Real-World Treatment Characteristics and Clinical Outcomes in Medicare Beneficiaries with Newly Diagnosed Multiple Myeloma (NDMM) Treated with Bortezomib in Combination with Lenalidomide and Dexamethasone (VRd)

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Background

- The triple combination of bortezomib, lenalidomide, and dexamethasone (VRd) has become a standard of care for patients with newly diagnosed multiple myeloma (NDMM).[1]
- VRd is used as an induction regimen in both transplant-eligible and ineligible patients.[1, 2]
- Comprehensive real-world data reporting treatment characteristics and clinical outcomes in patients with NDMM receiving VRd are lacking.

Objectives

- This study assessed patient and treatment characteristics (including duration of therapy [DoT] and time to next treatment [TTNT]) and clinical outcomes (including real-world progression-free survival [rwPFS] and overall survival [rwOS]) during the first line (1L) in patients with NDMM (overall sample) and those receiving VRd in the 1L, stratified by the stem cell transplant (SCT) status.

Methods

- This retrospective cohort study included adult patients (≥18 years) who were diagnosed with multiple myeloma (MM), on continuous Parts A, B, and D coverage, and initiated 1L MM treatment between January 01, 2012 and December 31, 2018, using the Medicare Research Identifiable Files. This constituted the overall MM sample, which served as a reference while evaluating the results of patients who received VRd in 1L.
- Patients meeting the sample selection criteria were analyzed and stratified by the SCT status. Patient characteristics, Charlson Comorbidity Index (CCI) score, MM-associated comorbidities, treatment patterns (DoT and TTNT), and clinical outcomes (rwPFS and rwOS) were reported.
- For rwPFS, patients were observed from the line of treatment (LoT) initiation to the first event (next LoT initiation as proxy of disease progression) before subsequent LoT initiation (excluding SCT) or death (i.e., event), or the observation period was censored at the end of follow-up.
- For rwOS, patients were observed from the LoT initiation to death (i.e., event), or the observation period was censored at the end of follow-up.
- rwPFS and rwOS were estimated using the Kaplan–Meier (KM) method.
- Continuous measurements were summarized as the mean, standard deviation (SD), and median; categorical variables were presented as frequency and percentages.

Results

Patient characteristics

- A total of 13,573 patients diagnosed with MM (overall sample) were included between 2012 and 2018, of which 31.4% received VRd. Between 2016 and 2018, 43.9% of patients received VRd.
- Irrespective of the SCT status, patients receiving VRd were younger than those in the overall sample. In addition, a slight preponderance of female patients was observed in both overall sample (53.0%) and patients treated with VRd (50.7%) (**Table 1**).
- The proportion of patients receiving VRd in the 1L increased from 18.5% in 2016 to 24.2% in 2018 (**Table 1**).

Table 1: Patient characteristics among MM patients in 1L

Patient characteristic	Patients with MM receiving VRd			Patients with MM (overall sample)		
	1L (*n* = 4,266)	1L with SCT (*n* = 618)	1L without SCT (*n* = 3,648)	1L (*n* = 13,573)	1L with SCT (*n* = 1,332)	1L without SCT (*n* = 12,241)
Age, mean (SD), years	73.1 (7.3)	69.9 (5.4)	73.7 (7.5)	74.9 (8.4)	70.8 (7.4)	75.3 (8.4)
Female, n (%)	2,162 (50.7%)	295 (47.7%)	1,867 (51.2%)	7,199 (53.0%)	634 (47.6%)	6,565 (53.6%)
Calendar year, n (%)						
2012–2015	1,510 (35.4%)	285 (46.1%)	1,225 (33.6%)	7,293 (53.7%)	869 (65.2%)	6,424 (52.5%)
2016	788 (18.5%)	114 (18.4%)	674 (18.5%)	2,171 (16.0%)	173 (13.0%)	1,998 (16.3%)
2017	936 (21.9%)	139 (22.5%)	797 (21.8%)	2,087 (15.4%)	186 (14.0%)	1,901 (15.5%)
2018	1,032 (24.2%)	80 (12.9%)	952 (26.1%)	2,022 (14.9%)	104 (7.8%)	1,918 (15.7%)
MM with prior smoldering[a] MM, n (%)	437 (10.2%)	55 (8.9%)	382 (10.5%)	2,007 (14.8%)	153 (11.5%)	1,854 (15.1%)

[a]Smoldering MM was defined as a diagnosis for MM that occurred >365 days before the start of the 1L.
1L, first line; MM, multiple myeloma; n, number of patients; SD, standard deviation; SCT, stem cell transplant; VRd, bortezomib + lenalidomide + dexamethasone.

