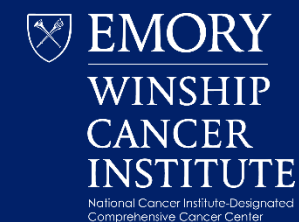




NEWLY DIAGNOSED MYELOMA IN THE ELDERLY PATIENT: QUADS

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This is a debate between...

The Great Nishadini

The Great Nishadini



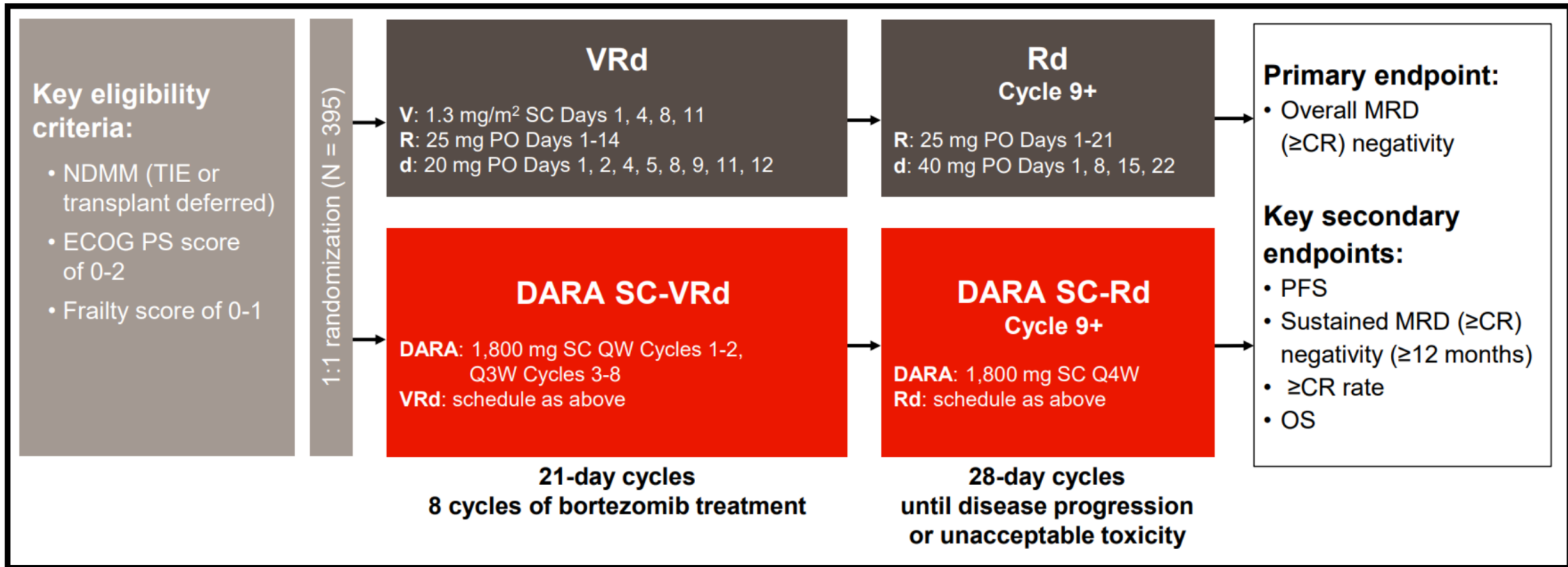
And...

