PS1712

Subcutaneous Daratumumab (Dara) + Bortezomib/ Lenalidomide/Dexamethasone With Dara + Lenalidomide Maintenance in Transplant-Eligible Patients With Newly Diagnosed Multiple Myeloma: Analysis of Sustained Minimal Residual Disease Negativity in the Phase 3 PERSEUS Trial

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Key Takeaway

These results reinforce the consistent benefit of DVRd + DR maintenance and further support the PERSEUS regimen as standard of care for transplant-eligible NDMM

Conclusions

- Higher rates of sustained MRD negativity (10^{-5}) ≥CR were achieved with DVRd + DR maintenance vs VRd + R maintenance, with nearly two-thirds of patients achieving sustained MRD negativity for ≥12 months and more than half achieving sustained MRD negativity for ≥24 months
- Sustained MRD negativity was associated with a PFS benefit with DVRd, with >95% of patients with ≥12-month or ≥24-month sustained MRD negativity remaining progression free at 48 months
- Rates of functionally high-risk myeloma, defined as relapse or progression within 18 months of treatment initiation, were lower than in previous daratumumab frontline trials[4] and were halved with DVRd vs VRd

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Poster

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Disclosures

PM reports a consulting/advisory role for AbbVie, Amgen, Celgene, GSK, Janssen, Pfizer, and Sanofi; and has received honoria from AbbVie, Amgen, Celgene, GSK, Janssen-Cilag, Pfizer, and Sanofi.

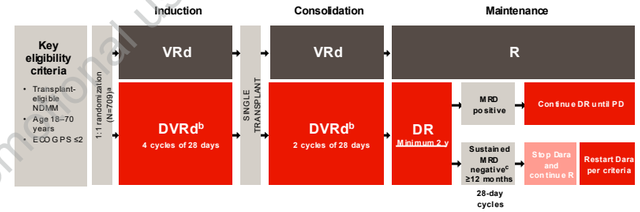
Introduction

- In PERSEUS, daratumumab, bortezomib, lenalidomide, and dexamethasone (DVRd) induction/consolidation and DR maintenance improved minimal residual disease (MRD) negativity and progression-free survival (PFS) vs VRd induction/consolidation and R maintenance[1-3]
- Functionally high-risk patients (with relapse or progression within 18 months of treatment initiation) have poorer survival outcomes[4,5]
  - Approved frontline daratumumab-containing regimens, including daratumumab, bortezomib, thalidomide, and dexamethasone and DRd, reduced the risk of early relapse at 12–24 months to <10–20%[4]
- Sustained MRD negativity, a key efficacy endpoint and prognostic marker, is linked to improved survival[6-8]
- This post hoc analysis explored 2 distinct aims in PERSEUS:
  - Aim 1: to determine whether DVRd + DR maintenance reduces the number of functionally high-risk patients
  - Aim 2: to explore the impact of sustained MRD negativity (10^{-5}) complete response or better (≥CR) on PFS

Methods

- PERSEUS is a phase 3, randomized clinical trial (**Figure 1**)
- The primary endpoint was PFS; MRD-negativity rate (defined as the proportion of patients who achieved both MRD negativity and ≥CR in the intent-to-treat [ITT] population) was one of the key secondary endpoints
- Sustained MRD negativity was defined as MRD negativity with ≥CR at least 12 months apart and without MRD positivity in between
  - Patients who were not evaluable were considered MRD positive
  - MRD was evaluated post consolidation; at the time of suspected CR/stringent CR (sCR); at 12, 18, 24, 30, and 36 months after cycle 1 day 1; and yearly thereafter

Figure 1: Study design



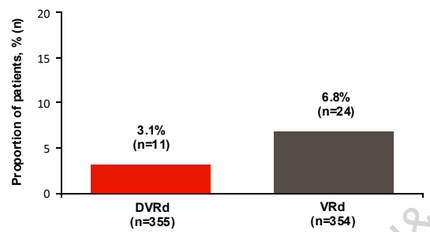
[a]Stratified by ISS stage and cytogenetic risk. [b]Dara 1800 mg co-formulated with rHuPH20 (2000 U/mL; ENHANZE® drug delivery technology, Halozyme, Inc., San Diego, CA, USA); VRd administered as in the VRd group. [c]MRD was assessed using the clonoSEQ assay (v.2.0; Adaptive Biotechnologies, Seattle, WA, USA) in patients with ≥VGPR post consolidation and at the time of suspected ≥CR. Dara, daratumumb; ECOG PS, Eastern Cooperative Oncology Group performance status; ISS, International Staging System; NDMM, newly diagnosed multiple myeloma; PD, progressive disease; rHuPH20, recombinant human hyaluronidase PH20; VGPR, very good partial response; y, year.