Comorbidity profile

- Patients receiving VRd were observed to have lower comorbidity burden and mean CCI score than the overall sample (**Table 2**).
- The most prevalent comorbidities in patients receiving VRd compared with the overall sample were cardiovascular disease (79.1% vs. 82.6%), hypertension (77.6% vs. 80.7%), and chronic pain/fibromyalgia (64.8% vs. 64.0%).

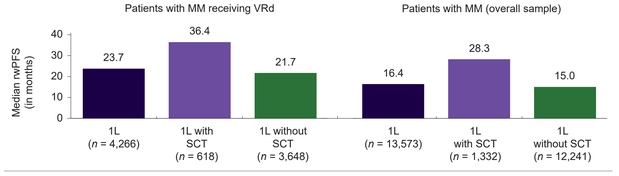
Table 2: Comorbidity profile in MM patients in 1L

	Patients with MM receiving VRd			Patients with MM (overall sample)		
	1L (*n* = 4,266)	1L with SCT (*n* = 618)	1L without SCT (*n* = 3,648)	1L (*n* = 13,573)	1L with SCT (*n* = 1,332)	1L without SCT (*n* = 12,241)
CCI, mean (SD)	2.4 (2.2)	2.2 (1.9)	2.5 (2.2)	3.0 (2.2)	2.8 (2.1)	3.0 (2.2)
MM-associated comorbidities (CRAB), n (%)						
Anemia	1,282 (30.1%)	155 (25.1%)	1,127 (30.9%)	4,468 (32.9%)	404 (30.3%)	4,064 (33.2%)
Hypercalcemia	741 (17.4%)	102 (16.5%)	639 (17.5%)	2,270 (16.7%)	219 (16.4%)	2,051 (16.8%)
Renal impairment	1,329 (31.2%)	150 (24.3%)	1,179 (32.3%)	5,582 (41.1%)	465 (34.9%)	5,117 (41.8%)
Skeletal-related events	1,257 (29.5%)	176 (28.5%)	1,081 (29.6%)	3,610 (26.6%)	354 (26.6%)	3,256 (26.6%)

1L, first line; CCI, Charlson Comorbidity Index; CRAB, calcium elevation, renal insufficiency, anemia, and bone abnormalities; MM, multiple myeloma; n, number of patients; SD, standard deviation; SCT, stem cell transplant; VRd, bortezomib + lenalidomide + dexamethasone.

Clinical outcomes

- The median rwPFS was longer in patients receiving VRd than in the overall sample in 1L (23.7 vs. 16.4 months, with SCT [36.4 vs. 28.3 months] or without SCT [21.7 vs. 15.0 months]) (**Figure 1**).

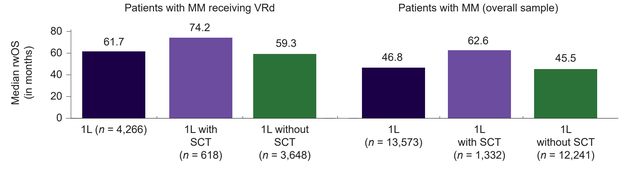


	1L (*n* = 4,266)	1L with SCT (*n* = 618)	1L without SCT (*n* = 3,648)	1L (*n* = 13,573)	1L with SCT (*n* = 1,332)	1L without SCT (*n* = 12,241)
1-year KM rates (95% CI)	71.2 (69.7, 72.6)	88.1 (85.2, 90.5)	67.9 (66.2, 69.6)	59.0 (58.1, 59.8)	82.6 (80.4, 84.6)	56.2 (55.3, 57.1)
Patients at risk (%)	51.6%	74.6%	47.7%	47.9%	74.2%	45.0%
2-year KM rates (95% CI)	49.6 (47.8, 51.4)	66.3 (61.9, 70.4)	46.3 (44.3, 48.3)	38.1 (37.2, 39.0)	56.9 (54.0, 59.8)	35.9 (34.9, 36.8)
Patients at risk (%)	24.4%	40.1%	21.7%	24.2%	41.1%	22.4%

Figure 1: Real-world progression-free survival in MM patients in 1L

1L, first line; CI, confidence interval; KM, Kaplan–Meier; MM, multiple myeloma; rwPFS, real-world progression-free survival; SCT, stem cell transplant; VRd, bortezomib + lenalidomide + dexamethasone.

- The median rwOS was also longer in patients receiving VRd than in the overall sample in 1L (61.7 vs. 46.8 months, with SCT [74.2 vs. 62.6 months] or without SCT [59.3 vs. 45.5 months]) (**Figure 2**).



