Poster number: PA-414

Cost per Responder Model of Daratumumab, Bortezomib, Lenalidomide and Dexamethasone (DVRd) for Transplant-Ineligible or Transplant-Deferred Newly Diagnosed Multiple Myeloma

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Introduction

- For patients with newly diagnosed multiple myeloma (NDMM) who are ineligible for stem cell transplant (TIE), the current standard of care consists of triplet regimens such as daratumumab (D) plus lenalidomide (R) and dexamethasone (DRd) or bortezomib (V), lenalidomide (R), and dexamethasone (VRd)[1]
- In the phase 3 CEPHEUS trial, eight 21-day cycles of subcutaneous D combined with VRd (DVRd) followed by monthly DRd (DVRd/DRd) demonstrated superior efficacy compared to eight 21-day cycles of VRd followed by monthly Rd (VRd/Rd) in TIE/transplant-deferred (TD) patients with NDMM[2]
  - Patients in the DVRd/DRd cohort achieved higher rates of minimal residual disease (MRD)-negative status compared to VRd/Rd cohort (60.9% versus 39.4% by 58.7 months; odds ratio: 2.37, p<0.0001)[2]
  - The sustained MRD-negativity rate (≥12 months) was similarly higher in the DVRd/VRd cohort compared to the VRd/Rd cohort (48.7% versus 26.3%; odds ratio: 2.63, p<0.0001)
- In this study, the economic value associated with achieving and sustaining MRD-negative status for TIE/TD patients with NDMM treated with DVRd/DRd versus VRd/Rd was assessed

Objective

- To evaluate costs per MRD-negative patient, among TIE/TD patients with NDMM in the United States (US) treated with DVRd/DRd versus VRd/Rd based on the findings of the CEPHEUS trial

Methods

Model framework/structure

- An economic model was developed from a US mixed payer perspective (80% Medicare, 20% commercial, as observed in the CEPHEUS trial[2])
- Costs were assessed over a 60-month time horizon
  - Outcomes were additionally reported at 12, 24, 36, and 48 months

Model inputs

- Clinical efficacy informed by the CEPHEUS trial:[2]
  - Cumulative proportion of patients achieving MRD-negative status (sensitivity threshold of 10^{-5})
  - Proportion of patients achieving sustained MRD-negativity (i.e., MRD-negative for ≥12 months) at 60 months
  - Time on first-line (1L) treatment as well as time to initiation of second-line (2L) treatment
  - Grade 3+ adverse events (AEs) of interest
- Costs of treatment acquisition were derived from the average sales price 2025 Q1 pricing file[3] (Medicare) and IBM Micromedex® RED BOOK® wholesale acquisition costs[4] (commercial)
- Costs of treatment administration and AE management were obtained from CMS[5] and HCUP[6], respectively; costs of medical visits and MRD testing were obtained from the literature[7,8]

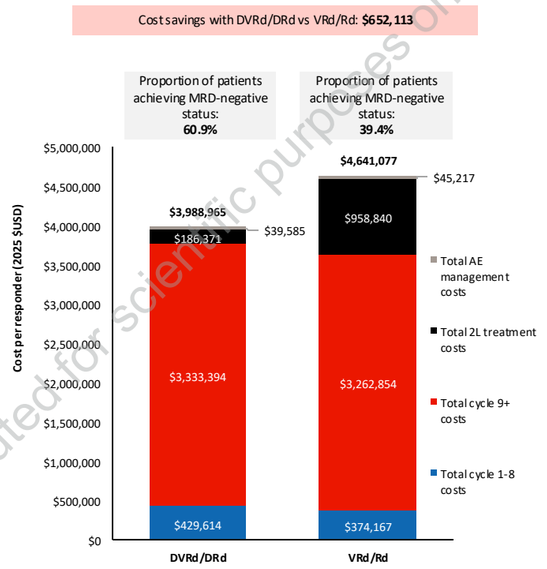
Model outputs

- Cost per MRD-negative patient was calculated based on the cumulative proportion of patients achieving MRD-negativity at 60 months after randomization
  - Reported overall and by treatment phase (i.e., cycles 1-8, cycle 9+, and 2L)
- Cost per patient achieving sustained MRD negativity (i.e., MRD-negative for ≥12 months) was calculated based on the proportion of patients with MRD-negative status on ≥2 occasions that were ≥12 months apart during the 60 months post-randomization
- Costs were reported in 2025 US dollars

