3760

Real-World Characteristics and Treatment Patterns of Transplant-Eligible Patients with Newly Diagnosed Multiple Myeloma Treated with Daratumumab, Bortezomib, Lenalidomide, and Dexamethasone (DVRd) as Front-line Treatment: Results from A Multicenter Chart Review Study

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Key Takeaway

This real-world study complements evidence from the PERSEUS[1] and GRIFFIN[2] clinical trials, indicating that DVRd is an effective FL treatment regimen in TE NDMM patients, with favorable outcomes when D is added to R maintenance.

Conclusions

- Compared to patients in the pivotal clinical trials, the TE NDMM patients treated with FL DVRd identified in this real-world study were largely similar, with the exception of DVRd patients being older in the real world.
- DR maintenance was more commonly used in the older patients and in patients with high-risk disease, however it was less frequently used in Black or African American patients.
- Although all patients enrolled in this study were deemed TE, only 67% received an SCT, with transplant deferral being the most common reason for not receiving FL SCT.
- Patients who received DR maintenance had a higher CR+ rate and longer TTNT compared to those who received R-only maintenance.

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Introduction

- On July 30, 2024, the Food and Drug Administration approved DVRd for induction and consolidation in transplant-eligible (TE) patients with newly diagnosed multiple myeloma (NDMM) based on the results from the PERSEUS and GRIFFIN studies.
- Both studies showed that the addition of daratumumab, a CD38-directed monoclonal antibody, to VRd (the DVRd regimen) during induction/consolidation followed by daratumumab + lenalidomide (DR) maintenance improved response rates and minimal residual disease (MRD) negativity rates, as well as progression-free survival compared to VRd followed by lenalidomide only (R) maintenance[1,2], leading to a current shift in treatment paradigm from front-line (FL) triplet therapy to daratumumab-based quadruplets.
- However, patient characteristics and treatment patterns, including maintenance therapy selection, may differ in the real-world setting compared to clinical trials.
- This study aimed to describe the real-world demographic and clinical characteristics as well as treatment patterns (overall and stratified by maintenance regimen [i.e., DR and R maintenance]) among TE NDMM patients treated with DVRd as FL therapy.

Methods

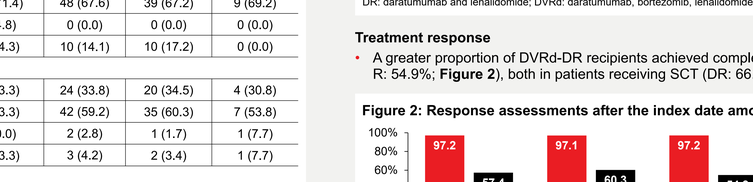
Data source and study design

- A retrospective multi-center chart review study was conducted at 10 clinical sites in the United States.
- All eligible adults who initiated FL DVRd therapy for treating TE NDMM between January 1, 2019, and June 30, 2022, were included.
  - Except at one site, where eligible patients were randomly selected because of an abundance of eligible patients

Inclusion criteria

- Confirmed NDMM (must meet at least 1 SLiM CRAB criterion[3] at the time of diagnosis)
- Were eligible for stem cell transplant (SCT) at MM diagnosis per physician assessment
- Received DVRd (first date of administration defined as index date; **Figure 1**) as FL therapy between January 1, 2019, and June 30, 2022
- Aged ≥18 years as of index date

Figure 1: Study design schema



DVRd: daratumumab, bortezomib, lenalidomide, and dexamethasone; MM: multiple myeloma

Exclusion criteria

- Received/initiated any recommended treatment for MM (except corticosteroids) for more than 30 days prior to the index date
- Initiated FL DVRd treatment more than one year after initial MM diagnosis
- Participated in an interventional clinical trial related to MM prior to the index date
- Had any invasive malignancy other than MM during the baseline period (except for basal and squamous cell carcinomas and carcinomas in-situ)
- Previously diagnosed with amyloidosis

Limitations

- Data was recorded as part of routine care and not for research purposes; thus, some information may be missing.
- There may be differences in missingness across sites.
- The data analyzed for this study are limited to the information collected in records and medical charts available at the sites, which do not constitute a closed system.

