Daratumumab (DARA) + Bortezomib/Lenalidomide/ Dexamethasone (VRd) in Transplant-eligible Patients With Newly Diagnosed Multiple Myeloma (NDMM): Analysis of Minimal Residual Disease (MRD) in the PERSEUS Trial*

*ClinicalTrials.gov Identifier: NCT03710603; sponsored by EMN in collaboration with Janssen Research & Development, LLC.

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Disclosures of Conflicts of Interest

HE has served in a consulting/advisory role for Amgen, BMS, Celgene, GSK, Janssen, and Sanofi; has received honoraria from Amgen, BMS, Celgene, GSK, Janssen, and Sanofi; and has received research funding from Amgen, BMS, Celgene, GSK, Janssen, and Sanofi. **PRO** has received honoraria from Amgen, BMS, Celgene, GSK, Janssen, Oncopeptides, Regeneron, and Sanofi. **PM** has served in a consulting/advisory role for AbbVie, Amgen, Celgene, GSK, Janssen, Oncopeptides, Sanofi; and has received honoraria from AbbVie, Amgen, Celgene, GSK, Janssen, Oncopeptides, and Sanofi**. MAD** has served in a consulting/advisory role for Amgen, Beigene, BMS, Janssen-Cilag, Takeda; and has received honoraria from Amgen, Beigene, BMS, Janssen-Cilag, Takeda. **MB** has served in a consulting/advisory role for Amgen, Celgene, Janssen-Cilag, Oncopeptides, Sanofi Pasteur, Takeda; and has received honoraria from Amgen, Celgene, Janssen-Cilag, Oncopeptides, Sanofi Pasteur, and Takeda**. AP** has served in a consulting/advisory role for AbbVie, Amgen, BMS, Janssen, Pfizer, Sanofi, and Takeda; and has received honoraria from AbbVie, Amgen, BMS, Janssen, Pfizer, Sanofi, and Takeda**. AB** has served in a consulting/advisory role for Amgen, BMS, Janssen, and Sanofi; and has received honoraria from Amgen, BMS, Janssen, and Sanofi**. FG** has served in a consulting/advisory role for AbbVie, Adaptive Biotechnologies, Amgen, Bluebird Bio, BMS, Celgene, GSK, Janssen, Oncopeptides, Roche, Sanofi, and Takeda; and has received honoraria from AbbVie, Adaptive Biotechnologies, Amgen, Bluebird Bio, BMS, Celgene, GSK, Janssen, Oncopeptides, Roche, Sanofi, and Takeda**. RM** has served in a consulting/advisory role for Amgen, BMS, Celgene, Janssen, Sanofi, Takeda; and has received honoraria from Amgen, BMS, Celgene, Janssen, Sanofi, Takeda**. NWCJvdD** has served in a consulting/advisory role for AbbVie, Adaptive Biotechnologies, Amgen, Bayer, BMS, Celgene, Janssen, Kite Pharma, Merck, Novartis, Pfizer, Roche, Servier, and Takeda; and has received research funding from Amgen, BMS, Celgene, Cellectis, Janssen, and Novartis**. FS** has served in a consulting/advisory role for, received honoraria from, and received research funding from AbbVie, Amgen, BMS, Celgene, Daiichi Sankyo, GSK, Janssen-Cilag, Novartis, Oncopeptides, Pfizer, Sanofi, SkylineDx, Takeda, and Targovax**. MD** has served in a consulting/advisory role for Amgen, BMS, GSK, Janssen, Sanofi, Stemline Therapeutics, and Takeda**. AS** has served in a consulting/advisory role for AbbVie, Amgen, BMS, Haemalogix, Janssen, Pfizer; is a member of the Board of Directors or advisory committee for Roche; and has received honoraria from AbbVie, Amgen, BMS, Haemalogix, Janssen, Pfizer, and Roche**. SL** has nothing to disclose. **DV, ASA,** and **RC** are employees/hold stock and other ownership interests in Janssen. **JB** has served in a consulting/advisory role for and received honoraria from Amgen, Celgene, Janssen, and Takeda**. MB** has served in a consulting/advisory role for GSK and Janssen; has received honoraria from AbbVie, Amgen, BMS, Celgene, GSK, Janssen, Novartis, and Sanofi; and has received research funding from Amgen, BMS, Celgene, Janssen, Mundipharma, Novartis, and Sanofi**. PS** has received honoraria from Amgen, BMS, Celgene, Janssen, Karyopharm, Pfizer, and Takeda; and has received research funding from Amgen, BMS, Celgene, Janssen, Karyopharma, SkylineDx, and Takeda**.**

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PERSEUS: Introduction

- In NDMM, MRD negativity has been associated with longer PFS and OS, and deeper responses (10^{-6}) have been associated with superior PFS compared with MRD negativity at 10^{-5} or 10^{-4} sensitivity[1,2]
- An increasing number of patients are achieving OS of 10 years or longer. Current MRD testing at a sensitivity level of 10^{-6} and sustained MRD at this level for over 5 years translates into very long survival and potentially a "cure" for patients with standard-risk features[3-5]
- In the primary analysis of PERSEUS, D-VRd induction/consolidation + D-R maintenance improved depth of response and PFS versus VRd induction/consolidation + R maintenance in transplant-eligible NDMM[6]
  - 64% of patients receiving D-R maintenance stopped DARA after ≥2 years due to achieving sustained MRD negativity (10^{-5})[a]
- **Here, we report further results from PERSEUS on deepening of response and MRD negativity during maintenance therapy**

[a]MRD-negativity rate was defined as the proportion of patients who achieved both MRD negativity and ³CR in the ITT population.
MRD was assessed using bone marrow aspirates and evaluated via NGS (clonoSEQ assay, version 2.0; Adaptive Biotechnologies, Seattle, WA, USA).
CR, complete response; DARA, daratumumab; D-R, daratumumab plus lenalidomide; D-VRd, daratumumab plus bortezomib/lenalidomide/dexamethasone; ITT, intent to treat; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; NGS, next-generation sequencing OS, overall survival; PFS, progression-free survival; R, lenalidomide; VRd, bortezomib/lenalidomide/dexamethasone.

1. Munshi NC, et al. *Blood Adv* 2020;4(23):5988-99. 2. Perrot A, et al. *Blood* 2018;132(23):2456-64. 3. International Myeloma Foundation. A deeper understanding of 'cure' in multiple myeloma. Accessed May 14, 2024. https://www.myeloma.org/blog/dr-duries/deeper-understanding-of-cure-in-myeloma. 4. Engelhardt M, et al. *Haematologica* 2024;109(8):2420-35. 5. Rodriguez-Otero P, et al. *Cancer Treat Rev* 2021;100:102284. 6. Sonneveld P, et al. *N Engl J Med* 2024;390(4):301-13.

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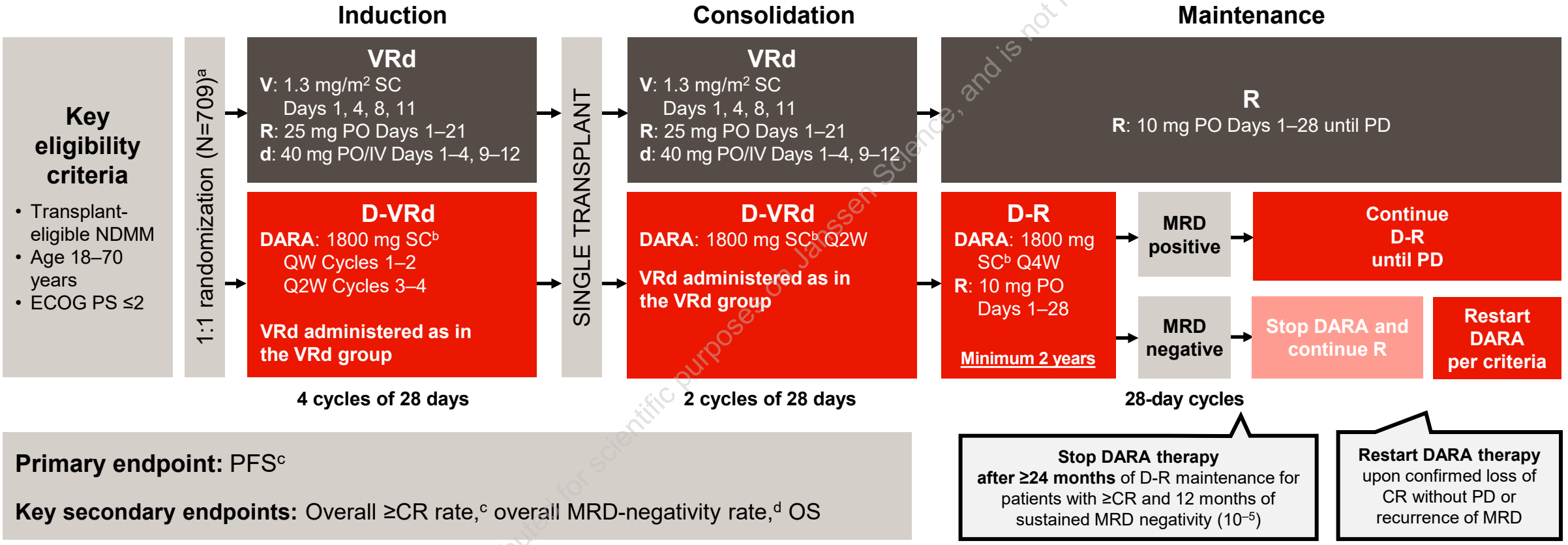
PERSEUS: Study Design