Results

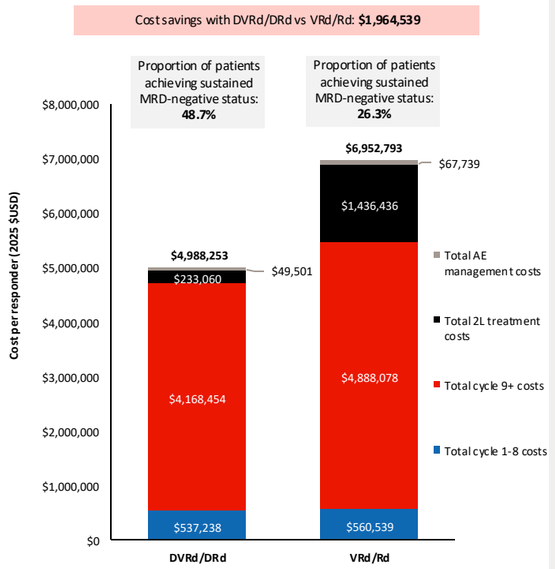
- At 60 months, treatment with DVRd/DRd resulted in cost savings of $652,113 per MRD-negative patient compared to treatment with VRd/Rd (DVRd/DRd: $3,988,965; VRd/Rd: $4,641,077; **Figure 1**), explained by:
  - A higher proportion of patients achieving MRD-negative status by 60 months (DVRd/DRd: 60.9%; VRd/Rd: 39.4%)
  - Lower 2L treatment costs per MRD-negative patient (DVRd/DRd: $186,371; VRd/Rd: $958,840; $772,469 difference)
    - A lower proportion of patients progressed to 2L at 60 months (DVRd/DRd: 11.2%; VRd/Rd: 33.3%)
- The cost per patient achieving sustained MRD-negative status was $1,964,539 lower in the DVRd/DRd cohort compared to the VRd/Rd cohort (DVRd/DRd: $4,988,253; VRd/Rd: $6,952,793; **Figure 2**), explained by:
  - A higher proportion of patients achieving MRD-negative status (DVRd/DRd: 48.7%; VRd/Rd: 26.3%)
  - Lower 2L treatment costs per patient achieving sustained MRD-negative status (DVRd/DRd: $233,060; VRd/Rd: $1,436,436; $1,203,376 difference)
- DVRd/DRd demonstrated consistent cost savings per MRD-negative patient relative to VRd/Rd across all assessed time frames (12 months: $7,684; 24 months: $216,612; 36 months: $412,034; 48 months: $564,816; **Figure 3**)
  - This was explained by higher cumulative rates of MRD-negativity in the DVRd/DRd cohort relative to VRd/Rd cohort at all time intervals (**Figure 3**)

Figure 1. Cost per MRD-negative patient (10^{-5} threshold) at 60 months



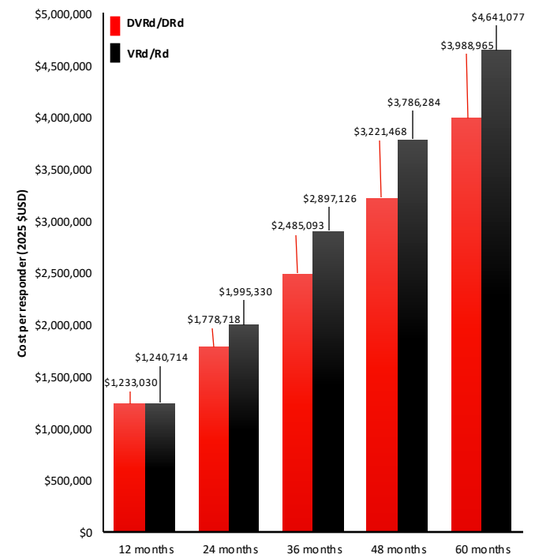
2L: second-line; AE: adverse event; DRd: daratumumab, lenalidomide, and dexamethasone; DVRd: daratumumab, bortezomib, lenalidomide, and dexamethasone; MRD: minimal residual disease; Rd: lenalidomide and dexamethasone; USD: United States Dollar; VRd: bortezomib, lenalidomide, and dexamethasone.

Figure 2. Cost per patient achieving sustained MRD-negativity (10^{-5} threshold sustained for ≥12 months) at 60 months



2L: second-line; AE: adverse event; DRd: daratumumab, lenalidomide, and dexamethasone; DVRd: daratumumab, bortezomib, lenalidomide, and dexamethasone; MRD: minimal residual disease; Rd: lenalidomide and dexamethasone; USD: United States Dollar; VRd: bortezomib, lenalidomide, and dexamethasone.

Figure 3. Cost per MRD-negative patient (10^{-5} threshold) at 12, 24, 36, 48, and 60 months



DRd: daratumumab, lenalidomide, and dexamethasone; DVRd: daratumumab, bortezomib, lenalidomide, and dexamethasone; MRD: minimal residual disease; Rd: lenalidomide and dexamethasone; VRd: bortezomib, lenalidomide, and dexamethasone.

Limitations

- The modeling approach was based on data available from the CEPHEUS trial[2] which may limit the generalizability of study findings
- The model assumed a blend of commercial- or Medicare-insured patients, based on the age composition observed in the CEPHEUS trial; as such, results may not be representative of other TIE/TD patients with NDMM

Conclusions

- Among TIE/TD patients with NDMM, treatment with DVRd/DRd was associated with a lower cost per MRD-negative patient and a lower cost per patient achieving sustained MRD-negativity compared to treatment with VRd/Rd
- These findings demonstrate the potential cost savings associated with the use of DVRd/DRd as 1L treatment for TIE/TD patients with NDMM, complementing the superior efficacy benefits observed compared to VRd/Rd as demonstrated in the CEPHEUS trial[2]

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Acknowledgments

This study was funded by Johnson & Johnson

Disclosures

Santosh Gautam, Brian Macomson, Vipin Khare, Xin Yin and Rohan Medhekar are employees of Johnson & Johnson, and may own Johnson & Johnson stock/stock options.
Laura Morrison, Philippe Thompson-Leduc, Bronwyn Moore and Avani Samandur are employees of Analysis Group, Inc., a consulting company that has provided paid consulting services to Johnson & Johnson, which funded the development and conduct of this study

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Presented by V Khare at the International Myeloma Society 2025, Toronto, Canada, September 17-20, 2025