therapy(4–6). Prior to the advent of novel agents, this approach incorporating ASCT has shown higher response rates and overall survival when compared to conventional chemotherapy, and has become the accepted standard treatment schema(3, 7).

Stem cell mobilization, usually using granulocyte colony stimulating factor (G-CSF) or a combination of cyclophosphamide and G-CSF (C+G-CSF) followed by SC harvest is a crucial component of the treatment in these patients. Prior studies have determined that infusion of  $< 2.5 \times 10^6$  CD34+ cells/kg during transplant was associated with delayed platelet and white blood cell engraftment;(8–11) most institutional practices aim at collecting enough SCs for at least two ASCTs, (i.e. a minimum of  $4\text{--}5 \times 10^6$  CD34+ cells/kg). Several risk factors, including age, prolonged exposure to lenalidomide, low platelet count and G-CSF monotherapy as mobilization regimen, have been associated with decreased stem cell harvest when using G-CSF.(12, 13) We and others have shown that cyclophosphamide used in combination with G-CSF can overcome the negative impact on SC mobilization of some of these risk factors including prior exposure to lenalidomide.(14–16)

In 2008, the United States Food and Drug Administration approved plerixafor + G-CSF (P+G-CSF) for use in SC collection in patients with MM and non-Hodgkin's lymphoma. Plerixafor is a hematopoietic SC mobilizer which selectively and reversibly binds to the chemokine receptor CXCR4 and blocks its interaction with stromal cell-derived factor-1 $\alpha$ . Through this mechanism, SCs are released from the bone marrow into the peripheral blood. (17–19) In a phase III, multicenter, randomized study, the superiority of P+G-CSF was established over G-CSF monotherapy. Indeed, a higher percentage of MM patients in the P+G-CSF group reached the primary endpoint of  $\geq 6 \times 10^6$  CD34+ cells/kg in two aphereses when compared to the G-CSF group (71.6% vs. 34.4%,  $p < 0.001$ ). Also, the percentage of patients failing to collect at least  $2 \times 10^6$  CD34+ cells/kg – regardless of the number of aphereses – was only 4.7% with P+G-CSF.(20) Although the efficacy of plerixafor for SC mobilization appears well established, the *clinically relevant* failure rate of plerixafor in myeloma patients, which one could safely define as the inability to collect  $\geq 5 \times 10^6$  CD34+ cells/kg for two ASCT, regardless of the number of aphereses, is not clearly determined and validated. In addition, only two small studies have attempted to identify risk factors associated with mobilization failure using plerixafor.(12, 13) The purpose of this study was to determine the *clinically relevant* SC mobilization failure rate and efficiency associated with plerixafor mobilization and to identify the risk factors associated with inadequate SC mobilization, including the potential deleterious effect of prior exposure to lenalidomide-based regimens.

## METHODS

### Patient population

This retrospective study examined all consecutive patients with MM who were mobilized with P+G-CSF upfront as part of initial therapy following induction treatment at Memorial Sloan Kettering Cancer Center (MSKCC) between April 1<sup>st</sup>, 2009 and August 1<sup>st</sup>, 2013. Patients received a variable number of induction cycles, which included various combinations of drugs. For the purpose of this analysis, the patients were divided into three groups: (1) Those exposed to lenalidomide only (lenalidomide/dexamethasone); (2) bortezomib only (bortezomib/dexamethasone or bortezomib/dexamethasone/cyclophosphamide); and (3) both (lenalidomide/bortezomib/dexamethasone). Patients who were mobilized with high dose cyclophosphamide along with plerixafor and patients who had previously failed a stem cell mobilization/collection attempt were excluded. Waiver of authorization and waiver of informed consent were granted by the Institutional Review Board.

### Retrospective data collection

The data sources for this study included the pharmacy database and the patients' electronic medical records. Baseline characteristics collected included: patients' age, gender, race, staging according to the International Staging System (ISS), platelets at baseline prior to therapy and before SC collection, WBC before SC collection, baseline cytogenetic risk based on Mayo Stratification of Myeloma and Risk-Adapted Therapy (mSmart) criteria,(21, 22) and percentage of bone marrow plasmacytosis in bone marrow aspirates prior to mobilization. The treatment characteristics included: Type of induction regimen, number of treatment cycles received, time between last chemotherapy received and SC mobilization, time between start of induction and SC mobilization, and history of prior radiation therapy. Outcome measurements were based on the total number of CD34+ cells/kg collected during the upfront mobilization and collection, and number of aphereses performed, allowing measurement of failure rate and efficiency of SC collection as defined below in the Statistical analysis section.