Primary endpoint: PFS[c]

Key secondary endpoints: Overall ≥CR rate,[c] overall MRD-negativity rate,[d] OS

Stop DARA therapy after ≥24 months of D-R maintenance for patients with ≥CR and 12 months of sustained MRD negativity (10^{-5})

Restart DARA therapy upon confirmed loss of CR without PD or recurrence of MRD

[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). [c]Response and disease progression were assessed using a computerized algorithm based on IMWG response criteria. [d]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. Overall, the MRD-negativity rate was defined as the proportion of patients who achieved both MRD negativity (10^{-5} threshold) and ≥CR at any time.

CR, complete response; DARA, daratumumab; d, dexamethasone; D-R, daratumumab plus lenalidomide; D-VRd, daratumumab plus bortezomib/lenalidomide/dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; IMWG, International Myeloma Working Group; ISS, International Staging System; IV, intravenous; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; OS; overall survival; PD, progressive disease; PFS, progression-free survival; PO, oral; Q2W, every 2 weeks; Q4W, every 4 weeks; QW, weekly; R, lenalidomide; rHuPH20, recombinant human hyaluronidase PH20; SC, subcutaneous; V, bortezomib; VGPR, very good partial response; VRd, bortezomib/lenalidomide/dexamethasone.

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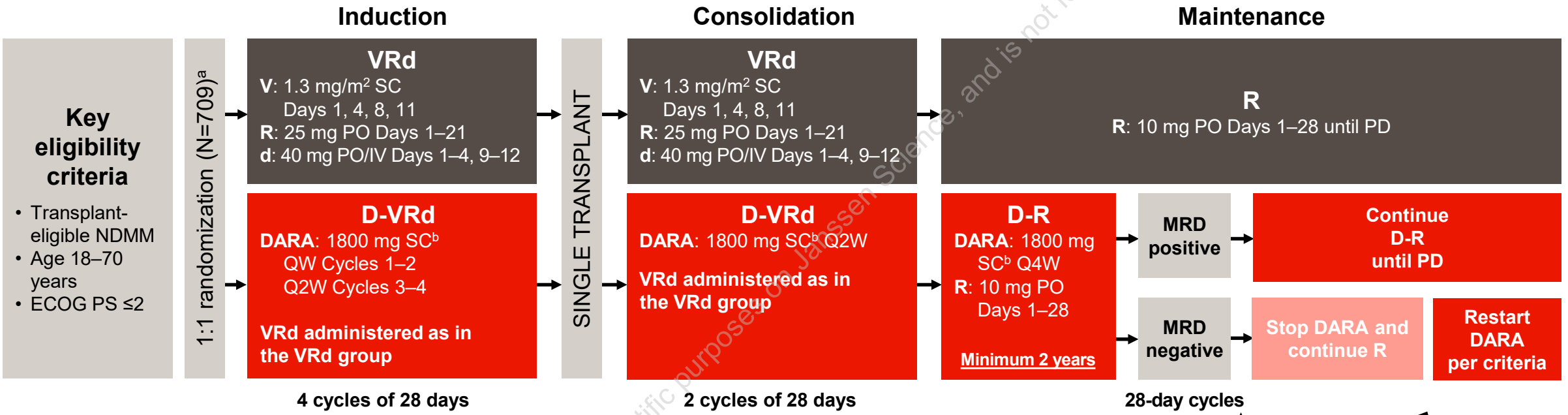
PERSEUS: Study Design



Primary endpoint: PFS[c]

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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.

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PERSEUS: Endpoints and Statistical Analyses

- **Endpoints**
  - The primary endpoint was PFS
  - Overall ≥CR rate and overall MRD-negativity (10^{-5}) rate were key secondary endpoints
- **MRD endpoint definitions**
  - MRD negativity was defined as the patients who achieved both MRD negativity and ≥CR response
    - Patients who were not evaluable or had indeterminate results were considered MRD positive
  - Overall MRD-negativity rate was defined as the proportion of patients in the ITT population who achieved both MRD negativity and ≥CR
  - Sustained MRD-negativity (≥12 months) rate was defined as the proportion of patients in the ITT population with 2 consecutive MRD-negative results ≥12 months apart, without any MRD-positive results in between
- **Statistical analyses**
  - Odds ratios and *P* values for the difference between the 2 treatment groups were calculated for overall MRD-negativity rate and sustained MRD-negativity rate
    - Stratified Mantel–Haenszel odds ratios and stratified *P* values were calculated for the ITT population
    - Unstratified Mantel–Haenszel odds ratios and unstratified *P* values were calculated for subgroup analyses
    - Stratification factors were ISS disease stage (I, II, vs III) and cytogenetic risk (high risk vs standard risk or indeterminate)
    - *P* values were based on the Cochran–Mantel–Haenszel chi-square test

CR, complete response; ISS, International Staging System; ITT, intent to treat; MRD; minimal residual disease; PFS, progression-free survival.

