ELSEVIER

Blood 142 (2023) 6633–6635

The 65th ASH Annual Meeting Abstracts

ONLINE PUBLICATION ONLY

652.MULTIPLE MYELOMA: CLINICAL AND EPIDEMIOLOGICAL

Impact of Daratumumab on Hematopoietic Stem Cell Mobilization with G-CSF and on-Demand Plerixafor in Newly-Diagnosed Multiple Myeloma Patients

Roberto Mina, MD[1], *Bruno Garibaldi*[2], *Giuseppe Bertuglia*[3], *Andrea Casson*[1], *Barbara Sarina*[4], *Francesca Gay, MD PhD*[5], *Silvio Mercadante, PhD*[6], *Jacopo Mariotti*[7], *Mattia D'Agostino, MD*[3], *Daniela Taurino*[8], *Stefania Oliva, MD PhD*[3], *Alessandra Larocca, MD PhD*[9], *Daniele Mannina, MD*[10], *Chiara De Philippis*[11], *Giulia Benevolo*[12], *Tiziana Francisci*[13], *Marco Lorenzi*[14], *Benedetto Bruno, MD PhD*[15], *Armando Santoro, MD*[16], *Sara Bringhen, MDPhD*[17], *Stefania Bramanti*[10]

[1] Division of Hematology, Department of Molecular Biotechnology and Health Sciences, University of Torino, Torino, Italy
[2] IRCCS Humanitas Research Hospital, Transplantation Unit Department of Oncology and Haematology, Milan, Italy, Rozzano, Italy
[3] Myeloma Unit, Division of Hematology, Azienda Ospedaliero-Universitaria Città della Salute e della Scienza di Torino, University of Torino, Torino, Italy
[4] Istituto Clinico Humanitas, Rozzano, ITA
[5] University of Torino, Torino, Italy
[6] Division of Hematology, Department of Molecular Biotechnology and Health Sciences, University of Torino and Division of Hematology, Azienda Ospedaliero-Universitaria Città della Salute e della Scienza di Torino, Torino, Italy, Torino, Italy
[7] IRCCS Humanitas Research Hospital, Transplantation Unit Department of Oncology and Haematology, Milan, Italy, Rozzano (milan), ITA
[8] Bone Marrow Unit, IRCCS Humanitas Research Hospital, Humanitas Cancer Center, Rozzano, ITA
[9] SSD Clinical Trial in Oncoematologia e Mieloma Multiplo, Department of Oncology, Azienda Ospedaliero-Universitaria Città della Salute e della Scienza di Torino, Torino, Italy
[10] Humanitas Clinical and Research Center, IRCCS, Rozzano, Italy
[11] IRCCS Humanitas Research Hospital, Transplantation Unit Department of Oncology and Haematology, Rozzano, ITA
[12] Azienda Ospedaliero Universitaria, Turin, ITA
[13] S.C. Banca del Sangue e Immunoematologia, Azienda Ospedaliero-Universitaria Città della Salute e della Scienza di Torino, Torino, Italy, Torino, Italy
[14] S.C. Banca del Sangue e Immunoematologia, Azienda Ospedaliero-Universitaria Città della Salute e della Scienza di Torino, Torino, Italy, torino, Italy
[15] Division of Hematology and Stem Cell Transplant Unit, University Hospital AOU Città della Salute e della Scienza, Torino, Italy
[16] Humanitas Cancer Center, Rozzano, Italy
[17] Citta' Della Salute E Della Scienza, Torino, Italy

Introduction

Autologous stem cell transplantation (ASCT) is a standard of care for transplant eligible (TE) patients with newly diagnosed (ND) multiple myeloma (MM); therefore, an adequate hematopoietic stem cell (HSC) collection is crucial to allow patients to proceed to ASCT and ensure optimal hematologic recovery. A more frequent use of plerixafor (PLX) and lower HSC yields have been reported in patients treated with daratumumab, a backbone of induction therapy for NDMM patients. Chemotherapy-free mobilization with G-CSF and on-demand PLX is an effective mobilization strategy lacking chemotherapy-related toxicities. Here we present the results of a multicenter, retroprospective and prospective, observational study, aiming to compare the impact of daratumumab on HSC mobilization with G-CSF + on-demand PLX in patients with NDMM treated with bortezomib-thalidomide-dexamethasone (VTd) or VTd plus daratumumab (D-VTd).