### Mobilization regimens and strategy

During the period of time encompassed by this study, which followed the FDA approval of plerixafor, the choice of mobilization regimen was mainly based on physician preference. The decision of choice of mobilization approach was also driven, in significant part, by clinical trials -- most mandating the use of cyclophosphamide and G-CSF at the time-- as well as insurance constraints since all third party payers had yet to accept the upfront use of plerixafor for SC mobilization. For standardized upfront mobilization procedure with P+G-CSF during the period of the study, patients initiated G-CSF, at least two weeks from any anti-myeloma therapy, at a dose of 10 mcg/kg subcutaneously for 4 consecutive days. On the evening of the fourth day, plerixafor 0.24 mg/kg was administered, approximately 11 hours prior to initiation of apheresis. Apheresis was initiated on day 5 if adequate peripheral blood CD34+ cell count (at least 5 CD34+ cells/mcL) was reached on that day. Plerixafor, G-CSF, and apheresis were repeated on subsequent days until the target number of stem cells was reached (up to a maximum of four apheresis sessions). The standard target number of stem

cells collected at the conclusion of the upfront stem cell collection attempt was, per MSKCC guidelines, set at  $10 \times 10^6$  CD34+ cells/kg to safely allow the potential performance of two ASCT. The final products were cryopreserved in 10% DMSO using a controlled rate freezer and stored in liquid nitrogen.

Patients who were deemed to have failed upfront SC collection as determined by their treating physician usually had a salvage attempt at stem cell collection. They were remobilized with either chemotherapy + G-CSF (which included cyclophosphamide or VDT-PACE chemotherapy) or remobilized with P+G-SCF with the addition of cyclophosphamide. Patients collecting less than  $5 \times 10^6$  CD34+ cells/kg during the upfront stem cell collection procedure were considered mobilization failures for the purpose of this analysis.

### Statistical analysis

The goal of the study was to evaluate the efficiency of SC collection using plerixafor upfront and identify risk factors impacting SC mobilization. The primary endpoint was to determine the SC mobilization failure rate, defined as the inability to collect  $5 \times 10^6$  CD34+ cells/kg. This target goal is predicated upon the need to collect enough SCs to safely perform two ASCTs and the evidence that infusion of  $< 2.5 \times 10^6$  CD34+ cells/kg is associated with delayed engraftment. We acknowledge that collection targets subjectively set by individual physicians may influence SC collection outcome. To circumvent this bias, a secondary endpoint was the efficiency of SC mobilization measured by the total number of CD34+ cells/kg yielded per apheresis performed. Linear regression was used to compare the mean efficiency level across selected patients and treatment characteristics on either endpoint using linear regression for both univariate and multivariate analyses. Variables significant at the 0.05 level were entered into multivariable model. All analyses were done using the R statistical platform (R Core Team (2014). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL <http://www.R-project.org/>).

## RESULTS

### Patients and Treatment Characteristics

The current study covered the period from April 1<sup>st</sup>, 2009 to August 1<sup>st</sup>, 2013 and involved 306 patients identified as having received plerixafor. All patients proceeded to have SC mobilization. One hundred and sixty-eight patients were excluded due to the following reasons: 143 patients did not have a diagnosis of MM; 7 patients received high dose cyclophosphamide along with plerixafor for SC mobilization; and 18 patients had incomplete data records. The baseline and treatment characteristics of the 138 patients included in the retrospective analysis are shown in Table 1.

Among these 138 patients, the median age at time of diagnosis was 60 years, and there was predominance of male gender (58%). At the time of diagnosis, 84 patients (61%) had ISS Stage I disease while 27 (19.5%) had ISS stage II and 27 (19.5%) ISS stage III. Using the Mayo Clinic mSmart criteria 104 (75 %) were considered standard risk, 16 (12 %)

intermediate risk and 18 (13%) high risk. 27 patients (19.5%) received lenalidomide only, 25 (18.1%) bortezomib only, and 86 (62.3%) both. The median number of induction treatment cycles received is 4 (range 1–11) for the entire population and 4 (range 1–6) for patients who received lenalidomide-based therapy during induction. The median time from start of induction therapy to SC collection is 4.8 months (range 1.8–38.3). The median time from last therapy to SC collection is 1.1 months (range 0.8–6.1).

