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Health-Related Quality of Life in Transplant-Eligible Patients With Newly Diagnosed Multiple Myeloma: Data From the PERSEUS Trial of Subcutaneous Daratumumab Combined With Bortezomib, Lenalidomide, and Dexamethasone

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Key Takeaway

Together with favorable efficacy data, these HRQoL data support DVRd-DR as a new standard of care for TE NDMM

Conclusions

- Quadruplet therapy with DVRd plus DR maintenance provides durable improvements in overall HRQoL, MM symptoms, and functioning; these HRQoL data are consistent with the efficacy and safety of this regimen
- HRQoL improvements are comparable to those seen with VRd-R, indicating no detriment to HRQoL with the addition of Dara during induction, consolidation, and maintenance phases
- In both treatment arms, GHS, physical functioning, and pain and fatigue symptoms improved through maintenance, and the PRO benefits were sustained over time

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Poster

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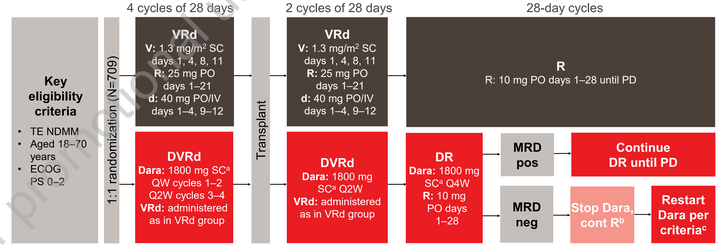
Introduction

- In PERSEUS (NCT03710603), patients with transplant-eligible (TE) newly diagnosed multiple myeloma (NDMM) received daratumumab (Dara) subcutaneous (SC) plus bortezomib, lenalidomide, and dexamethasone (VRd) induction and consolidation therapy and Dara plus lenalidomide (R) maintenance therapy (DVRd-DR), or VRd induction and consolidation therapy and lenalidomide maintenance therapy alone (VRd-R)[1]
  - In the primary analysis (47.5-month median follow-up), progression-free survival (PFS; primary endpoint) was significantly improved with DVRd-DR vs VRd-R (hazard ratio, 0.42 [95% CI, 0.30–0.59], *P*<0.001)
    - Median PFS was not reached in either arm; 48-month rates were 84.3% vs 67.7%, respectively)
  - The addition of Dara was well tolerated with manageable side effects
- Maintaining health-related quality of life (HRQoL) is an important treatment goal for patients with multiple myeloma (MM)[2]
- We report patient-reported outcomes (PROs) in PERSEUS

Methods

- PERSEUS is a phase 3, randomized clinical trial (**Figure 1**)
- PROs were secondary endpoints
- PROs were assessed using the European Organisation for Research and Treatment of Cancer (EORTC) QoL questionnaire core 30 (QLQ-C30), EORTC Multiple Myeloma module QoL questionnaire (QLQ-MY20), and EuroQol 5-Dimension 5-Level (EQ-5D-5L) instruments
  - For EORTC scales, all raw scores were linearly transformed and presented on a scale of 0–100
  - For 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 and fatigue)
- Least squares (LS) mean change from baseline at each time point was derived via a mixed-effects model with repeated measures
- Clinically meaningful changes were defined as ≥10-point changes on EORTC scales and 7 points for EQ-5D-5L VAS[3-5]

Figure 1: Study design



[a]Co-formulated with rHuPH20 (2000 U/mL; ENHANZE® drug delivery technology, Halozyme, Inc., San Diego, CA, USA) [b]After ≥24 months of DR maintenance for patients with ≥CR and 12 months of sustained MRD negativity (10^{-5}). [c]Upon confirmed loss of CR without PD or recurrence of MRD. cont, continue; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; MRD, minimal residual disease; neg, negative; PD, disease progression; PO, orally; pos, positive; Q2W, every other week; Q4W, every 4 weeks; QW, weekly.

Results

Study population

- In the intent-to-treat (ITT) population, 355 patients were randomized to DVRd-DR and 354 to VRd-R
- Baseline characteristics and PRO scores were well balanced (**Tables 1** and **2**)
- Median follow-up was 47.5 (range, 0–54.4) months
- At maintenance cycle 34 (MC34), 254 patients in the DVRd-DR arm and 164 in the VRd-R arm remained on study

Table 1: Baseline characteristics (ITT)

	DVRd-DR (n=355)	VRd-R (n=354)
Age, years, median (range)	61 (32–70)	59 (31–70)
Male, n (%)	211 (59.4)	205 (57.9)
Race, n (%)		
Asian	4 (1.1)	6 (1.7)
Black	5 (1.4)	4 (1.1)
White	330 (93.0)	323 (91.2)
Other/not reported	16 (4.5)	21 (5.9)
ECOG PS, n (%)		
0	221 (62.3)	230 (65.0)
1	114 (32.1)	108 (30.5)
2	19 (5.4)	16 (4.5)
3	1 (0.3)	0
International Staging System stage, n/N (%)		
I	186/355 (52.4)	178/353 (50.4)
II	114/355 (32.1)	125/353 (35.4)
III	55/355 (15.5)	50/353 (14.2)
Cytogenetic risk,[a] n (%)		
Standard	264 (74.4)	266 (75.1)
High	76 (21.4)	78 (22.0)
Indeterminate	15 (4.2)	10 (2.8)

[a]Assessed by fluorescence in situ hybridization; high risk was defined as the presence of del(17p), t(4;14), and/or t(14;16).

