PA-408

Real-World Progression-Free Survival Among Non-Transplanted Newly Diagnosed Multiple Myeloma Patients Initiating Frontline DVRd vs VRd

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Key Takeaway

Real-world use of DVRd as 1L treatment significantly improved PFS compared with VRd for non-transplanted patients with NDMM, regardless of age and frailty status

Conclusions

DVRd was associated with a 46% (hazard ratio=0.54; 95% confidence interval=0.42–0.68) lower risk of disease progression or death compared with VRd among patients with NDMM who did not receive SCT

The PFS benefit of DVRd was also observed in patients aged ≥70 years and frail patients, supporting its use in these patient populations

These real-world findings are consistent with the CEPHEUS trial[1] and demonstrate a consistent benefit of 1L DVRd over VRd in patients with NDMM who did not receive SCT

Poster

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https://www.congresshub.com/Oncology/IMS2026/Daratumumab/Friend

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Disclosures

RF has served on an advisory board for Bristol Myers Squibb, JH, EC, XY, RM and SK are employees and stockholders of Johnson & Johnson, VK was an employee and stockholder of Johnson & Johnson at the time of study, PTL and ATS are employees of Analysis Group ULC, a consulting company that has provided paid consulting services to Johnson & Johnson Innovative Medicine, which funded the development and conduct of this study. MJP has served on an advisory board for Johnson & Johnson, Bristol Myers Squibb, GlaxoSmithKline, Kite, Regeneron, Sanofi, and Pfizer, and has received research funding from AbbVie, Bristol Myers Squibb, CellCentric, C4 Therapeutics, GlaxoSmithKline, Johnson & Johnson, Pfizer, Regeneron, Sanofi.

Introduction

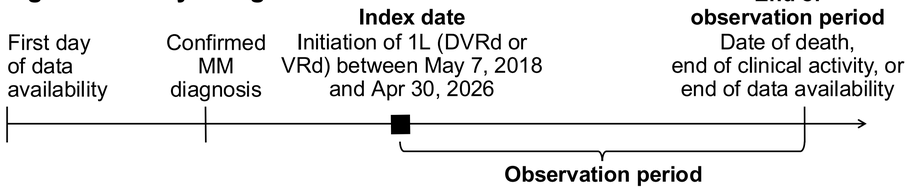
- Daratumumab-based quadruplet regimens are the new standard of care for patients with newly diagnosed multiple myeloma (NDMM) who are ineligible for or have deferred stem cell transplant (SCT)[1]
- In the pivotal phase III CEPHEUS trial, daratumumab, bortezomib, lenalidomide, and dexamethasone (DVRd) significantly improved outcomes compared with bortezomib, lenalidomide, and dexamethasone (VRd), including higher rates of minimal residual disease (MRD) negativity (60.9% vs 39.4%) and longer progression-free survival (PFS; hazard ratio [HR] 0.57; median PFS: not reached for DVRd vs 50.2 months for VRd)[2]
- These results have led to increasing adoption of DVRd as frontline therapy (1L) for SCT-ineligible patients with NDMM
- However, older and frail patients are often underrepresented in clinical trials, including CEPHEUS (eligibility criteria: age ≤80 years, International Myeloma Working Group [IMWG] frailty index <2); real-world evidence comparing DVRd with VRd remains limited, particularly in these patients
- The objective of this study is to compare PFS among non-transplanted patients with NDMM initiating DVRd vs VRd in routine clinical practice in the United States, including older and frail patients

Methods

Data source and study design

- Retrospective observational study using the Flatiron Health Research database **(Figure 1)**
  - Index date: Date of 1L initiation following multiple myeloma diagnosis
  - Observation period: Time between index date and earliest of death, end of continuous activity, or end of data availability

Figure 1. Study design scheme



Abbreviations: 1L: frontline therapy; DVRd: daratumumab, bortezomib, lenalidomide, and dexamethasone; MM: multiple myeloma; VRd: bortezomib, lenalidomide, and dexamethasone.