### Predictors of SC collection failure and efficiency by univariate and multivariate analysis

When considering the primary objective of the study, a total of ten patients failed to collect  $5 \times 10^6$  CD34+ cells/kg; therefore, the overall SC collection failure rate was 7.2%. Note that if a less stringent criterion were used to define SC collection failure, yet allowing for the possibility of performing two ASCT (i.e. threshold set at  $4 \times 10^6$  CD34+ cells/kg, since a number of  $2 \times 10^6$  CD34+ cells/kg is often considered adequate to safely perform a single ASCT by many centers as opposed to  $2.5 \times 10^6$  CD34+ cells/kg), the failure rate would have been 4.3% (n = 6). Likewise, only 1.4% of patients (n = 2) failed to collect at least  $2 \times 10^6$  CD34+ cells/kg. Table 2 shows the characteristics of the 10 patients who failed SC collection. Among these patients, seven were exposed to lenalidomide-based therapy while three patients were not. Since the failure rate was so low, we could not identify independent risk factors associated with SC mobilization failure.

Since SC collection total yield may be influenced by predetermined SC collection targets, individual physicians' practice, and number of aphereses performed, we analyzed the effect of the various baseline and treatment characteristics on SC collection *efficiency* defined as the number of SCs collected per apheresis session performed. When considering SC efficiency as outcome, the median and mean efficiency for the entire cohort were  $7.25 \times 10^6$  and  $5.82 \times 10^6$  CD34+ cells/kg/apheresis, respectively. As shown in Table 3, univariate linear regression identified that variables associated with a lowered SC collection efficiency included more than four months between start of induction treatment and SC collection (p=0.001), more than four cycles received during induction treatment (p=0.038), WBC count below  $4 \times 10^3$  cells/mcL just prior to mobilization (p = 0.017), and prior exposure to lenalidomide only (p=0.008). Of note, we found a statistically significant difference between patients mobilized after exposure to lenalidomide only versus those exposed to bortezomib only, but no statistical difference could be shown between those exposed to bortezomib only and those exposed to both drugs. African American race was associated with higher efficiency compared to Caucasians (p=0.017). Gender, age, and platelet counts prior to GCSF were not associated with efficiency. In the multivariate model, lower WBC prior to GCSF (p = 0.01), prior exposure to lenalidomide only (p = 0.038) and race (p=0.019) maintained statistically significant association.

## DISCUSSION

This analysis that includes 138 patient with MM who underwent upfront SC mobilization and collection using P+G-CSF has shown that the SC collection failure rate is very low and affected 7.2% of all patients, when using a threshold of  $5 \times 10^6$  CD34+ cells/kg (which safely allows two ASCT), and only 1.4% when using a less stringent threshold of  $2 \times 10^6$

CD34+ cells/kg (a threshold most often reported in the literature allowing cross comparison between studies). These findings confirm, using an endpoint *relevant to clinicians*, the high success rate achieved using plerixafor in the setting of upfront stem cell collection in patients with MM.

The SC collection failure rate reported in this study compares very favorably with previously reported failure rates using G-CSF alone, which have ranged from 18.6% to as high as 38%. (23–27) This reports supports the findings of a large phase III trial of upfront mobilization in patients with MM(20). Although the primary end point of that randomized phase III study was the percentage of patients who collected more than  $6 \times 10^6$  CD34+ cells/kg in 2 aphereses, an endpoint that may not be as relevant to clinicians, the percentage of patients failing to collect at least  $2 \times 10^6$  CD34+ cells/kg – regardless of the number of aphereses– was only 4.7%, comparable to 1.4% in the current study. Likewise, the present study supports the findings of Russell *et al.* who examined the efficacy of plerixafor used in upfront mobilization in 90 patients with MM and reported a failure rate (defined using a threshold of  $2 \times 10^6$  CD34+ cells/kg) in only 2 % of patients(28). In addition, Shaughnessy *et al.* reported that among 54 MM patients, 89% met the target of  $> 6 \times 10^6$  CD34+ cells/kg and 93% of patients had  $> 2 \times 10^6$  CD34+ cells/kg collected(29). One can surmise, based on the current and prior studies, and despite the disparities pertaining to the definition of failure rates between studies, that the collection failure rate for P+G-CSF is reliably low and significantly lower than previous reports using G-CSF alone.