	1L (*n* = 4,266)	1L with SCT (*n* = 618)	1L without SCT (*n* = 3,648)	1L (*n* = 13,573)	1L with SCT (*n* = 1,332)	1L without SCT (*n* = 12,241)
1-year KM rates (95% CI)	89.0 (88.0, 90.0)	95.5 (93.5, 96.9)	87.8 (86.6, 88.9)	83.0 (82.3, 83.6)	88.5 (86.7, 90.2)	82.3 (81.6, 83.0)
Patients at risk (%)	65.3%	81.4%	62.5%	68.2%	79.9%	66.9%
2-year KM rates (95% CI)	79.2 (77.7, 80.6)	87.9 (84.6, 90.5)	77.5 (75.8, 79.1)	70.1 (69.2, 70.9)	77.9 (75.3, 80.1)	69.2 (68.2, 70.1)
Patients at risk (%)	39.7%	53.4%	37.4%	45.1%	56.5%	43.9%

Figure 2: Real-world overall survival in MM patients in 1L

1L, first line; CI, confidence interval; KM, Kaplan–Meier; MM, multiple myeloma; rwOS, real-world overall survival; SCT, stem cell transplant; VRd, bortezomib + lenalidomide + dexamethasone.

Treatment patterns

- During the 1L, patients who received VRd had a longer DoT, by ~1 month (median: 7.7 vs. 6.3 months), and TTNT, by ~3 months (median: 12.2 vs. 9.2 months), than the overall sample (**Table 3**).

Table 3: Treatment pattern in MM patients in 1L

	Patients with MM receiving VRd			Patients with MM (overall sample)		
	1L (*n* = 4,266)[a]	1L with SCT (*n* = 618)	1L without SCT (*n* = 3,648)	1L (*n* = 13,573)[a]	1L with SCT (*n* = 1,332)	1L without SCT (*n* = 12,241)
DoT[a], median (months)	7.7	14.8	6.9	6.3	12.9	5.7
TTNT[b], median (months)	12.2	--	--	9.2	--	--

[a]Among patients who received VRd in 1L, 37.2% were still on the LoT when assessing DoT (DoT was assessed including patients still on the line at the end of data, and DoT might have been underestimated due to data availability); in the overall sample, 21.8% were still on 1L when assessing DoT.
[b]TTNT was assessed among patients observed with a next LoT: VRd, *n* = 1,403 (32.9%); overall sample, *n* = 5,534 (40.8%). TTNT might have been underestimated due to data availability.
1L, first line; DoT, duration of treatment; LoT, line of treatment; SD, standard deviation; SCT, stem cell transplant; TTNT, time to next treament; VRd, bortezomib + lenalidomide + dexamethasone.

Limitations

- These results are not representative of patients with MM with commercial or no health insurance.
- Claims data in real-world analyses inherently reflect the individual decisions of physicians as they evaluate and treat patients, which differ from the controlled and standardized methods used in clinical studies.
- Laboratory results, risk stratification of MM cases, and clinical information (e.g., disease stage, cytogenetic risk status, and performance status) were not available from the claims data.
- Since clinical information was not available, the next LoT initiation was used as a proxy for progression (in addition to death event) in the rwPFS analysis, which could have led to misclassifications of toxicity-based treatment switches as an indication of disease progression.
- There was a lack of data availability for daratumumab in the front-line treatment comparators as data were collected between 2012 and 2018.

Conclusions

- In the real-world setting, NDMM Medicare beneficiaries receiving VRd had a lower comorbidity burden and better clinical outcomes than the overall sample in 1L, irrespective of the SCT status.
- The median rwPFS and rwOS were shorter than that in clinical trials evaluating VRd as a standard frontline treatment among patients with NDMM with no intent to transplant/no transplant (SWOGS0777; VRd superior to Rd [median PFS: 41.0 vs. 29.0 months; median OS: not reached vs. 69.0 months])[2] as well as in transplant-eligible patients (IFM2009; VRd+SCT superior to VRd [median PFS: 50.0 vs. 36.0 months; median OS: not reached in either group]).[3]
- Early initiation of therapeutic regimens with good efficacy and minimal toxicity may help improve clinical outcomes in patients with NDMM.

References

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Conflicts of Interest

JR: A member of Speakers Bureau: Janssen, Celgene, Adaptive Biotechnologies; Consulting/Advisory Board: Celgene, Janssen, BMS, Karyopharm, Antengene, Sanofi, X4 Pharmaceuticals, Oncopeptides, Adaptive Biotechnologies, Secura Bio, and AstraZeneca.

DLV: Employee of Analysis Group, which received funding from Sanofi for this research.

ES, PL, and CT: Employees and stockholders of Sanofi.

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