Patient eligibility criteria

- Inclusion criteria
  - Aged ≥18 years with NDMM
  - Did not receive an SCT prior to or during 1L
  - To provide sufficient opportunity to observe whether SCT occurred during 1L, patients were also required to meet ≥1 of the following criteria:
    - Second-line treatment or death was observed
    - ≥120 days after 1L end date
    - Follow-up time from index date was ≥215 days
    - Frailty score, assessed using the simplified Intergroup Francophone of Myeloma (IFM) score,[3] was ≥2
  - Initiated either the DVRd (**DVRd cohort**) or VRd regimen (**VRd cohort**) as 1L between May 7, 2018 and Apr 30, 2026
  - Had ≥60 days of clinical activity after the index date to adequately identify the treatment regimen
- Exclusion criteria
  - Initiated 1L ≥1 year after the confirmed multiple myeloma diagnosis
  - Had other cancer or amyloid light chain amyloidosis prior to index date
  - Received chimeric antigen receptor T-cell therapy (CAR-T) prior to index date
  - Participated in a clinical trial during 1L

Statistical analysis

- Demographic and clinical characteristics were compared between cohorts using standardized mean differences, with values <10% indicating balance between cohorts
  - Propensity score matching (1 DVRd: 1 VRd) based on demographic and clinical characteristics presented in Table 1 was used to reduce confounding
- A Kaplan-Meier analysis was conducted to assess PFS in each cohort
  - Time (in months) from the index date to earliest of disease progression (event) or death (event)
  - Patients without an event were censored at initiation of second-line treatment, end of clinical activity or end of data availability, whichever occurred first
- A Cox proportional hazards model, further adjusting for characteristics that remained imbalanced after matching, was used to compare PFS between cohorts
- Two subgroup analyses were conducted separately among (1) patients aged ≥70 years and (2) frail patients (i.e., frailty score ≥2)

Results

Sample size and patient characteristics

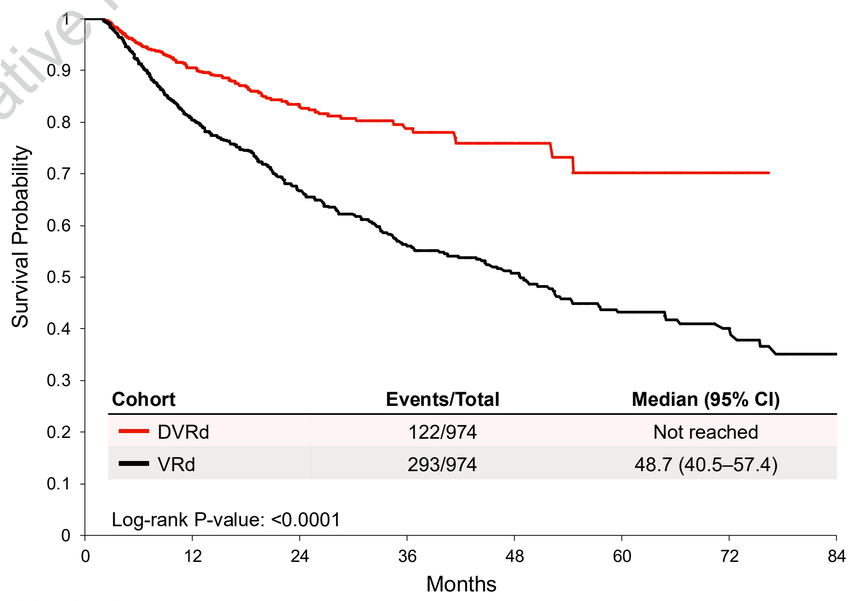
- Before matching:
  - **DVRd cohort:** 992 patients, mean age [range] = 66 [19–85] years, 54% male, 29% frail, 40% with high cytogenetic risk, 22% treated in academic setting **(Figure 2)**
  - **VRd cohort:** 1,946 patients, mean age [range] = 69 [32–85] years, 52% male, 36% frail, 33% with high cytogenetic risk, 11% treated in academic setting
- After matching, each cohort included 974 patients
  - Demographic and clinical characteristics were well balanced except for age group and year of index date due to increasing adoption of DVRd across the years **(Table 1)**

