Post-ASCT Outcomes in Multiple Myeloma Patients Who Underwent ASCT with G-CSF + Plerixafor Versus G-CSF Mobilized Graft

Harsh Shah, DO , Seongho Kim, Ph.D , Paramveer Singh, MD , Asif Alavi, MD , Lois Ayash, MD, Voravit Ratanatharathorn, MD, Joseph P. Uberti, M.D., Ph.D., and Abhinav Deol, MD.
Department of Oncology, Blood and Marrow Stem Cell Transplant Program, Karmanos Cancer Institute/Wayne State University, Detroit, MI

Introduction and Objectives:

Impact of Plerixafor (P) mobilized stem cells on immune reconstitution of autologous stem cell transplant (ASCT) patients has not been established. Early lymphocyte recovery (Absolute lymphocyte count of > 1 K/uL at day 30 after transplant) has been established to predict outcomes in multiple myeloma (MM) patients. The purpose of this study was to evaluate lymphocyte recovery in MM patients who underwent ASCT with stem cells mobilized with G-CSF vs G-CSF+P. Secondary objective was to evaluate the survival outcomes.

METHODS

- This was a retrospective analysis of MM patients who underwent first ASCT between 2008 and 2016 with either G-CSF or G-CSF+P mobilization at Karmanos Cancer Institute in Detroit, Michigan. Plerixafor was used per institutional guidelines when the peripheral CD-34+ve cell-count was < 20/ uL on day 5 of G-CSF mobilization.
- End Points:** The primary endpoint was the Absolute Lymphocyte Count at day 30 (ALC30). Secondary endpoints were PFS and OS. Overall survival (OS) was calculated as the time from the date of transplantation to death from any cause. Progression-free survival (PFS) was calculated as the time from the date of transplantation to the date of progression or death from any cause.
- Statistical Methods:** Univariable and multivariable Cox proportional hazards regression models were fit to assess associations between ten pre chosen predictors(age, race, stage at diagnosis, doublet vs. triplet therapy, lines of treatment, disease status, mobilization agents, melphalan dose, ALC at day 30, post-transplant maintenance) and survival benefit (PFS and OS).

RESULTS

610 total patients were identified. Mobilization agents used were G-CSF alone (n= 469) or G-CSF+P (n= 141). All patients underwent transplant after Melphalan (M) conditioning and dose of M was at treating physician's discretion (140 vs 200 mg/m²).

RESULTS

Table 1. Baseline characteristics

	G-CSF (N = 469)	G-CSF + Plerixafor (N = 141)	All (N = 610)	Signif.
Age at transplant, year – median (range)	60 (30-76)	62 (41-76)	61 (30-76)	0.006
Sex – no. (%)				0.770
Male	274 (58)	85 (60)	359 (59)	
Female	195 (42)	56 (40)	251 (41)	
Race – no. (%)				0.445
Caucasian	330 (70)	107 (76)	437 (72)	
African-American	129 (28)	32 (23)	161 (26)	
Others	10 (2)	2 (1)	12 (2)	
Stage at Diagnosis – no. (%)				>0.99
1	70 (15)	20 (14)	90 (15)	
2	110 (23)	32 (23)	142 (23)	
3	269 (57)	77 (55)	346 (57)	
Unknown	20 (4)	12 (9)	32 (5)	
Disease status at transplant – no. (%)				0.575
CR	77 (16)	21 (15)	98 (16)	
VGPR	153 (33)	47 (33)	200 (33)	
PR	163 (35)	44 (31)	207 (34)	
SD	47 (10)	21 (15)	68 (11)	
PD	28 (6)	8 (6)	36 (6)	
Unknown	1 (0)	0 (0)	1 (0)	
CMV status – no. (%)				0.922
+	279 (59)	83 (59)	362 (59)	
-	190 (41)	58 (41)	248 (41)	
Sig CoExit Disease – no. (%)				0.147
Yes	413 (88)	117 (83)	530 (87)	
No	54 (12)	23 (16)	77 (13)	
Unknown	2 (0)	1 (1)	3 (0)	
Doublet vs Triplet Therapy – no. (%)				0.015
Doublet	132 (28)	25 (18)	157 (26)	
Triplet Therapy	337 (72)	116 (82)	453 (74)	
Post transplant treatment – no. (%)				0.892
Yes	323 (69)	83 (59)	406 (67)	
No	81 (17)	22 (16)	103 (17)	
Unknown	65 (14)	36 (26)	101 (17)	
Infused CD34 – median (range)	3.19 (1.77-16.9)	2.88 (1.71-7.2)	3.125 (1.71-16.9)	0.001
G500 – median (range)	12 (10-27)	12 (10-18)	12 (10-27)	0.810
Unknown	0	1	1	
G1000 – median (range)	13 (11-46)	13 (11-63)	13 (11-63)	0.427
Unknown	7	7	14	
ALC30 – median (range)	1.3 (0.1-4.5)	1.2 (0.1-5.1)	1.3 (0.1-5.1)	0.608
AMC30 – median (range)	0.7 (0-2.4)	0.7 (0-2.1)	0.7 (0-2.4)	0.237
Day – median (range)	30 (13-42)	31 (12-39)	30 (12-42)	0.407
Lines of Tx – median (range)	1 (1-6)	1 (1-5)	1 (1-6)	0.002
Melphalan dose – median (range)	<200	59 (42)	205 (34)	0.020
200	146 (31)	82 (58)	405 (66)

