Daratumumab (DARA)/Bortezomib/ Lenalidomide/Dexamethasone (D-VRd) With D-R Maintenance in Transplant-Eligible (TE) Newly Diagnosed Myeloma (NDMM): Analysis of PERSEUS Based on Cytogenic Risk

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CD has nothing to disclose. **MAD** has served in a consulting/advisory role for and received honoraria from Amgen, BeiGene, BMS, Janssen-Cilag, Takeda. **PS** has received honoraria from Amgen, BMS, Celgene, Janssen, Karyopharm, Pfizer, Takeda; received research funding from Amgen, BMS, Celgene, Janssen, Karyopharm, Takeda, Skyline DX. **PRO** has received honoraria from Amgen, BMS, Celgene, GSK, Janssen, Oncopeptides, Regeneron, Sanofi. **HQ** has served in a consulting/advisory role for Amgen, Antengene, BMS, CSL, GSK, Janssen, Karyopharm, Sanofi; received honoraria from Amgen, Antengene, BMS, CSL, GSK, Janssen, Karyopharm; received research funding from AbbVie, Amgen, Antengene, BMS, GSK, Karyopharm, Sanofi. **PJH** has nothing to disclose. **MB** has served in a consulting/advisory role for Amgen, Janssen, Oncopeptides, Sanofi, Takeda. **CH** has served in a consulting/advisory role for Celgene; received honoraria from AbbVie, Amgen, Celgene, Janssen. **EA** has nothing to disclose. **XL** has nothing to disclose. **SM** has served in a consulting/advisory role for BMS, Janssen, Sanofi, Takeda; received honoraria from Amgen, BMS, GSK, Janssen, Sanofi, Takeda. **AP** has served in a consulting/advisory role for and received honoraria from AbbVie, Amgen, BMS, Janssen, Pfizer, Sanofi, Takeda. **MC** has received honoraria from AbbVie, Adaptive Biotechnologies, Amgen, BMS, Celgene, GSK, Janssen, Mundipharma, Sanofi, Takeda. **ABe** has nothing to disclose. **ABr** has served in a consulting/advisory role for and received honoraria from Amgen, BMS, Janssen, Sanofi. **FG** has served in a consulting/advisory role for and received honoraria from AbbVie, Adaptive Bluebird Bio, Biotechnologies, Amgen, BMS, Celgene, GSK, Janssen, Oncopeptides, Roche, Sanofi, Takeda. **RM** has served in a consulting/advisory role for and received honoraria from Amgen, BMS, Celgene, Janssen, Sanofi, Takeda. **ISN** has nothing to disclose. **NWCJvdD** has served as a consultant or advisor to AbbVie, Adaptive Biotechnologies, Amgen, Bayer, BMS, Celgene, Janssen, Novartis, Pfizer, Roche, Servier, Takeda; received research funding from Amgen, BMS, Celgene, Cellectis, Janssen, Novartis. **EK** has served in a consulting/advisory role for Amgen, Janssen-Cilag; received honoraria and research funding from Amgen, Genesis Pharma, Janssen-Cilag, Takeda; received travel and accommodation funding from Genesis Pharma, Takeda. **FS** has served in a consulting/advisory role for AbbVie, Celgene, GSK, Janssen, Oncopeptides, Sanofi, Takeda; received honoraria from AbbVie, Amgen, BMS, Daiki-Sankyo, GSK, Janssen, Novartis, Oncopeptides, Pfizer, Sanofi, Skyline Dx, Takeda; received research funding from Celgene, GSK, Janssen, Oncopeptides, Sanofi, Targovax. **ASB** has served in a consulting/advisory role for BMS, Celgene, Gilead Sciences, Janssen, Novartis, Takeda; received honoraria from BMS, Celgene, Gilead Sciences, Janssen-Cilag, Merck Sharp & Dohm, Novartis, Roche, Sanofi, Takeda; received travel and accommodation funding from Gilead Sciences/Kite; other relationships with Celgene, Gilead, Roche, Sanofi, Takeda. **LR** has served in a consulting/advisory role for Amgen, Celgene, Janssen-Cilag, Sanofi; received honoraria from Amgen, Celgene, GSK, Janssen-Cilag, Sanofi, Takeda. **MD** has served as a consultant/advisor for Amgen, BMS, GSK, Janssen, Sanofi, Stemline Therapeutics, Takeda. **WR** has served as a consultant/advisor for AbbVie, BMS, Takeda; received honoraria from Amgen, BMS, Janssen, Sanofi. **AV** has nothing to disclose. **HE** served as a consultant or advisor for, and received honoraria and research funding from Amgen, BMS, Celgene, GSK, Janssen, Sanofi. **AS** has served in a consulting/advisory role for AbbVie, Antengene, BMS, Haemalogix, Janssen, Regeneron, Roche, Skyline; holds patent/copyright licensing for AbbVie; received honoraria from AbbVie, Antengene, BMS, Haemalogix, Janssen; Regeneron, Roche, Skyline; received research funding from AbbVie, Antengene, BMS, Haemalogix, Janssen. **RH** has served in a consulting/advisory role for AbbVie, Amgen, BMS, Janssen, Novartis, Pharma Mar, Takeda; received honoraria from AbbVie, Amgen, Janssen, Pharma Mar, Takeda; received research funding from Amgen, BMS, Janssen, Novartis, Takeda. **AJ** has nothing to disclose. **SL** has nothing to disclose. **YL, JW, DV, EMJvB, VV, ASA, CJdB**, 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, Takeda. **MB** has served in a consulting/advisory role for GSK, Janssen; received honoraria from AbbVie, Amgen, BMS, Celgene, GSK, Janssen, Novartis, Sanofi; received research funding from Amgen, BMS, Celgene, Janssen, Mundipharma, Novartis, Sanofi. **PM** has served in a consulting/advisory role for and received honoraria from AbbVie, Amgen, Celgene, GSK, Janssen, Oncopeptides, Sanofi.