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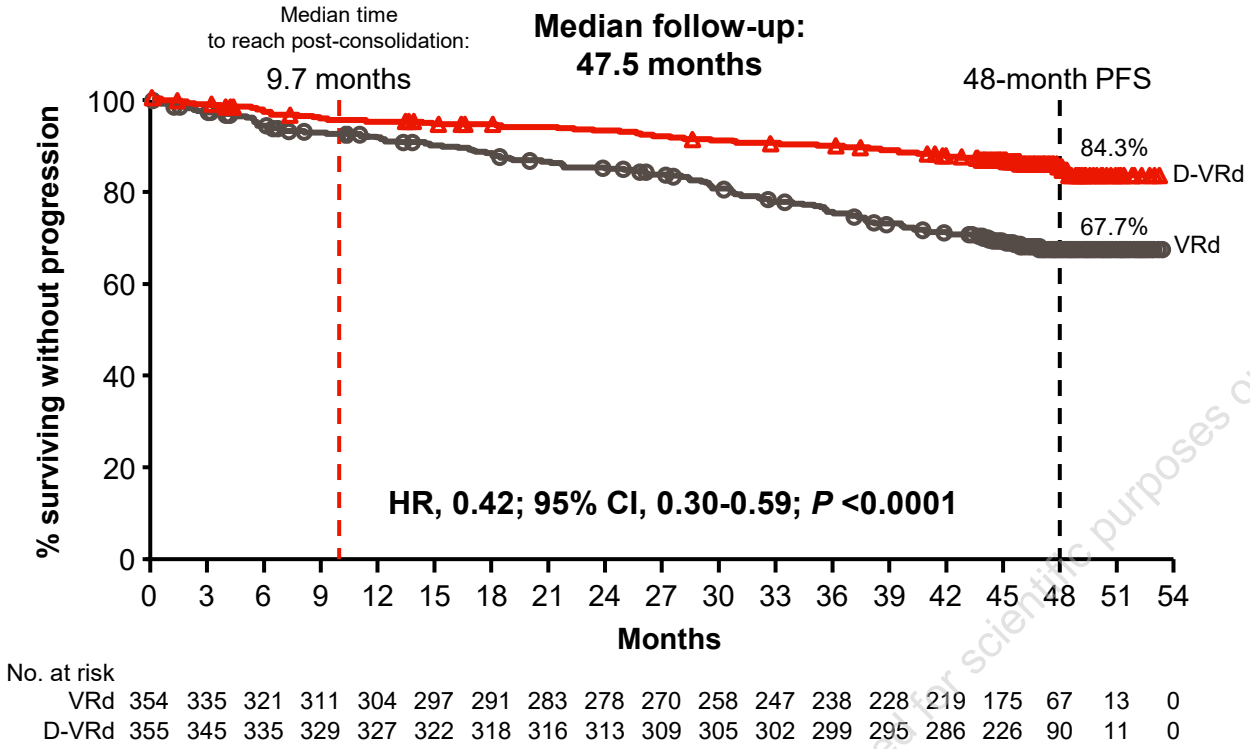
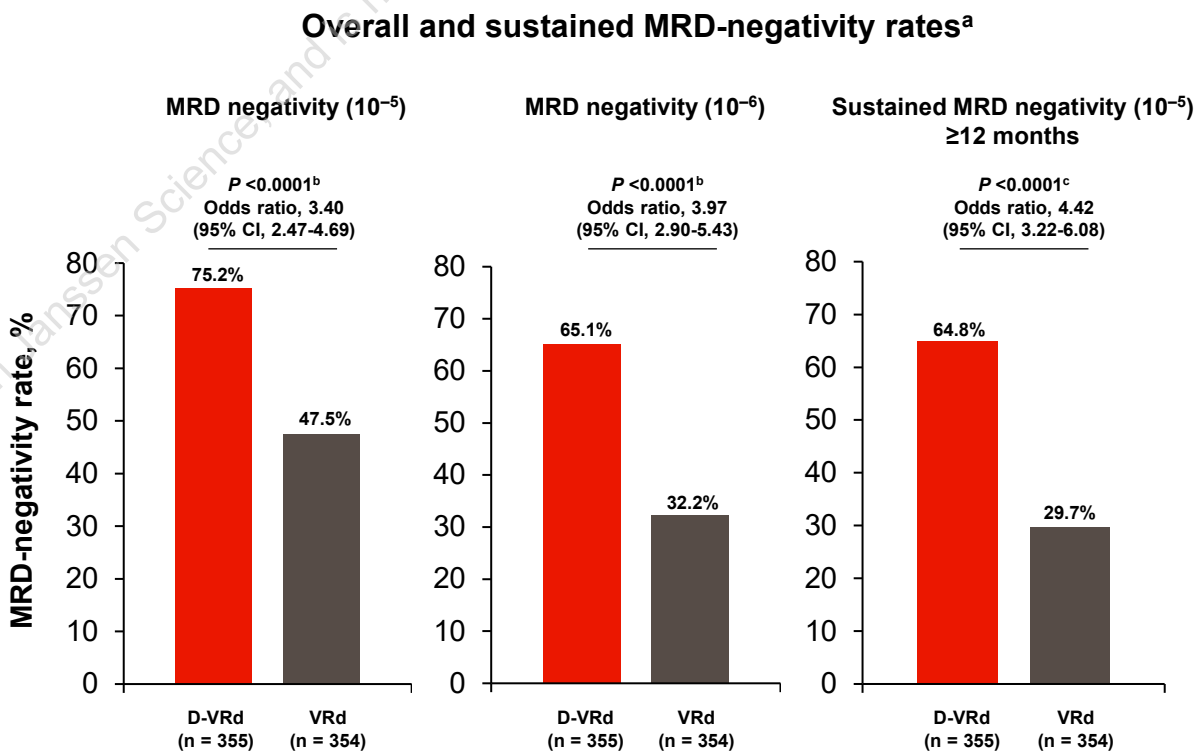
PERSEUS Primary Analysis: D-VRd Followed by D-R Maintenance Significantly Improved PFS and Depth of Response Versus VRd Followed by R Maintenance[1]





58% reduction in the risk of progression or death in patients receiving D-VRd

Deep and durable MRD negativity achieved with D-VRd

[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).
[b]*P* values were calculated with the use of the stratified Cochran–Mantel–Haenszel chi-square test. [c]*P* value was calculated with the use of Fisher's exact test.
CI, confidence interval; D-R, daratumumab plus lenalidomide; D-VRd, daratumumab plus bortezomib/lenalidomide/dexamethasone; HR, hazard ratio; MRD; minimal residual disease; NGS, next-generation sequencing; PFS, progression-free survival; R, lenalidomide; VRd, bortezomib/lenalidomide/dexamethasone.

1. Sonneveld P, et al. *N Engl J Med* 2024;390(4):301-13.

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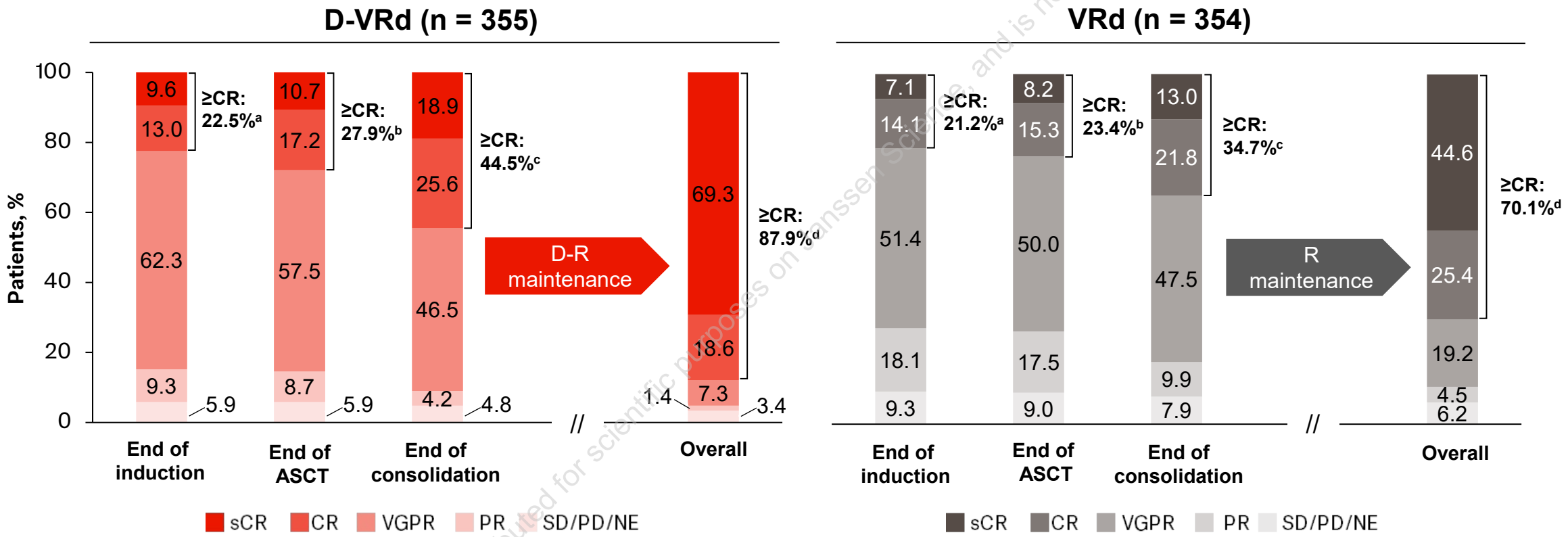
PERSEUS: Responses Over Time (ITT)



Responses deepened to a greater extent with D-VRd + D-R versus VRd + R

P values were calculated using the stratified Cochran–Mantel–Haenszel chi-square test. [a]*P* = 0.6680. [b]*P* = 0.1774. [c]*P* = 0.0078. [d]*P* <0.0001.
ASCT, autologous stem cell transplant; CR, complete response; D-R, daratumumab plus lenalidomide; D-VRd, daratumumab plus bortezomib/lenalidomide/dexamethasone; ITT, intent to treat; PR, partial response; R, lenalidomide; sCR, stringent complete response; SD/PD/NE, stable disease/progressive disease/not evaluable; VRd, bortezomib/lenalidomide/dexamethasone.