Results

Aim 1: Rates of functionally high risk

- Functionally high-risk incidence was halved with DVRd vs VRd (**Figure 2**)
- Rates of functionally high-risk disease, including pre-progression deaths, (those who progressed or died within 18 months of treatment initiation), were lower with DVRd (5.4%; n=19) vs VRd (11.0%; n=39)

Figure 2: Rates of functionally high risk[a]

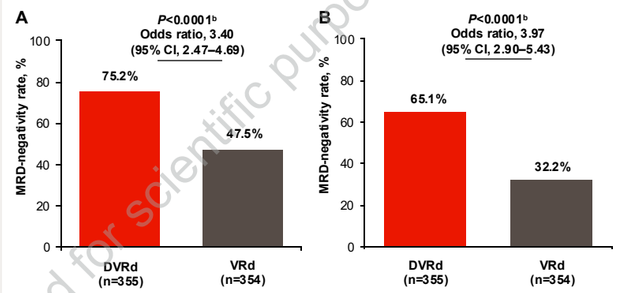


[a]Defined as those experiencing relapse or progression within 18 months of treatment initiation.

Aim 2: Impact of sustained MRD negativity (10^{-5}) ≥CR on PFS

- At a median follow-up of 47.5 months, DVRd and DR maintenance achieved deep and durable MRD negativity at 10^{-5} (**Figure 3A**) and 10^{-6} (**Figure 3B**)

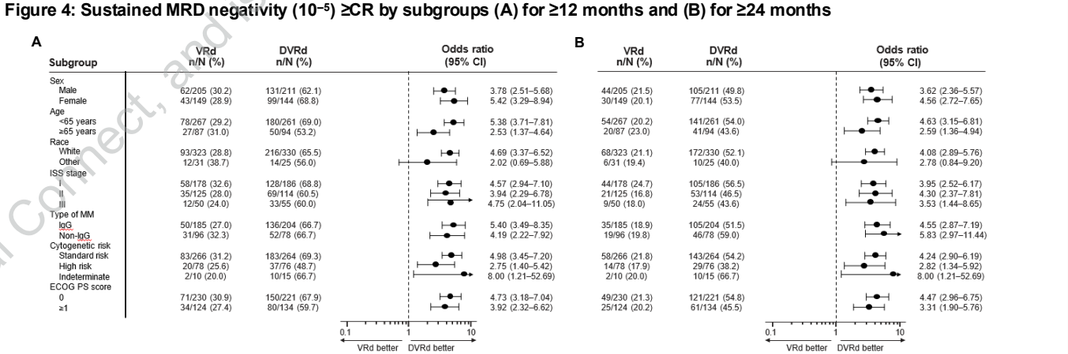
Figure 3: Overall MRD-negativity ≥CR rates[a] at (A) 10^{-5} and (B) 10^{-6}



[a]MRD-negativity rate was defined as the proportion of patients who achieved both MRD negativity and ≥CR and was assessed using bone marrow aspirates and evaluated via NGS (clonoSEQ assay version 2.0; Adaptive Biotechnologies, Seattle, WA, USA). [b]*P* values were calculated with the use of the stratified Cochran-Mantel-Haenszel chi-square test.