Results

Patient characteristics

- Baseline characteristics of FL DVRd recipients were similar to patients in the GRIFFIN[2] trial.
- 216 FL DVRd patients were included, of whom 176 initiated maintenance, including 68 with DR maintenance ("DVRd-DR recipients") and 71 with R maintenance ("DVRd-R recipients").
- DVRd-DR recipients were older than DVRd-R recipients (median age DR: 65 years, R: 62 years; **Table 1**).
- DVRd-DR seemed to be used less frequently in Black or African American patients compared to DVRd-R (DR: 5.9%, R: 14.1%; **Table 1**).
- In comparison with DVRd-R recipients, DVRd-DR recipients had:
  - Lower ECOG score (ECOG=0; DR: 47.1%, R: 33.8%)
  - Higher Revised ISS disease stage (stage III MM: DR: 13.2%, R: 5.6%)
  - Slightly higher rate of high cytogenetic risk abnormalities (DR: 13.2%, R: 11.3%)
- The patients who did not receive SCT were older than those who did, and the DVRd-DR recipients without SCT had more high cytogenetic risk disease compared to the DVRd-R recipients without SCT (**Table 1**).

Table 1: Baseline demographic and clinical characteristics overall and by maintenance therapy and receipt of SCT

	DVRd N=216	DVRd-DR N=68	DVRd-DR (SCT) N=47	DVRd-DR (No SCT) N=21	DVRd-R N=71	DVRd-R (SCT) N=58	DVRd-R (No SCT) N=13
Age (years), median [IQR]	63 [55-68]	65 [56-68]	62 [54-67]	69 [66-72]	62 [54-69]	62 [54-67]	69 [62-72]
Age ≥65, n (%)	99 (45.8)	36 (53.0)	18 (38.3)	18 (85.7)	29 (40.8)	21 (36.2)	8 (61.6)
Male, n (%)	124 (57.4)	44 (64.7)	31 (66.0)	13 (61.9)	38 (53.5)	31 (53.4)	7 (53.8)
Race, n (%)							
Asian	15 (6.9)	5 (7.4)	3 (6.4)	2 (9.5)	3 (4.2)	3 (5.2)	0 (0.0)
Black or African American	28 (13.0)	4 (5.9)	4 (8.5)	0 (0.0)	10 (14.1)	6 (10.3)	4 (30.8)
White	141 (65.3)	48 (70.6)	33 (70.2)	15 (71.4)	48 (67.6)	39 (67.2)	9 (69.2)
Other	2 (0.9)	1 (1.5)	0 (0.0)	1 (4.8)	0 (0.0)	0 (0.0)	0 (0.0)
Unknown	30 (13.9)	10 (14.7)	7 (14.9)	3 (14.3)	10 (14.1)	10 (17.2)	0 (0.0)
ECOG score, n (%)							
0	94 (43.5)	32 (47.1)	25 (53.2)	7 (33.3)	24 (33.8)	20 (34.5)	4 (30.8)
1 or 2	98 (45.4)	28 (41.2)	21 (44.7)	7 (33.3)	42 (59.2)	35 (60.3)	7 (53.8)
3 or 4	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.8)	1 (1.7)	1 (7.7)
Unknown	22 (10.2)	8 (11.8)	1 (2.1)	7 (33.3)	3 (4.2)	2 (3.4)	1 (7.7)
Revised ISS stage, n (%)							
I	30 (13.9)	14 (20.6)	11 (23.4)	3 (14.3)	12 (16.9)	11 (19.0)	1 (7.7)
II	50 (23.1)	15 (22.1)	15 (31.9)	0 (0.0)	17 (23.9)	16 (27.6)	1 (7.7)
III	24 (11.1)	9 (13.2)	6 (12.8)	3 (14.3)	4 (5.6)	4 (6.9)	0 (0.0)
Unknown	112 (51.8)	30 (44.1)	15 (31.9)	15 (71.4)	38 (53.5)	27 (46.5)	11 (84.6)
Cytogenetic risk, n (%)							
High risk[1]	44 (20.4)	9 (13.2)	3 (6.4)	6 (28.6)	8 (11.3)	8 (13.8)	0 (0.0)
Standard risk	143 (66.2)	52 (76.5)	40 (85.1)	12 (57.1)	45 (63.4)	35 (60.3)	10 (76.9)
Unknown	29 (13.4)	7 (10.3)	4 (8.5)	3 (14.3)	18 (25.4)	15 (25.9)	3 (23.1)

DR: daratumumab and lenalidomide; DVRd: daratumumab, bortezomib, lenalidomide, and dexamethasone; ECOG: Eastern Cooperative Oncology Group; IQR: interquartile range; ISS: International Staging System; R: lenalidomide; SCT: stem cell transplant

Notes:
1. Presence of del17p, t[14;16], t[14;20], or t[4;14] abnormalities.

