Transplant non eligible IMW 2024

מפגש חוג מיאלומה 11.2024

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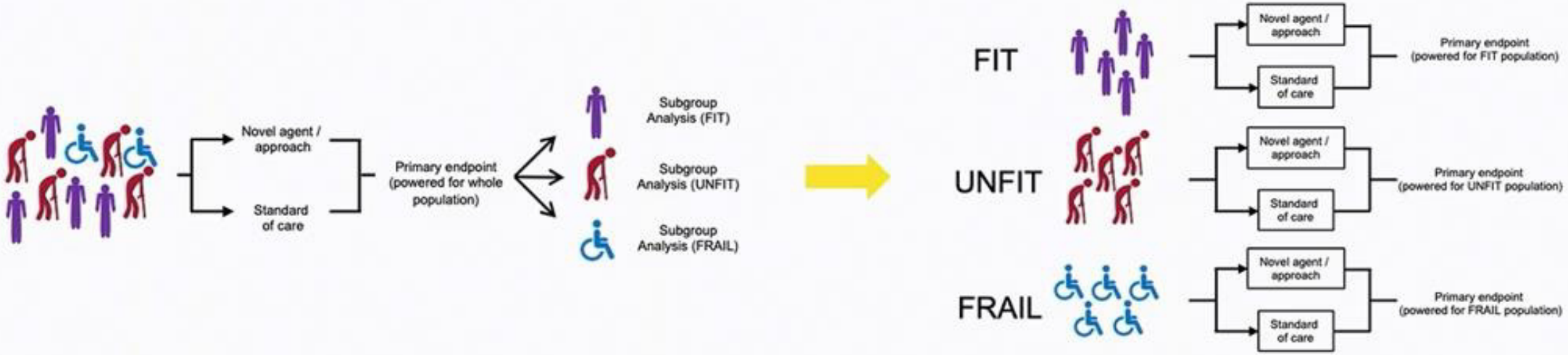
Paradigm switch for management of elderly patients



	IMWG frailty score	R-MCI	UKMRA MRP	Mayo risk score	Ancona Vulnerability Score	IFM simplified frailty scale
Biological / Clinical components	Age CCI	eGFR PFTs Age Cytogenetics	Age R-ISS CRP	Age NT-proBNP	CCI	Age CCI
Functionality tests	ADL IADL	PS (Karnofsky)	PS (WHO)	PS (WHO)	PS (WHO)	ECOG
Population	Clinical trials	Clinical trials, real world	Clinical trials, real world	Real world	Real world	Clinical trials

Need for frailty scores
- **to compare clinical trials**
- **to guide the clinical practice**

Tailoring patients upfront and adapting therapy based on frailty

Adapted from Pawlyn, Khan & Freeman, *Hematology* 2023;

Main recent phase 3 trials in elderly patients

PAST

Trials	Age limit	Frailty limit
FIRST	≥ 65 or TNE	none
ALCYONE	≥ 65 or TNE	none
MAIA	≥ 65 or TNE	none

CURRENT

Trials	Age limit	Frailty limit
IFM2017-03	≥ 65	Frailty score ≥ 2
IMROZ	TNE and ≤ 80	none
BENEFIT IFM	≥ 65 and < 80	Frailty score <2
CEPHEUS	TNI	Frailty score <2
MAJESTEC-7	TNI	Frailty score <2 Or 2 if age only
CARTITUDE-5	TNI	Frailty score <2

TNE = transplant not eligible; TNI = transplant not intended

IMWG frailty score

Score assessment		Score
Age (year)	≤75	0
	76-80	1
	>80	2
Activity of Daily Living	>4	0
	≥4	1
Instrumental Activity of Daily Living	>5	0
	≤5	1
Charlson Comorbidity Index	≤1	0
	≥2	1

Score assessment	Total score
Fit	0
Intermediate	1
Frail	≥2

Quadruplet in TI

	CEPHEUS	IMROZ	BENEFIT
	Dara VRD vs VRD 8 cycles x 21d Velcade 2 weekly Len for 14 days Dara every week 1 cycle, every 3 weeks for 8 cycles, than every 4 weeks Maintenance: DaraRD vs RD Cycle 28 days	**Isa VRD vs VRD** Induction 4 cycles x 42d Continue: Isa RD vs RD After cycle 18, Isa every 4 weeks) Crossover in case of progression	**IsaVRD vs IsaRD** Induction 12 cycles x 28-d Consolidation: IsaVR vs IsaR Cycle 13-18, 28-d (6 cycles) IsaR until progression
N. of patients	395	446	270
Primary EP	Overall MRD 10^{-5}	PFS	MRD 10^{-5} on 18 months
Median follow up	58.7 months	59.7 months	
Age limit	Transplant non intent 27% transplant differed	TNE and ≤ 80	65 ≤ and ≤ 80
Frailty limit	<2	None	<2

CEPHEUS: Baseline Demographic and Clinical Characteristics (ITT Population)

	D-VRd (n = 197)	VRd (n = 198)
Age		
Median (range), years	70.0 (42-79)	70.0 (31-80)
Category, n (%)		
<65 years	36 (18.3)	35 (17.7)
65 to <70 years	52 (26.4)	53 (26.8)
≥70 years	109 (55.3)	110 (55.6)
Male, n (%)	87 (44.2)	111 (56.1)
ECOG PS score, n (%)[a]		
0	71 (36.0)	84 (42.4)
1	103 (52.3)	100 (50.5)
2	23 (11.7)	14 (7.1)
Frailty score, n (%)[b]		
0 (fit)	124 (62.9)	132 (66.7)
1 (intermediate fitness)	73 (37.1)	66 (33.3)
Transplant deferred, n (%)	53 (26.9)	53 (26.8)
Transplant ineligible, n (%)	144 (73.1)	145 (73.2)

	D-VRd (n = 197)	VRd (n = 198)
Type of myeloma by immunofixation or serum FLC assay, n (%)		
IgG	130 (66.0)	114 (57.6)
IgA	38 (19.3)	52 (26.3)
IgD	2 (1.0)	3 (1.5)
Light chain	22 (11.2)	25 (12.6)
Biclonal	5 (2.5)	3 (1.5)
Unknown	0	1 (0.5)
Extramedullary plasmacytomas, n (%)	11 (5.6)	13 (6.6)
ISS disease stage, n (%)[c]		
I	68 (34.5)	68 (34.3)
II	73 (37.1)	75 (37.9)
III	56 (28.4)	55 (27.8)
Cytogenetic risk profile, n (%)[d]		
Standard risk	149 (75.6)	149 (75.3)
High risk	25 (12.7)	27 (13.6)
Indeterminate[e]	23 (11.7)	22 (11.1)

Treatment arms were well balanced

ITT, intent-to-treat; FLC, free light chain; ISS, International Staging System; [a]ECOG PS is scored on a scale from 0 to 5, with 0 indicating no symptoms and higher scores indicating increasing disability. [b]Total additive frailty is scored on a scale of 0 to 5 based on age, comorbidities, and cognitive and physical conditions, with 0 indicating fit, 1 indicating intermediate fitness, and ≥2 indicating frail, per the Myeloma Geriatric Assessment score (http://www.myelomafrailtyscorecalculator.net/). [c]Based on the combination of serum β2-microglobulin and albumin levels. Higher stages indicate more advanced disease. [d]Based on fluorescence in situ hybridization; high risk was defined as the presence of del(17p), t(4;14), and/or t(14;16). [e]Indeterminate includes patients with missing or unevaluable samples.