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PERSEUS: Introduction

- DARA is a human IgGκ monoclonal antibody targeting CD38 with a direct on-tumor[1-4] and immunomodulatory[5-7] MOA, demonstrating greater cytotoxicity toward MM cells ex vivo vs analogs of other CD38 antibodies[8]
  - DARA is approved in combination with other SOC regimens in NDMM[9,10] and has been used to treat >518,000 patients worldwide[11]
  - DARA has consistently demonstrated efficacy in pivotal clinical trials[12-15]
- Patients with HRCAs often have a poor prognosis and experience poor disease outcomes[16]
  - In the primary analysis of the phase 3 PERSEUS study, D-VRd + D-R maintenance significantly improved PFS and increased depth of response, including ≥CR, vs VRd + R maintenance alone in TE patients with NDMM at median follow-up of 47.5 months[17]
    - Overall and sustained MRD-negativity rates were significantly higher with D-VRd + D-R maintenance vs VRd + R maintenance[17,18]
    - Overall (10^{-5}): 75.2% vs 47.5% (*P*<0.0001)
    - Overall (10^{-6}): 65.1% vs 32.2% (*P*<0.0001)
    - Sustained (≥12 months; 10^{-5}): 64.8% vs 29.7% (*P*<0.0001)
    - Sustained (≥12 months; 10^{-6}): 47.3% vs 18.6% (*P*<0.0001)
  - Consistent benefits were observed across subgroups, including in patients with HRCAs (ie, del[17p], t[4;14], or t[14;16])
- We report an expanded analysis of PERSEUS clinical outcomes (PFS, overall MRD negativity, and sustained MRD negativity) based on the presence of HRCAs, including gain(1q21) and amp(1q21)

CR, complete response; D-R, daratumumab plus lenalidomide; D-VRd, subcutaneous daratumumab plus bortezomib, lenalidomide, and dexamethasone; DARA, daratumumab; HRCA, high-risk cytogenetic abnormality; Ig, immunoglobulin; MM, multiple myeloma; MOA, mechanism of action; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; PFS, progression-free survival; R, lenalidomide; SOC, standard of care; TE, transplant-eligible; VRd, bortezomib, lenalidomide, and dexamethasone.

1. de Weers M, et al. *J Immunol* 2011;186:1840-8. 2. Lammerts van Bueren J, et al. *Blood* 2014;124:3474. 3. Overdijk MB, et al. *MAbs* 2015;7:311-21. 4. Overdijk MB, et al. *J Immunol* 2016;197:807-13. 5. Krejcik J, et al. *Blood* 2016;128:384-94. 6. Adams HC III, et al. *Cytometry A* 2019;95:279-89. 7. Casneuf T, et al. *Leukemia* 2021;35:573-84. 8. Kinder M, et al. *Haematologica* 2021;106:2004-8. 9. DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj) injection, for subcutaneous use [package insert]. Janssen Biotech, Inc.; December 2022. 10. European Medicines Agency. DARZALEX 20 mg/mL concentrate for solution for infusion. Summary of product characteristics. Accessed May 10, 2024. https://www.ema.europa.eu/en/documents/product-information/darzalex-epar-product-information_en.pdf. 11. Data on file. 12. Mateos MV, et al. *Lancet* 2020;395:132-41. 13. Moreau P, et al. *Lancet Oncol* 2021;22:1378-90. 14. Voorhees PM, et al. *Lancet Haematol* 2023;10:e825-37. 15. Facon T, et al. *Lancet Oncol* 2021;22:1582-96. 16. Hanamura I. *Int J Hematol* 2022;115:762-77. 17. Sonneveld P, et al. *N Engl J Med* 2024;390:301-13. 18. Rodriguez-Otero P, et al. Presented at ASCO; May 31–June 4, 2024; Chicago, IL, USA.

