Treatment Patterns Among Patients With Relapsed/Refractory Multiple Myeloma (RRMM) Receiving Second- and Third-Line Therapy in a Medicare Population

Poster No. MM-451

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Background

Treatment response and survival outcomes for patients with multiple myeloma (MM) diminish as patients advance through lines of therapy (LoT).[1-3]

While novel treatment classes have improved survival outcomes, treatment options for patients with relapsed or refractory MM (RRMM) are limited, partly due to prior exposure to multiple agents in prior LoTs, sometimes in doublet and triplet regimens.

When selecting subsequent treatment after each relapse, several factors such as the following may be considered.

- The patient's disease characteristics and progression, including cytogenetic risk and severity of previous relapse, which will influence the optimal treatment choice.[1]
- Patients should generally be treated with a regimen containing at least one drug class that they have not previously received.[1]
- Re-treatment with a previously used treatment class may be considered if the prior treatment provided a clinically meaningful response of adequate duration, although the risk of cumulative toxicity must be considered.[1]

Analyzing real-world treatment patterns in early LoTs in patients with RRMM may help identify the challenges physicians face in optimizing strategies with the available treatment options.

As MM primarily affects the elderly population, Medicare beneficiaries represent an appropriate population for investigation of real-world US treatment patterns.

Aim

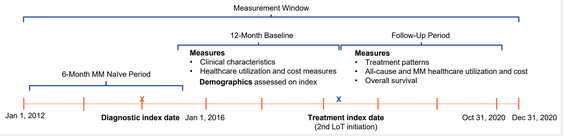
To describe treatment patterns in 2nd and 3rd LoTs as well as in different multiple exposure cohorts in US Medicare patients with RRMM.

Methods

Study design

This was a retrospective observational cohort study of adult patients with RRMM using data from the 100% US Medicare Fee-for-Service (FFS) claims database. The analysis included adult patients with ≥1 inpatient or ≥2 outpatient claims with a diagnosis code for MM (ICD-9 203.0, ICD-10 C90.0) between January 1, 2012 and December 31, 2020. Study design is shown in **Figure 1**.

Figure 1. Study design



All patients had evidence of treatment with ≥2 LoTs for MM after diagnostic index, with 2nd LoT beginning on or after January 1, 2016. Patients were excluded if they presented with a diagnosis of a primary cancer or had clinical trial participation during the study period.

Treatment patterns were assessed in the follow-up period across the following cohorts:

- **2nd LoT initiators:** Patients who began a 2nd LoT (full sample).
- **3rd LoT initiators:** Patients who began a 3rd LoT.
- **DCE:** Patients treated with only 2 drug classes in prior LoTs (exclusively double-class exposed).
- **TCE:** Patients treated with ≥3 drug classes in prior LoTs (triple-class exposed).

Results

Patient population and characteristics

A total of 4560 patients with MM were 2nd LoT initiators and qualified for inclusion in the study (**Table 1**). A subset of 1991 (44%) patients subsequently initiated a 3rd LoT during the study period.

- The mutually exclusive DCE and TCE cohorts included 2464 (54%) and 224 (5%) patients, respectively.
- Of the 3rd LoT initiator cohort, 1391 patients (70%) were identified as DCE and 215 (11%) patients as TCE.

The mean ± standard deviation (SD) age of the 2nd LoT initiator cohort was 75.1 ± 7.9 years, 48.4% were male, and 36% presented with a Charlson Comorbidity Index ≥4.

Prior treatments are shown in **Table 2**.