Presented by S.Z Usmani at the 21st International Myeloma Society (IMS) Annual Meeting; September 25-28, 2024; Rio de Janeiro, Brazil

CEPHEUS: Patient Disposition (ITT Population)

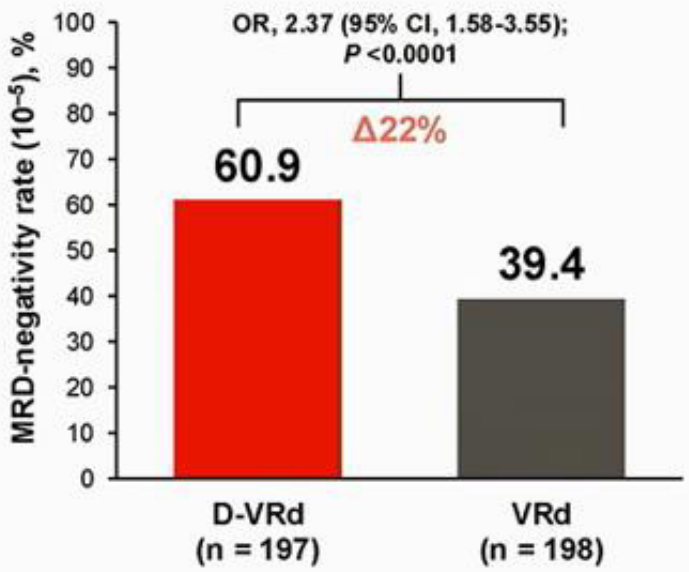
Median follow-up: 58.7 months

	D-VRd	VRd
Randomized patients (ITT)	197	198
Number of patients treated	197	195
Median treatment duration, months	56.3	34.3
Patients who discontinued study treatment,[a] n (%)	95 (48.2)	128 (65.6)
Reason for treatment discontinuation,[a] n (%)		
Progressive disease	27 (13.7)	51 (26.2)
Adverse events	16 (8.1)	32 (16.4)
Death[b]	34 (17.3)	24 (12.3)
Death due to COVID-19	12 (6.1)	6 (3.1)
Other[c]	18 (9.1)	21 (10.8)

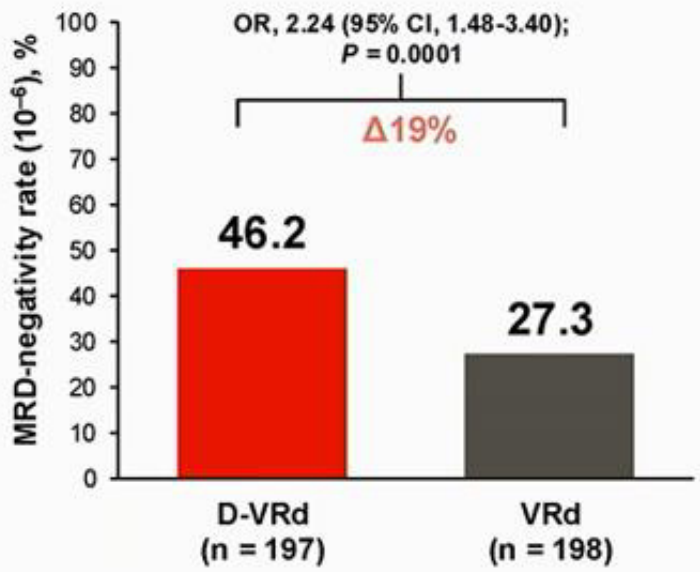
CEPHEUS: Overall and Sustained MRD-negativity Rates[a] (ITT Population)

Primary endpoint

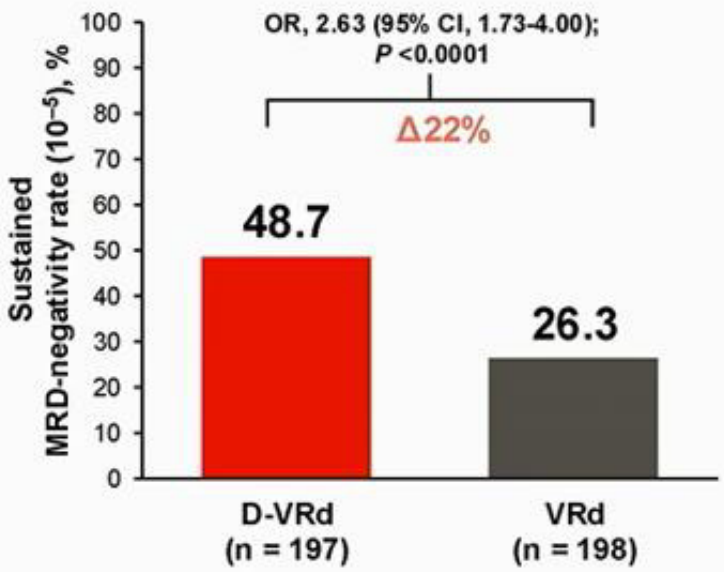
Overall MRD-negativity rate (10^{-5})



Overall MRD-negativity rate (10^{-6})

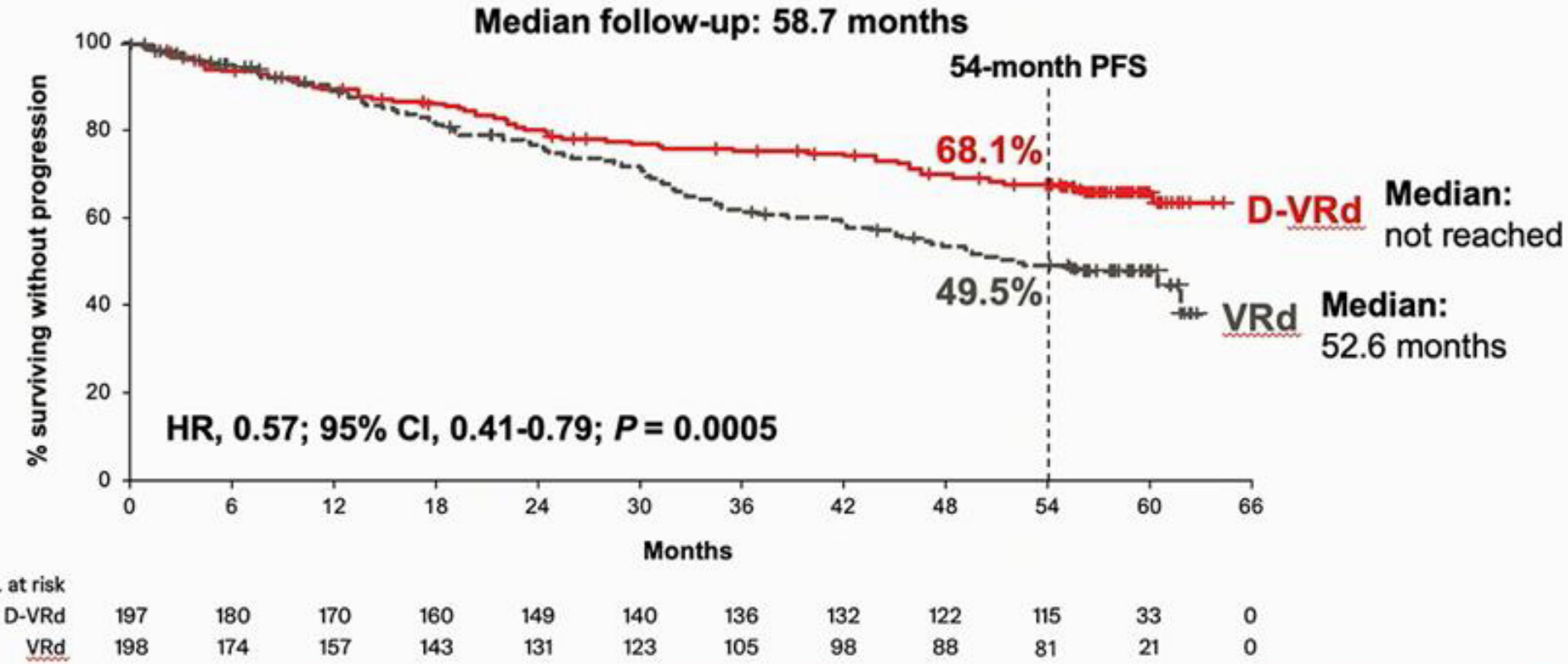


Sustained MRD-negativity rate (10^{-5}) ≥12 months



Daratumumab led to deeper MRD responses at 10^{-6} and a higher sustained MRD-negativity rate

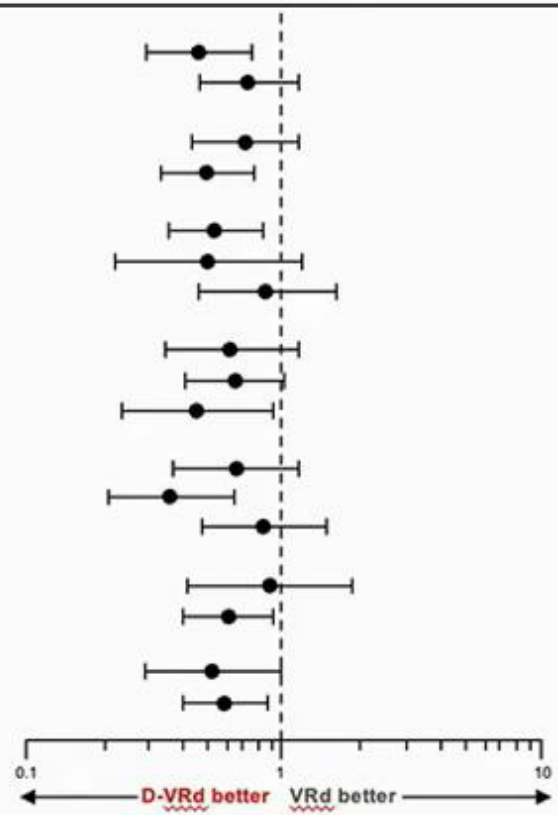
CEPHEUS: PFS (ITT Population)