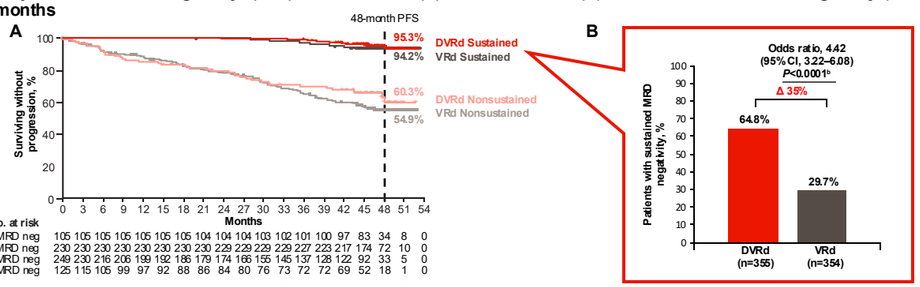
- DVRd led to higher rates of sustained MRD negativity (10^{-5}) ≥CR vs VRd across subgroups for both ≥12 and ≥24 months (**Figure 4**)
- Sustained MRD-negativity (10^{-5}) ≥CR rates for ≥12 months were twice as high with DVRd vs VRd; among these patients, 48-month PFS rates were ~95% in both arms (sustained [≥12 months] hazard ratio [HR], 0.83 [95% CI, 0.3–2.3]; nonsustained [≥12 months] HR, 0.80 [95% CI, 0.6–1.2]; **Figure 5**)
- Sustained MRD-negativity (10^{-5}) ≥CR rates for ≥24 months were more than twice as high with DVRd vs VRd; among these patients, 48-month PFS rates exceeded 95% in both arms (**Figure 6**)

Figure 4: Sustained MRD negativity (10^{-5}) ≥CR by subgroups (A) for ≥12 months and (B) for ≥24 months



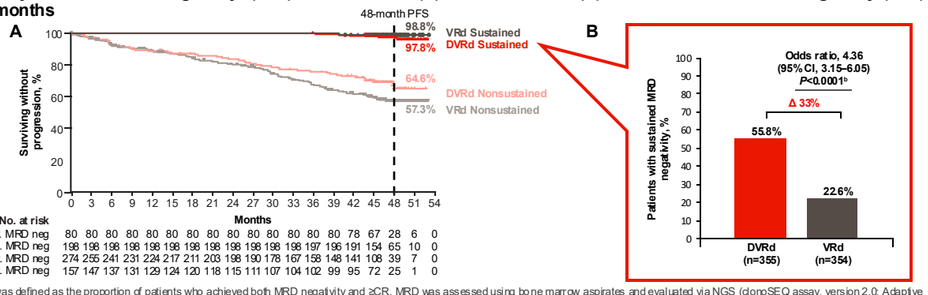
Sustained MRD negativity is defined as 2 consecutive MRD-negative reads at least 24 months (–3) apart without MRD positive in between. MRD-negativity rate was defined as the proportion of patients who achieved both MRD negativity and ≥CR in the ITT population. Patients who were not evaluable or had indeterminate results were considered MRD positive. The subgroup analysis for type of MM was performed on data from patients who had measurable disease in serum. Cytogenetic risk was assessed by fluorescence in situ hybridization; high risk was defined as the presence of del(17p), t(4;14), and/or t(14;16). Ig, immunoglobulin; MM, multiple myeloma.

Figure 5: PFS by sustained MRD negativity[a] (10^{-5}) ≥CR status for (A) ≥12 months and (B) rates of sustained MRD negativity (10^{-5}) ≥CR for ≥12 months



[a]MRD-negativity rate was defined as the proportion of patients who achieved both MRD negativity and ≥CR. MRD was assessed using bone marrow aspirates and evaluated via NGS (clonoSEQ assay, version 2.0; Adaptive Biotechnologies, Seattle, WA, USA). Sustained MRD negativity is defined as MRD negative and confirmed by at least 1 year apart without MRD positive in between. [b]*P* value was calculated from the stratified Cochran-Mantel-Haenszel chi-squared test.

Figure 6: PFS by sustained MRD negativity[a] (10^{-5}) ≥CR status for (A) ≥24 months and (B) rates of sustained MRD negativity (10^{-5}) ≥CR for ≥24 months



[a]MRD-negativity rate was defined as the proportion of patients who achieved both MRD negativity and ≥CR. MRD was assessed using bone marrow aspirates and evaluated via NGS (clonoSEQ assay, version 2.0; Adaptive Biotechnologies, Seattle, WA, USA). Sustained MRD negativity is defined as 2 consecutive MRD-negative reads at least 24 months (–3) apart without MRD positive in between. [b]*P* value was calculated from the stratified Cochran-Mantel-Haenszel chi-squared test.

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Multiple Myeloma

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