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PERSEUS: Study Design

- In PERSEUS (NCT03710603), patients aged 18–70 years with NDMM and eligible for high-dose chemotherapy and ASCT were randomized 1:1 to receive D-VRd followed by D-R maintenance or VRd followed by R maintenance
- Patients in both arms received up to six 28-day cycles (4 pre-ASCT induction; 2 post-ASCT consolidation) of VRd (V: 1.3 mg/m^2 SC on days 1, 4, 8, and 11; R: 25 mg PO once daily on days 1–21; d: 40 mg PO/IV on days 1–4 and 9–12) followed by R maintenance (10 mg PO once daily on days 1–28)
- Patients in the D-VRd/D-R arm also received DARA SC (DARA 1800 mg + rHuPH20; 2000 U/mL; Halozyme) QW in cycles 1–2, Q2W in cycles 3–6, and Q4W during maintenance until progressive disease or unacceptable toxicity

ASCT, autologous stem cell transplant; d, dexamethasone; D-R, daratumumab plus lenalidomide; D-VRd, subcutaneous daratumumab plus bortezomib, lenalidomide, and dexamethasone; DARA, daratumumab; IV, intravenously; NDMM, newly diagnosed multiple myeloma; PO, orally; Q2W, every 2 weeks; Q4W, every 4 weeks; QW, weekly; R, lenalidomide; rHuPH20, recombinant human hyaluronidase PH20; SC, subcutaneous; V, bortezomib; VRd, bortezomib, lenalidomide, and dexamethasone.

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PERSEUS: Cytogenetic Risk Subgroups

- The following cytogenetic risk subgroups were explored in this analysis:
  - Standard risk (per protocol) – none of the HRCAs del(17p), t(4;14), t(14;16)
  - High risk (per protocol) – ≥1 HRCA: del(17p), t(4;14), t(14;16)
  - Revised standard risk – none of the HRCAs: del(17p), t(4;14), t(14;16), gain(1q21), amp(1q21)
  - Revised high risk – ≥1 HRCA: del(17p), t(4;14), t(14;16), gain(1q21), amp(1q21)
  - Gain(1q21) – 3 copies of chromosome 1q21 ± other HRCAs
  - Amp(1q21) – ≥4 copies of chromosome 1q21 ± other HRCAs
  - Gain(1q21) or amp(1q21) – gain(1q21) or amp(1q21) ± other HRCAs
  - Isolated gain(1q21) – 3 copies of chromosome 1q21, with no other HRCAs
  - Isolated amp(1q21) – ≥4 copies of chromosome 1q21, with no other HRCAs
  - 1 revised HRCA – presence of 1 revised HRCA only
  - ≥2 revised HRCAs – presence of ≥2 revised HRCAs
- Cytogenetic risk was centrally assessed by FISH[a]

[a]Patients were considered positive for a chromosome abnormality when test result met or exceeded the threshold established by the central laboratory.
FISH, fluorescence in situ hybridization; HRCA, high-risk cytogenetic abnormality.

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PERSEUS: Assessments

- PFS (primary endpoint) was defined as the time from the date of randomization to the date of first disease progression (as per International Myeloma Working Group response criteria)[1] or death, whichever occurred first
  - PFS was compared between treatment groups using a log-rank test; the Kaplan-Meier method was used to estimate PFS distributions
  - Treatment effect (HR) and corresponding 95% CIs were estimated using a Cox regression model, with treatment as the sole variable
- Overall MRD negativity rate was defined as the proportion of patients who achieved MRD negativity (at or below 10^{-5}) and ≥CR at any time during the study
  - Sustained MRD negativity was defined as 2 consecutive MRD-negative results (at or below 10^{-5}) ≥12 months apart without any MRD positive (10^{-4} or higher) results in between
  - MRD was assessed using bone marrow aspirates by next-generation sequencing (clonoSEQ® Assay, version 2.0; Adaptive Biotechnologies)
  - Treatment effect (OR) and corresponding 95% CIs were estimated using a Mantel-Haenszel estimation

CR, complete response; HR, hazard ratio; MRD, minimal residual disease; OR, odds ratio; PFS, progression-free survival.