Daratumumab significantly improved PFS, with a 43% reduction in the risk of disease progression or death

CEPHEUS: PFS in Prespecified Subgroups (ITT Population)

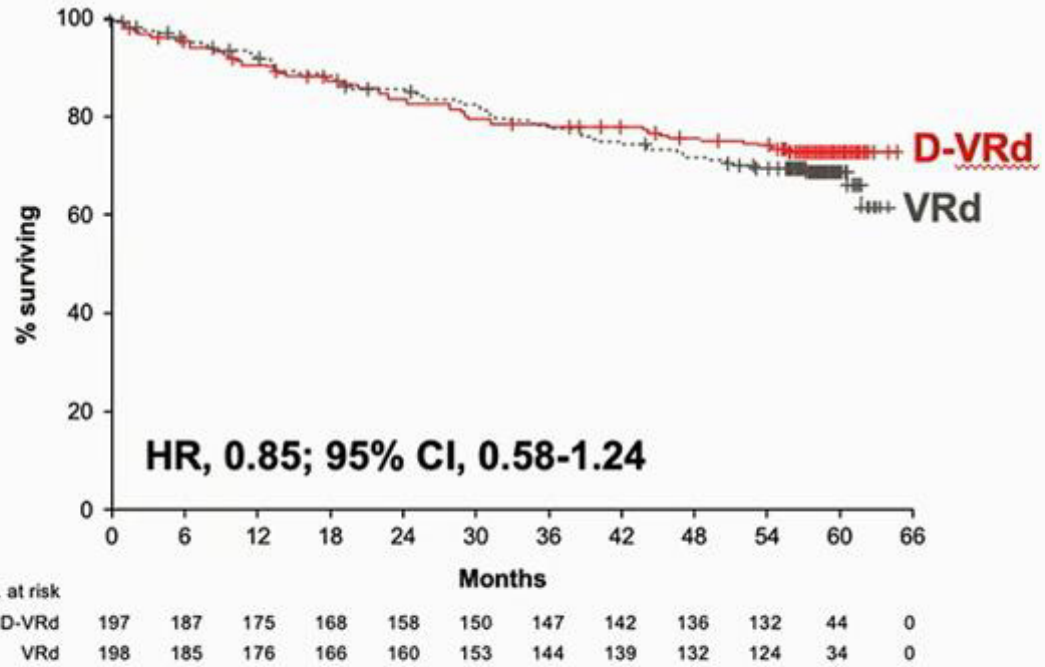
Subgroup	Disease progression or death, n/N		Median PFS, months		HR (95% CI)
	D-VRd	VRd	D-VRd	VRd	
Sex					
Male	24/87	53/111	NE	49.2	0.46 (0.29-0.75)
Female	39/110	38/87	NE	NE	0.73 (0.47-1.15)
Age					
<70 years	30/88	38/88	NE	NE	0.72 (0.44-1.16)
≥70 years	33/109	53/110	NE	49.4	0.50 (0.33-0.78)
Region					
Europe	37/120	54/116	NE	51.1	0.54 (0.36-0.82)
North America	10/37	13/31	NE	50.2	0.51 (0.22-1.17)
Other	16/40	24/51	NE	NE	0.87 (0.46-1.64)
Weight					
≤65 kg	17/58	24/63	NE	NE	0.62 (0.34-1.16)
>65-85 kg	34/101	40/88	NE	51.1	0.65 (0.41-1.02)
>85 kg	12/38	27/47	NE	41.9	0.46 (0.23-0.91)
ISS disease stage					
I	21/68	28/68	NE	60.6	0.66 (0.37-1.16)
II	18/73	37/75	NE	45.6	0.36 (0.21-0.64)
III	24/56	26/55	NE	49.2	0.84 (0.48-1.46)
Cytogenetic risk					
High risk	13/25	17/27	39.8	31.7	0.88 (0.42-1.84)
Standard risk	43/149	60/149	NE	60.6	0.61 (0.41-0.91)
ECOG PS score					
0	16/71	30/84	NE	NE	0.53 (0.29-0.97)
≥1	47/126	61/114	NE	43.8	0.59 (0.40-0.86)



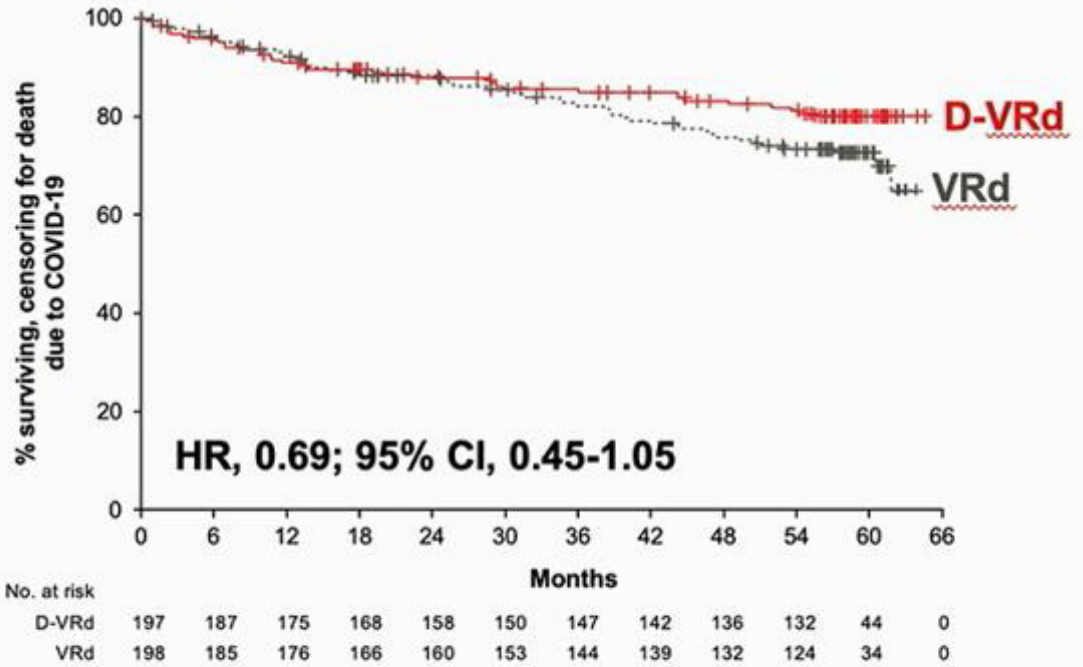
Daratumumab benefit was generally consistent across prespecified subgroups

CEPHEUS: OS

OS (ITT population)



OS
Censoring for death due to COVID-19



OS trended favorably for the daratumumab arm and further improved when censoring for death due to COVID-19

CEPHEUS: Safety[a]

	D-VRd (n = 197)	VRd (n = 195)
Median (range) treatment duration, months	56.3 (0.1-64.6)	34.3 (0.5-63.8)
Any grade 3 or 4 TEAE, n (%)	182 (92.4)	167 (85.6)
TEAE leading to discontinuation of all study drugs, n (%)	15 (7.6)	31 (15.9)
Grade 5 non–COVID-19 TEAE,[b] n (%)	21 (10.7)	15 (7.7)
Grade 5 COVID-19 TEAE,[b,c] n (%)	12 (6.1)	6 (3.1)
Exposure-adjusted grade 5 TEAE rate, patient-months	0.39/100	0.31/100

- **Comparable rate of grade 5 TEAEs, adjusting for a ~2-year difference in treatment duration**
- **The impact of COVID-19 on grade 5 TEAEs was greatest at the peak of the global pandemic**

CEPHEUS: Safety[a]