Figure 2. Demographic and clinical characteristics before and after matching

	Before Matching			After Matching[1]		
	DVRd (N = 992)	VRd (N = 1,946)	SMD	DVRd (N = 974)	VRd (N = 974)	SMD
Age at index, years, mean (min–max)	66.3 (19–85)	69.4 (32–85)	31.5%	66.5 (30–85)	66.6 (32–85)	1.0%
Male	533 (53.7%)	1,014 (52.1%)	3.2%	520 (53.4%)	533 (54.7%)	2.6%
Race/ethnicity n (%)						
White	560 (56.5%)	1,042 (53.5%)	6.0%	547 (56.2%)	544 (55.9%)	0.6%
Black or African American	193 (19.5%)	388 (19.9%)	1.0%	191 (19.6%)	184 (18.9%)	1.8%
Asian or other race	80 (8.1%)	232 (11.9%)	12.7%	79 (8.1%)	87 (8.9%)	2.9%
Unknown	159 (16.0%)	284 (14.6%)	3.9%	157 (16.1%)	159 (16.3%)	0.5%
Insurance type n (%)						
Commercial/ Private	437 (44.1%)	820 (42.1%)	4.0%	427 (43.8%)	441 (45.3%)	3.0%
Medicare or Medicare Advantage	79 (8.0%)	191 (9.8%)	6.3%	79 (8.1%)	86 (8.8%)	2.5%
Other[2]	199 (20.1%)	328 (16.9%)	8.2%	194 (19.9%)	181 (18.6%)	3.3%
Multiple or unknown	277 (27.9%)	607 (31.2%)	7.2%	274 (28.1%)	266 (27.3%)	1.8%
Practice type n (%)						
Academic	221 (22.3%)	210 (10.8%)	31.3%	204 (20.9%)	191 (19.6%)	3.2%
Community	771 (77.7%)	1,736 (89.2%)	31.3%	770 (79.1%)	783 (80.4%)	3.2%
ISS stage n (%)						
Stage I	249 (25.1%)	477 (24.5%)	1.4%	246 (25.3%)	241 (24.7%)	1.2%
Stage II	221 (22.3%)	414 (21.3%)	2.4%	215 (22.1%)	215 (22.1%)	0.0%
Stage III	177 (17.8%)	334 (17.2%)	1.8%	174 (17.9%)	176 (18.1%)	0.5%
Unknown/ not documented	345 (34.8%)	721 (37.1%)	4.7%	339 (34.8%)	342 (35.1%)	0.6%
ECOG score n (%)						
0	293 (29.5%)	651 (33.5%)	8.4%	291 (29.9%)	290 (29.8%)	0.2%
1	317 (32.0%)	616 (31.7%)	0.6%	309 (31.7%)	316 (32.4%)	1.5%
2+	159 (16.0%)	314 (16.1%)	0.3%	157 (16.1%)	163 (16.7%)	1.7%
Missing	223 (22.5%)	365 (18.8%)	9.2%	217 (22.3%)	205 (21.0%)	3.0%
Cytogenetic risk status[3] n (%)						
High	400 (40.3%)	648 (33.3%)	14.6%	388 (39.8%)	388 (39.8%)	0.0%
Standard risk	166 (16.7%)	333 (17.1%)	1.0%	164 (16.8%)	159 (16.3%)	1.4%
Missing	426 (42.9%)	965 (49.6%)	13.4%	422 (43.3%)	427 (43.8%)	1.0%
Frailty n (%)						
Frail	287 (28.9%)	690 (35.5%)	14.0%	285 (29.3%)	287 (29.5%)	0.5%
Non-frail	705 (71.1%)	1,256 (64.5%)	14.0%	689 (70.7%)	687 (70.5%)	0.5%

Abbreviations: BMI: body mass index; CRAB: hypercalcemia, renal impairment, anemia, or bone lesions; ECOG: Eastern Cooperative Oncology Group; ISS: International Staging System; Quan-CCI: Quan-Charlson Comorbidity Index; SMD: standardized mean difference. **Notes:** [1]Variables included in the calculation of the propensity score also included region of residence, time from initial diagnosis to index date, Quan-CCI score (*Am J Epidemiol*. 2011;173(6):676–82), BMI, and presence of ≥1 CRAB feature. [2]Other included patient assistance programs or others (e.g., Medicaid, government, self-pay, other type). [3]Defined as del(17p), t(4;14), t(14;16), t(14;20), or 1q21 amplification.

Figure 3. Progression-free survival after 1:1 matching

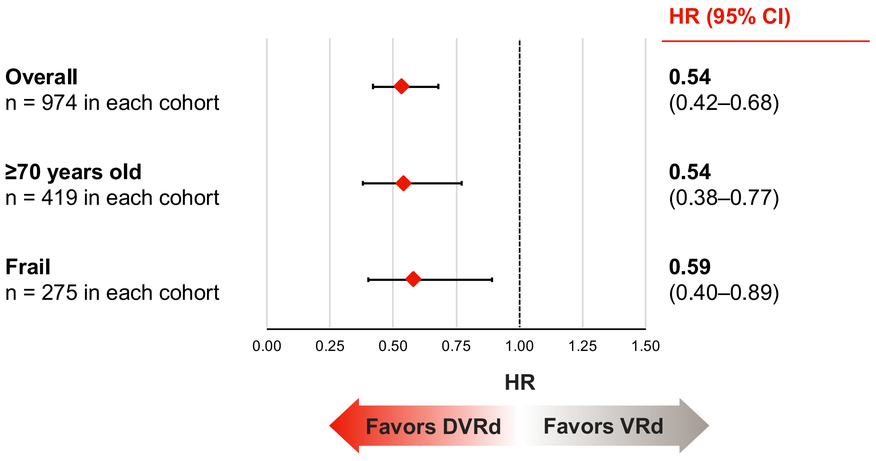


Patients at risk

Months	0	12	24	36	48	60	72	84
DVRd	974	536	251	106	41	12	4	0
VRd	974	476	279	189	120	72	37	17