1. Rajkumar SV, et al. *Blood* 2011;117:4691-5.

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PERSEUS: Demographic and Baseline Characteristics of the ITT Population[a]

- In total, 709 patients were randomized (D-VRd, n=355; VRd, n=354)
  - Patient demographic and baseline characteristics were well balanced between groups[1]

Characteristic	D-VRd (n=355)	VRd (n=354)
Age		
Median (range), years	61.0 (32–70)	59.0 (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	4 (1.1)	3 (0.8)
Not reported	12 (3.4)	18 (5.1)
ISS disease 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,[b] n (%)		
Standard risk	264 (74.4)	266 (75.1)
High risk	76 (21.4)	78 (22.0)
del(17p)	36 (10.1)	34 (9.6)
t(4;14)	33 (9.3)	38 (10.7)
t(14;16)	11 (3.1)	14 (4.0)
Indeterminate	15 (4.2)	10 (2.8)
Revised cytogenetic risk,[c] n (%)		
Revised standard risk	174 (49.0)	167 (47.2)
Revised high risk	130 (36.6)	148 (41.8)
Indeterminate	51 (14.4)	39 (11.0)

[a]The ITT population included all randomized patients. [b]Cytogenetic risk was based on FISH; high risk was defined as the presence of del(17p), t(4;14), or t(14;16). [c]Revised cytogenetic risk was defined as the presence of del(17p), t(4;14), t(14;16), gain(1q21), or amp(1q21).

D-VRd, daratumumab plus bortezomib, lenalidomide, and dexamethasone; FISH, fluorescence in situ hybridization; ISS, International Staging System; ITT, intent-to-treat; VRd, bortezomib, lenalidomide, and dexamethasone.

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

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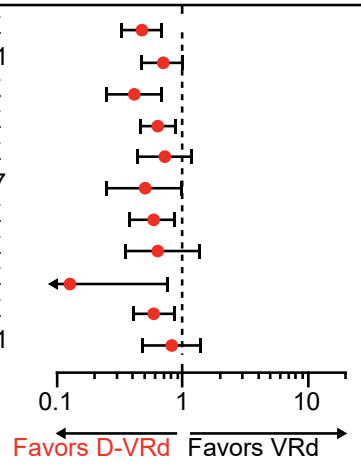
PERSEUS: PFS in Cytogenetic Risk Subgroups

- After median follow-up of 47.5 months, PFS favored D-VRd followed by D-R maintenance vs VRd followed by R maintenance across all cytogenetic risk subgroups
  - Revised standard (HR, 0.29; 95% CI, 0.15–0.56; *P*=0.0001)
  - Revised high cytogenetic risk (HR, 0.53; 95% CI, 0.35–0.81; *P*=0.0027)
  - HR point estimates for PFS also favored D-VRd in patients with the presence of gain(1q21), amp(1q21), and gain(1q21) or amp(1q21), irrespective of other HRCAs

Cytogenetic risk subgroup analysis of PFS (ITT)

	D-VRd		VRd			
	n/N	Median PFS (mo)	n/N	Median PFS (mo)	HR (95% CI)	*P* value
Standard risk	25/264	NE	62/266	NE	0.35 (0.22–0.56)	<0.0001
High risk	24/76	NE	38/78	44.1	0.59 (0.36–0.99)	0.0439
Revised standard risk	12/174	NE	35/167	NE	0.29 (0.15–0.56)	0.0001
Revised high risk	33/130	NE	62/148	NE	0.53 (0.35–0.81)	0.0027
Gain(1q21)	15/59	NE	26/71	NE	0.62 (0.33–1.18)	0.1400
Amp(1q21)	6/28	NE	17/36	46.7	0.37 (0.15–0.94)	0.0306
Gain(1q21) or amp(1q21)	21/87	NE	43/107	NE	0.52 (0.31–0.88)	0.0133
Isolated gain(1q21)	8/37	NE	15/47	NE	0.57 (0.24–1.36)	0.2004
Isolated amp(1q21)	1/17	NE	9/23	NE	0.11 (0.01–0.87)	0.0115
1 revised HRCA	21/97	NE	43/110	NE	0.47 (0.28–0.79)	0.0035
≥2 revised HRCAs	12/33	NE	19/38	44.1	0.73 (0.35–1.50)	0.3878



D-R, daratumumab plus lenalidomide; D-VRd, daratumumab plus bortezomib, lenalidomide, and dexamethasone; HR, hazard ratio; HRCA, high-risk cytogenetic abnormality; ITT, intent-to-treat; NE, not estimable; PFS, progression-free survival; R, lenalidomide; VRd, bortezomib, lenalidomide, and dexamethasone.