TEAE, n (%)	D-VRd (n = 197)		VRd (n = 195)	
	Any grade	Grade 3 or 4	Any grade	Grade 3 or 4
HEMATOLOGIC				
Blood and lymphatic system disorders	163 (82.7)	126 (64.0)	126 (64.6)	98 (50.3)
Neutropenia	110 (55.8)	87 (44.2)	76 (39.0)	58 (29.7)
Thrombocytopenia	92 (46.7)	56 (28.4)	66 (33.8)	39 (20.0)
Anemia	73 (37.1)	26 (13.2)	62 (31.8)	23 (11.8)
NONHEMATOLOGIC				
Gastrointestinal disorder	157 (79.7)	41 (20.8)	159 (81.5)	40 (20.5)
Diarrhea	112 (56.9)	24 (12.2)	115 (59.0)	18 (9.2)
Constipation	75 (38.1)	4 (2.0)	82 (42.1)	5 (2.6)
General disorders and administration-site conditions	159 (80.7)	40 (20.3)	147 (75.4)	28 (14.4)
Peripheral edema	83 (42.1)	4 (2.0)	76 (39.0)	1 (0.5)
Fatigue	63 (32.0)	18 (9.1)	60 (30.8)	16 (8.2)
Psychiatric disorders	91 (46.2)	10 (5.1)	96 (49.2)	10 (5.1)
Insomnia	63 (32.0)	4 (2.0)	63 (32.3)	2 (1.0)
Infections	181 (91.9)	79 (40.1)	167 (85.6)	62 (31.8)
Upper respiratory tract infection	78 (39.6)	1 (0.5)	64 (32.8)	1 (0.5)
COVID-19	75 (38.1)	22 (11.2)	48 (24.6)	9 (4.6)
Second primary malignancies	15 (7.6)	–	18 (9.2)	–

	Any grade	Grade 2	Grade 3 or 4	Any grade	Grade 2	Grade 3 or 4
Peripheral sensory neuropathy	110 (55.8)	60 (30.5)	16 (8.1)	119 (61.0)	70 (35.9)	16 (8.2)

Safety data was consistent with the established safety profile of each individual drug

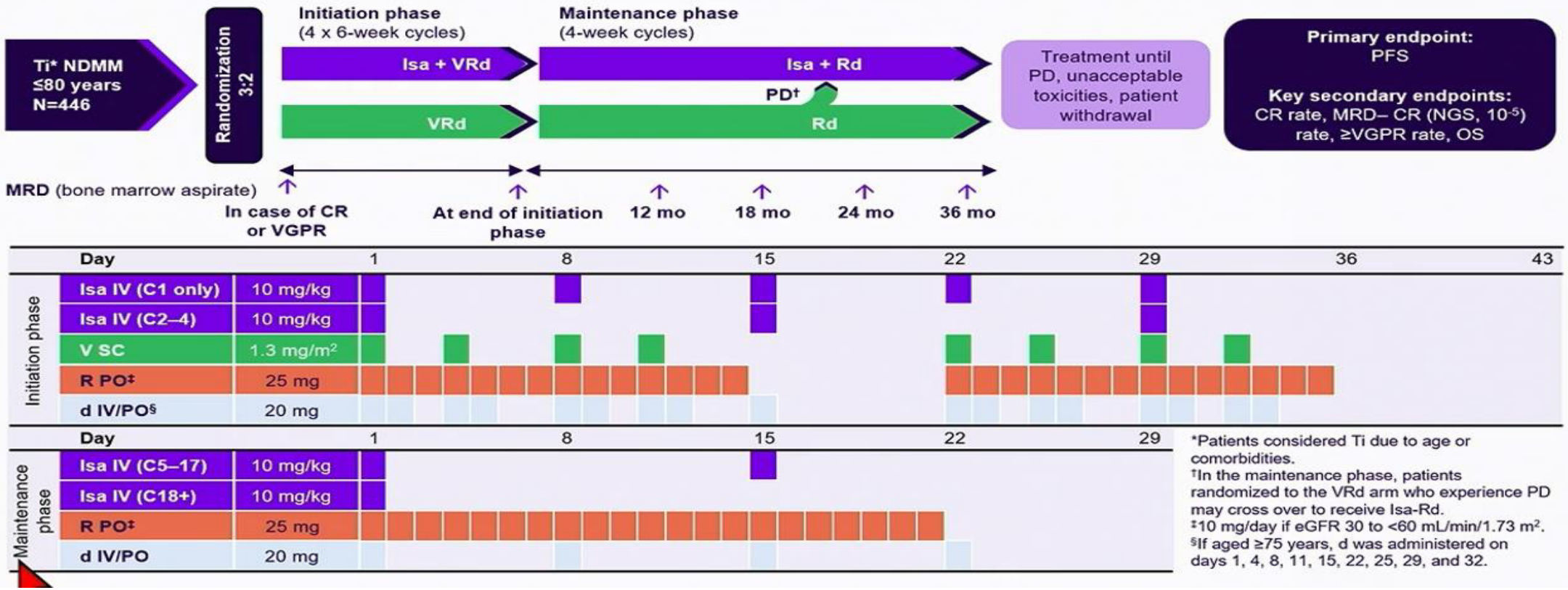
CEPHEUS: Conclusions

- CEPHEUS is the first phase 3 daratumumab trial with a primary endpoint of MRD negativity
- Adding daratumumab to VRd significantly improved depth and duration of response
  - Primary endpoint of overall MRD negativity (10^{-5}): 60.9% vs 39.4%
  - Overall MRD-negativity (10^{-6}): 46.2% vs 27.3%
  - Sustained MRD-negativity (10^{-5}): 48.7% vs 26.3%
- Risk of disease progression or death was 43% lower for D-VRd, HR: 0.57
- OS trended favorably for D-VRd, improving further when censored for COVID-19 deaths, HR: 0.69
- D-VRd quadruplet has the potential to improve clinical outcomes for TIE or transplant-deferred patients with NDMM who can tolerate bortezomib

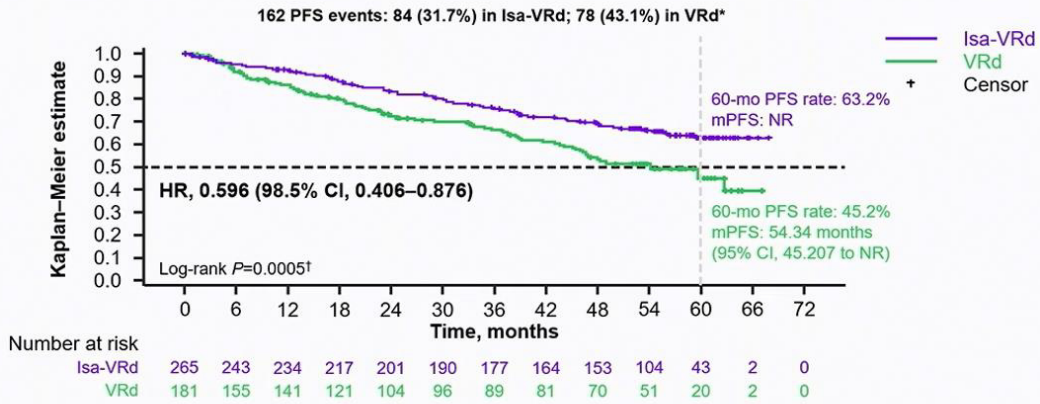
CEPHEUS complements MAIA (D-Rd), supporting a daratumumab-based quadruplet or triplet standard-of-care option across TIE patients and those deferring transplant

IMROZ Phase 3 Study Results of Isatuximab, Bortezomib, Lenalidomide, and Dexamethasone (Isa-VRd) Versus VRd for Transplant-Ineligible Patients With Newly Diagnosed Multiple Myeloma (IMROZ)

Thierry Facon,[1] Meletios-Athanasios Dimopoulos,[2] Xavier Leleu,[3] Meral Beksac,[4,5] Ludek Pour,[6] Roman Hajek,[7] Zhuogang Liu,[8] Jiri Minarik,[9] Philippe Moreau,[10] Joanna Romejko-Jarosinska,[11] Ivan Spicka,[12] Vladimir Vorobyev,[13] Michele Cavo,[14] Hartmut Goldschmidt,[15] Thomas Martin,[16] Salomon Manier,[17] Marie-France Brégeault,[18] Sandrine Macé,[18] Christelle Berthou,[18] Robert Z. Orlowski[19]



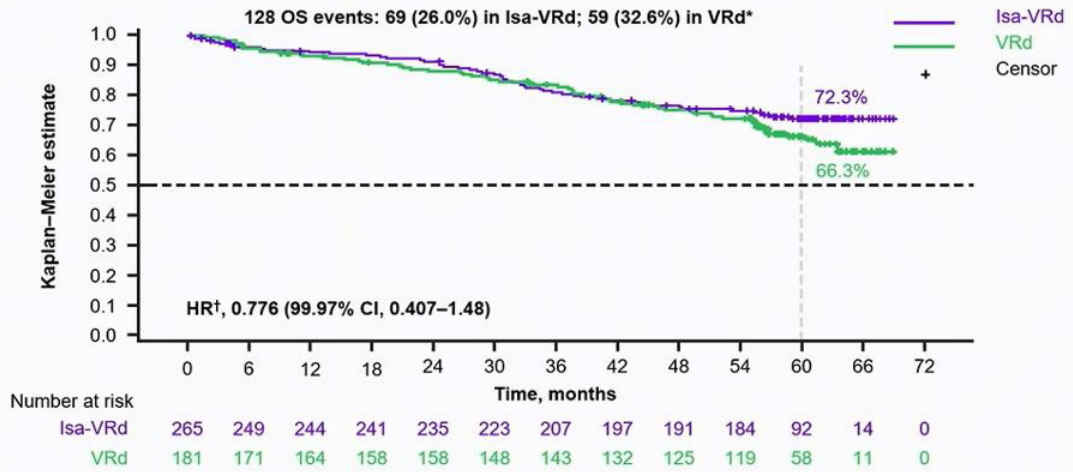
Primary endpoint met: Interim PFS analysis–IRC assessment in ITT population



At a median follow-up of 5 years (59.7 months), Isa-VRd followed by Isa-Rd led to a statistically significant reduction in the risk of progression or dea

*Cutoff ... for PFS analysis: September 26, 2023 (median follow-up ~5 years). †Nominal one-sided P value.

