PS1763

Health-Related Quality of Life in Patients With Transplant-Ineligible or Transplant-Deferred Newly Diagnosed Multiple Myeloma in the Phase 3 CEPHEUS Trial

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Key Takeaway

Along with the improved MRD negativity and PFS response data from CEPHEUS, these PRO findings show the benefit of DVRd quadruplet therapy for TIE or TD NDMM

Conclusions

- As measured by the EORTC QLQ-C30, EORTC QLQ-MY20, and EQ-5D-5L VAS scales, DVRd-treated patients in CEPHEUS had improved HRQoL, physical functioning, and symptom reduction from baseline
- Improvements with DVRd were similar vs VRd with no apparent differences between arms, indicating no detriment to HRQoL with a daratumumab-based quadruplet therapy, as reported in other daratumumab clinical trials
- The TIE subgroup in CEPHEUS also showed similar PRO results, indicating no detriment to HRQoL in this older subgroup

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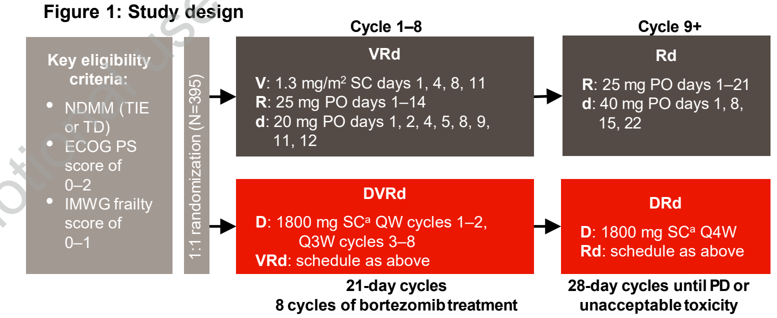
Introduction

- In MAIA (NCT02252172), improvement in health-related quality of life (HRQoL), including pain, was faster in patients treated with daratumumab plus lenalidomide and dexamethasone (DRd) vs lenalidomide and dexamethasone in transplant-ineligible (TIE) newly diagnosed multiple myeloma (NDMM)[1]
- In PERSEUS (NCT03710603), in patients with transplant-eligible NDMM treated with daratumumab-based quadruplet therapy (subcutaneous [SC] daratumumab plus bortezomib, lenalidomide, and dexamethasone [DVRd]), durable improvements in overall HRQoL, multiple myeloma symptoms, and functioning were reported[2]
- In the phase 3 CEPHEUS trial (NCT03652064), minimal residual disease (MRD) negativity and progression-free survival (PFS) improved with DVRd vs VRd in patients with TIE or transplant-deferred (TD) NDMM[3]
- In addition to improved efficacy outcomes, it is important to understand how DVRd quadruplet therapy impacts HRQoL in patients not undergoing autologous stem cell transplantation
- Here, we report the HRQoL findings of DVRd vs VRd in the CEPHEUS trial

Methods

- CEPHEUS is a randomized, open-label, multicenter phase 3 trial (**Figure 1**)
- Patient-reported outcomes (PROs) were secondary endpoints evaluated at:
  - Baseline
  - Once each cycle (C, 28 days [D]) to C8D1
  - Every third C from C9D1 until disease progression
- PROs were assessed using the European Organisation for Research and Treatment of Cancer quality of life questionnaire core 30 (EORTC QLQ-C30), EORTC QLQ-Multiple Myeloma 20 (EORTC QLQ-MY20), and the EuroQol 5-Dimension 5-Level (EQ-5D-5L)
  - For EORTC scales, all raw scores were linearly transformed and presented on a scale of 0–100
  - EQ-5D-5L visual analogue scale (VAS) scores range from 0–100
  - Higher scores indicate improved overall HRQoL (eg, global health status [GHS], physical functioning, and EQ-5D-5L VAS) and worsened disease symptoms (eg, pain)
- Least squares (LS) mean change from baseline at each time point was derived via a mixed-effects model with repeated measures

Figure 1: Study design



[a]Daratumumab 1800 mg co-formulated with recombinant human hyaluronidase PH20 ([rHuPH20; 2000 U/mL; ENHANZE® drug delivery technology; Halozyme, Inc., San Diego, CA, USA). CR, complete response; D, daratumumab; d, dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; IMWG, International Myeloma Working Group; PD, disease progression; PO, orally; Q3W, every 3 weeks; Q4W, every 4 weeks; QW, weekly; R, lenalidomide; V, bortezomib.