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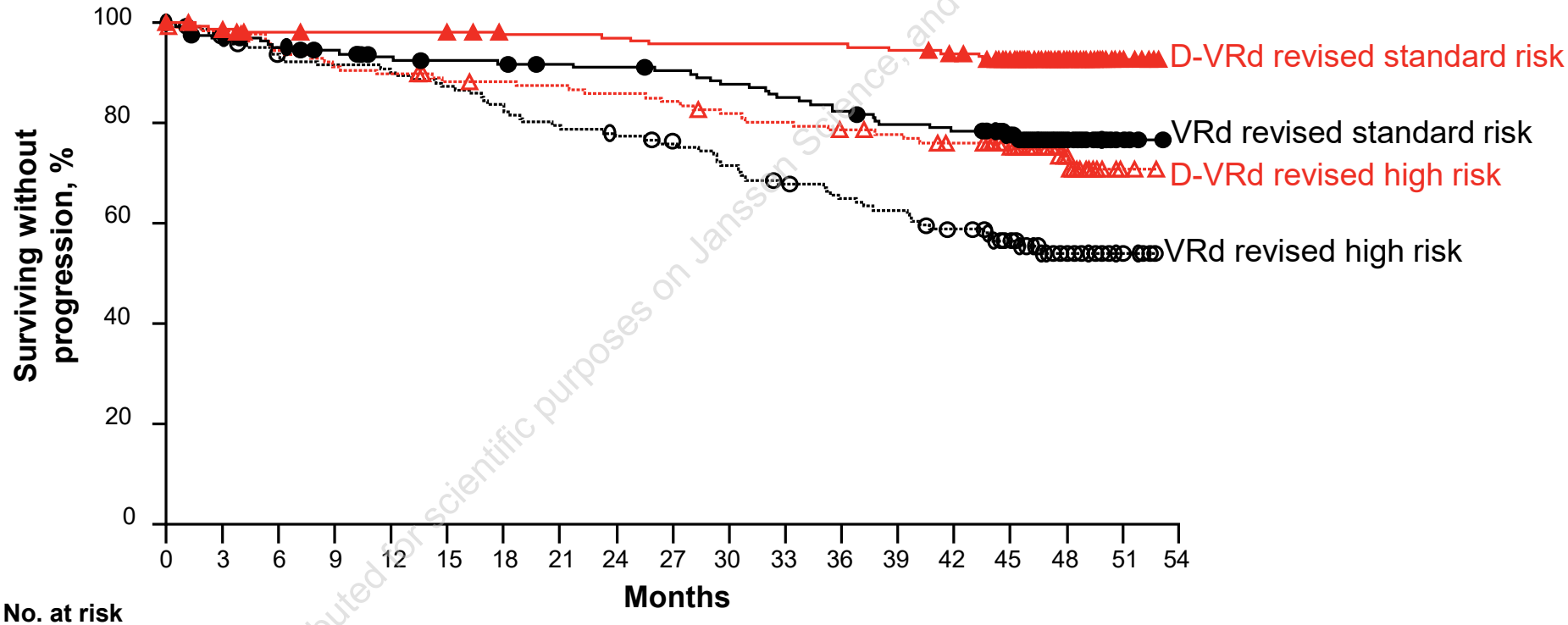
PERSEUS: PFS Based on Revised Cytogenetic Risk Status

Subgroup analysis of PFS based on revised[a] cytogenetic risk status (ITT)



No. at risk																			
VRd revised standard risk	167	157	152	148	143	141	140	138	137	135	131	127	123	118	116	96	36	6	0
D-VRd revised standard risk	174	167	163	162	162	162	159	158	157	155	155	155	155	153	149	124	52	7	0
VRd revised high risk	148	139	132	129	127	123	118	112	109	105	98	92	87	84	77	64	22	4	0
D-VRd revised high risk	130	127	121	117	115	111	110	109	107	105	101	99	96	94	90	76	31	2	0

[a]Revised high risk defined as the presence of 1 or more of the following HRCAs: del(17p), t(4;14), t(14;16), gain(1q21), amp(1q21).
D-VRd, daratumumab plus bortezomib, lenalidomide, and dexamethasone; HRCA, high-risk cytogenetic abnormality; ITT, intent-to-treat; PFS, progression-free survival; VRd, bortezomib, lenalidomide, and dexamethasone.