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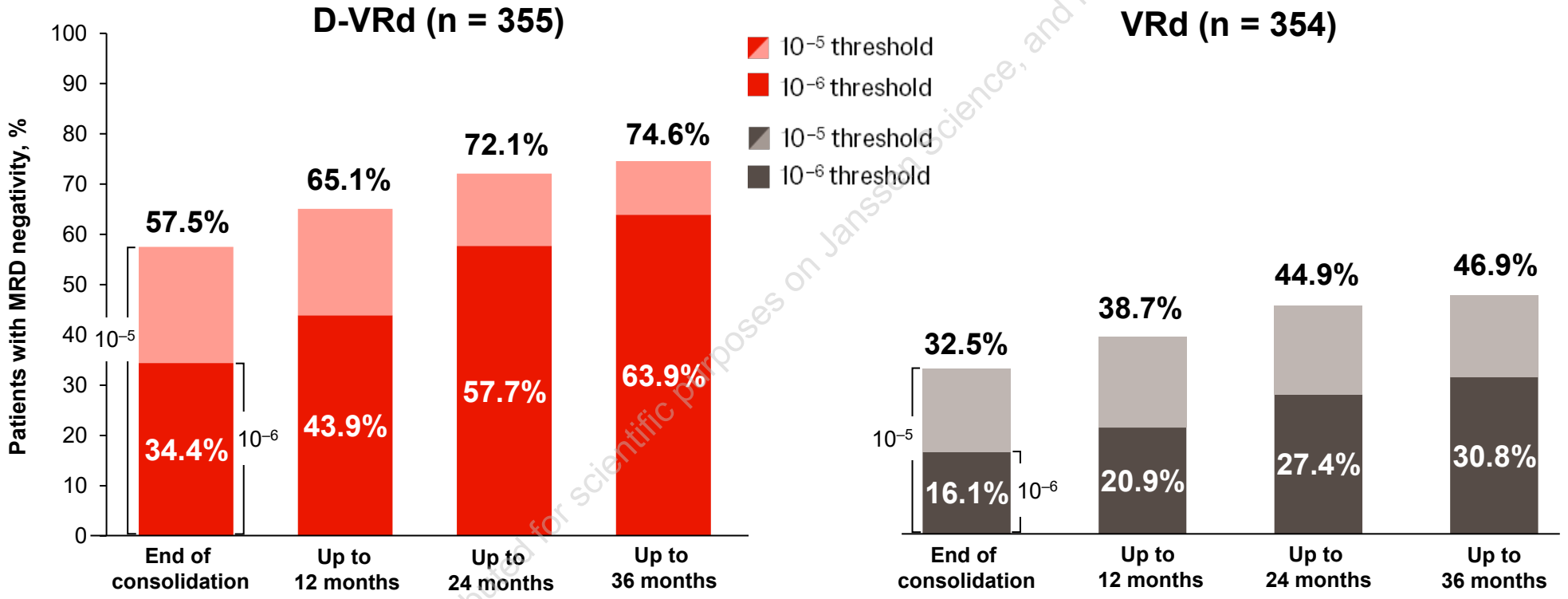
PERSEUS: MRD Negativity Rates 10^{-5} and 10^{-6} (ITT)

Cumulative MRD-negativity rates (%) measured from first treatment dose



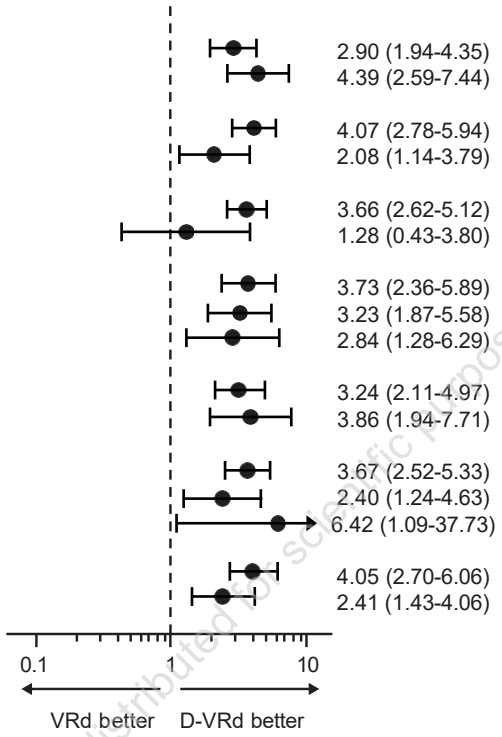
- **D-VRd + D-R doubled the rates of deeper MRD negativity at 10^{-6} versus VRd + R**
- **MRD negativity at 10^{-6} increased by approximately 30% during maintenance with D-R**

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. *P* values were calculated using the stratified Cochran–Mantel–Haenszel chi-square test. *P* <0.0001 for all comparisons of D-VRd versus VRd.
CR, complete response; D-R, daratumumab plus lenalidomide; D-VRd, daratumumab plus bortezomib/lenalidomide/dexamethasone; ITT, intent to treat; MRD; minimal residual disease; R, lenalidomide; VRd, bortezomib/lenalidomide/dexamethasone.

PERSEUS: MRD-negativity Rates in Prespecified Subgroups (ITT)

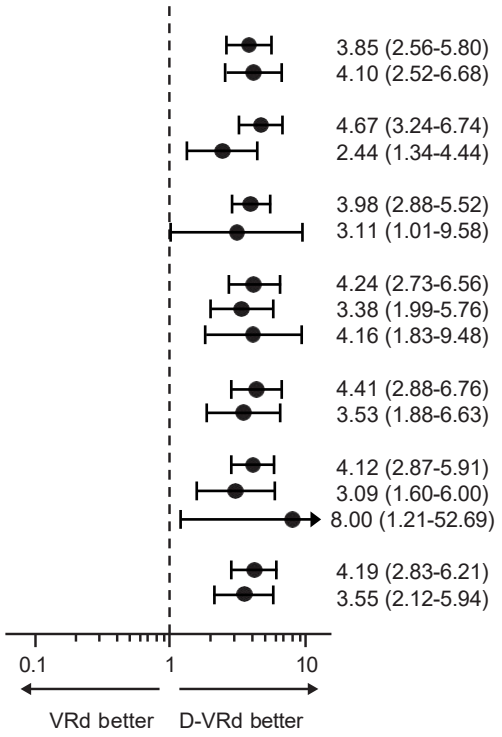
Overall MRD negativity (10^{-5})

Subgroup	VRd n/N (%)	D-VRd n/N (%)	Odds ratio (95% CI)
Sex			
Male	94/205 (45.9)	150/211 (71.1)	2.90 (1.94-4.35)
Female	74/149 (49.7)	117/144 (81.3)	4.39 (2.59-7.44)
Age			
<65 years	125/267 (46.8)	204/261 (78.2)	4.07 (2.78-5.94)
≥65 years	43/87 (49.4)	63/94 (67.0)	2.08 (1.14-3.79)
Race			
White	150/323 (46.4)	251/330 (76.1)	3.66 (2.62-5.12)
Other	18/31 (58.1)	16/25 (64.0)	1.28 (0.43-3.80)
ISS stage			
I	88/178 (49.4)	146/186 (78.5)	3.73 (2.36-5.89)
II	58/125 (46.4)	84/114 (73.7)	3.23 (1.87-5.58)
III	21/50 (42.0)	37/55 (67.3)	2.84 (1.28-6.29)
Type of MM			
IgG	89/185 (48.1)	153/204 (75.0)	3.24 (2.11-4.97)
Non-IgG	50/96 (52.1)	63/78 (80.8)	3.86 (1.94-7.71)
Cytogenetic risk			
Standard risk	128/266 (48.1)	204/264 (77.3)	3.67 (2.52-5.33)
High risk	37/78 (47.4)	52/76 (68.4)	2.40 (1.24-4.63)
Indeterminate	3/10 (30.0)	11/15 (73.3)	6.42 (1.09-37.73)
ECOG PS score			
0	101/230 (43.9)	168/221 (76.0)	4.05 (2.70-6.06)
≥1	67/124 (54.0)	99/134 (73.9)	2.41 (1.43-4.06)



Overall MRD negativity (10^{-6})

Subgroup	VRd n/N (%)	D-VRd n/N (%)	Odds ratio (95% CI)
Sex			
Male	62/205 (30.2)	132/211 (62.6)	3.85 (2.56-5.80)
Female	52/149 (34.9)	99/144 (68.8)	4.10 (2.52-6.68)
Age			
<65 years	83/267 (31.1)	177/261 (67.8)	4.67 (3.24-6.74)
≥65 years	31/87 (35.6)	54/94 (57.4)	2.44 (1.34-4.44)
Race			
White	106/323 (32.8)	218/330 (66.1)	3.98 (2.88-5.52)
Other	8/31 (25.8)	13/25 (52.0)	3.11 (1.01-9.58)
ISS stage			
I	59/178 (33.1)	126/186 (67.7)	4.24 (2.73-6.56)
II	41/125 (32.8)	71/114 (62.3)	3.38 (1.99-5.76)
III	14/50 (28.0)	34/55 (61.8)	4.16 (1.83-9.48)
Type of MM			
IgG	56/185 (30.3)	134/204 (65.7)	4.41 (2.88-6.76)
Non-IgG	36/96 (37.5)	53/78 (67.9)	3.53 (1.88-6.63)
Cytogenetic risk			
Standard risk	88/266 (33.1)	177/264 (67.0)	4.12 (2.87-5.91)
High risk	24/78 (30.8)	44/76 (57.9)	3.09 (1.60-6.00)
Indeterminate	2/10 (20.0)	10/15 (66.7)	8.00 (1.21-52.69)
ECOG PS score			
0	75/230 (32.6)	148/221 (67.0)	4.19 (2.83-6.21)
≥1	39/124 (31.5)	83/134 (61.9)	3.55 (2.12-5.94)