Table 1. Baseline demographics

	2nd LoT initiators (n=4560)	3rd LoT initiators (n=1991)	DCE (n=2464)*†‡	TCE (n=224)*
Male, n (%)	2205 (48.4)	929 (46.7)	1174 (47.7)	109 (48.7)
Age, years, mean (SD)	75.1 (7.9)	74.5 (7.7)	74.1 (7.3)	74.3 (6.9)
Charlson comorbidity index score 4+, n (%)	1646 (36.1)	669 (33.6)	790 (32.1)	65 (29.0)
Census region, n (%)				
South	1691 (37.1)	741 (37.2)	931 (37.8)	86 (38.4)
Midwest	1147 (25.2)	488 (24.5)	604 (24.5)	47 (21.0)
Northeast	860 (18.9)	388 (19.5)	465 (18.9)	49 (21.9)
West	854 (18.7)	368 (18.5)	457 (18.6)	42 (18.8)
Treatment index year, n (%)				
2020	1160 (25.4)	240 (12.1)	591 (24.0)	70 (31.3)
2019	1017 (22.3)	453 (22.8)	547 (22.2)	84 (37.5)
2018	900 (19.7)	459 (23.1)	518 (21.0)	45 (20.1)
Prior to and including 2017	2722 (59.7)	1358 (68.2)	1482 (60.1)	101 (45.1)
Follow-up duration from treatment index, months, mean (SD)	18.9 (14.7)	24.7 (14.6)	20.8 (15.0)	16.1 (9.8)

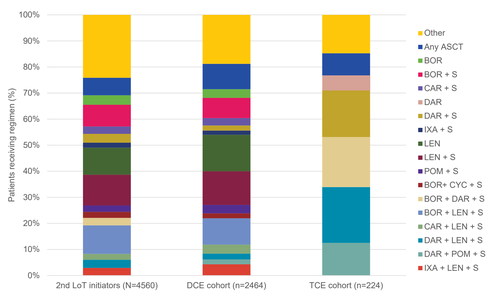
*DCE and TCE cohorts are reported for 2nd LoT only; †DCE patients had received only 2 drug classes in prior LoTs; ‡n=2103 for Charlson comorbidity index and prior treatments
DCE, double-class exposed; LoT, line of therapy; SD, standard deviation; TCE, triple-class exposed

Table 2. Prior treatments

	2nd LoT initiators (n=4560)	3rd LoT initiators (n=1991)	DCE (n=2464)*†	TCE (n=224)*
Time between diagnostic and treatment index, months, mean (SD)	16.9 (16.3)	24.2 (17.3)	15.9 (14.7)	16.0 (14.5)
Duration of therapy, months, mean (SD)	6.5 (7.0)	6.1 (6.6)	6.6 (7.2)	6.1 (6.0)
Time to next treatment, months, mean (SD)	8.7 (8.3)	7.4 (7.7)	9.0 (8.6)	6.8 (6.1)
Treatment gap, months, mean (SD)	2.2 (4.9)	1.3 (3.2)	2.5 (5.1)	0.8 (1.6)
Drug class, n (%)				
PI	2529 (55.5)	978 (49.1)	1308 (53.1)	77 (34.4)
Immunomodulatory agent	2820 (61.8)	1183 (59.4)	1662 (67.5)	115 (51.3)
Anti-CD38 monoclonal antibody	727 (15.9)	553 (27.8)	236 (9.6)	213 (95.1)
ASCT	329 (7.2)	82 (4.1)	240 (9.7)	19 (8.5)
Reason for LoT termination, n (%)				
Discontinuation	2317 (50.8)	898 (45.1)	1174 (47.7)	67 (29.9)
Switch	942 (20.7)	478 (24.0)	615 (25.0)	127 (56.7)
End of enrolment, study period or death	1301 (28.5)	615 (30.9)	675 (27.4)	30 (13.4)

*DCE and TCE cohorts are reported for 2nd LoT only; †DCE patients had received only 2 drug classes in prior LoTs.
ASCT, autologous stem cell transplant; DCE, double-class exposed; LoT, line of therapy; PI, protease inhibitor; SD, standard deviation; TCE, triple-class exposed

Figure 2. Percentage of patients receiving treatment regimens used at 2nd LoT in 2nd LoT initiators (N=4560) and in the DCE (n=2464) and TCE cohorts (n=224)*



*Other includes triplet therapies.
ASCT , autologous stem cell transplant; BOR, bortezomib; CAR, carfilzomib; CYC, cyclophosphamide; DAR, daratumumab; IXA, ixazomib; LEN, lenalidomide; LoT, line of therapy;
MEL, melphalan; POM, pomalidomide; S, steroids (dexamethasone, prednisone)

Treatment patterns

The mean ± SD time between diagnostic index date and treatment index date was 16.9 ± 16.3 months for 2nd LoT initiators and 24.2 ± 17.3 months for 3rd LoT initiators; the mean ±SD duration of therapy was 6.5 ± 7.0 months and 6.1 ± 6.6 months for each of the 2 cohorts, respectively.