Table 2: Baseline PRO scores[a]

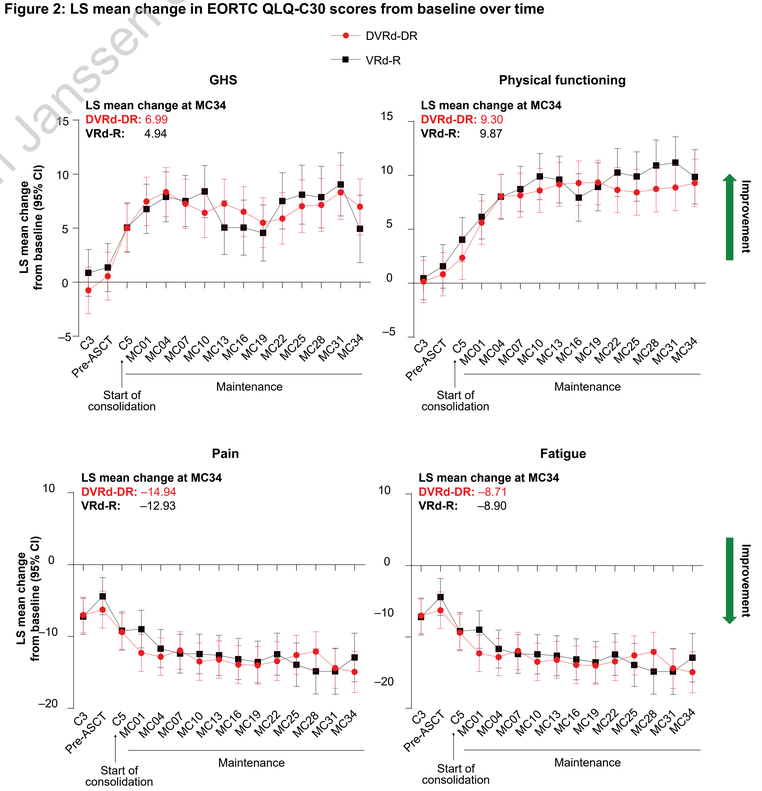
	DVRd-DR (n=355)	VRd-R (n=354)
EORTC QLQ-C30, mean (SD)		
GHS	64.2 (23.1)	65.2 (23.7)
Physical functioning	74.2 (27.1)	74.8 (25.6)
Pain	32.8 (30.4)	33.5 (30.6)
Fatigue	31.7 (24.7)	33.5 (25.4)
EQ-5D-5L, mean (SD)		
VAS	69.3 (21.6)	69.0 (22.3)
EORTC QLQ-MY20, mean (SD)		
Disease symptoms	23.4 (19.6)	25.9 (22.1)

[a]Scores ranged from 0–100 (after linear transformation for EORTC scales).

PROs

- Compliance rates for PRO assessments were high and comparable between both treatment arms
  - Compliance was >93.5% at baseline and >80.0% for the majority of time points, ranging from 75.0–96.7%, through MC34 for the EORTC QLQ-C30, EORTC QLQ-MY20, and EQ-5D-5L
- LS mean changes from baseline in PRO scores showed improvements for EORTC QLQ-C30 GHS (overall quality of life), physical functioning, and pain and fatigue (MM-related symptoms), EORTC QLQ-MY20 disease symptoms (MM symptom burden) scores, and EQ-5D-5L VAS (self-rated overall health) that were apparent by the start of maintenance and sustained through MC34 (**Figures 2–4**)
  - Comparable improvements in HRQoL were observed across other EORTC QLQ-C30, EORTC QLQ-MY20, and EQ-5D-5L domains

Figure 2: LS mean change in EORTC QLQ-C30 scores from baseline over time



ASCT, autologous stem cell transplant; C, cycle.

Figure 3: LS mean change in EORTC QLQ-MY20 disease symptom scores from baseline over time

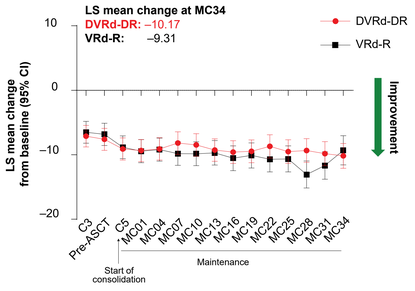
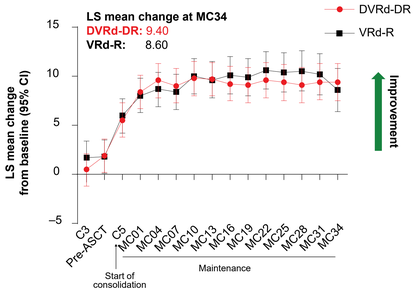
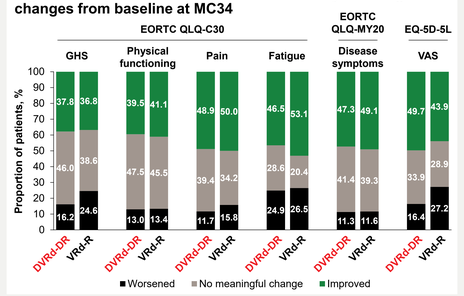


Figure 4: LS mean change in EQ-5D-5L VAS scores from baseline over time



- Similar proportions of each arm reported clinically meaningful improvement and worsening across PRO instruments (**Figure 5**)

Figure 5: Proportions of patients with clinically meaningful changes from baseline at MC34



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Multiple Myeloma

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