Characterizing real-world treatment utilization and clinical outcomes in patients with relapsed/refractory multiple myeloma after lenalidomide and anti-CD38 exposure in the United States

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Introduction

- Guidelines for treatment of multiple myeloma (MM) include the use of lenalidomide (LEN) and an anti-CD38 monoclonal antibody (mAb) in early lines of treatment (LOT)[1]
- Given that treatment is recommended until progressive disease (PD), particularly for LEN and daratumumab (DARA), most patients will likely be refractory to one or both agents as early as the first progression, and subsequent outcomes for those patients are poor[2,3]
- With the anticipated introduction of novel treatments for patients previously exposed to LEN and anti-CD38 mAbs, an understanding of current clinical practices, treatment outcomes, and the existing standard of care is crucial in this population of patients with relapsed/refractory (RR) MM

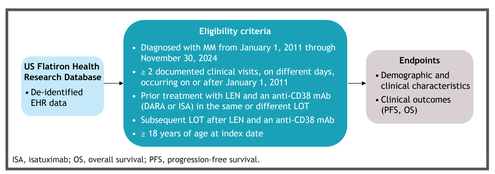
Objective

- To describe real-world treatment utilization and clinical outcomes in patients with RRMM treated with the most commonly prescribed regimens after exposure to LEN and an anti-CD38 mAb

Methods

- This retrospective study used the US-based, electronic health record (EHR)-derived Flatiron Health Research Database[4]
- Patient eligibility criteria are shown in **Figure 1**; prior treatment with LEN and an anti-CD38 mAb assumed RR status

Figure 1. Study design



ISA, isatuximab; OS, overall survival; PFS, progression-free survival.

- Refractoriness was defined as patients who progressed on current treatment, progressed within 60 days after the current LOT end date, or initiated subsequent LOT within 60 days after the current LOT end date without evidence of progression events, whichever came first
- The index date was defined as the date of initiation of the first treatment regimen after LEN and an anti-CD38 mAb
- The baseline period was defined as the time between MM diagnosis and the index date
- Baseline demographic and clinical characteristics and clinical outcomes (PFS and OS) were evaluated for the overall population and for patients receiving the 4 most commonly prescribed index regimens in this study
- Subgroup analyses were also conducted for PFS and OS according to LOT of index regimen and anti-CD38 mAb refractory status
- PFS and OS were estimated using the Kaplan-Meier method
  - PFS was defined as time from index date to next treatment, PD, or death, whichever occurred first
  - OS was defined as time from index date to death or end of follow-up (last documented clinical activity within the study period)

Results

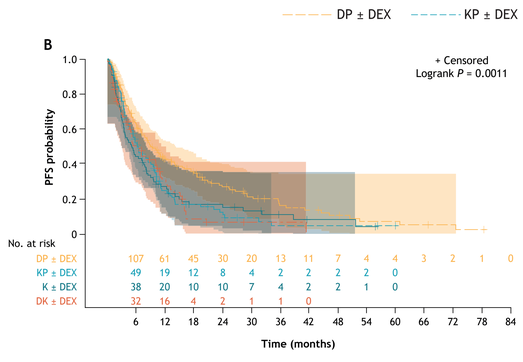
- Overall, 1684 patients with RRMM were included
- Demographic characteristics were similar across the 4 most frequent index regimens (± dexamethasone [DEX]): DARA + pomalidomide (POM) (DP ± DEX), carfilzomib (CFZ) + POM (KP ± DEX), CFZ (K ± DEX), and DARA + CFZ (DK ± DEX) (**Table 1**)
- K ± DEX was more frequently observed in combinations in the second and third LOTs (2L and 3L), whereas K ± DEX alone was more frequently seen in later LOTs (4L and 5L+; **Table 2**)
- A higher proportion of patients receiving K ± DEX had prior exposure to POM (51.1% vs 15.4% for DP ± DEX, 18.2% KP ± DEX, and 48.1% DK ± DEX)
- A lower proportion of patients receiving DP ± DEX were triple-class refractory (67.0% vs 75.5% KP ± DEX, 77.3% K ± DEX, and 82.7% DK ± DEX)