When trying to compare P+G-CSF versus chemotherapy (most often cyclophosphamide) based stem cell mobilization, phase III trials that prospectively compare these two options are not available. However, several retrospective studies have been published and have reached somewhat diverging conclusions although plerixafor appears overall to fair favorably compared to cyclophosphamide. Shaughnessy *et al.* found a significantly higher percentage of patients collecting  $5 \times 10^6$  cells/kg in the plerixafor group compared to the cyclophosphamide group (94% vs. 76%). Note that only 66 patients were included in the study and only 40 had a diagnosis of MM(30). Costa *et al.* reported a significantly higher rate of mobilization failure with the cyclophosphamide-based regimen when comparing with an algorithm using G-CSF plus “on-demand” plerixafor, an approach that would be expected to spare the use of plerixafor in a substantial percentage of patients(31). Likewise, Micallef *et al.* have described a similar approach and concluded that plerixafor “on demand” lowered the failure rate, days of apheresis, and total days of collection.(32) On the other hand, Awan *et al.* comparing intermediate-dose CY (ID-CY) and G-CSF versus P+G-CSF in MM patients, reported a higher CD34+ cell yield on day 1 and higher total yield ( $16.6 \times 10^6$  cells/kg vs.  $11.6 \times 10^6$  cells/kg,  $p < 0.001$ ) in the ID-CY group(33). Overall, a prospective trial aimed at comparing the efficacy, cost and quality of life assessment of these two stem cell mobilization approaches may be warranted.

In this study we also aimed at identifying risk factors associated with mobilization failure as defined (  $5 \times 10^6$  CD34+ cel/kg) when using plerixafor; but the failure rate observed was too low to achieve this goal. However, since SC collection failure is dependent on compensation afforded by an increase in the number of apheresis sessions, we reasoned that SC collection efficiency, defined as the number of SC collected per apheresis performed,



may be a more revealing outcome to analyze in order to identify risk factors. Indeed, multivariate analysis using a linear regression model revealed that exposure to lenalidomide alone during induction, lower WBC prior to G-CSF, and non African American race were associated with a decreased SC collection efficiency. These risk factors would identify patients in whom stem cell collection may necessitate an increased number of apheresis sessions.

Interestingly, while exposure to lenalidomide alone during induction negatively impacted SC collection efficiency, the simultaneous exposure to lenalidomide and bortezomib or to bortezomib alone did not. We hypothesize that this observation may be related to the higher dose of lenalidomide received during induction by patients on lenalidomide alone compared to those who receive it in association with bortezomib, which usually amounts to a 50% increase in dose exposure to lenalidomide (25 mg for 21 days vs. 25 mg for 14 days, respectively). Alternatively, bortezomib may have a protective effect, although this mechanism is completely speculative. Other studies have investigated the impact of lenalidomide on SC mobilization failure when using plerixafor. Micallef *et al.* examined in a retrospective study the efficacy of P+G-CSF among 60 patients with MM previously treated with lenalidomide and could not identify lenalidomide as a risk factor when using plerixafor upfront(14). Indeed, the minimum number of CD34+ cells ( $2 \times 10^6$  CD34+ cells/kg) was collected in 100% of patients who underwent frontline mobilization, suggesting a predictably successful collection with P+G-CSF, at least using this SC threshold, in patients previously exposed to lenalidomide. On the other hand, Costa *et al.* in order to determine if preemptive combination of P+G-CSF would overcome lenalidomide exposure in MM patients, stratified patients into three groups based on exposure to lenalidomide: Group A (n = 40), no prior exposure; group B (n = 30), 1–4 cycles; or group C (n = 19), > 4 cycles. Forty five percent of patients in group A needed plerixafor use vs. 63% in group B and 84% in group C, a finding that is expected in view of the known negative impact of lenalidomide when using single agent G-CSF. Importantly, and in agreement with our findings, 100% of patients in group A, 90% in group B, and 79% in group C achieved the mobilization target of the study ( $6 \times 10^6$  CD34+ cells/kg) despite the addition of plerixafor, supporting the deleterious effect of lenalidomide(31).