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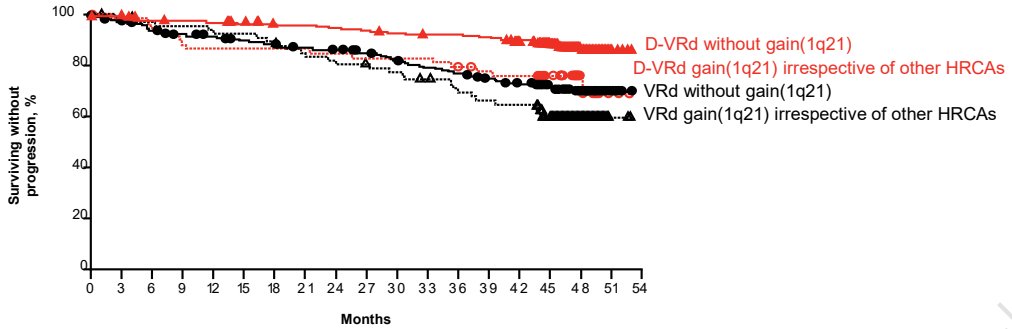
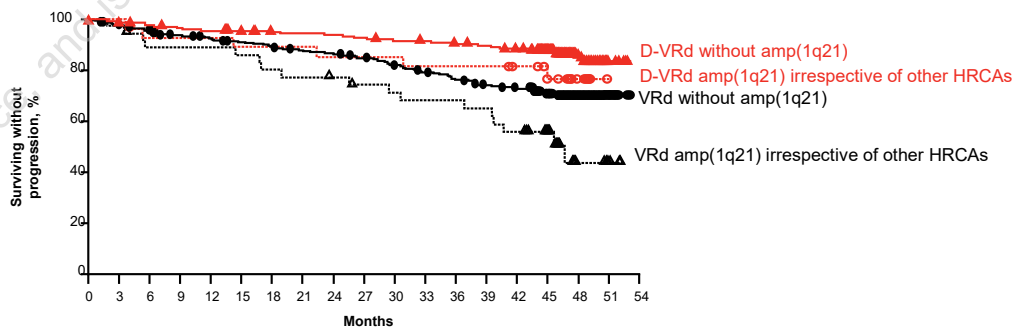
PERSEUS: PFS Based on Chromosome 1q21 Status

PFS by gain(1q21)



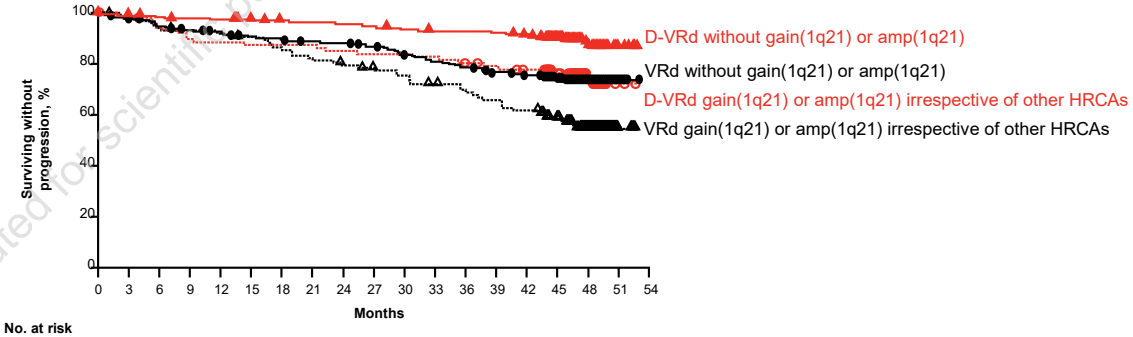
No. at risk																		
VRd without amp(1q21)	283	269	257	248	243	236	232	227	224	217	208	200	195	187	179	142	55	12	0
D-VRd without amp(1q21)	296	288	280	278	277	272	268	266	264	261	257	254	254	252	244	192	78	9	0
VRd amp(1q21) irrespective of other HRCAs	71	66	64	63	61	61	59	56	54	53	50	47	43	41	40	33	12	1	0
D-VRd amp(1q21) irrespective of other HRCAs	59	57	55	51	50	50	50	50	49	48	48	48	45	43	42	34	12	2	0

PFS by amp(1q21)



No. at risk																		
VRd without amp(1q21)	318	300	290	280	273	267	263	256	252	246	235	225	216	207	201	160	64	11	0
D-VRd without amp(1q21)	327	317	310	304	302	298	294	292	290	286	282	280	277	273	266	209	82	11	0
VRd amp(1q21) irrespective of other HRCAs	36	35	31	31	31	30	28	27	26	24	23	22	22	21	18	15	3	2	0
D-VRd amp(1q21) irrespective of other HRCAs	28	28	25	25	25	24	24	24	23	23	23	22	22	22	20	17	8	0	0

PFS by gain(1q21) or amp(1q21)



No. at risk																		
VRd without gain or amp	247	234	226	217	212	206	204	200	198	193	185	178	173	166	161	127	52	10	0
D-VRd without gain or amp	268	260	255	253	252	248	244	242	241	238	234	232	232	230	224	175	70	9	0
VRd gain or amp irrespective of other HRCAs	107	101	95	94	92	91	87	83	80	77	73	69	65	62	58	48	15	3	0
D-VRd gain or amp irrespective of other HRCAs	87	85	80	76	75	74	74	74	72	71	71	70	67	65	62	51	20	2	0

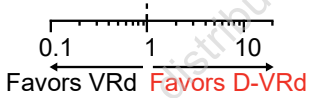
D-VRd, daratumumab plus bortezomib, lenalidomide, and dexamethasone; HRCA, high-risk cytogenetic abnormality; PFS, progression-free survival; VRd, bortezomib, lenalidomide, and dexamethasone.