In this real-world study of patients with RRMM previously exposed to LEN and anti-CD38 mAbs, DP ± DEX, KP ± DEX, K ± DEX, and DK ± DEX were the most utilized regimens; however, survival outcomes were suboptimal with these 4 regimens, highlighting a significant unmet medical need

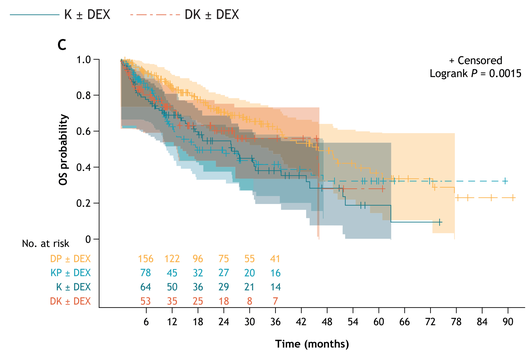
Figure 2. Most common index regimens (A), PFS (B), and OS (C) in patients with RRMM with prior LEN and anti-CD38 mAb treatment

A

Index regimen[a]	Patients, n (%) (N = 1684)
DP ± DEX	182 (10.8)
KP ± DEX	110 (6.5)
K ± DEX	88 (5.2)
DK ± DEX	81 (4.8)
BORT + DARA ± DEX	63 (3.7)
CFZ + cyclophosphamide ± DEX	55 (3.3)
POM ± DEX	53 (3.1)
DARA ± DEX	52 (3.1)
Elotuzumab + POM ± DEX	49 (2.9)
DARA + LEN ± DEX	42 (2.5)



	Overall	DP ± DEX	KP ± DEX	K ± DEX	DK ± DEX
Median PFS (95% CI), months	7.0 (6.5-7.5)	9.0 (7.4-12.2)	6.4 (5.1-9.1)	5.2 (3.4-7.6)	6.0 (4.7-10.2)



	Overall	DP ± DEX	KP ± DEX	K ± DEX	DK ± DEX
Median OS (95% CI), months	31.5 (27.9-35.4)	46.0 (37.2-58.0)	17.7 (12.3-44.3)	25.8 (16.9-37.3)	45.7 (13.5-NR)

[a]DARA index regimen includes those listed as "DARA/hyaluronidase". Shading represents 95% Hall-Wellner bands. CI, confidence interval; NR, not reached.

Table 1. Demographic and clinical characteristics

Characteristic	Overall (N = 1684)	DP ± DEX (n = 182)	KP ± DEX (n = 110)	K ± DEX (n = 88)	DK ± DEX (n = 81)
Age at index, years					
Mean	69	70	69	71	69
Median	70	71	71	74	70
Sex, n (%)					
Female	778 (46.2)	84 (46.2)	52 (47.3)	38 (43.2)	39 (48.1)
Male	906 (53.8)	98 (53.8)	58 (52.7)	50 (56.8)	42 (51.9)
Race, n (%)					
White	1023 (60.7)	110 (60.4)	67 (60.9)	45 (51.1)	48 (59.3)
Black/African American	306 (18.2)	40 (22.0)	24 (21.8)	25 (28.4)	7 (8.6)
Asian	52 (3.1)	5 (2.7)	2 (1.8)	4 (4.5)	2 (2.5)
Other[a]	173 (10.3)	9 (4.9)	8 (7.3)	4 (4.5)	9 (11.1)
Missing	130 (7.7)	18 (9.9)	9 (8.2)	10 (11.4)	15 (18.5)
Cytogenetic risk,[b] (%)					
High	597 (35.5)	45 (24.7)	47 (42.7)	34 (38.6)	32 (39.5)
Low	164 (9.7)	21 (11.5)	10 (9.1)	4 (4.5)	8 (9.9)
Uncertain	923 (54.8)	116 (63.7)	53 (48.2)	50 (56.8)	41 (50.6)