Methods

NDMM patients undergoing a first HSC mobilization attempt with G-CSF (10 mcg/kg/day) were enrolled and observed up to 30 days after ASCT. According to its label, on-demand PLX was administered in patients with <20 CD34$^+$ cells/μL after ≥ 4 days of G-CSF or in case $<1\times10^6$ CD34$^+$ cells/kg were collected on the first day of apheresis. The primary endpoint of the

study was the rate of poor mobilizing patients (≤2x10 ^{6} CD34 $^{+}$ cells/Kg collected or need for PLX to reach an adequate HSC harvest). Key secondary endpoints included: the rate of suboptimal (2 to 4 CD34 $^{+}$ cells/kg) and optimal (≥4 CD34 $^{+}$ cells/Kg) collection; the median number of apheresis required to obtain ≥2x10 ^{6} CD34 $^{+}$ cells/Kg; the impact of daratumumab on HSC engraftment.

Results

A total of 190 NDMM patients (median age, 62 years) were enrolled in 2 Italian centres (IRCSS Istituto Clinico Humanitas and Città della Salute e della Scienza di Torino) and analyzed; of these, 70% (133/190) were treated with VTd and 30% (57/190) with D-VTd. The median number of induction cycles was 4 in both groups. Best response after the induction phase was at least very good partial response (VGPR) in 87/133 (65%) and 41/57 (72%) of patients treated with VTd or D-VTd, respectively (p=0.4). The median time from the end of induction to G-SCF administration was 24 days in the VTd group and 29 days in the D-VTd group (p=0.5).

The rate of poor mobilizing patients was 31% (41/133) in the VTd group and 54% (31/57) in the D-VTd group (p=0.002), mainly due to a higher rate of PLX use in the D-VTd as compared to the VTd group (53% vs. 28%; p=0.001), while the rate of patients who failed HSC mobilization (≤2x10 ^{6} CD34 $^{+}$ cells/kg collected) was similar in the two groups (2% vs. 3%; p=1). Despite a numerically higher median number of CD34 $^{+}$ cells collected in the VTd group (7.9) as compared to the D-VTd group (7.1; p=0.009), no difference in the rate of patients who collected 2-4 (5% vs. 5%; p=1) and ≥4 CD34 $^{+}$ cells/Kg (95% vs. 95%; p=1) was observed in the VTd and D-VTd groups, respectively. A higher median number of CD34 $^{+}$/μL on the first day of count was observed in the VTd as compared to the D-VTd group (24.5 vs. 19, p=<0.001). Among patients who had <20 CD34 $^{+}$/μL [32% (43/133) vs. 51% (29/57)] on the first day of count, a similar increase in the CD34 $^{+}$/μL (48.5 vs. 55) was observed in the two groups after PLX administration. The median number of apheresis session needed to complete the harvestwas 1 fo the VTd group and 2 in the D-VTd group (p=0.1).

Neutrophil and platelet recovery were achieved in 100% of patients with a median time to neutrophil recovery of 15 and 13 days in the VTd and D-VTd groups, respectively (p=<0.001) and a median time to platelet recovery of 16 and 14 days in the VTd and D-VTd groups, respectively (p=0.001).

Conclusion

G-CSF plus on-demand PLX for HSC mobilization demonstrated to be an effective strategy in NDMM patients treated with VTd with or without daratumumab, resulting in very low rates of mobilization failures irrespective of the use of daratumumab during induction. Despite a higher rate of patients requiring PLX for HSC collection and lower CD34 $^{+}$ yields, the incorporation of daratumumab as part of the induction treatment did not negatively impact the possibility to achieve an optimal HSC collection. Our results, along with the lack of chemotherapy-associated toxicity, support the use of a chemotherapy-free HSC mobilization with G-CSF and on-demand plerixafor also in patients receiving daratumumab upfront.