Figure 1. Kaplan-Meier curves of progression-free survival (PFS) according to G-CSF and G-CSF+Plerixafor (G-CSF+P). The median PFS is 2.46 years (95% CI, 2.14 to 3.15) and 2.77 years (95% CI, 1.99 to 3.27) for G-CSF and G-CSF+P, respectively. The median follow-up time of PFS is 2.99 years (95% CI, 2.48 to 3.13) and 1.92 years (95% CI, 1.20 to 2.53) for G-CSF and G-CSF+P, respectively. The follow-up time was calculated using the reverse Kaplan-Meier estimate.

Figure 2. Kaplan-Meier curves of overall survival (OS) according to G-CSF and G-CSF+Plerixafor (G-CSF+P). The median OS is 6.09 years (95% CI, 4.55 to NR) and 3.73 years (95% CI, 3.20 to NR) for G-CSF and G-CSF+P, respectively. The median follow-up time of OS is 2.53 years (95% CI, 2.13 to 2.99) and 1.59 years (95% CI, 1.17 to 2.02) for G-CSF and G-CSF+P, respectively. The follow-up time was calculated using the reverse Kaplan-Meier estimate. Note that NR represents 'not reached'.

RESULTS

- Median age of patients was older in G-CSF+P group (62 vs 60 years, p=. 006) and they were more likely to receive triplet therapy (82 vs 72%, p=. 015) for induction compared to G-CSF group (Table 1). Patients in G-CSF group were more likely to receive greater than one line of treatment before transplant (p=. 006). Disease status at transplant was similar between the two groups. G-CSF patients received higher dose of M (at 200mg/ m2) more frequently (69 vs. 58%, p = 0.010) and median cell dose infused was higher in G-CSF group (3.19 vs 2.88 x10⁶ CD 34+ve-cells/Kg, p= 0.001).
- Primary endpoint, ALC30, was 1.3 K/uL (1-4.5) and 1.2 K/uL (1-5.1) for G-CSF and G-CSF+P, (p=. 608). Median day to neutrophil recovery were similar in both groups (Day 12). Post-transplant maintenance use was similar between the two groups.
- The median PFS was 2.46 years (95% CI, 2.14 to 3.15) and 2.77 years (95% CI, 1.99 to 3.27) for G-CSF and G-CSF+P, respectively (HR: 1.128; 95% CI, (.843-1.509); p=. 417) (Figure 1). The median OS was 6.09 years (95% CI, 4.55 to NR) and 3.73 years (95% CI, 3.20 to NR) for G-CSF and G-CSF+P, respectively (HR: 1.638; 95% CI, (1.118-2.399); p=. 011) (Figure 2) .
- In MVA, higher stage at diagnosis, less than PR before ASCT, and no post-transplant maintenance therapy were associated with worse PFS and OS. Use of G-CSF+P for mobilization and Melphalan dose <200-mg/ m² adversely impacted OS. ALC30 did not impact PFS or OS in MVA.

CONCLUSIONS

In this large, retrospective analysis of MM patients mobilized with G-CSF vs G-CSF + P, there was no significant difference in lymphocyte recovery. Higher Melphalan dose resulted in improved OS in the MVA. There was an overall survival difference favoring the G-CSF group, however, differences in baseline characteristics not accounted for in the MVA may be responsible for this observation. A Prospective study comparing these mobilization regimens including patients with similar baseline characteristics is necessary to confirm this finding.

REFERENCES

Hiwashe et al. Higher Infused Lymphocyte Dose Predicts Higher Lymphocyte Recovery, Which in Turn, Predicts Superior Overall Survival following Autologous Hematopoietic Stem Cell Transplantation for Multiple Myeloma. Biology of Blood and Marrow Transplantation 14:116-124, 2008.