At 2nd LoT, the most common regimens used at 2nd LoT were lenalidomide (LEN) + steroid (13%), bortezomib (BOR) + LEN + steroid (12%), and LEN (11%) (**Figure 3**).

- The most common 2nd LoT regimens in the DCE cohort (n=2464) were LEN (14%), LEN + steroid (13%), and BOR + LEN + steroid (10%).
- The most common 2nd LoT regimens in the TCE cohort (n=224) were daratumumab (DAR) + LEN + steroid (21%), BOR + DAR + steroid (19%), and DAR + steroid (18%).

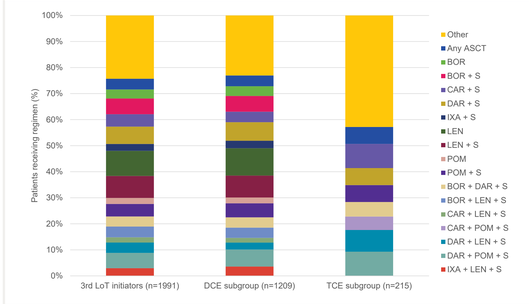
At 3rd LoT, the most commonly used regimens were LEN (10%), LEN + steroid (8%), and DAR + steroid (7%) (**Figure 4**).

- In the DCE cohort (n=1209), the most common 3rd LoT regimens were also LEN (10%), LEN + steroid (8%) and DAR + steroid (7%).
- In the TCE cohort (n=215), the most common 3rd LoT regimens were carfilzomib (CAR) + steroid (9%), DAR + pomalidomide (POM) + steroid (9%), and DAR + LEN + steroid (8%).

At both 2nd and 3rd LoT, the TCE cohort received triplet combinations more frequently than the DCE cohort, particularly those containing DAR.

Patients who received LEN at 3rd LoT were largely treated with LEN (27%) or BOR (40%) and/or received autologous stem cell transplant (ASCT, 44%) as part of their treatment in 2nd LoT; for those who received LEN at 2nd LoT, most were treated with BOR, LEN, or ASCT in some combination at 1st LoT (99%).

Figure 3. Percentage of patients receiving treatment regimens used at 3rd LoT in 3rd LoT initiators (n=1991) and in the DCE (n=1209) and TCE cohorts (n=215)*



*Other includes triplet therapies.
ASCT, autologous stem cell transplant; BOR, bortezomib; CAR, carfilzomib; CYC, cyclophosphamide; DAR, daratumumab; IXA, ixazomib; LEN, lenalidomide; LoT, line of therapy;
MEL, melphalan; POM, pomalidomide; S, steroids (dexamethasone, prednisone)

Key Takeaway

While the treatment landscape for RRMM is rapidly evolving, the pattern of increasing use of complex combination regimens in more treatment-exposed cohorts indicates an unmet need for novel treatment classes.

Conclusions

A broad range of regimens were used in 2nd and 3rd LoTs for patients with RRMM; selection of regimens appeared more complex in 2nd and 3rd LoTs and for patients who had prior exposure to 2 or 3 drug classes.

Bortezomib and lenalidomide were the most prevalent treatment regimens in 2nd and 3rd LoTs, along with daratumumab in 3rd LoT.

Over the study period, retreatment with individual treatment classes and combinations may have contributed to the high proportions of patients using lenalidomide and bortezomib in 3rd LoT settings; further investigation would be necessary to understand the extent of this specific effect.

Abbreviations

BOR, bortezomib; CAR, carfilzomib; CYC, cyclophosphamide; DAR, daratumumab; DCE, double-class exposed, not triple class exposed; FFS, Fee-for-Service; IXA, ixazomib; LEN, lenalidomide; LoT, line of therapy; MEL, melphalan; MM, multiple myeloma; POM, pomalidomide; RRMM, relapsed or refractory multiple myeloma; S, steroids; SD, standard deviation; TCE, triple-class exposed

Disclosures

JT, **WJ**, and **AS** are employees of Inovalon. **BG**, **NB**, **PFW**, **SP**, **SL**, **MH**, and **PP** are employees of GSK and hold stocks/shares in GSK. **AM** is an employee of Rutgers University.

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