Abbreviation: CI: confidence interval.

Figure 4. Risk of disease progression or death associated with DVRd vs VRd after 1:1 matching



Abbreviation: HR: hazard ratio.

Progression-free survival

- Following 1:1 propensity score matching, DVRd was associated with significantly improved PFS compared with VRd
- Median follow-up was 19 months in the DVRd cohort and 41 months in the VRd cohort
- Disease progression or death occurred in 13% of patients in the DVRd cohort vs 30% of patients in the VRd cohort (log-rank P<0.0001, **Figure 3**)
- Median PFS was not reached in the DVRd cohort and was 48.7 months in the VRd cohort
- After adjustment for characteristics that remained imbalanced after matching, DVRd was associated with a 46% lower risk of disease progression or death compared with VRd (hazard ratio=0.54; 95% confidence interval=0.42–0.68; P<0.0001)
- Similar findings were observed in the subgroup analyses:
  - Among patients aged ≥70 years (N = 419 in each cohort after matching), DVRd was associated with a 46% lower risk of disease progression or death compared with VRd (hazard ratio=0.54; 95% confidence interval=0.38–0.77; P=0.0005; **Figure 4**)
  - Among frail patients (N = 275 in each cohort after matching), DVRd was associated with a 41% lower risk of disease progression or death compared with VRd (hazard ratio=0.59; 95% confidence interval=0.40–0.89; P=0.0114; **Figure 4**)

Limitations

- Results may not be generalizable beyond patients represented in the Flatiron Health Research database
- Despite the use of propensity score matching, residual confounding of unobserved characteristics may remain
- Comorbidity profiles may not have been fully captured in the data source
- The absence of del(1p32) data in the Flatiron Health Research database precluded alignment with the most recent definition of high cytogenetic risk[4]

Table 1. Characteristics included as covariates in Cox regression

	Before Matching			After Matching		
	DVRd	VRd	SMD	DVRd	VRd	SMD
Age category at index, years, n (%)[1,2]						
<65	371 (41.0%)	533 (59.0%)	21.5%	359 (48.8%)	376 (51.2%)	3.5%
65 to 69	194 (37.2%)	327 (62.8%)	7.3%	190 (52.2%)	174 (47.8%)	4.1%
70 to 74	229 (38.2%)	371 (61.8%)	9.8%	227 (58.5%)	161 (41.5%)	17.1%
≥75	198 (21.7%)	715 (78.3%)	37.7%	198 (43.0%)	263 (57.0%)	15.8%
Year of index date, n (%)[1,2,3]						
2018	0 (0.0%)	236 (100.0%)	52.5%	0 (0.0%)	130 (100.0%)	55.4%
2019	7 (1.8%)	379 (98.2%)	65.7%	6 (3.4%)	169 (96.6%)	61.4%
2020	34 (8.2%)	380 (91.8%)	52.3%	32 (13.7%)	201 (86.3%)	55.3%
2021	71 (17.6%)	332 (82.4%)	30.7%	68 (27.2%)	182 (72.8%)	35.5%
2022	131 (33.6%)	259 (66.4%)	0.3%	128 (50.4%)	126 (49.6%)	0.6%
2023	196 (45.7%)	233 (54.3%)	21.5%	194 (64.7%)	106 (35.3%)	25.1%
2024	256 (72.5%)	97 (27.5%)	60.2%	253 (83.5%)	50 (16.5%)	60.2%
2025	280 (90.6%)	29 (9.4%)	81.0%	276 (96.5%)	10 (3.5%)	83.7%
2026	17 (94.4%)	1 (5.6%)	17.0%	17 (100.0%)	0 (0.0%)	18.6%

Notes: [1]n (%) are reported as row percentages. [2]SMDs show the difference in the proportion of patients relative to the size of their cohort within each row. [3]Proportions illustrate the uptake of DVRd over time.

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Multiple Myeloma

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