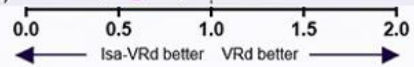
Interim OS analysis–ITT population



At a median follow-up of 5 years, OS is still immature; however, a favorable trend was observed for the Isa-VRd arm, with a 22.4% risk reduction compared with the VRd arm

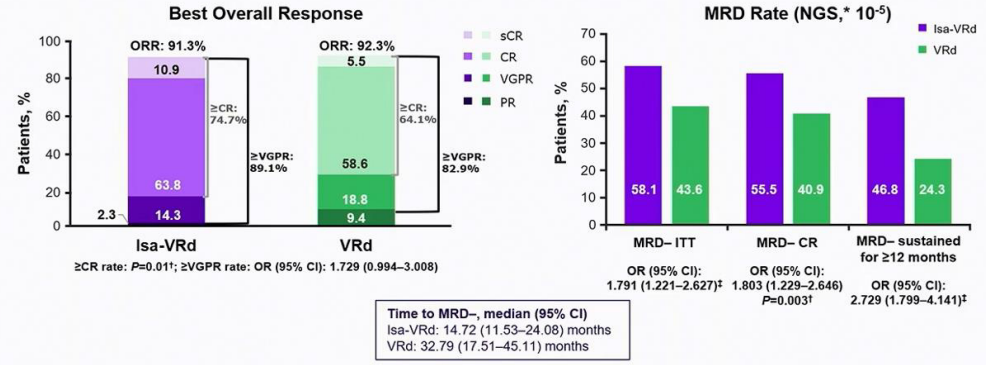
PFS subgroup analyses

Characteristic		Subgroup	Isa-VRd Events/total	Median PFS (95% CI)	VRd Events/total	Median PFS (95% CI)	Hazard ratio (95% CI)
All patients			84/265	NR (NR–NR)	78/181	54.341 (45.207–NR)	0.596 (0.438–0.812)
Age*	70-year threshold:	<70 years	22/80	NR (NR–NR)	27/56	53.914 (37.52–NR)	0.441 (0.251–0.775)
		≥70 years	62/185	NR (NR–NR)	51/125	54.341 (43.598–NR)	0.671 (0.463–0.972)
	Multiple subgroups:	<65 years	1/8	NR (48.066–NR)	5/9	31.524 (12.189–NR)	0.126 (0.014–1.095)
		65 to <70 years	21/73	NR (NR–NR)	22/47	59.663 (37.52–NR)	0.503 (0.276–0.915)
		70 to <75 years	39/115	NR (56.214–NR)	25/68	NR (45.207–NR)	0.781 (0.472–1.291)
		75 to 80 years	23/69	NR (53.06–NR)	26/57	45.864 (23.819–NR)	0.582 (0.331–1.02)
Baseline ECOG PS		0 or 1	74/235	NR (NR–NR)	69/162	54.341 (45.864–NR)	0.589 (0.424–0.818)
		>1	10/30	NR (29.503–NR)	9/19	43.598 (5.29–NR)	0.606 (0.246–1.493)
Baseline eGFR (MDRD)		<60 mL/min/1.73 m^2	25/66	NR (48.066–NR)	31/62	43.598 (33.117–NR)	0.63 (0.371–1.068)
		≥60 mL/min/1.73 m^2	59/197	NR (NR–NR)	47/119	59.663 (46.62–NR)	0.604 (0.412–0.887)
Extramedullary disease at baseline		Yes	6/19	NR (35.91–NR)	5/7	17.873 (2.825–NR)	0.174 (0.045–0.666)
		No	78/246	NR (NR–NR)	73/174	59.663 (46.16–NR)	0.618 (0.449–0.851)
R-ISS stage at study entry		I or II	67/234	NR (NR–NR)	65/157	59.663 (46.62–NR)	0.551 (0.391–0.776)
		III	16/29	45.602 (21.027–NR)	12/21	37.52 (4.6–NR)	0.736 (0.347–1.561)
Cytogenetic risk at baseline		High	18/40	NR (30.259–NR)	14/34	NR (37.454–NR)	0.971 (0.481–1.96)
		Standard	61/207	NR (NR–NR)	62/140	53.914 (43.006–NR)	0.517 (0.363–0.737)
HRCA† and 1q21+‡		Yes	8/19	NR (22.998–NR)	9/15	37.52 (5.782–NR)	0.491 (0.187–1.293)
		No	70/227	NR (NR–NR)	65/157	59.696 (45.864–NR)	0.604 (0.431–0.847)



A PFS benefit was observed with Isa-VRd vs VRd across most subgroups, including some difficult-to-treat populations with negative prognostic factors

Depth of response in ITT population



Isa-VRd followed by Isa-Rd resulted in deep response rates, with a significant improvement in the MRD– CR rate, as well as higher rates of MRD– and sustained MRD– for ≥12 months

Safety summary (Safety population)

TEAE overview, n (%)	Isa-VRd (n=263)	VRd (n=181)
Median treatment duration	**53.2 months**	**31.3 months**
Patients still on treatment	**125 (47.2)**	**44 (24.3)**
Any TEAE	262 (99.6)	178 (98.3)
Grade ≥3 TEAEs	241 (91.6)	152 (84.0)
Grade 5 TEAEs*	29 (11.0)	10 (5.5)
Serious TEAEs	186 (70.7)	122 (67.4)
Any TEAE leading to definitive treatment discontinuation	60 (22.8)	47 (26.0)
Event rate per patient-year†		
Any TEAE	13.39	12.69
Grade ≥3 TEAEs	1.17	0.99
Grade 5 TEAEs	0.03	0.02
Serious TEAEs	0.37	0.43
Any TEAE leading to definitive treatment discontinuation	0.07	0.09

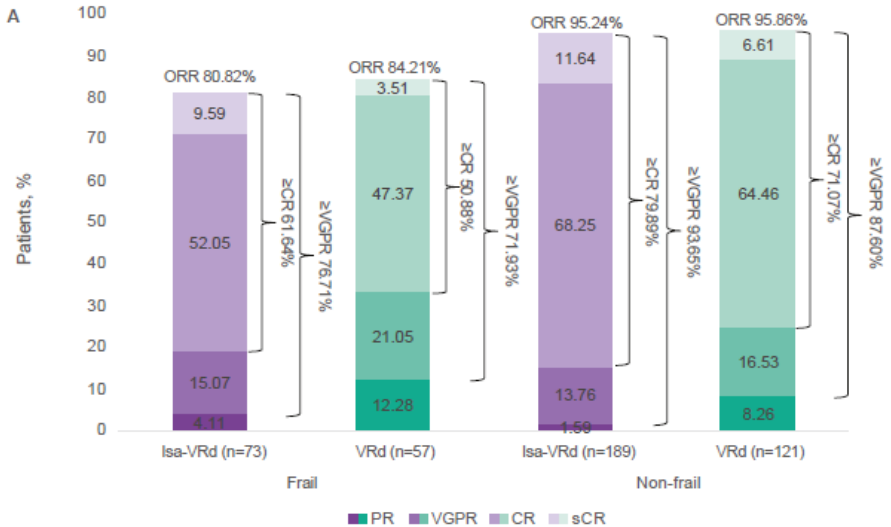
The exposure-adjusted incidence rates suggest the difference in incidence of grade 5 TEAEs between arms was largely driven by the difference in treatment exposure