In summary, we have validated in this study the high success rate of stem cell collection with plerixafor in the upfront setting in patients with MM, using an outcome measurement that is *relevant to clinicians*, i.e. using a target stem cell collection adequate to perform at least two ASCT. We have also shown that despite this low failure rate, risk factors affecting the SC collection efficiency could be identified and include lower WBC count prior to mobilization, prior exposure to lenalidomide alone, and non African American race. We hypothesize, based on our observations, that the effect of lenalidomide may be dose dependent. These risk factors would allow identification of patients in whom an increased number of apheresis sessions may be anticipated for a successful outcome. It is important to note that although this study shows excellent efficacy of plerixafor when used for stem cell mobilization upfront, the drug remains at the present time costly and others have advocated the use of “on demand plerixafor”, an approach that would be expected to lower the financial burden of plerixafor mobilization, since a significant percentage of patients would be spared plerixafor(34, 35). Further prospective studies may be warranted to address this issue.

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**Table 1**

## Patients' Baseline and Treatment Characteristics

| Baseline characteristics                                | Patients (n= 138) |
|---|-------------------|
| Age, median (Range)                                     | 60 (40–77)        |
| Male gender, N (%)                                      | 80 (58)           |
| Race, N (%)   |                   |
| Caucasian   | 102(74)           |
| African American  | 20 (14.4)         |
| Asian   | 6 (4.3)           |
| Non-specified   | 10 (7.3)          |
| Isotype, N (%)  |                   |
| IgA kappa   | 17 (12.3)         |
| IgA lambda  | 14 (10.1)         |
| IgG kappa   | 79(57.2)          |
| IgG lambda  | 23 (16.7)         |
| IgM kappa   | 1 (0.7)           |
| Kappa only  | 3 (2.2)           |
| Unknown   | 1 (0.7)           |
| ISS, N (%)  |                   |
| I   | 84 (61)           |
| II  | 27 (19.5)         |
| III   | 27 (19.5)         |
| Cytogenetic risk, N (%)                                 |                   |
| Standard  | 104 (75)          |
| Intermediate  | 16 (12)           |
| High  | 18 (13)           |
| Prior therapy, N (%)                                    |                   |
| RVD   | 86 (62.3)         |
| RD  | 27 (19.6)         |
| CyBorD  | 10 (7.2)          |
| BD  | 15 (10.9)         |
| Number of induction cycles, median (Range)              | 4 (1–11)          |
| Prior radiation, N (%)                                  |                   |
| Yes   | 24 (17)           |
| Plasmacytosis prior to mobilization (%), median (Range) | 3 (0–28)          |

Abbreviations: RVD: Revlimid (Lenalidomide), Velcade (bortezomib), and dexamethasone; RD: Lenalidomide and dexamethasone; CyBorD: Cyclophosphamide, bortezomib, and dexamethasone; BD: Bortezomib and dexamethasone.

**Table 2**

Characteristics of patient who failed stem cell collection

| Patient | Age | Race             | WBC Count<br>Prior to<br>Mobilization | Platelet Count<br>Prior to<br>Mobilization | Induction<br>Treatment | Number of<br>Induction<br>cycles | Total<br>CD34+<br>cells/kg |
|---------|-----|------------------|---------------------------------------|--|------------------------|----------------------------------|----------------------------|
| 1       | 75  | Caucasian        | 5.6                                   | 109  | RVD                    | 6                                | 4.48                       |
| 2       | 61  | Nonspecified     | 0.1                                   | 20   | RD                     | 1                                | 0.05                       |
| 3       | 61  | Caucasian        | 7.8                                   | 219  | RVD                    | 3                                | 2.63                       |
| 4       | 60  | African American | 7                                     | 115  | RVD                    | 4                                | 4.74                       |
| 5       | 67  | Caucasian        | 5.8                                   | 191  | RVD                    | 4                                | 2.11                       |
| 6       | 73  | Nonspecified     | 3.2                                   | 222  | RVD                    | 5                                | 4.28                       |
| 7       | 67  | Caucasian        | 6.2                                   | 186  | CyBorD                 | 5                                | 4.96                       |
| 8       | 72  | African American | 6.7                                   | 235  | BD                     | 4                                | 3.02                       |
| 9       | 57  | Asian            | 3.2                                   | 361  | BD                     | 5                                | 0.7                        |
| 10      | 71  | Caucasian        | 3.4                                   | 233  | RD                     | 8                                | 3.1                        |

Abbreviations: WBC: White blood Cell; RD: Revlimid (lenalidomide) and dexamethasone; RVD: Revlimid (lenalidomide), Velcade (bortezomib) and dexamethasone; CyBorD: Cyclophosphamide, bortezomib and dexamethasone;