MRD-negativity rates were improved with D-VRd + D-R versus VRd + R across subgroups

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).
CR, complete response; D-R, daratumumab plus lenalidomide; D-VRd, daratumumab plus bortezomib/lenalidomide/dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; IgG, immunoglobulin G; ISS, International Staging System; ITT, intent to treat; MM, multiple myeloma; MRD; minimal residual disease; R, lenalidomide; VRd, bortezomib/lenalidomide/dexamethasone.

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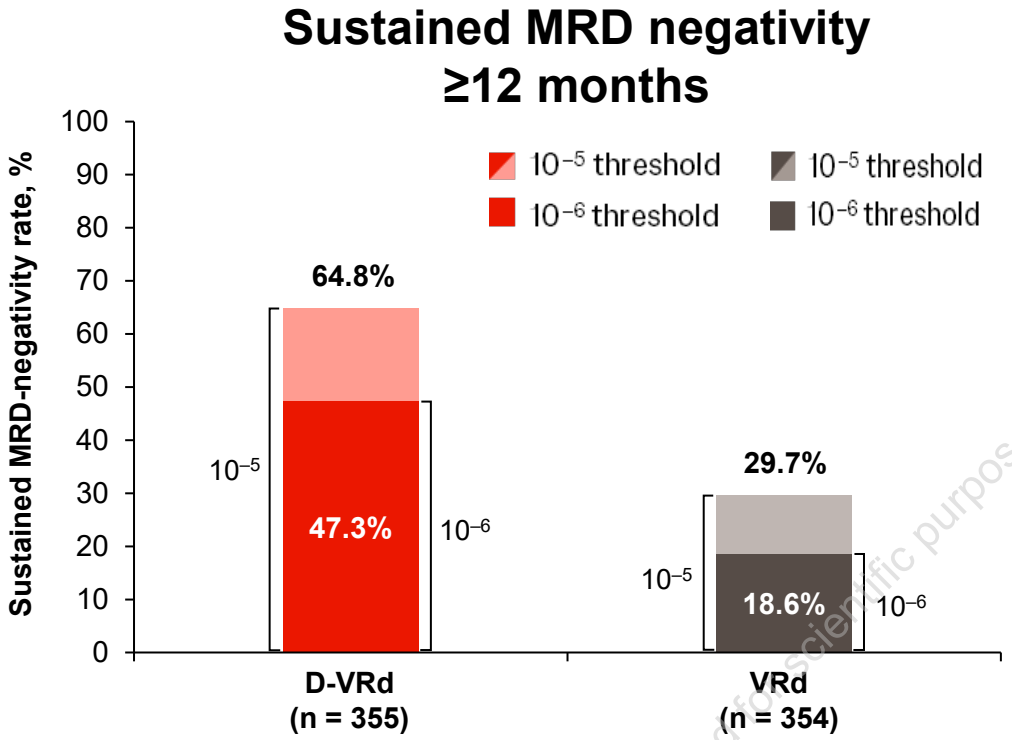
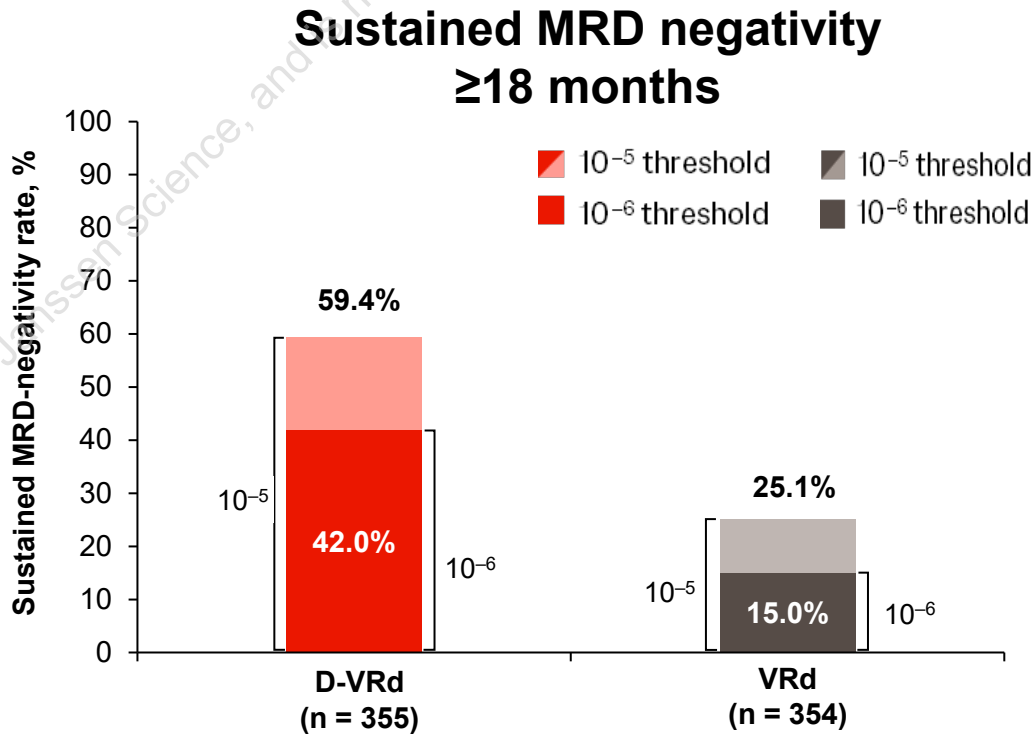
PERSEUS: Sustained MRD-negativity Rates (10^{-5} and 10^{-6} ; ITT)





- **Rates of sustained MRD negativity at 10^{-6} were 2.5-fold higher for D-VRd + D-R versus VRd + R**
- **More than 40% of patients had sustained MRD negativity at 10^{-6} for ≥18 months with D-VRd + D-R**

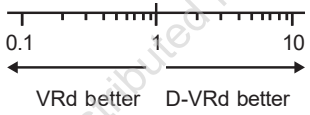
MRD-negativity rate was defined as the proportion of patients who achieved both MRD negativity and ≥CR in the ITT population. Patients who were not evaluable or had indeterminate results were considered MRD positive. *P* values were calculated using the stratified Cochran–Mantel–Haenszel chi-square test. *P* <0.0001 for all comparisons of D-VRd versus VRd.
CR, complete response; D-R, daratumumab plus lenalidomide; D-VRd, daratumumab plus bortezomib/lenalidomide/dexamethasone; ITT, intent to treat; MRD; minimal residual disease; R, lenalidomide; VRd, bortezomib/lenalidomide/dexamethasone.