Isatuximab Plus Bortezomib, Lenalidomide, and Dexamethasone (VRd) for Newly Diagnosed Multiple Myeloma (NDMM) Transplant-Ineligible Patients: Frailty Subgroup Analysis of IMROZ

Salomon Manier[1], Meletios-Athanasios Dimopoulos[2], Xavier P. Leleu[3], Philippe Moreau[4], Michele Cavo[5], Hartmut Goldschmidt[6], Robert Z. Orlowski[7], Muriel Tron[8], Christina Tekle[9], Marie-France Brégeault,[10] Andrea T. Shafer[9], Meral Beksac[11,12], Thierry Facon[1,13]

[1]Department of Haematology, Lille University Hospital, Lille, France; [2]Plasma Cell Dyscrasia Unit, Department of Clinical Therapeutics, National and Kapodistrian University of Athens, Greece; [3]Service d'Hématologie et Thérapie Cellulaire, CHU and CIC Inserm 1402, Poitiers Cedex, France; [4]Department of Hematology, University Hospital Hôtel-Dieu, Nantes, France; [5]Dipartimento di Scienze Mediche e Chirurgiche, Università di Bologna, Italy; [6]Department of Internal Medicine V, University of Heidelberg, Heidelberg, Germany; [7]Department of Lymphoma and Myeloma, University of Texas MD Anderson Cancer Center, Houston, TX, USA; [8]Sanofi, Vitry, France; [9]Sanofi, Cambridge, MA, USA; [10]Sanofi R&D, Vitry-sur-Seine, France; [11]Department of Hematology, Ankara University, Ankara, Turkey; [12]Istinye University Ankara Liv Hospital, Ankara, Turkey; [13]French National Academy of Medicine, Paris, France

Figure 2. (A) Depth of response and (B) MRD-negativity rates across the frail and non-frail subgroups



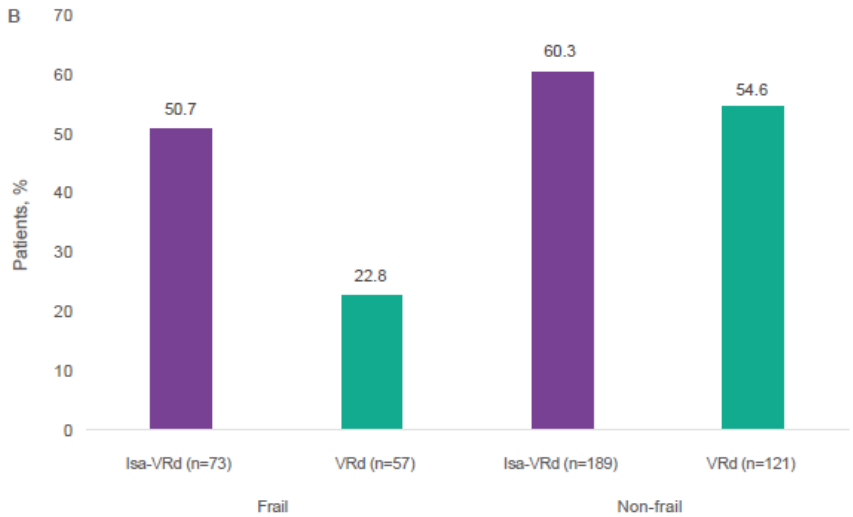


Table 2. Overview of TEAEs in the safety population by patient-year

	Frail (N=129)				Non-frail (N=309)			
	Isa-VRd (n=72)		VRd (n=57)		Isa-VRd (n=188)		VRd (n=121)	
	n (%)	Event rate per patient-year	n (%)	Event rate per patient-year	n (%)	Event rate per patient-year	n (%)	Event rate per patient-year
Patients with any TEAE	72 (100.0)	16.761	56 (98.25)	29.991	187 (99.47)	19.588	119 (98.35)	18.727
Patients with any grade ≥3 TEAE	66 (91.67)	2.221	49 (85.96)	3.248	172 (91.49)	1.832	100 (82.64)	2.141
Patients with any grade 5 TEAE*	9 (12.50)	0.975	5 (8.77)	1.979	20 (10.64)	0.509	5 (4.13)	0.416
Patients with any TEAE leading to definitive treatment discontinuation	21 (29.17)	0.957	20 (35.09)	0.965	39 (20.74)	0.530	27 (22.31)	0.525
Patients with any treatment-emergent SAE†	56 (77.78)	1.051	47 (82.46)	1.340	130 (69.15)	0.989	74 (61.16)	1.296

Table 3. Most common grade ≥3 TEAEs within the frail subgroup

Grade ≥3 TEAEs, n (%)	Isa-VRd (n=72)	VRd (n=57)
Neutropenia	28 (38.89)	9 (15.79)
Pneumonia	18 (25.00)	12 (21.05)
Cataract	9 (12.50)	3 (5.26)
Diarrhea	7 (9.72)	5 (8.77)
COVID-19 pneumonia	7 (9.72)	1 (1.75)
Fall	6 (8.33)	2 (3.51)
Thrombocytopenia	6 (8.33)	9 (15.79)
Fatigue	4 (5.56)	1 (1.75)

du myélome

Isatuximab plus lenalidomide and dexamethasone with weekly bortezomib versus isatuximab plus lenalidomide and dexamethasone in newly diagnosed transplant ineligible Multiple Myeloma. The BENEFIT (IFM 2020-05) study