Data

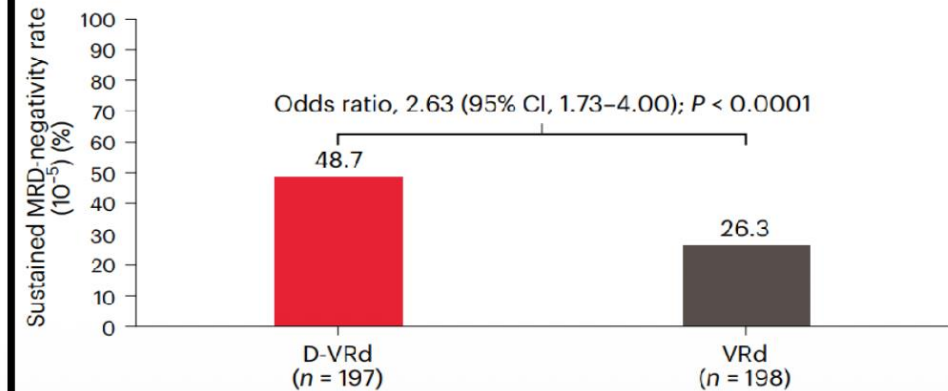
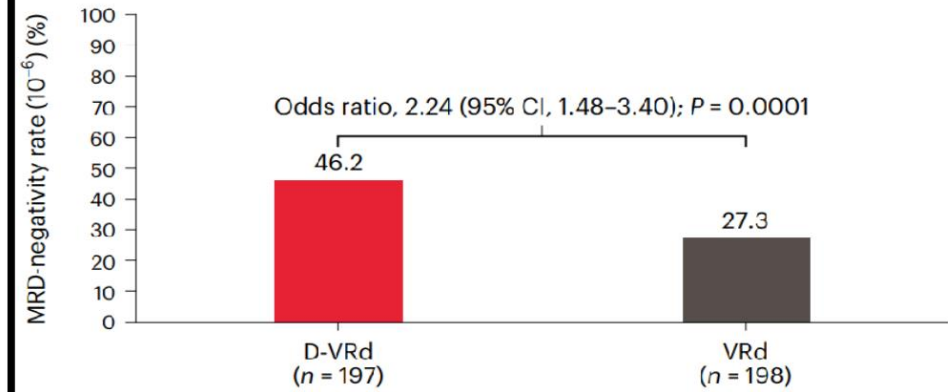
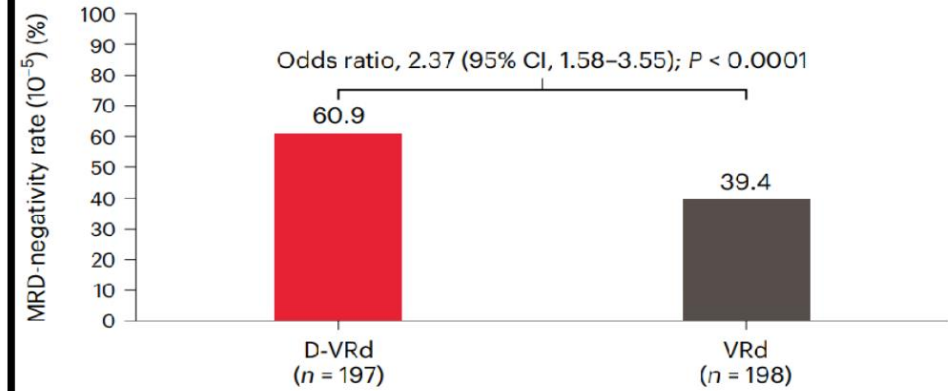
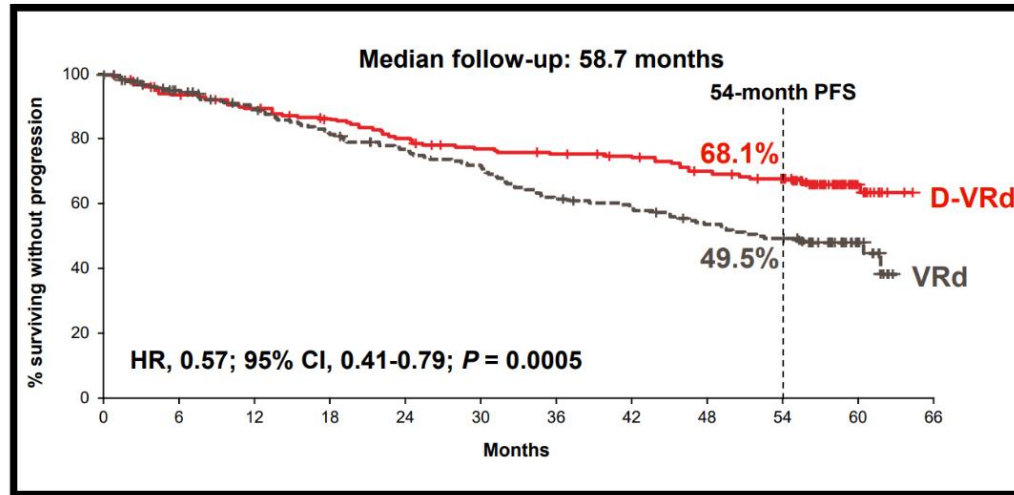
Landmark studies in TiE NDMM

Doublet	FIRST Rd cont vs Rd 18 vs MPT			
Triplet	S0777 RVd vs Rd	MAIA DRd vs Rd	IFM 2017-03 DR(d) vs Rd	
Quadruplet	ALCYONE D-VMP	CEPHEUS D-VRd vs VRd	IMROZ Isa-VRd vs VRd	IFM 2020-05/ BENEFIT IsaVRd vs IsaRd
Immunotherapy	IFM 2021-01-A (TecLille) (Ph2 N=37)	LINKER-MM4 (Ph1/2)	AZD0120 (Ph1) (TE N=22, TIE N=8)	CAREMM-001 BCMA CAR-T (Ph2 N=35)