PERSEUS: MRD Negativity (10^{-5}) in Cytogenetic Risk Subgroups

Subgroup analysis of overall and sustained (≥12 months) MRD negativity (10^{-5} and 10^{-6}) with ≥CR rates based on cytogenetic risk markers favored treatment with D-VRd followed by D-R maintenance over VRd followed by R maintenance, regardless of high-risk cytogenetic markers

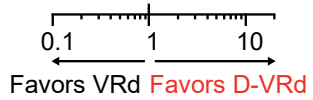
Subgroup analysis of MRD negativity (10^{-5}) with ≥CR

	D-VRd n/N (%)	VRd n/N (%)	OR (95% CI)	*P* value
Standard risk	204/264 (77.3)	128/266 (48.1)	3.67 (2.52–5.33)	<0.0001
High risk	52/76 (68.4)	37/78 (47.4)	2.40 (1.24–4.63)	0.0086
Revised standard risk	131/174 (75.3)	79/167 (47.3)	3.39 (2.14–5.37)	<0.0001
Revised high risk	95/130 (73.1)	73/148 (49.3)	2.79 (1.68–4.62)	<0.0001
Gain(1q21)	41/59 (69.5)	33/71 (46.5)	2.62 (1.27–5.41)	0.0086
Amp(1q21)	24/28 (85.7)	20/36 (55.6)	4.80 (1.38–16.69)	0.0104
Gain(1q21) or amp(1q21)	65/87 (74.7)	53/107 (49.5)	3.01 (1.63–5.56)	0.0004
Isolated gain(1q21)	27/37 (73.0)	23/47 (48.9)	2.82 (1.12–7.10)	0.0268
Isolated amp(1q21)	16/17 (94.1)	13/23 (56.5)	12.31 (1.39–109.10)	0.0093
1 revised HRCA	73/97 (75.3)	55/110 (50.0)	3.04 (1.68–5.51)	0.0002
≥2 revised HRCAs	22/33 (66.7)	18/38 (47.4)	2.22 (0.85–5.83)	0.1044



Subgroup analysis of sustained MRD negativity (10^{-5}) ≥12 months

	D-VRd n/N (%)	VRd n/N (%)	OR (95% CI)	*P* value
Standard risk	183/264 (69.3)	83/266 (31.2)	4.98 (3.45–7.20)	<0.0001
High risk	37/76 (48.7)	20/78 (25.6)	2.75 (1.40–5.42)	0.0032
Revised standard risk	115/174 (66.1)	53/167 (31.7)	4.19 (2.67–6.59)	<0.0001
Revised high risk	77/130 (59.2)	41/148 (27.7)	3.79 (2.30–6.26)	<0.0001
Gain(1q21)	37/59 (62.7)	21/71 (29.6)	4.00 (1.92–8.34)	0.0002
Amp(1q21)	20/28 (71.4)	10/36 (27.8)	6.50 (2.17–19.48)	0.0006
Gain(1q21) or amp(1q21)	57/87 (65.5)	31/107 (29.0)	4.66 (2.54–8.56)	<0.0001
Isolated gain(1q21)	25/37 (67.6)	15/47 (31.9)	4.44 (1.77–11.17)	0.0012
Isolated amp(1q21)	15/17 (88.2)	6/23 (26.1)	21.25 (3.71–121.61)	0.0001
1 revised HRCA	60/97 (61.9)	31/110 (28.2)	4.13 (2.31–7.41)	<0.0001
≥2 revised HRCAs	17/33 (51.5)	10/38 (26.3)	2.97 (1.10–8.04)	0.0303



CR, complete response; D-R, daratumumab plus lenalidomide; D-VRd, daratumumab plus bortezomib, lenalidomide, and dexamethasone; HRCA, high-risk cytogenetic abnormality; MRD, minimal residual disease; OR, odds ratio; R, lenalidomide; VRd, bortezomib, lenalidomide, and dexamethasone.

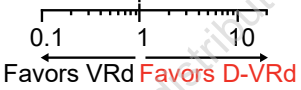
Presented by C Driessen at the Annual Meeting of the German, Austrian and Swiss Associations of Hematology and Medical Oncology (DGHO); October 11–14, 2024; Basel, Switzerland

PERSEUS: MRD Negativity (10^{-6}) in Cytogenetic Risk Subgroups

Subgroup analysis of overall and sustained (≥12 months) MRD negativity (10^{-5} and 10^{-6}) with ≥CR rates based on cytogenetic risk markers favored treatment with D-VRd followed by D-R maintenance over VRd followed by R maintenance, regardless of high-risk cytogenetic markers