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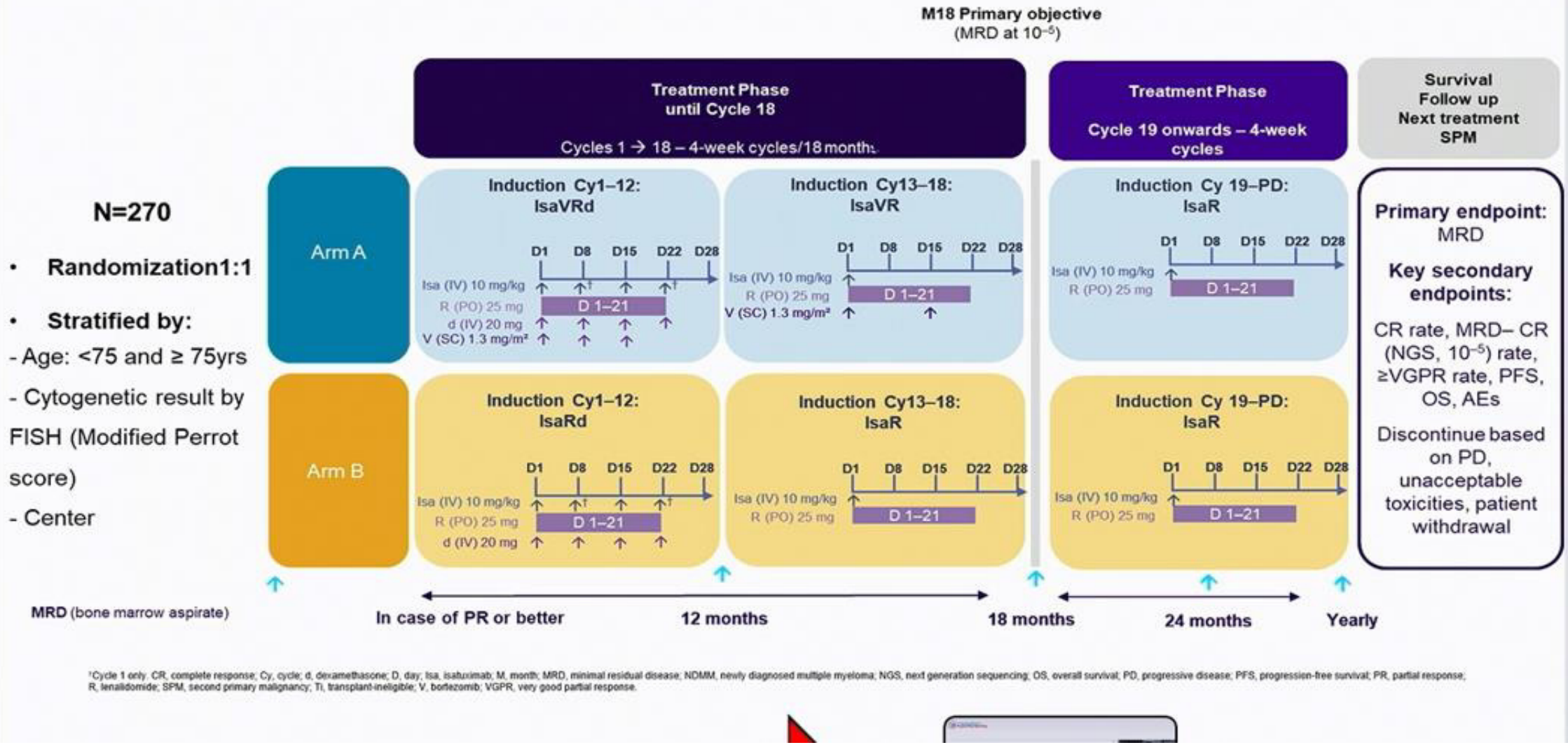
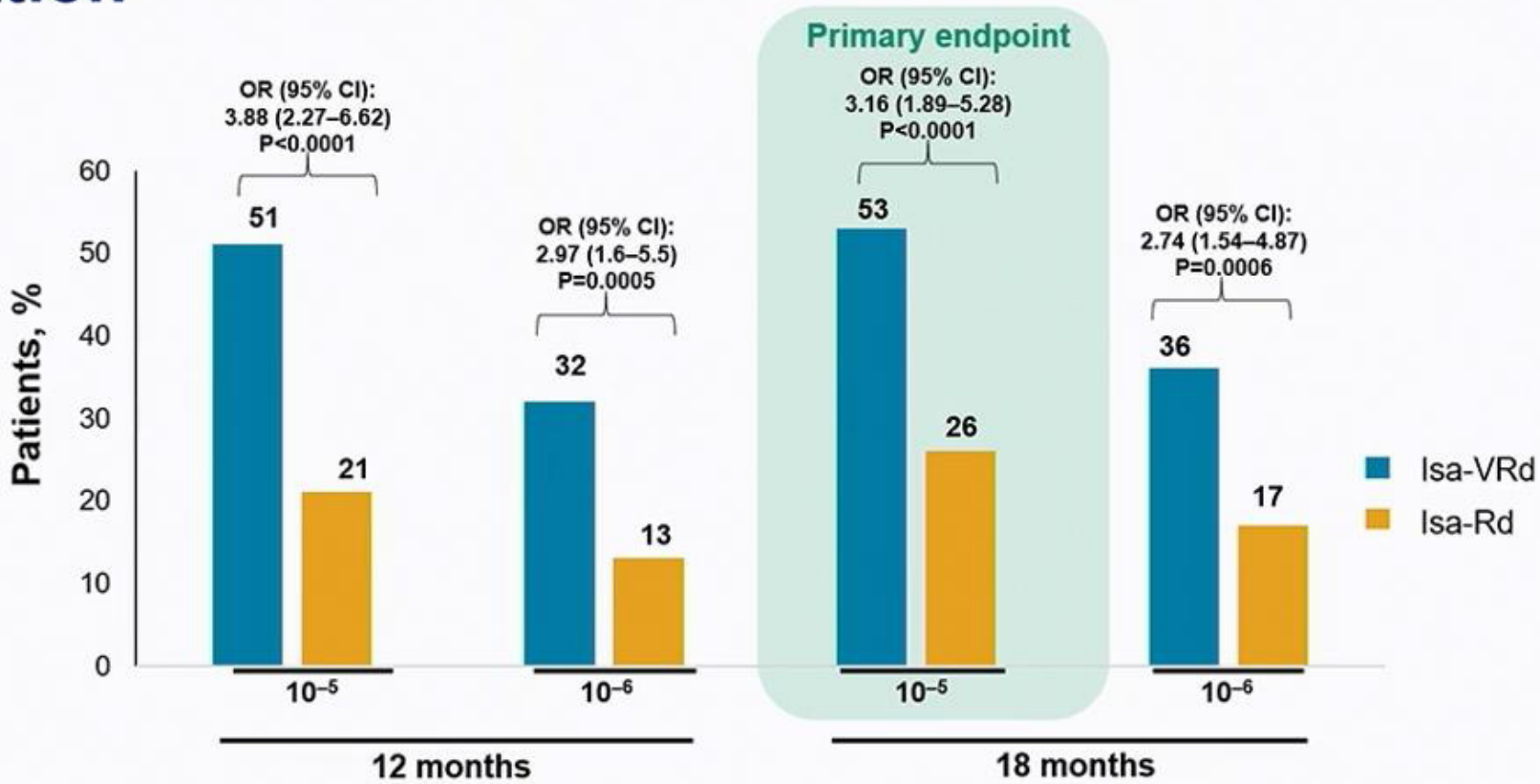
Study design: Isa-VRd vs Isa-Rd in Ti NDMM



[1]Cycle 1 only. CR, complete response; Cy, cycle; d, dexamethasone; D, day; Isa, isatuximab; M, month; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; NGS, next generation sequencing; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; R, lenalidomide; SPM, second primary malignancy; Ti, transplant-ineligible; V, bortezomib; VGPR, very good partial response.

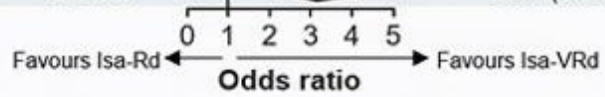
Primary endpoint: MRD–* rate at 18 months – ITT population



Isa-VRd resulted in deep response rates, with a significant improvement in the MRD at 12 and 18 months, and at 10^{-5} and 10^{-6} in the ITT population

MRD subgroup analyses

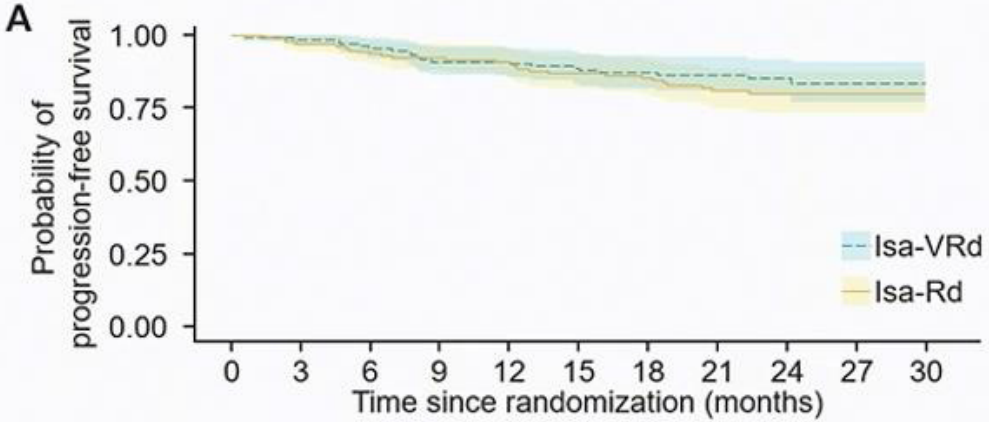
Subset		Isa-VRd Events/Pts	Isa-Rd Events/Pts	OR (95% CI)	P-value for interaction
Sex	Male	37/74	16/71	3.44 (1.67–7.06)	0.79
	Female	34/61	19/64	2.98 (1.43–6.23)	
Age	≤ 75 yr	48/93	22/87	3.15 (1.68–5.93)	0.95
	> 75 yr	23/42	13/48	3.26 (1.35–7.86)	
Cytogenetic profile (LP FISH)	LP HR-	62/119	31/124	3.26 (1.9–5.62)	0.66
	LP HR+	9/16	4/11	2.25 (0.47–10.88)	
Cytogenetic profile (NGS)	Standard risk	58/107	29/112	3.39 (1.92–5.98)	0.62
	High risk	10/22	4/15	2.29 (0.55–9.47)	
ISS	I	27/50	15/51	2.82 (1.24–6.4)	0.91
	II	33/64	13/57	3.6 (1.64–7.93)	
	III	11/21	7/27	3.14 (0.93–10.58)	
eGFR (MRDR Formula)	<60	8/19	8/28	1.82 (0.53–6.19)	0.34
	≥60	63/116	27/107	3.52 (1.99–6.22)	
	All patients	71/135	35/125	3.17 (1.9–5.29)	



A consistent MRD benefit was observed with Isa-VRd vs Isa-Rd across most subgroups, including difficult-to-treat populations with negative prognostic factors