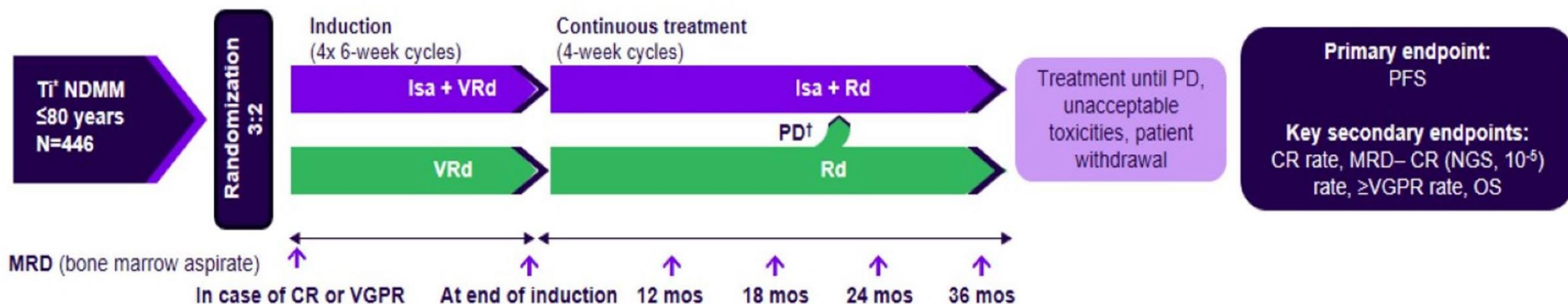
Quadruplet- CEPHEUS: D-VRd vs VRd



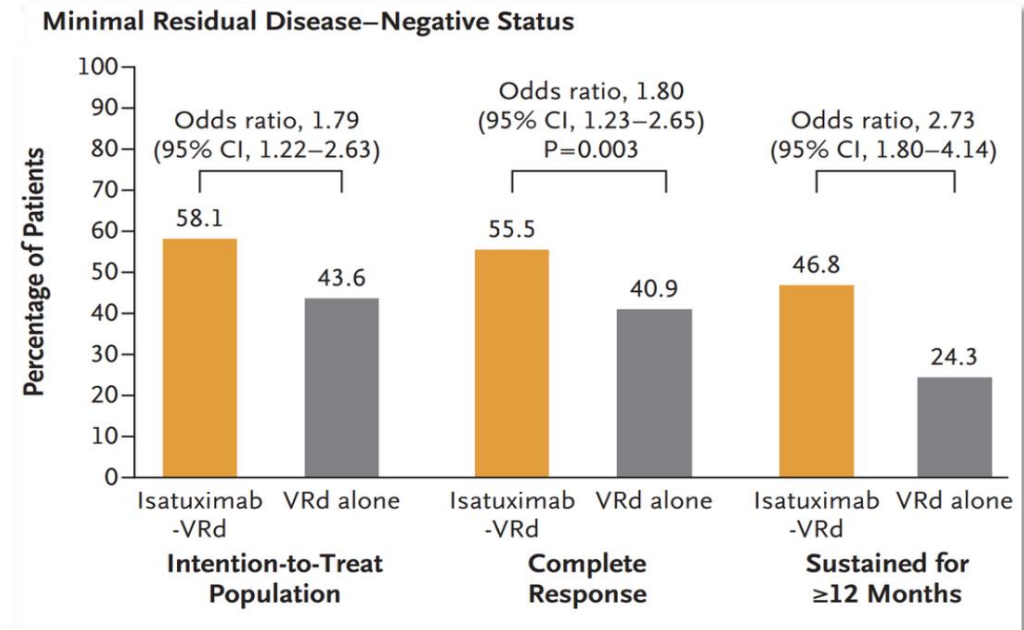
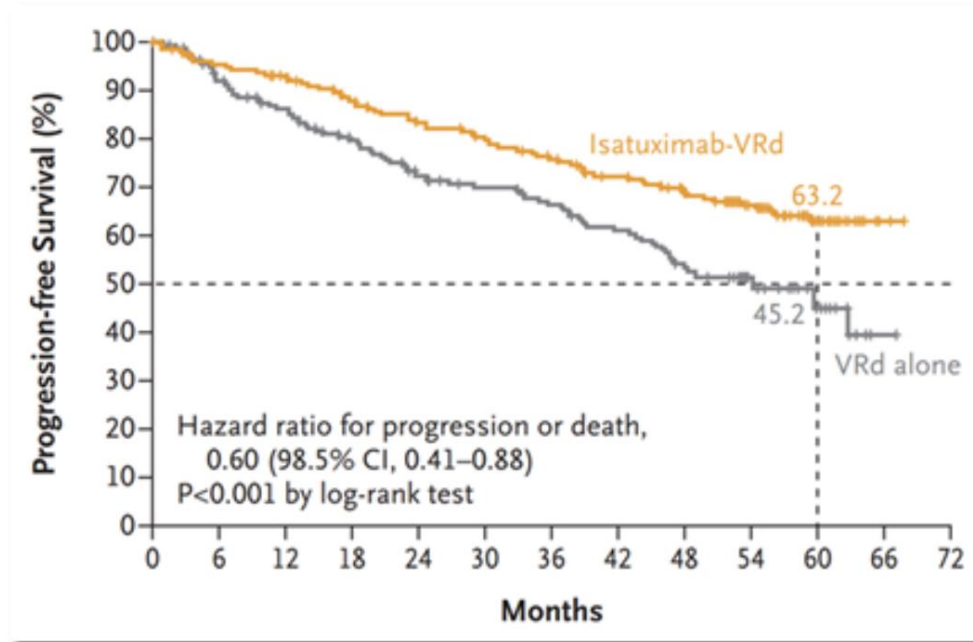
CEPHEUS