Results

- The intent-to-treat (ITT) population had 395 patients (DVRd, n=197; VRd, n=198)
- Baseline characteristics (not shown) and PRO scores were similar across treatment arms, with slight numerical differences (**Table 1**)
- Median follow-up was 58.7 months
- At C36, 135 patients in the DVRd arm and 106 in the VRd arm remained on-study

Table 1: Baseline PRO scores (ITT)

	DVRd (n=197)	VRd (n=198)
EORTC QLQ-C30, mean (SD)		
GHS	57.9 (22.9)	60.6 (23.5)
Physical Functioning	65.8 (27.1)	66.9 (26.1)
Pain	44.3 (35.4)	41.2 (32.0)
Fatigue	38.8 (26.6)	35.0 (26.6)
EORTC QLQ-MY20, mean (SD)		
Disease symptoms	31.0 (23.6)	30.9 (25.1)
EQ-5D-5L, mean (SD)		
VAS	63.0 (20.9)	65.8 (20.2)

- Compliance was >85% at baseline and >81% through C36 in both arms (**Table 2**)
- **Figure 2** shows improvements in LS mean changes from baseline in PRO scores in the ITT population for EORTC QLQ-C30 GHS, physical functioning, pain, and fatigue (data not shown); EORTC QLQ-MY20 disease symptoms score; and EQ-5D-5L VAS (data not shown)
- For all scales, a similar median time to worsening and time to improvement were observed across both arms
- LS mean changes from baseline in PRO scores of the CEPHEUS TIE subgroup had similar results as the ITT population (**Figure 3**) for EORTC QLQ-C30 GHS, physical functioning, pain, and fatigue (data not shown), EORTC QLQ-MY20 disease symptoms scores, and EQ-5D-5L VAS (data not shown)

Table 2: Compliance[a] with the questionnaires (ITT)

	DVRd (n=197)	VRd (n=198)
EORTC QLQ-C30		
Baseline, n/N (%)	191/197 (97.0)	190/198 (96.0)
C2–36, range, n/N (%)	117/136 (86.0) – 185/191 (96.4)	106/128 (82.8) – 176/179 (97.8)
EORTC QLQ-MY20		
Baseline, n/N (%)	188/197 (95.4)	188/198 (94.9)
C2–36, range, n/N (%)	139/162 (85.3) – 174/181 (96.1)	104/128 (81.3) – 188/198 (97.1)
EQ-5D-5L, (%)		
Baseline, n/N (%)	169/197 (85.8)	173/198 (87.4)
C2–36, range, n/N (%)	153/174 (87.9) – 174/183 (95.1)	106/128 (82.8) – 174/179 (96.7)

[a]Compliance was defined as the number of forms received as a percentage of the number of forms expected. Forms were expected from all patients who were on study treatment at each visit. Percentages were calculated with the number of expected forms in each group as denominator.

Figure 2: LS mean change in HRQoL scores from baseline over time in the CEPHEUS ITT population