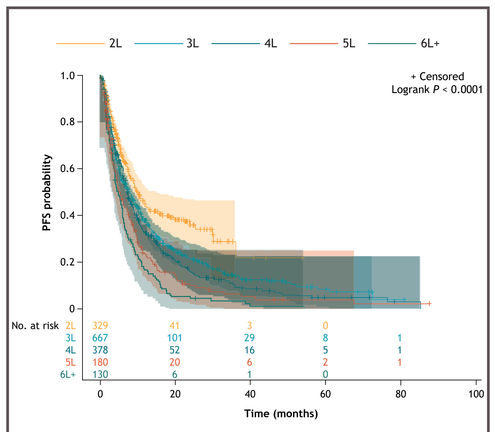
[a]Patients with race "Hispanic or Latino" and "Other race" were reported under "Other". [b]If any 1 of the 5 cytogenetic markers were present, risk was categorized as "High"; if all 5 markers were absent, risk was categorized as "Low"; otherwise, risk was categorized as "Uncertain". Percentages may not total 100% due to rounding.

Table 2. Prior treatment and refractory status

Characteristic	Overall (N = 1684)	DP ± DEX (n = 182)	KP ± DEX (n = 110)	K ± DEX (n = 88)	DK ± DEX (n = 81)
Prior MM treatment, n (%)					
LEN	1684 (100)	182 (100)	110 (100)	88 (100)	81 (100)
POM	514 (30.5)	28 (15.4)	20 (18.2)	45 (51.1)	39 (48.1)
BORT	1428 (93.8)	149 (92.0)	97 (96.0)	83 (96.5)	71 (95.9)
CFZ	436 (28.6)	41 (25.3)	12 (11.9)	11 (12.8)	11 (14.9)
Ixazomib	174 (11.4)	22 (13.6)	8 (7.9)	15 (17.4)	6 (8.1)
DARA	1655 (98.3)	180 (98.9)	109 (99.1)	88 (100)	79 (97.5)
ISA	29 (1.7)	2 (1.1)	1 (0.9)	0	2 (2.5)
Triple-class exposed[a], n (%)	1522 (90.4)	162 (89.0)	101 (91.8)	86 (97.7)	74 (91.4)
Prior refractory status[b], n (%)					
LEN + anti-CD38 mAb	1404 (83.4)	147 (80.8)	96 (87.3)	68 (77.3)	75 (92.6)
Triple-class refractory	1239 (73.6)	122 (67.0)	83 (75.5)	68 (77.3)	67 (82.7)
HSCT prior to index, n (%)	623 (37.0)	74 (40.7)	49 (44.5)	31 (35.2)	33 (40.7)
No. of prior LOTs, median	2	2	2	3	2
LOT at index, n (%)					
2L	329 (19.5)	22 (12.1)	23 (20.9)	9 (10.2)	18 (22.2)
3L	667 (39.6)	89 (48.9)	49 (44.5)	30 (34.1)	32 (39.5)
4L	378 (22.4)	46 (25.3)	26 (23.6)	28 (31.8)	18 (22.2)
5L+	310 (18.4)	25 (13.7)	12 (10.9)	21 (23.9)	13 (16.0)

[a]Immunomodulatory drug, proteasome inhibitor, and anti-CD38 mAb. [b]Refractory was defined as (LOT start < progression date ≤ LOT end) or (LOT start < progression date ≤ minimum [LOT end + 60 days, next LOT start]) or (LOT end < next LOT start ≤ LOT end + 60 days). Percentages may not total 100% due to rounding. BORT, bortezomib; HSCT, hematopoietic stem cell transplant.

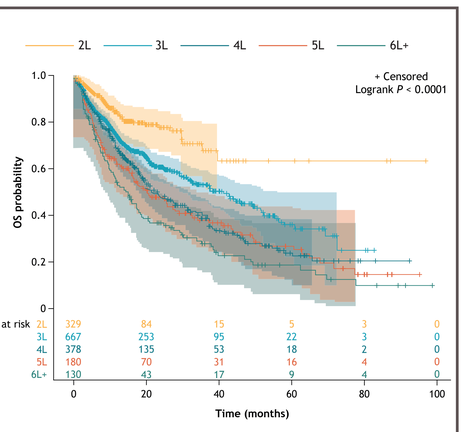
Figure 3. PFS by LOT at index



LOT	Patients, n	Median PFS (95% CI), months
2L	329	9.7 (8.1-12.2)
3L	667	7.5 (6.2-8.6)
4L	378	6.9 (6.3-8.1)
5L	180	5.1 (4.2-6.9)
6L+	130	4.8 (3.8-6.0)

Shading represents 95% Hall-Wellner bands. Index date ranged from 2015 to 2024.

