

Effectiveness of Daratumumab plus Bortezomib, Lenalidomide, and Dexamethasone Versus VRd as Frontline Treatment for Transplant-Eligible Newly Diagnosed Multiple Myeloma: A Chart Review Study

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Key Takeaway

These findings highlight the clinical effectiveness of the daratumumab-based quadruplet regimen DVRd in real-world clinical practice, underscoring its superiority over VRd as frontline (FL) treatment for TE patients with NDMM

Conclusions

In this real-world, multicenter chart review study, TE patients with NDMM treated with FL DVRd-DR/R had a 63% lower risk of disease progression or death (HR: 0.37; 95% CI: 0.17–0.80; P=0.006) compared with those treated with FL VRd-R

These real-world findings are consistent with the pivotal PERSEUS and GRIFFIN trials

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Poster

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Introduction

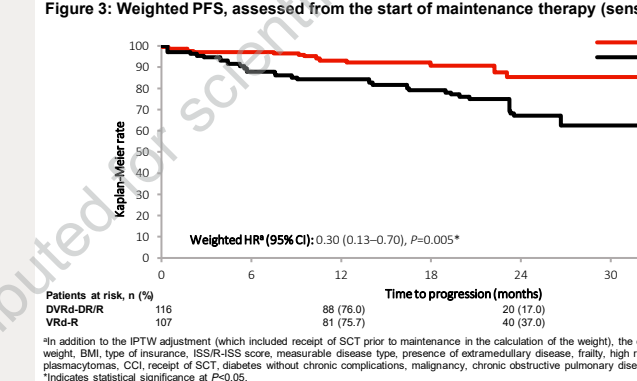
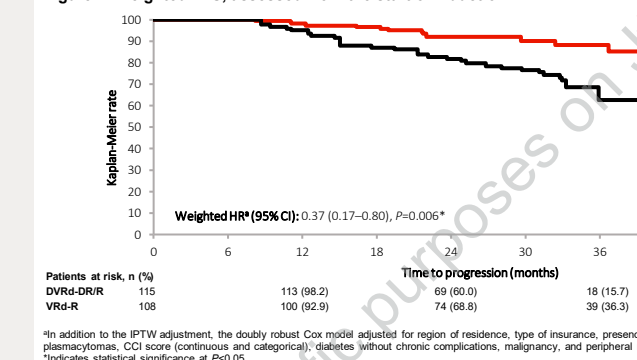
- In July 2024, the US Food and Drug Administration (FDA) approved the quadruplet regimen of daratumumab (D) in combination with bortezomib (V), lenalidomide (R), and dexamethasone (d; DVRd) for induction and consolidation in transplant-eligible (TE) patients with newly diagnosed multiple myeloma (NDMM) based on results from the PERSEUS and GRIFFIN trials¹
 - These pivotal trials demonstrated that DVRd during induction/consolidation followed by DR maintenance yielded improved minimal residual disease (MRD) negativity rates and progression-free survival (PFS) compared with VRd followed by R maintenance^{2,3}
- In light of these findings, a change in the FL treatment strategy for TE patients has been observed, more specifically, a shift from triplet regimens (eg, VRd) to quadruplet regimens (eg, DVRd)
- While improved efficacy with DVRd over VRd has been established in these pivotal trials, there is a need to assess the comparative effectiveness in the real-world setting

Objective

- To compare PFS among TE patients with NDMM receiving DVRd induction/consolidation plus DR or R maintenance (DVRd-DR/R) versus VRd induction/consolidation plus R maintenance (VRd-R) in the real world

Methods

- Study design and population**
 - A retrospective, multi-center chart review study was conducted at 10 clinical sites in the US
 - Inclusion criteria: Adult TE (based on physician assessment) patients with NDMM who initiated FL DVRd-DR/R or VRd-R between 1/1/2020 and 6/30/2022
 - DR and R maintenance were both examined in those with DVRd induction/consolidation, as both regimens are common in the real world
 - Exclusion criteria: Previously received any MM treatment for ≥30 days; participated in an MM-related clinical trial; treated for another invasive malignancy <12 months prior to induction; had amyloid light-chain amyloidosis at induction
 - The index date was defined as the date of initiation of FL DVRd or VRd and patients were followed up to the earliest of the date of death, date of last clinical activity (ie, last available assessment at the site), or the last date of data collection (ie, 10/28/2024; Figure 1)
- Statistical analysis**
 - Descriptive statistics were used to assess patient characteristics and compared using standardized differences (<10% = balanced)
 - Inverse probability of treatment weighting (IPTW) was used to balance differences in baseline characteristics between cohorts
 - A Kaplan-Meier (KM) analysis was conducted to assess PFS
 - PFS: time from the index date until disease progression or death
 - A sensitivity analysis was conducted whereby PFS was assessed from the initiation of maintenance until disease progression or death
 - Patients were censored at the end of maintenance therapy, date of last clinical activity, or the last date of data collection
 - A doubly-robust Cox proportional hazards model, additionally adjusting for baseline characteristics that remained unbalanced after IPTW, was used to estimate the hazard ratio (HR) for PFS associated with DVRd-DR/R compared with VRd-R



