Sequential use of Carfilzomib and Pomalidomide in Relapsed Multiple Myeloma: A Multi-Institutional Report from the Canadian Myeloma Research Group (CMRG) Database

Arleigh McCurdy [1], Christopher P Venner[2], Martha Louzada[3], Richard LeBlanc[4], Michael Sebag[5], Kevin Song[6], Victor H Jimenez-Zepeda[7], Rami Kotb[8], Esther Masih-Khan[9], Eshetu Atenafu[10], Hira Mian[11], Darrell White[12], Julie Stakiw[13], Muhammad Aslam[14], Anthony Reiman[15], Engin Gul[10], Donna Reece[9]

Introduction:
The treatment of relapsed multiple myeloma (MM) is not standardized due to both the heterogeneity of the illness and a data gap regarding the optimal sequencing of the available agents. Carfilzomib (CAR) and Pomalidomide (POM) are commonly used treatments for relapsed multiple myeloma (MM). However, the efficacy and optimal sequencing of each therapy with respect to one another is unknown. Therefore, the goal of our study was to understand the efficacy of two commonly used treatments in the relapsed setting: 1) POM after CAR based therapy and 2) CAR after POM based therapy.

Methods:
We performed a retrospective observational study using the Canadian Myeloma Research Group Database (CMRG-DB), analyzed up to 30/06/2020. The CMRG-DB (Formerly 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. All patients with MM who were treated for relapsed disease with approved regimens using POM after CAR, or CAR after POM were included. Our primary outcomes were overall response rates (ORR) in each respective cohort. Secondary outcomes were progression free survival (PFS), overall survival (OS), and a landmark OS analysis from treatment initiation with the first of the two agents. Survival was estimated using Kaplan-Meier methods and compared between groups using log rank test.

Results:
A total of 121 patients were included: 49 treated with POM after CAR, and 72 with CAR after POM. In the POM after CAR group, the median line of treatment was 4th for POM and 3rd for CAR. In the CAR after POM group, the median line of treatment was 4th for POM and 5th for CAR. In 79/121 patients (65%), the two therapies were directly sequential, 40/49 (82%) for the POM after CAR group, and 38/72 (54%) in the CAR after POM group. Baseline characteristics and treatment details are shown in Table 1.

The ORR was 51.35% for patients treated with POM after CAR, and 49.18% for patients treated with CAR after POM. The median PFS for POM after CAR was 4.93 months (95% CI, 2.76-7.07), and for CAR after POM was 5.36 months (95% CI, 3.75-6.94). The median OS for patients treated POM after CAR was 11.01 months (95% CI, 4.50-19.13), and for patients treated with CAR after POM the median OS was 10.98 months (95% CI, 8.98-19.17) (Figure 1). In a landmark analysis using the time of the treatment initiation with the first of the two agents, the median OS of patients treated with CAR after POM was 37.61 months (95% CI 26.66-46.52) and 25.32 months (95% CI 14.56-41.19) for patients treated with POM after CAR (p=0.1270) (Figure 2).

Conclusion:

In this real-world observational study, we demonstrated that Carfilzomib and Pomalidomide based therapies were effective treatment options for patients with advanced relapsed MM. The ORR and PFS rates were comparable to what has been observed in clinical trials leading to the approval of these agents in this setting. Further, a landmark analysis shows that using both agents sequentially late in treatment provided reasonable overall survival outcomes, regardless of the order in which they were sequenced. Further studies prospective studies could help optimize this challenging area.

Table 1: Baseline Characteristics and Treatment details

	All (N= 121)	POM after CAR (N=49/121)	CAR after POM (N=72/121)
Baseline Characteristics			
Age, median (range)			
Male, N (%)	71 (58.68)	26 (53.06)	45 (62.50)
MM Subtype, N (%)			
IgG	68 (59.13)	28 (60.87)	40 (57.97)
IgA	30 (26.09)	13 (28.26)	17 (24.64)
IgD	1 (0.87)	0 (0)	1 (1.45)
FLC	16 (13.91)	5 (10.87)	11 (15.94)
Unknown	6	3	3
ISS Stage, N (%)			
I	27 (29.56)	8 (19.51)	19 (34.55)
II	35 (38.99)	16 (39.02)	19 (34.55)
III	34 (31.45)	17 (41.46)	17 (30.91)
Unknown	25	8	17
High Risk FISH*, N (%)			
Present	24 (25.53)	15 (42.86)	9 (15.25)
Not Present	70 (74.47)	20 (57.14)	50 (84.75)
Unknown	27	14	13
Treatment			
Pomalidomide based			
PC	2 (1.65)	1 (2.04)	1 (1.39)
PCD	58 (47.93)	33 (67.35)	25 (34.72)
PCP	4 (3.31)	3 (6.12)	1 (1.39)
PD	52 (42.98)	11 (22.45)	41 (56.94)
PDB	1 (0.83)	0 (0)	1 (1.39)
PVD	4 (3.31)	1 (2.04)	3 (4.17)
Carfilzomib based			
K	7 (5.79)	1 (2.04)	6 (8.33)
KCD	20 (16.53)	12 (24.49)	8 (11.11)
KD	74 (61.16)	22 (44.90)	52 (72.22)
KP	2 (1.65)	0 (0)	2 (2.78)
KRD	18(14.88)	14 (28.57)	4 (5.56)

*High risk cytogenetics defined as del 17p, t(4;14) and/or t(14;16)

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, P, Pomalidomide; C, cyclophosphamide; D, dexamethasone; P, prednisone; V, bortezomib; K, carfilzomib; R, lenalidomide; B, biaxin

Figure 1: OS Analysis

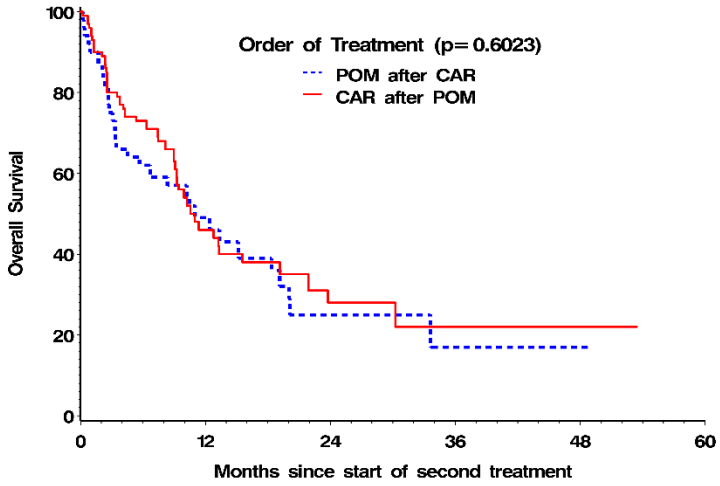

Figure 2: Landmark OS Analysis