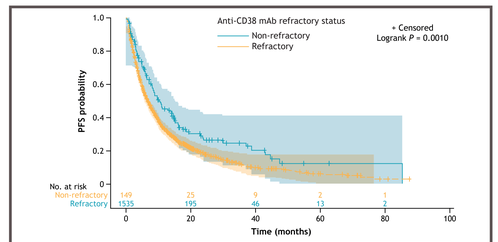
Figure 4. OS by LOT at index



LOT	Patients, n	Median OS (95% CI), months
2L	329	NR (39.5-NR)
3L	667	40.1 (31.5-49.2)
4L	378	23.2 (18.5-28.1)
5L	180	20.6 (15.5-27.9)
6L+	130	14.2 (10.0-18.1)

Shading represents 95% Hall-Wellner bands. Index date ranged from 2015 to 2024.

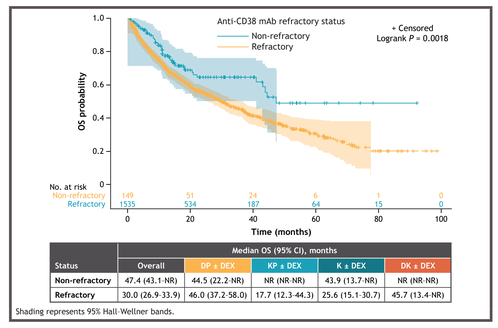
Figure 5. PFS by anti-CD38 mAb refractory status



Status	Median PFS (95% CI), months				
	Overall	DP ± DEX	KP ± DEX	K ± DEX	DK ± DEX
Non-refractory	10.4 (8.2-14.2)	44.5 (3.5-NR)	11.1 (5.9-NR)	5.2 (1.3-9.7)	16.1 (11.3-NR)
Refractory	6.7 (6.2-7.4)	8.9 (7.0-11.6)	6.4 (4.5-8.5)	5.2 (3.4-8.0)	5.4 (4.6-10.1)

Shading represents 95% Hall-Wellner bands.

Figure 6. OS by anti-CD38 mAb refractory status



Status	Median OS (95% CI), months				
	Overall	DP ± DEX	KP ± DEX	K ± DEX	DK ± DEX
Non-refractory	47.4 (43.1-NR)	44.5 (22.2-NR)	NR (NR-NR)	43.9 (13.7-NR)	NR (NR-NR)
Refractory	30.0 (26.9-33.9)	46.0 (37.2-58.0)	17.7 (12.3-44.3)	25.6 (15.1-30.7)	45.7 (13.4-NR)

Shading represents 95% Hall-Wellner bands.

Strengths and limitations

- Real-world EHR data from Flatiron Health Research Database provide contemporary, detailed demographic, clinical, and outcomes data across a geographically diverse US population
- Limitations inherent to using EHR data apply to this study, including incomplete data/medical history and potential errors in coding and natural language processing-based data extraction
- The data are derived from a US population mostly from community oncology practices, which may limit the applicability of the findings to other settings

Conclusions

- In this real-world study of patients with RRMM previously exposed to LEN and anti-CD38 mAbs, DP ± DEX was the most utilized regimen, followed by K ± DEX-containing regimens (KP ± DEX, K ± DEX, and DK ± DEX)
- Real-world survival outcomes were suboptimal in patients receiving these 4 treatments relative to clinical trial outcomes, with median PFS ranging from 5.2 to 9.0 months, highlighting a significant unmet medical need (**Figure 2**)
- Subgroup analyses showed that:
  - Median PFS and OS were shorter with each subsequent LOT from 2L to 6L+ (**Figure 3** and **Figure 4**)
  - Median PFS and OS were generally shorter in patients who were refractory to anti-CD38 mAbs than in those who were non-refractory (**Figure 5** and **Figure 6**)
- Number of prior LOTs, prior MM treatments, refractoriness to prior treatments, baseline patient characteristics, and other prognostic indicators should be considered when interpreting these results

References

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