- Limitations**
 - Patients were required to be TE at initial MM diagnosis and findings may not translate to other populations
 - Results could be subject to residual confounding from variables that were not collected during data entry
 - PFS between DR and R maintenance after DVRd induction/consolidation could not be compared at this time due to limited follow-up
 - Comparability with clinical trials may be limited by differences in patients' treatment patterns, including lower rates of consolidation and longer length of induction therapy in the real world
 - Since multiple sites contributed data, it is possible that there were some differences in the level of missingness for some data elements across sites

References
1. FDA approves daratumumab and hyaluronidase-fihj with bortezomib, lenalidomide, and dexamethasone for multiple myeloma. U.S. Food & Drug Administration. Accessed September 03, 2022. <https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-daratumumab-and-hyaluronidase-fihj-bortezomib-lenalidomide-and-dexamethasone-multiple>. 2. Sonneveld P, et al. *N Engl J Med* 2024;390(4):301-13. 3. Voorhes M, et al. *Lancet Haematol* 2023;10(10):e825-37.

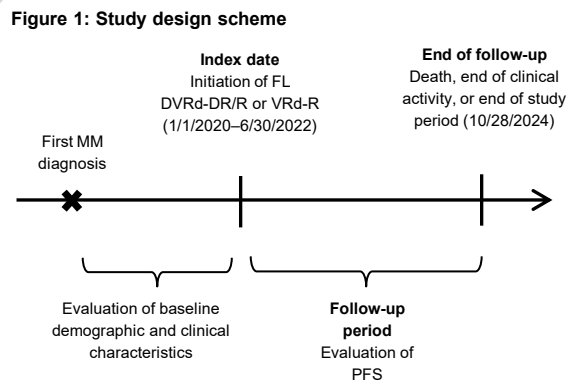
Results

- Sample size and patient characteristics**
 - DVRd-DR/R: 137 patients (DR maintenance: 67; R maintenance: 70)
 - Median age: 63
 - 42% female
 - 69% White, 10% Black
 - VRd-R: 86 patients
 - Median age: 65
 - 51% female
 - 76% White, 9% Black
- After IPTW, age, sex, race, ethnicity, performance status, ISS/R-ISS stage, frailty, and 1q21 gain/amplification were balanced (Table 1)
 - Region of residence, type of insurance, extramedullary disease, comorbidity index, diabetes, and malignancy, remained imbalanced and were included as covariates