Survival analysis-IRC assessment in ITT population

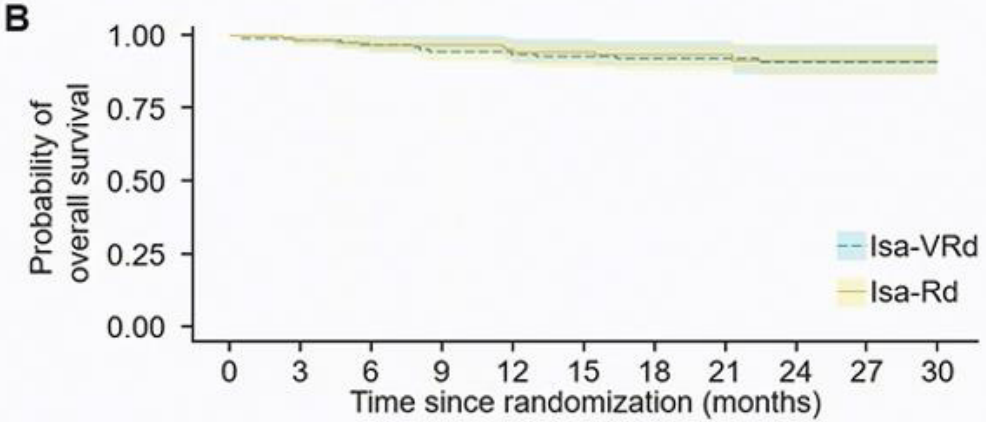
A



Isa-VRd	135	131	127	121	119	117	114	87	56	11	0
Isa-Rd	135	128	123	121	117	112	108	83	52	14	0

Estimated 24 months PFS
85.2% (95%CI 79.2–91.7) for Isa-VRd
80.0% (95% CI 73.3–87.4) for Isa-Rd

B

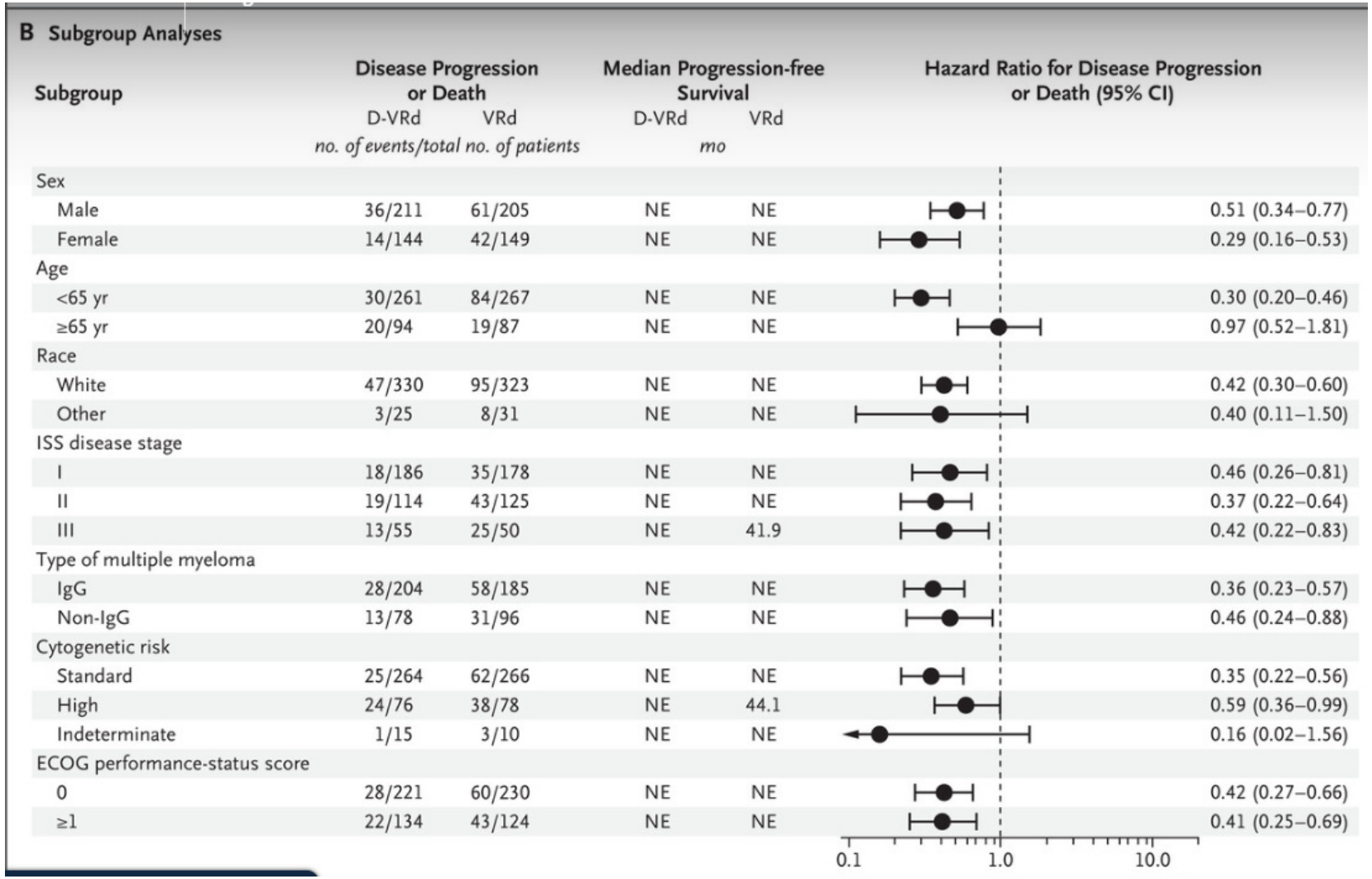


Isa-VRd	135	131	129	124	122	118	115	88	56	11	0
Isa-Rd	135	130	125	123	118	115	112	88	53	14	0

Estimated 24 months OS
91.1% (95%CI 86.1–96.4) for Isa-VRd
91.5% (95%CI 86.5–96.8) for Isa-Rd

At a median follow-up of 23.5 months, survival is still immature

Perseus subgroup analysis



B Subgroup Analyses

Subgroup	Disease Progression or Death		Median Progression-free Survival		Hazard Ratio for Disease Progression or Death (95% CI)
	D-VRd	VRd	D-VRd	VRd	
	no. of events/total no. of patients		*mo*		
Sex					
Male	36/211	61/205	NE	NE	0.51 (0.34–0.77)
Female	14/144	42/149	NE	NE	0.29 (0.16–0.53)
Age					
<65 yr	30/261	84/267	NE	NE	0.30 (0.20–0.46)
≥65 yr	20/94	19/87	NE	NE	0.97 (0.52–1.81)
Race					
White	47/330	95/323	NE	NE	0.42 (0.30–0.60)
Other	3/25	8/31	NE	NE	0.40 (0.11–1.50)
ISS disease stage					
I	18/186	35/178	NE	NE	0.46 (0.26–0.81)
II	19/114	43/125	NE	NE	0.37 (0.22–0.64)
III	13/55	25/50	NE	41.9	0.42 (0.22–0.83)
Type of multiple myeloma					
IgG	28/204	58/185	NE	NE	0.36 (0.23–0.57)
Non-IgG	13/78	31/96	NE	NE	0.46 (0.24–0.88)
Cytogenetic risk					
Standard	25/264	62/266	NE	NE	0.35 (0.22–0.56)
High	24/76	38/78	NE	44.1	0.59 (0.36–0.99)
Indeterminate	1/15	3/10	NE	NE	0.16 (0.02–1.56)
ECOG performance-status score					
0	28/221	60/230	NE	NE	0.42 (0.27–0.66)
≥1	22/134	43/124	NE	NE	0.41 (0.25–0.69)

Daratumumab Plus Bortezomib, Lenalidomide, and Dexamethasone in Transplant-eligible Patients With Multiple Myeloma: A Pooled Analysis of Patients Aged ≥65 Years From Both PERSEUS and GRIFFIN Studies

- ≥65 yrs 25.5% of pts in PERSEUS (D-VRd, 94/355; VRd, 87/354) and 27.1% of pts in GRIFFIN (D-VRd, 28/104; VRd, 28/103).
- aged ≥65 yrs, 9.0% in D-VRd and 13.0% in VRd
- Median PFS was not reached in either treatment group or study.
- Stratified by ISS and cytogenetic risk and not censoring pts on basis of 2 consecutive missing disease assessments,
- PFS HRs favored D-VRd in PERSEUS (HR 0.61 [95% CI 0.32-1.14]), GRIFFIN (HR 0.33 [95% CI 0.06-1.76]), and the pooled dataset (HR 0.56 [95% CI 0.31-1.01]).
- Rates of MRD neg (10^{-5}) were also higher with D-VRd vs VRd in PERSEUS (67.0% vs 49.4%; OR 2.08 [95% CI 1.14-3.79]), GRIFFIN (64.3% vs 17.9%; OR 6.40 [95% CI 1.80-22.75]), and the pooled dataset (66.4% vs 41.7%; OR 2.75 [95% CI 1.61-4.71]).