Presented by H Einsele at the Annual Meeting of the German, Austrian and Swiss Associations of Hematology and Medical Oncology (DGHO); October 11–14, 2024; Basel, Switzerland

PERSEUS: Sustained MRD Negativity by Prespecified Subgroups (ITT)

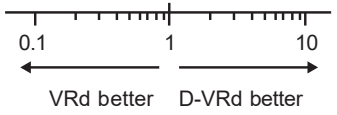
Sustained MRD negativity (10^{-5}) ≥12 months

Subgroup	VRd n/N (%)	D-VRd n/N (%)	Odds ratio (95% CI)
Sex			
Male	62/205 (30.2)	131/211 (62.1)	3.78 (2.51-5.68)
Female	43/149 (28.9)	99/144 (68.8)	5.42 (3.29-8.94)
Age			
<65 years	78/267 (29.2)	180/261 (69.0)	5.38 (3.71-7.81)
≥65 years	27/87 (31.0)	50/94 (53.2)	2.53 (1.37-4.64)
Race			
White	93/323 (28.8)	216/330 (65.5)	4.69 (3.37-6.52)
Other	12/31 (38.7)	14/25 (56.0)	2.02 (0.69-5.88)
ISS stage			
I	58/178 (32.6)	128/186 (68.8)	4.57 (2.94-7.10)
II	35/125 (28.0)	69/114 (60.5)	3.94 (2.29-6.78)
III	12/50 (24.0)	33/55 (60.0)	4.75 (2.04-11.05)
Type of MM			
IgG	50/185 (27.0)	136/204 (66.7)	5.40 (3.49-8.35)
Non-IgG	31/96 (32.3)	52/78 (66.7)	4.19 (2.22-7.92)
Cytogenetic risk			
Standard risk	83/266 (31.2)	183/264 (69.3)	4.98 (3.45-7.20)
High risk	20/78 (25.6)	37/76 (48.7)	2.75 (1.40-5.42)
Indeterminate	2/10 (20.0)	10/15 (66.7)	8.00 (1.21-52.69)
ECOG PS score			
0	71/230 (30.9)	150/221 (67.9)	4.73 (3.18-7.04)
≥1	34/124 (27.4)	80/134 (59.7)	3.92 (2.32-6.62)



Sustained MRD negativity (10^{-6}) ≥12 months

Subgroup	VRd n/N (%)	D-VRd n/N (%)	Odds ratio (95% CI)
Sex			
Male	37/205 (18.0)	96/211 (45.5)	3.79 (2.42-5.93)
Female	29/149 (19.5)	72/144 (50.0)	4.14 (2.46-6.97)
Age			
<65 years	47/267 (17.6)	131/261 (50.2)	4.72 (3.17-7.02)
≥65 years	19/87 (21.8)	37/94 (39.4)	2.32 (1.21-4.48)
Race			
White	63/323 (19.5)	158/330 (47.9)	3.79 (2.67-5.38)
Other	3/31 (9.7)	10/25 (40.0)	6.22 (1.48-26.12)
ISS stage			
I	36/178 (20.2)	93/186 (50.0)	3.94 (2.48-6.28)
II	23/125 (18.4)	47/114 (41.2)	3.11 (1.73-5.59)
III	7/50 (14.0)	28/55 (50.9)	6.37 (2.44-16.60)
Type of MM			
IgG	31/185 (16.8)	96/204 (47.1)	4.42 (2.75-7.09)
Non-IgG	18/96 (18.8)	43/78 (55.1)	5.32 (2.70-10.50
Cytogenetic risk			
Standard risk	54/266 (20.3)	137/264 (51.9)	4.24 (2.88-6.22)
High risk	11/78 (14.1)	23/76 (30.3)	2.64 (1.18-5.90)
Indeterminate	1/10 (10.0)	8/15 (53.3)	10.29 (1.03-102.75)
ECOG PS score			
0	47/230 (20.4)	106/221 (48.0)	3.59 (2.37-5.44)
≥1	19/124 (15.3)	62/134 (46.3)	4.76 (2.62-8.63)

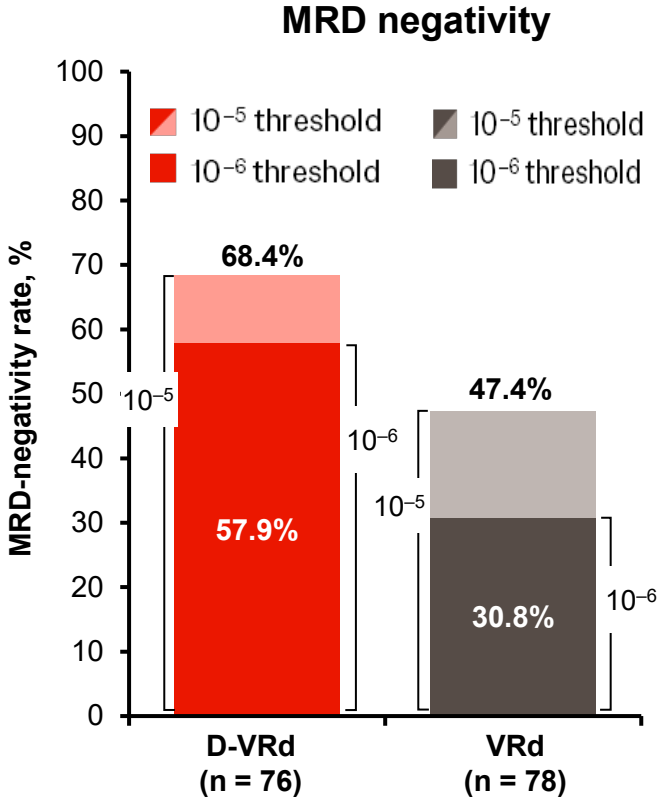


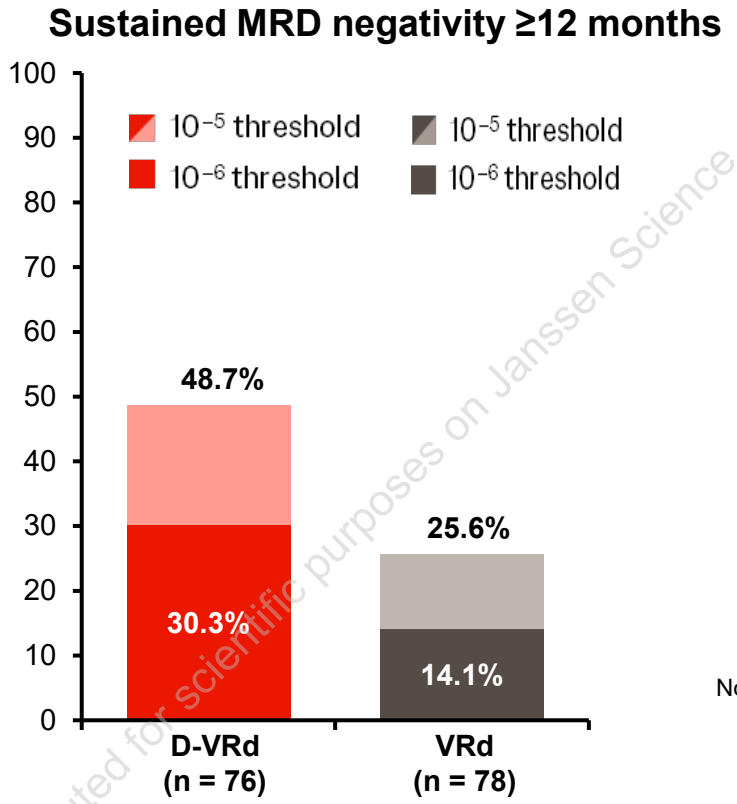
Sustained MRD-negativity rates were improved with D-VRd + D-R versus VRd + R across subgroups

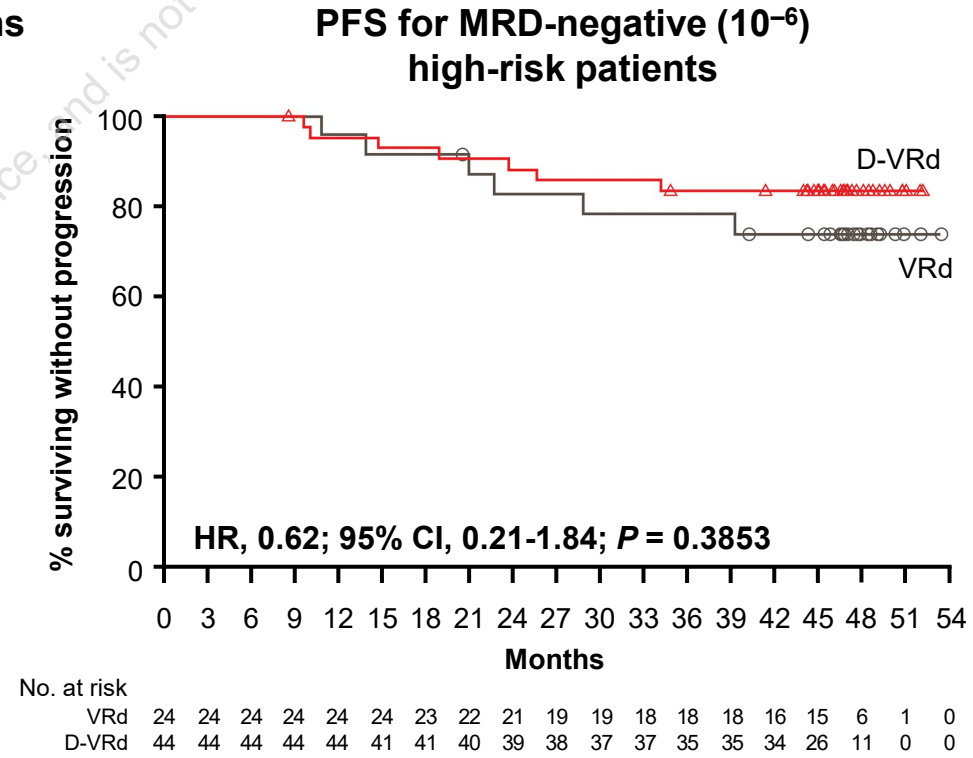
MRD-negativity rate was defined as the proportion of patients who achieved both MRD negativity and ≥CR in the ITT population. Patients who were not evaluable or had indeterminate results were considered MRD positive. The subgroup analysis for type of MM was performed on data from patients who had measurable 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).
CR, complete response; D-R, daratumumab plus lenalidomide; D-VRd, daratumumab plus bortezomib/lenalidomide/dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; IgG, immunoglobulin G; ISS, International Staging System; ITT, intent to treat; MM, multiple myeloma; MRD; minimal residual disease; R, lenalidomide; VRd, bortezomib/lenalidomide/dexamethasone.