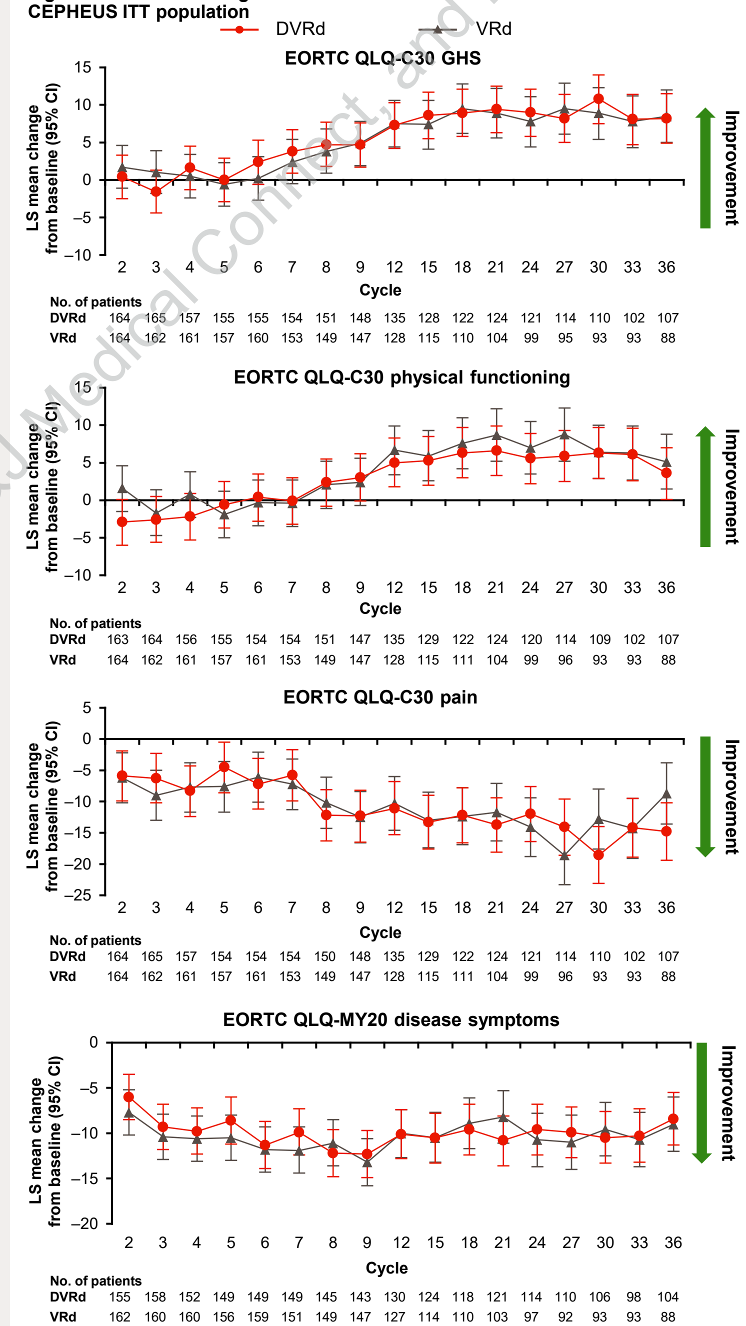
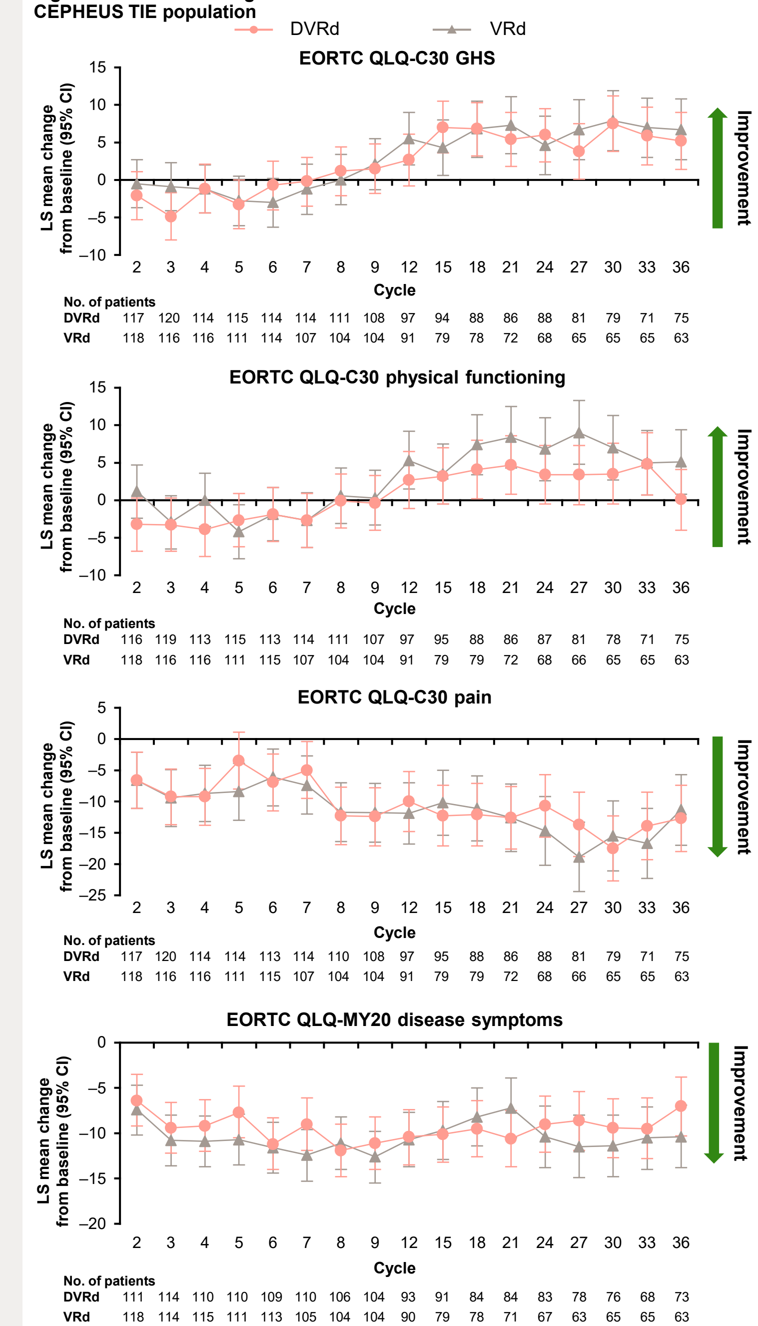


Figure 3: LS mean change in HRQoL scores from baseline over time in the CEPHEUS TIE population



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Disclosures
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Multiple Myeloma