Disclosures Mina: *Sanofi:* Consultancy; *Bristol Myers Squibb:* Membership on an entity's Board of Directors or advisory committees; *Pfizer:* Honoraria; *Amgen:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Takeda:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *Celgene:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Janssen:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees. **Gay:** *AbbVie:* Honoraria, Other: Advisory board; *Roche:* Other: Advisory board; *Takeda:* Honoraria, Other: Advisory board; *Pfizer:* Honoraria, Other: Advisory board; *Sanofi:* Honoraria, Other: Advisory board; *Bristol Myers Squibb/Celgene:* Honoraria, Other: Advisory board; *Oncopeptides:* Other: Advisory board; *Janssen:* Honoraria, Other: Advisory board; *Amgen:* Honoraria, Other: Advisory board; *GlaxoSmithKline:* Honoraria, Other: Advisory board. **D'Agostino:** *GlaxoSmithKline:* Membership on an entity's Board of Directors or advisory committees, Other: Honoraria for lectures; *Sanofi:* Membership on an entity's Board of Directors or advisory committees, Other: Honoraria for lectures; *Janssen:* Other: Honoraria for lectures; *Bristol Myers Squibb:* Membership on an entity's Board of Directors or advisory committees. **Oliva:** *Abbvie:* Honoraria; *Janssen:* Consultancy, Honoraria; *Takeda:* Honoraria; *Celgene/Bristol Myers Squibb:* Honoraria; *Amgen:* Consultancy, Honoraria; *Adaptive Biotechnologies:* Consultancy. **Larocca:** *Janssen-Cilag:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Bristol Myers Squibb:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Amgen:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Takeda:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Oncopeptides:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *GlaxoSmithKline:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Sanofi:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Karyopharm:* Honoraria, Membership on an entity's Board of Directors or advisory committees. **Benevolo:** *Bristol Myers Squibb:* Consultancy, Speakers Bureau; *Janssen:* Consultancy, Speakers Bureau; *Novartis:* Consultancy, Speakers Bureau. **Santoro:** *Eisai:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Pfizer:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Gilead:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Servier:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *BMS:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Incyte:* Consultancy; *Sanofi:* Consultancy; *Bayer:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Merck MSD:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Takeda:* Speakers Bureau; *Roche:* Speakers Bureau; *Abbvie:* Speakers Bureau; *Amgen:* Speakers Bureau; *Celgene (BMS):* Speakers Bureau; *AstraZeneca:* Speakers Bureau; *Eli Lilly:* Speakers Bureau; *Sandoz:* Speakers Bureau; *Novartis:* Speakers Bureau; *Arqule:* Other. **Bringhen:** *Amgen:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Janssen:* Consultancy,

Honoraria, Membership on an entity's Board of Directors or advisory committees; *Bristol Myers Squibb:* Consultancy, Honoraria; *GlaxoSmithKline:* Membership on an entity's Board of Directors or advisory committees; *Sanofi:* Membership on an entity's Board of Directors or advisory committees; *Takeda:* Consultancy; *Pfizer:* Membership on an entity's Board of Directors or advisory committees; *Celgene:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees.

Variables		VTd N=133	D-VTd N=57	P value
Poor mobilizing N (%)	No	92 (69)	26 (46)	0.002
	Yes	41 (31)	31 (54)	
PLX administration N (%)	No	96 (72)	27 (47)	0.001
	Yes	37 (28)	30 (53)	
Successful mobilization N (%)	No	4 (3)	1 (2)	1
	Yes	129 (97)	56 (98)	
CD34⁺ cells/µL on the first day of count	Median (IQR)	24.5 (14.8 - 42.3)	19 (8.5 - 30.5)	<0.001
	<20 N (%)	43 (32)	29 (51)	0.06
	≥ 20 N (%)	73 (55)	26 (46)	
CD34⁺ cells/µL increase after first PLX administration	Median (IQR)	55 (45 - 80)	48.5 (34.2 - 57)	0.05
CD34⁺ cells/Kg	Median (IQR)	7.92 (6.3 – 10.2)	7.12 (5.8 – 8.9)	0.009
	Optimal collection* N (%)	123 (95)	53 (95)	1
	Suboptimal collection** N (%)	7 (5)	3 (5)	
Apheresis sessions	Median	1	2	0.1

Table 1. Mobilization characteristics and harvesting outcomes
VTd, bortezomib-thalidomide-dexamethasone; DVTd; daratumumab-bortezomib-thalidomide-dexamethasone; PLX, plerixafor; IQR, interquartile range; N, number
* Optimal collection: total HSC collected over 4 CD34+/Kg,
* Suboptimal collection: yotal HSC collected between 2 and 4 x10^6 CD34/Kg,

Figure 1

https://doi.org/10.1182/blood-2023-180082