Presented by H Einsele at the Annual Meeting of the German, Austrian and Swiss Associations of Hematology and Medical Oncology (DGHO); October 11–14, 2024; Basel, Switzerland

PERSEUS: MRD Negativity in Patients With High-Risk MM (ITT)







- **Rates of MRD negativity at 10^{-6} and sustained MRD negativity ≥12 months were approximately doubled with D-VRd versus VRd**
- **PFS was improved with D-VRd versus VRd in MRD-negative high-risk patients**

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. 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).
CR, complete response; D-VRd, daratumumab plus bortezomib/lenalidomide/dexamethasone; HR, hazard ratio; ITT, intent to treat; MRD; minimal residual disease; PFS, progression-free survival; VRd, bortezomib/lenalidomide/dexamethasone.

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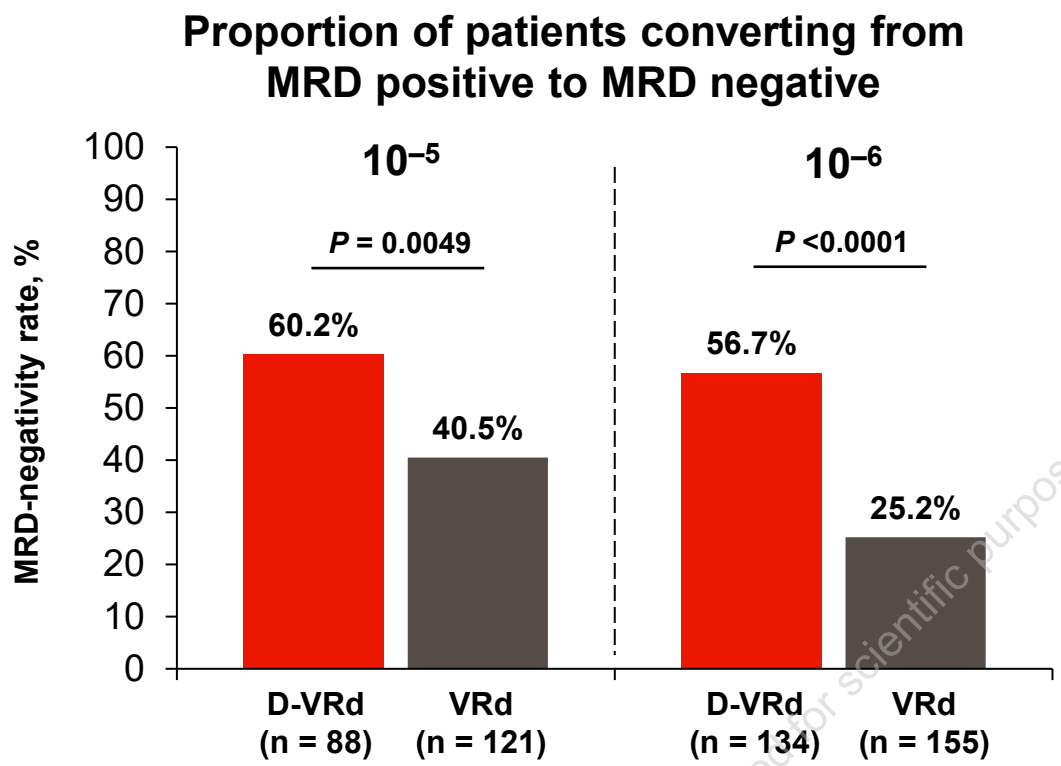
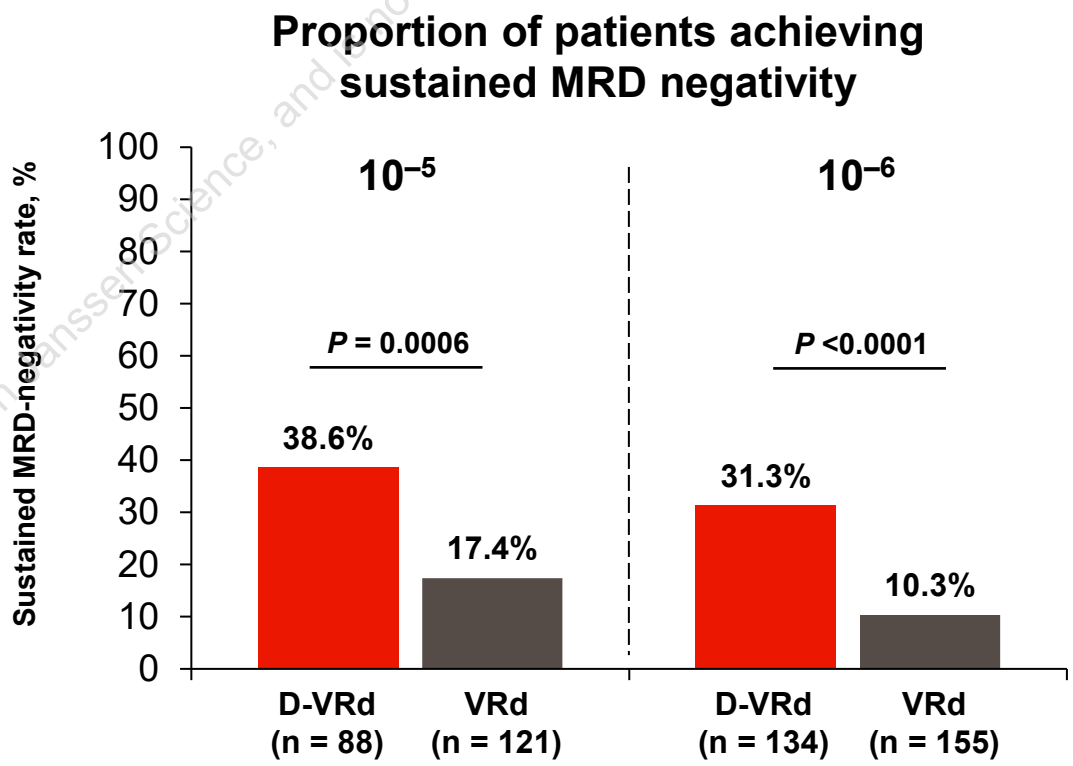
PERSEUS: MRD Conversion During Maintenance for Patients Remaining MRD Positive at the End of Consolidation





During maintenance, conversion to MRD negativity (10^{-6}) was doubled, and conversion to sustained MRD negativity was tripled, with D-R versus R

MRD-negativity rate was defined as the proportion of patients who achieved both MRD negativity and ≥CR. *P* values were calculated using the unstratified Cochran–Mantel–Haenszel chi-square test.
CR, complete response; D-R, daratumumab plus lenalidomide; D-VRd, daratumumab plus bortezomib/lenalidomide/dexamethasone; ITT, intent to treat; MRD; minimal residual disease; PFS, progression-free survival; R, lenalidomide; VRd, bortezomib/lenalidomide/dexamethasone.

