Efficacy of Daratumumab Containing Regimens Post Lenalidomide Maintenance in Transplant Eligible Patients: Real-World Experience from the Canadian Myeloma Research Group Database

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Introduction

Lenalidomide maintenance following autologous stem cell transplant (ASCT) remains a standard of care among transplant eligible patients with newly diagnosed multiple myeloma(NDMM). Many previous clinical trials done in patients following one prior line of therapy either excluded patients progressing on lenalidomide or included a very small proportion of these patients. Given the paucity of data in this setting, the optimal management of patients progressing on lenalidomide maintenance remains unknown. Daratumumab-containing triplet regimens have recently been introduced for these patients, typically in combination with pomalidomide (DPd), lenalidomide (DRd), or bortezomib (DVd). To our knowledge, there is no prospective data to allow comparison of the efficacy of these three regimens in patients progressing on lenalidomide maintenance, which is an increasingly common clinical scenario. Understanding the comparative efficacy, tolerability and toxicity of these regimens in patients progressing on lenalidomide maintenance in the 'real-world' is needed in order to help clinicians make appropriate decisions and guide future studies.

Methods

The Canadian Myeloma Research Group Database (formerly known as the Myeloma Canada Research Network Database, MCRN-DB) is a prospectively maintained disease specific database with over 7000 patients enrolled from 14 academic sites across Canada with legacy data collected from 2007. The Munster Myeloma database collects myeloma specific information in a German academic center and currently contains data from 800 patients collected from 2005. All consecutive patients treated with daratumumab based regimens in second line following relapse on lenalidomide maintenance were included in the analysis from the two databases analyzed up to 30/06/2020.

Results

A total of 1380 NDMM patients on lenalidomide maintenance post autologous stem cell transplant was identified in the two databases. From them, 73 patients were included in this analysis as they were treated with daratumumab containing regimen in second line. Specifically, 18 (24.7%) of these patients were treated with DPd, 32 (43.8%) patients with DRd, and 23 (31.5%) patients with DVd. The baseline characteristics, maintenance details, post-maintenance response rates and toxicity for each regimen are shown in Table 1. The median follow-up for the cohort from the time of daratumumab initiation was 8.3 months
(range 0.4 - 40.0). Although, a higher proportion of patients in the DPd arm obtained a

CR/VGPR compared to DRd or DVd, it did not reach statistical signi□cance (p-value 0.06). The median PFS of the entire cohort was 16.96 months (95% CI 11.47-23.44). The median PFS of the individual regimens was as follows: DPd 17.65 months, DRd not reached and DVd 11.47 months as demonstrated in Figure 1 (p-value =0.46).

Conclusion

In summary, our results show that daratumumab-based regimens are effective among patients progressing on lenalidomide maintenance in the real world. Despite the small sample size, the results presented here are in line with recent sub-analyses of phase III studies examining the common daratumumab-based regimens used in this setting (CASTOR with median PFS of DVd between 7.8 months in all lenalidomide refractory patients and 27 months in all patients in first relapse; MM014 with median PFS of DPd after lenalidomide refractoriness of 21.8 months). The efficacy of DRd, in which daratumumab is added to an increased dose of lenalidomide, is notable and warrants further evaluation to identify which patients are most likely to benefit. Additional studies with longer follow-up are required to assess the optimal daratumumab-based regimen to be used in this growing population of patients relapsing after lenalidomide maintenance.

Table 1: Baseline cohort characteristics and response rates

	All (N=73)	DPd (N=18)	DRd (N=32)	DVd (N=23)
Baseline characteristics				
Age, median (range)	60 (38-72)	53 (38-68)	59 (39-71)	64 (47-72)
Male, N (%)	47 (64)	15 (83)	19 (59)	13 (56)
MM subtype, N (%)				
IgG	40 (55)	14 (78)	14 (44)	12 (52)
IgA	17 (23)	3 (17)	7 (22)	7 (31)
FLC	14 (19)	1 (5)	10 (31)	3 (13)
Other	2 (3)	0	1 (3)	1 (4)
ISS Stage, N (%)				
I	23 (32)	4 (22)	11 (34)	8 (35)
II	32 (44)	10 (55)	12 (38)	10 (43)
III	13 (18)	3 (17)	7 (22)	3 (13)
Unknown	5 (7)	1 (6)	2 (6)	2 (9)
High-risk FISH*, N (%)				
Present	11 (15)	2 (11)	4 (12)	5 (22)
Not Present	52 (71)	14 (78)	23 (72)	15 (65)
Unknown	10 (14)	2 (11)	5 (16)	3 (13)
Maintenance Therapy				
Maintenance lenalidomide dose$^{\beta}$, N (%)				
5 mg	4 (5)	0	4 (13)	0
10 mg	64 (88)	17 (94)	25 (78)	22 (96)
15 mg	3 (4)	1 (6)	2 (6)	0
Unknown	2 (3)	0	1 (3)	1 (4)
Post-maintenance daratumumab therapy				
Reponses to post maintenance regimen				
CR/VGPR	33 (45)	13 (72)	16 (50)	4 (17)
PR	15 (21)	2 (11)	7 (22)	6 (26)
MR/SD/PD	14 (19)	2 (11)	6 (19)	6(26)
Unknown	11 (15)	1 (6)	3 (9)	7 (31)
Toxicity to post-maintenance regimen^				
Hematological	15 (20)	5 (28)	6 (19)	4 (17)
Non-hematological	21 (29)	6 (33)	9 (28)	6 (26)

*High risk cytogenetics defined as del 17p, t(4;14) and/or t(14;16) $^{\beta}$Dose at the start of therapy ^All grade toxicity
Abbreviations: MM, multiple myeloma; ISS, international staging system; CR, complete response; VGPR, very good partial response; PR, partial response; MR minimal response; SD, stable disease; PD progressive disease; PFS progression free survival

Figure 1 PFS of Daratumumab based regimens post Len maintenance