Treatment patterns

- Of the 216 patients that were considered as TE per physician assessment, 144 (66.7%) DVRd patients actually received an FL SCT (**Table 2**).
  - DVRd-DR recipients with SCT: n=47 (69.1% of 68)
  - DVRd-R recipients with SCT: n=58 (81.7% of 71)
  - Other types of maintenance or no maintenance with SCT: n=39 (50.6% of 77)
- Of the 51 DVRd patients who deferred SCT, 20 (39.2%) went straight to maintenance therapy.
  - 14 (70.0%) received >1 agent
- More DVRd-DR recipients deferred SCT (25.0%) compared with DVRd-R recipients (16.9%; **Table 2**).
- More DVRd-DR recipients received DVRd consolidation therapy following SCT (17.6%) than DVRd-R recipients (1.4%; **Table 2**).
- In addition to R and DR, maintenance regimens included VR (n=11), DV (n=7), DVR (n=8), D (n=5), V (n=4), R to V (n=1), R to D (n=1).
  - Due to the small sample size for these regimens, further analyses would be limited.

Table 2: Treatment patterns during FL DVRd therapy overall and by maintenance therapy

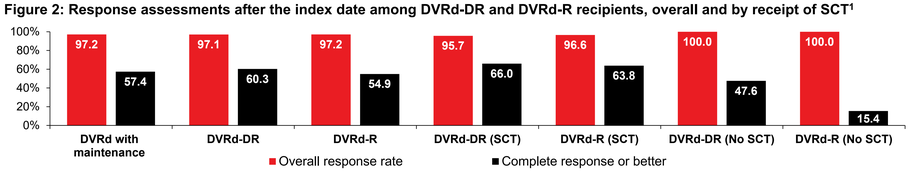
	DVRd N=216	DVRd-DR N=68	DVRd-R N=71
Length of follow-up (months), mean ± SD [median]	29.1 ± 8.3 [26.7]	28.3 ± 7.5 [26.5]	29.5 ± 8.2 [27.5]
Duration of induction phase (months), mean ± SD [median]	7.3 ± 4.7 [6.5]	6.4 ± 2.1 [6.4]	7.0 ± 3.2 [6.4]
Transplant			
Received an SCT during FL, n (%)	144 (66.7)	47 (69.1)	58 (81.7)
Did not receive an SCT, n (%)	71 (32.9)	21 (30.9)	13 (18.3)
Declined	10 (4.6)	4 (5.9)	1 (1.4)
Deferred	51 (23.6)	17 (25.0)	12 (16.9)
Unknown reason	10 (4.6)	0 (0.0)	0 (0.0)
Unknown SCT status, n (%)	1 (0.5)	0 (0.0)	0 (0.0)
Received DVRd consolidation, n (%)	18 (8.3)	12 (17.6)	1 (1.4)
Received maintenance, n (%)	176 (81.5)	68 (100.0)	71 (100.0)

DR: daratumumab and lenalidomide; DVRd: daratumumab, bortezomib, lenalidomide, and dexamethasone; FL: front-line; R: lenalidomide; SCT: stem cell transplant; SD: standard deviation

Treatment response

- A greater proportion of DVRd-DR recipients achieved complete response or better (CR+) compared to DVRd-R recipients (DR: 60.3%, R: 54.9%; **Figure 2**), both in patients receiving SCT (DR: 66.0%, R: 63.8%) as well as in patients not receiving SCT (DR: 47.6%, R: 15.4%).

Figure 2: Response assessments after the index date among DVRd-DR and DVRd-R recipients, overall and by receipt of SCT[1]



DR: daratumumab and lenalidomide; DVRd: daratumumab, bortezomib, lenalidomide, and dexamethasone; R: lenalidomide; SCT: stem cell transplant

Notes:
1. Response rates are shown only for patients who had at least one response assessment.

Time to next treatment

- Kaplan-Meier rates of patients who did not initiate the next line of therapy at 30 months were 87.9% among DVRd-DR recipients and 84.7% among DVRd-R recipients.
  - Among SCT recipients, rates were 91.1% and 85.3%, respectively.
  - Among non-SCT recipients, rates were 80.4% and 69.2%, respectively.

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Multiple Myeloma

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