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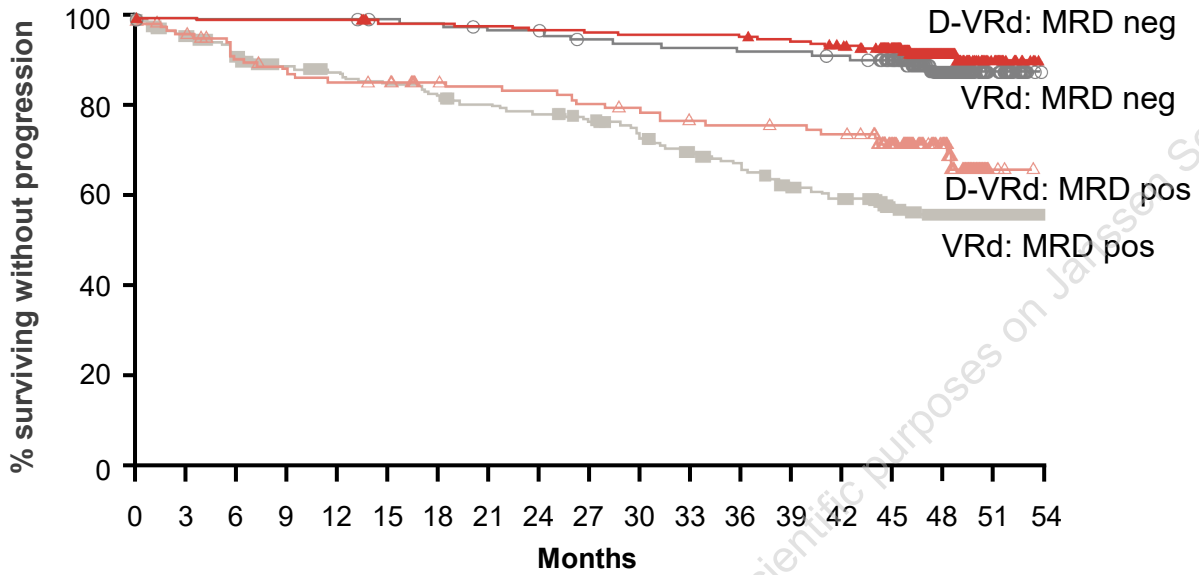
PERSEUS: PFS by MRD Negativity Status (10^{-6}; ITT)

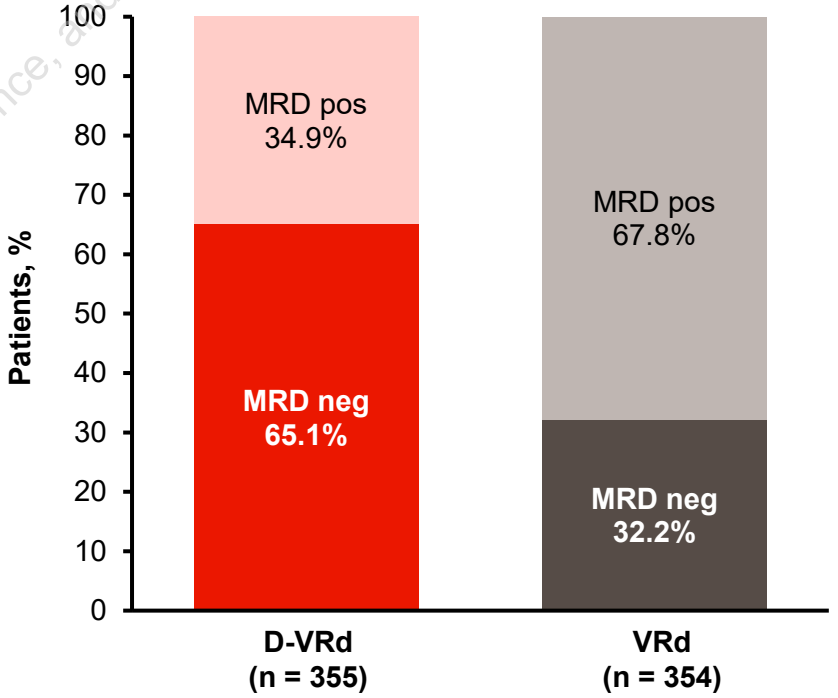
PFS according to MRD status (10^{-6})



No. at risk

VRd: MRD neg	114	114	114	114	114	112	111	108	107	104	103	102	101	101	98	87	34	9	0
D-VRd: MRD neg	231	231	230	230	230	226	226	225	223	222	221	221	219	216	210	169	70	10	0
VRd: MRD pos	240	221	207	197	190	185	180	175	171	166	155	145	137	127	121	88	33	4	0
D-VRd: MRD pos	124	114	105	99	97	96	92	91	90	87	84	81	80	79	76	57	20	1	0

Overall MRD negativity (10^{-6})



- **MRD negativity at 10^{-6} was associated with improved long-term outcomes**
- **Twice as many patients achieved MRD negativity at 10^{-6} with D-VRd + D-R versus VRd + R**
- **Patients remaining MRD positive had improved PFS with D-R maintenance versus R alone**

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.
CR, complete response; D-R, daratumumab plus lenalidomide; D-VRd, daratumumab plus bortezomib/lenalidomide/dexamethasone; ITT, intent to treat; MRD; minimal residual disease; PFS, progression-free survival; R, lenalidomide; VRd, bortezomib/lenalidomide/dexamethasone.

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PERSEUS: Conclusions From Analysis of MRD

- **The potential for a cure in NDMM is predicated on reaching sustained MRD negativity at 10^{-6}**
- **In the PERSEUS study, for D-VRd + D-R:**
  - 47% of patients achieved sustained MRD negativity (10^{-6}) for 12 months versus 19% with VRd + R
  - In high-risk patients: 58% of patients achieved MRD negativity (10^{-6}) and 30% achieved sustained MRD negativity (10^{-6}) versus 31% and 14%, respectively, with VRd + R
- **During D-R maintenance:**
  - The rate of MRD negativity (10^{-6}) increased by 30% versus 15% with R alone
  - 31% of MRD-positive patients converted to sustained MRD negativity (10^{-6}) versus 10% with R alone
  - 64% of patients stopped DARA after achieving sustained MRD negativity (10^{-5})[1]

These data further highlight the benefit of D-VRd and D-R maintenance as a new standard of care for transplant-eligible patients with NDMM

DARA, daratumumab; D-R, daratumumab plus lenalidomide; D-VRd, daratumumab plus bortezomib/lenalidomide/dexamethasone; MRD; minimal residual disease; NDMM, newly diagnosed multiple myeloma; R, lenalidomide; VRd, bortezomib/lenalidomide/dexamethasone.

1. Sonneveld P, et al. *N Engl J Med* 2024;390(4):301-13.

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PERSEUS: Future Directions

- PERSEUS evaluated the totality of a DARA-containing regimen, from induction through maintenance
  - CASSIOPEIA (double randomization) final analysis demonstrated that DARA maintenance post–D-VTd or VTd significantly improved PFS versus observation; the highest rates of MRD negativity were seen with D-VTd followed by DARA[1]
  - AURIGA is evaluating conversion from MRD positive to MRD negative with DARA + R versus R maintenance post-ASCT[2]
  - DRAMMATIC (SWOG) is evaluating DARA + R versus R maintenance post-ASCT, with data expected in 2028+[3]
- Longer follow-up for PFS and OS in PERSEUS will confirm if sustained MRD negativity at 10^{-6} for ≥5 years translates to functional cure, and in what proportion of patients
  - Potential to evaluate patient subgroups or clinical responses associated with greatest benefit
- PERSEUS sets a new benchmark for depth of response and PFS in transplant-eligible NDMM and should be considered a standard comparator for future frontline studies of novel approaches with CAR-T and bispecific antibodies

ASCT, autologous stem cell transplant; CAR-T, chimeric antigen receptor T cell; DARA, daratumumab; D-VTd, daratumumab plus bortezomib/thalidomide/dexamethasone; MRD; minimal residual disease; NDMM, newly diagnosed multiple myeloma; OS, overall survival; PFS, progression-free survival; R, lenalidomide; SWOG, Southwest Oncology Group; VTd, bortezomib/thalidomide/dexamethasone.

1. Moreau P, et al. To be presented at: European Hematology Association (EHA) Hybrid Congress; June 13-16, 2024; Madrid, Spain. Abstract S204. 2. ClinicalTrial.gov, Identifier: NCT03901963. 3. ClinicalTrial.gov, Identifier: NCT04071457.

PERSEUS: Acknowledgments

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- Data and safety monitoring committee
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EMN

https://www.congresshub.com/Oncology/DGHO2024/Daratumumab/Einsele-Dara

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