**Table 3**

Univariate and multivariate analyses using linear regression of risk factors associated with SC collection efficiency (n= 138)

| Variables                                      | N   | Mean Efficacy (SD) | Univariate Estimate (95% CI) | p value      | Multivariate Estimate (95% CI) | p value      |
|--|-----|--------------------|------------------------------|--------------|--------------------------------|--------------|
| <b>Gender</b>                                  |     |                    |                              |              |                                |              |
| Female   | 58  | 6.73 (4.46)        | (reference)                  | 0.356        |                                |              |
| Male   | 80  | 7.62 (6.21)        | 0.89 (-1.01,2.78)            |              |                                |              |
| <b>Age</b>                                     |     |                    |                              |              |                                |              |
| < 65 y/o                                       | 97  | 7.77 (5.68)        | (reference)                  | 0.089        |                                |              |
| 65 y/o   | 41  | 6.01 (5.05)        | -1.76 (-3.79,0.26)           |              |                                |              |
| <b>Race</b>                                    |     |                    |                              |              |                                |              |
| Caucasian                                      | 102 | 6.78 (5.3)         | (reference)                  |              | (reference)                    |              |
| African American                               | 20  | 10.01 (6.66)       | 3.23 (0.58,5.88)             | <b>0.017</b> | 3.03 (0.51,5.55)               | <b>0.019</b> |
| Asian  | 6   | 6.11 (4.28)        | -0.67 (-5.23,3.88)           | 0.77         | -1.1 (-5.4,3.2)                | 0.615        |
| Other  | 10  | 7.19 (5.31)        | 0.41 (-3.18,4)               | 0.822        | 0.7 (-2.69,4.1)                | 0.682        |
| <b>Regimens</b>                                |     |                    |                              |              |                                |              |
| Bortezomib only                                | 25  | 8.87 (8.19)        | (reference)                  |              | (reference)                    |              |
| Lenalidomide only                              | 27  | 4.84 (3.32)        | -4.04 (-7.02,-1.06)          | <b>0.008</b> | -3.21 (-6.23,-0.18)            | <b>0.038</b> |
| Both   | 86  | 7.53 (4.95)        | -1.34(-3.78,1.1)             | 0.28         | -1.23 (-3.6,1.13)              | 0.304        |
| <u>Plasmacytosis (prior to mobilization)</u>   | 126 |                    | -0.03 (0.13 to 0.06)         | 0.478        |                                |              |
| <b>Number of Induction Cycles</b>              |     |                    |                              |              |                                |              |
| 4  | 114 | 7.7 (5.76)         | (reference)                  |              | (reference)                    |              |
| > 4  | 24  | 5.12 (3.73)        | -2.58 (-5.01,-0.15)          | <b>0.038</b> | -1.94 (-4.35,0.47)             | 0.113        |
| <b>Treatment Start to Collection</b>           |     |                    |                              |              |                                |              |
| 4 months                                       | 43  | 9.57 (6.97)        | (reference)                  |              | (reference)                    |              |
| > 4 months                                     | 95  | 6.2 (4.41)         | -3.37 (-5.31,-1.43)          | <b>0.001</b> | -1.96 (-4.02,0.1)              | 0.063        |
| <b>Platelets Count (prior to mobilization)</b> |     |                    |                              |              |                                |              |
| 160  | 25  | 7.48 (7.23)        | (reference)                  |              |                                |              |
| > 160  | 113 | 7.20 (5.13)        | -0.27 (-2.7,2.16)            | 0.824        |                                |              |
| <b>WBC Count (prior to mobilization)</b>       |     |                    |                              |              |                                |              |

| Variables | N   | Mean<br>Efficacy (SD) | Univariate Estimate<br>(95% CI) | p value      | Multivariate<br>Estimate (95% CI) | p value     |
|-----------|-----|-----------------------|---------------------------------|--------------|-----------------------------------|-------------|
| < 4       | 34  | 5.29 (3.96)           | (reference)                     |              | (reference)                       |             |
| 4         | 104 | 7.89 (5.84)           | 2.6 (0.47,4.72)                 | <b>0.017</b> | 2.69 (0.66,4.72)                  | <b>0.01</b> |

Abbreviations: SD: Standard Deviation; CI: Confidence Interval; WBC: White Blood cells