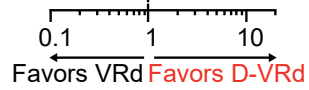
Subgroup analysis of MRD negativity (10^{-6}) with ≥CR

	D-VRd n/N (%)	VRd n/N (%)	OR (95% CI)	*P* value
Standard risk	177/264 (67.0)	88/266 (33.1)	4.12 (2.87–5.91)	<0.0001
High risk	44/76 (57.9)	24/78 (30.8)	3.09 (1.60–6.00)	0.0007
Revised standard risk	115/174 (66.1)	56/167 (33.5)	3.86 (2.47–6.05)	<0.0001
Revised high risk	82/130 (63.1)	48/148 (32.4)	3.56 (2.17–5.84)	<0.0001
Gain(1q21)	36/59 (61.0)	22/71 (31.0)	3.49 (1.69–7.20)	0.0006
Amp(1q21)	21/28 (75.0)	15/36 (41.7)	4.20 (1.42–12.39)	0.0082
Gain(1q21) or amp(1q21)	57/87 (65.5)	37/107 (34.6)	3.59 (1.98–6.52)	<0.0001
Isolated gain(1q21)	24/37 (64.9)	15/47 (31.9)	3.94 (1.58–9.80)	0.0028
Isolated amp(1q21)	14/17 (82.4)	9/23 (39.1)	7.26 (1.62–32.60)	0.0069
1 revised HRCA	63/97 (64.9)	35/110 (31.8)	3.97 (2.23–7.08)	<0.0001
≥2 revised HRCAs	19/33 (57.6)	13/38 (34.2)	2.61 (1.00–6.83)	0.0500



Subgroup analysis of sustained MRD negativity (10^{-6}) ≥12 months

	D-VRd n/N (%)	VRd n/N (%)	OR (95% CI)	*P* value
Standard risk	137/264 (51.9)	54/266 (20.3)	4.24 (2.88–6.22)	<0.0001
High risk	23/76 (30.3)	11/78 (14.1)	2.64 (1.18–5.90)	0.0160
Revised standard risk	87/174 (50.0)	35/167 (21.0)	3.77 (2.34–6.07)	<0.0001
Revised high risk	55/130 (42.3)	23/148 (15.5)	3.99 (2.27–7.01)	<0.0001
Gain(1q21)	25/59 (42.4)	11/71 (15.5)	4.01 (1.76–9.15)	0.0007
Amp(1q21)	17/28 (60.7)	6/36 (16.7)	7.73 (2.42–24.63)	0.0003
Gain(1q21) or amp(1q21)	42/87 (48.3)	17/107 (15.9)	4.94 (2.53–9.63)	<0.0001
Isolated gain(1q21)	19/37 (51.4)	9/47 (19.1)	4.46 (1.69–11.77)	0.0020
Isolated amp(1q21)	13/17 (76.5)	3/23 (13.0)	21.67 (4.15–113.02)	<0.0001
1 revised HRCA	45/97 (46.4)	18/110 (16.4)	4.42 (2.32–8.42)	<0.0001
≥2 revised HRCAs	10/33 (30.3)	5/38 (13.2)	2.87 (0.87–9.51)	0.0797



CR, complete response; D-R, daratumumab plus lenalidomide; D-VRd, daratumumab plus bortezomib, lenalidomide, and dexamethasone; HRCA, high-risk cytogenetic abnormality; MRD, minimal residual disease; OR, odds ratio; R, lenalidomide; VRd, bortezomib, lenalidomide, and dexamethasone.

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PERSEUS: Conclusions

- The addition of DARA SC to VRd induction/consolidation and R maintenance resulted in favorable PFS benefits across all cytogenetic risk subgroups, including those with revised high risk and the presence of gain(1q21) or amp(1q21) vs VRd followed by R maintenance
- D-VRd followed by D-R maintenance induced higher rates of deep and sustained MRD negativity vs VRd followed by R across all cytogenetic risk subgroups
- Results from this expanded subgroup analysis of PERSEUS based on the presence of HRCAs, including gain(1q21) and amp(1q21), support the addition of DARA SC to VRd therapy during both induction/consolidation and maintenance in this patient population

These results support the use of D-VRd induction/consolidation followed by D-R maintenance as a new standard of care for TE patients with NDMM, regardless of cytogenetic risk status

D-R, daratumumab plus lenalidomide; D-VRd, subcutaneous daratumumab plus bortezomib, lenalidomide, and dexamethasone; DARA, daratumumab; HRCA, high-risk cytogenetic abnormality; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; PFS, progression-free survival; R, lenalidomide; SC, subcutaneous; TE, transplant-eligible; VRd, bortezomib, lenalidomide, and dexamethasone.

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https://www.congresshub.com/Oncology/DGHO2024/Daratumumab/Driessen

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