Table 1: Baseline demographic and clinical characteristics

	DVRd n=137	VRd n=86	Standardized difference	DVRd n=115	VRd n=108	Standardized difference
Age, mean ±SD [median], y	61.7 ± 9.6 [63.0]	62.2 ± 8.3 [64.5]	4.8	61.9 ± 8.9 [64.0]	61.9 ± 9.5 [64.0]	0.2
Male sex, n (%)	80 (58.4)	42 (48.8)	19.3*	66 (57.2)	61 (56.4)	1.7
Race, n (%)						
White	94 (68.6)	65 (75.6)	15.6*	82 (71.2)	79 (73.3)	4.7
Black or African American	14 (10.2)	8 (9.3)	3.1	10 (9.0)	7 (6.6)	9.3
Other ^a	9 (6.6)	4 (4.7)	8.3	7 (5.7)	4 (3.9)	8.4
Unknown	20 (14.6)	9 (10.5)	12.5*	16 (14.1)	18 (16.3)	6.1
Ethnicity, n (%)						
Non-Hispanic or Non-Latino	107 (78.1)	72 (83.7)	14.3*	92 (79.7)	85 (79.0)	1.9
Hispanic or Latino	11 (8.0)	8 (9.3)	4.5	8 (7.2)	7 (6.7)	2.0
Other	7 (5.1)	2 (2.3)	14.8*	6 (4.8)	6 (6.0)	5.2
Unknown	12 (8.8)	4 (4.7)	16.5*	9 (8.2)	9 (8.3)	0.4
Region of residence, n (%)						
Northeast	74 (54.0)	41 (47.7)	12.7*	57 (49.4)	46 (42.5)	13.9*
West	37 (27.0)	27 (31.4)	9.7	34 (29.8)	37 (34.5)	10.0*
South	18 (13.1)	16 (18.6)	15.0*	19 (16.2)	22 (20.2)	10.3*
Midwest	8 (5.8)	2 (2.3)	17.8*	5 (4.5)	3 (2.8)	9.2
Type of insurance, n (%)						
Commercial/private	52 (38.0)	40 (46.5)	17.4*	47 (40.9)	48 (44.9)	8.0
Medicare/Medicare Advantage	37 (27.0)	33 (38.4)	24.4*	36 (31.6)	38 (35.6)	8.4
Medicaid	8 (5.8)	3 (3.5)	11.2*	6 (5.4)	6 (6.0)	2.7
Other ^d	7 (5.1)	2 (2.3)	14.8*	5 (4.0)	3 (2.8)	6.3
Unknown	33 (24.1)	8 (9.3)	40.5*	21 (18.1)	12 (10.7)	21.2*
ECOG performance status, n (%)						
0 or unknown	67 (48.9)	46 (53.5)	9.2	56 (48.4)	53 (49.3)	1.8
≥1	70 (51.1)	40 (46.5)	9.2	59 (51.6)	55 (50.7)	1.8
ISS/R-ISS score, n (%)						
I or unknown or not reported	61 (44.5)	47 (54.7)	20.4*	53 (46.0)	51 (46.9)	1.8
II or III	76 (55.5)	39 (45.3)	20.4*	62 (54.0)	57 (53.1)	1.8
Extramedullary disease, n (%)						
Yes	12 (8.8)	10 (11.6)	9.5	10 (8.6)	9 (8.5)	0.5
No	91 (66.4)	72 (83.7)	40.8*	84 (73.4)	87 (80.4)	16.7*
Unknown	34 (24.8)	4 (4.7)	59.4*	21 (18.0)	12 (11.1)	19.6*
Frailty assessment at clinic, n (%)						
Fit	53 (38.7)	32 (37.2)	3.0	47 (40.5)	47 (43.8)	6.5
Intermediate fitness	5 (3.6)	3 (3.5)	0.9	5 (3.9)	5 (4.8)	4.5
Frail	2 (1.5)	2 (2.3)	6.4	2 (1.8)	2 (1.7)	0.9
Unknown	77 (56.2)	49 (57.0)	1.6	62 (53.7)	54 (49.7)	8.0
1q21 amplification or gain, n (%)						
Yes	37 (27.0)	18 (20.9)	14.3*	29 (25.4)	28 (25.9)	1.0
No	93 (67.9)	58 (67.4)	0.9	79 (68.2)	72 (66.5)	3.6
Unknown	7 (5.1)	10 (11.6)	23.7*	7 (6.3)	8 (7.6)	5.0
CCI, mean ±SD [median]	0.7 ± 1.1 [0.0]	0.6 ± 1.1 [0.0]	11.1*	0.6 ± 0.9 [0.0]	0.5 ± 1.0 [0.0]	14.3*
0, n (%)	89 (65.0)	57 (66.3)	2.8	78 (67.6)	79 (72.8)	11.3*
1, n (%)	16 (11.7)	15 (17.4)	16.4*	14 (12.6)	14 (12.7)	0.4
2, n (%)	22 (16.1)	13 (15.1)	2.6	17 (15.1)	15 (13.9)	3.2
≥3, n (%)	10 (7.3)	1 (1.2)	30.9*	5 (4.8)	1 (0.6)	26.1*
Selected comorbidities, n (%)						
Diabetes without chronic complications	16 (11.7)	8 (9.3)	7.8	13 (11.3)	9 (8.2)	10.4*
Malignancy	13 (9.5)	6 (7.0)	9.2	9 (7.7)	5 (4.6)	13.1*
Moderate or severe renal disease	3 (3.5)	3 (3.5)	22.1*	8 (7.1)	6 (5.7)	5.9
Chronic obstructive pulmonary disease ^e	3 (2.2)	5 (5.8)	18.6*	3 (2.5)	4 (3.3)	4.5
Hypertension	55 (40.1)	41 (47.7)	15.2*	48 (42.1)	46 (42.7)	1.2
Obesity	23 (16.8)	19 (22.1)	13.4*	22 (19.1)	22 (20.2)	2.7




*Weighted were estimated using a multivariable logistic regression model with the following baseline covariates: age (continuous), male, race, ethnicity, type of insurance, region of residence, ECOG score of 1 or higher, ISS/R-ISS score of 1 or unknown or not reported, extramedullary disease, frailty, presence of 1q21 amplification or gain, CCI score (continuous and categorical) and selected comorbidities: diabetes without chronic complications, malignancy, moderate or severe renal disease, chronic obstructive pulmonary disease, hypertension, and obesity. ^aThe number of patients reported in this weighted population represent the sum of weights for the corresponding patients, rounded to the nearest integer. The proportions displayed were calculated prior to the rounding and may be slightly different than if they were calculated based on rounded numbers. ^bIncludes Asian, Hispanic or Latino, Native Hawaiian or other Pacific Islander, and American Indian or Alaska Native. ^cIncludes dual eligible, military and other. Dual eligible was defined as having both Medicare plus Medicaid insurance coverage. Military included Veterans Affairs and active military. ^dIncludes asthma ^eStandardized difference ≥10%. CCI, Charlson Comorbidity Index; ECOG, Eastern Cooperative Oncology Group; IPTW, inverse probability of treatment weighting; ISS, International Staging System; R-ISS, Revised International Staging System.



Multiple Myeloma



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