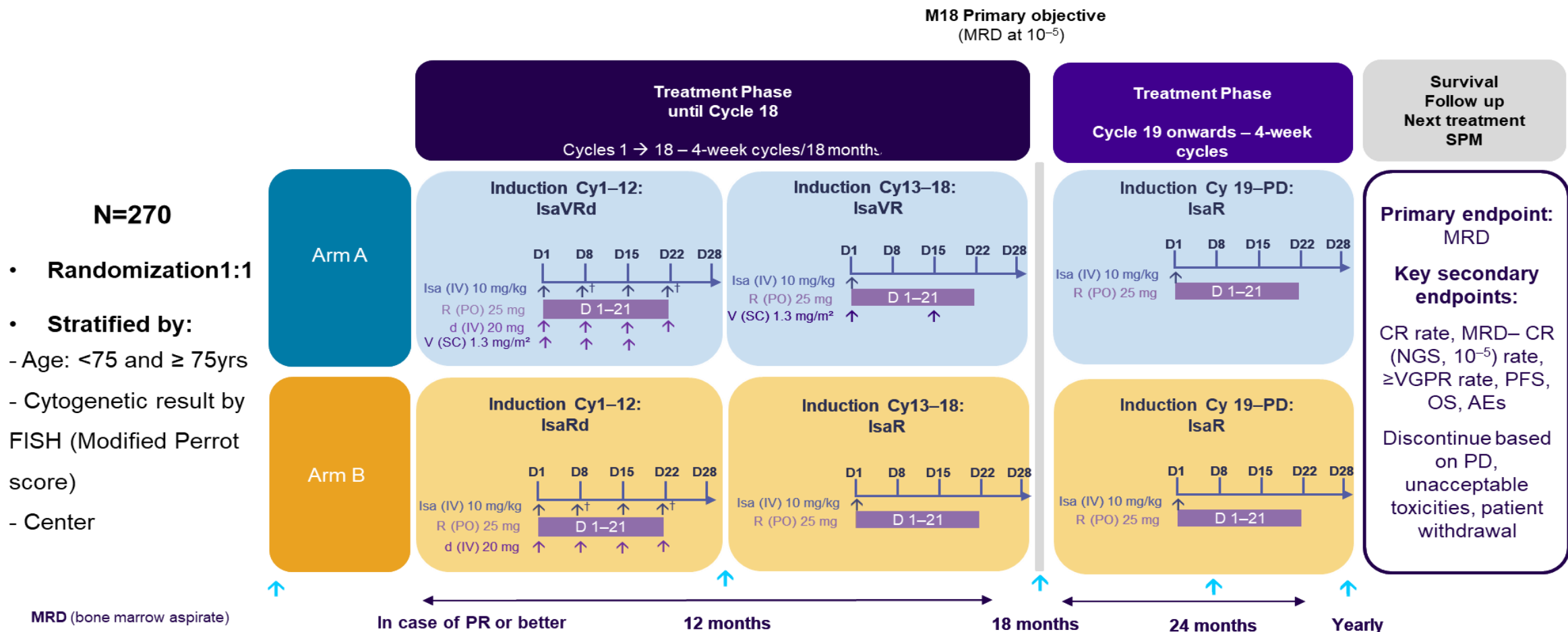
Quadruplet- IMROZ: Isa-VRd vs VRd



IMROZ



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



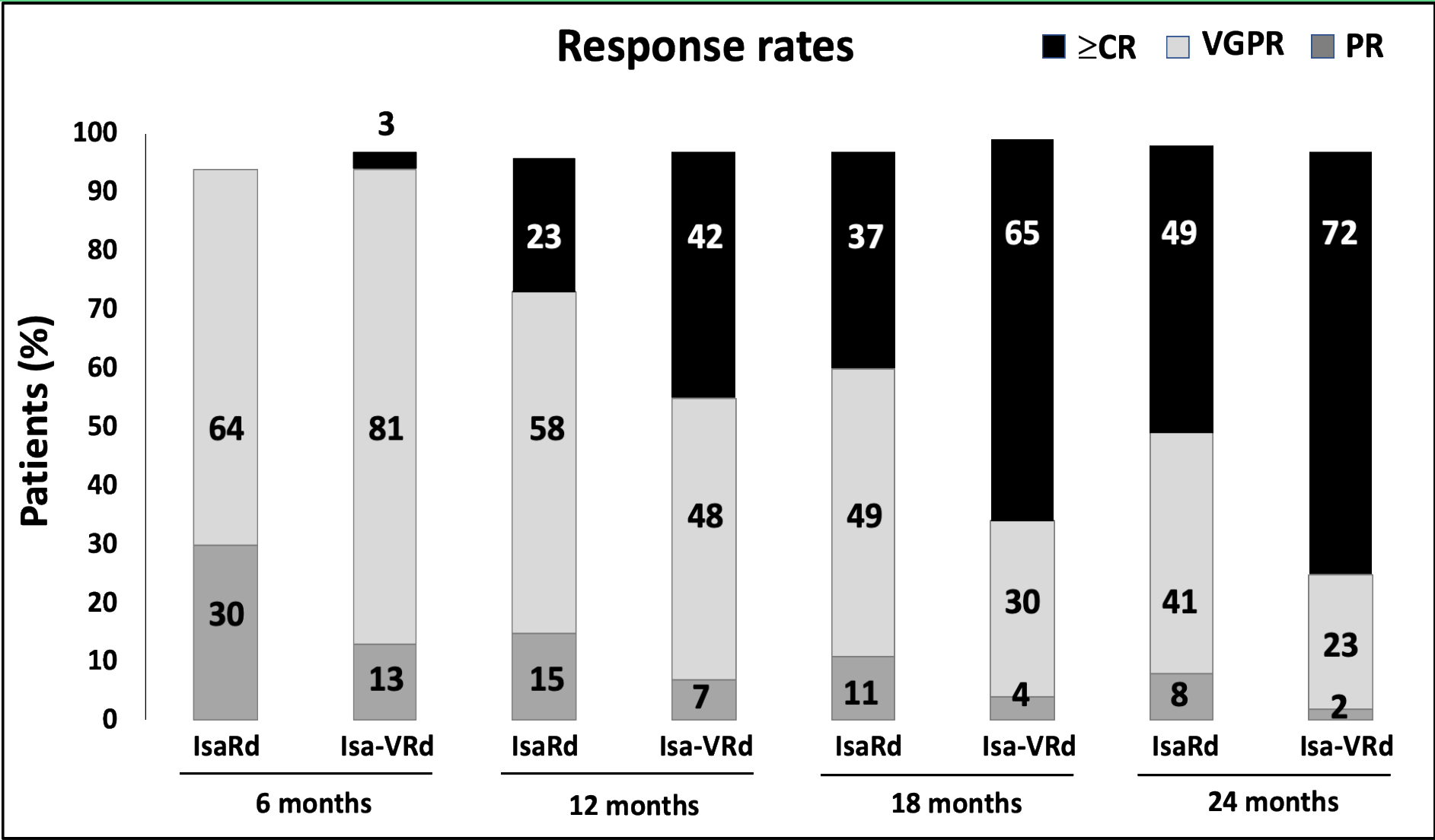
[†]Cycle 1 only. CR, complete response; Cy, cycle; d, dexamethasone; D, day; Isa, isatuximab; M, month; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; NGS, next generation sequencing; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response;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

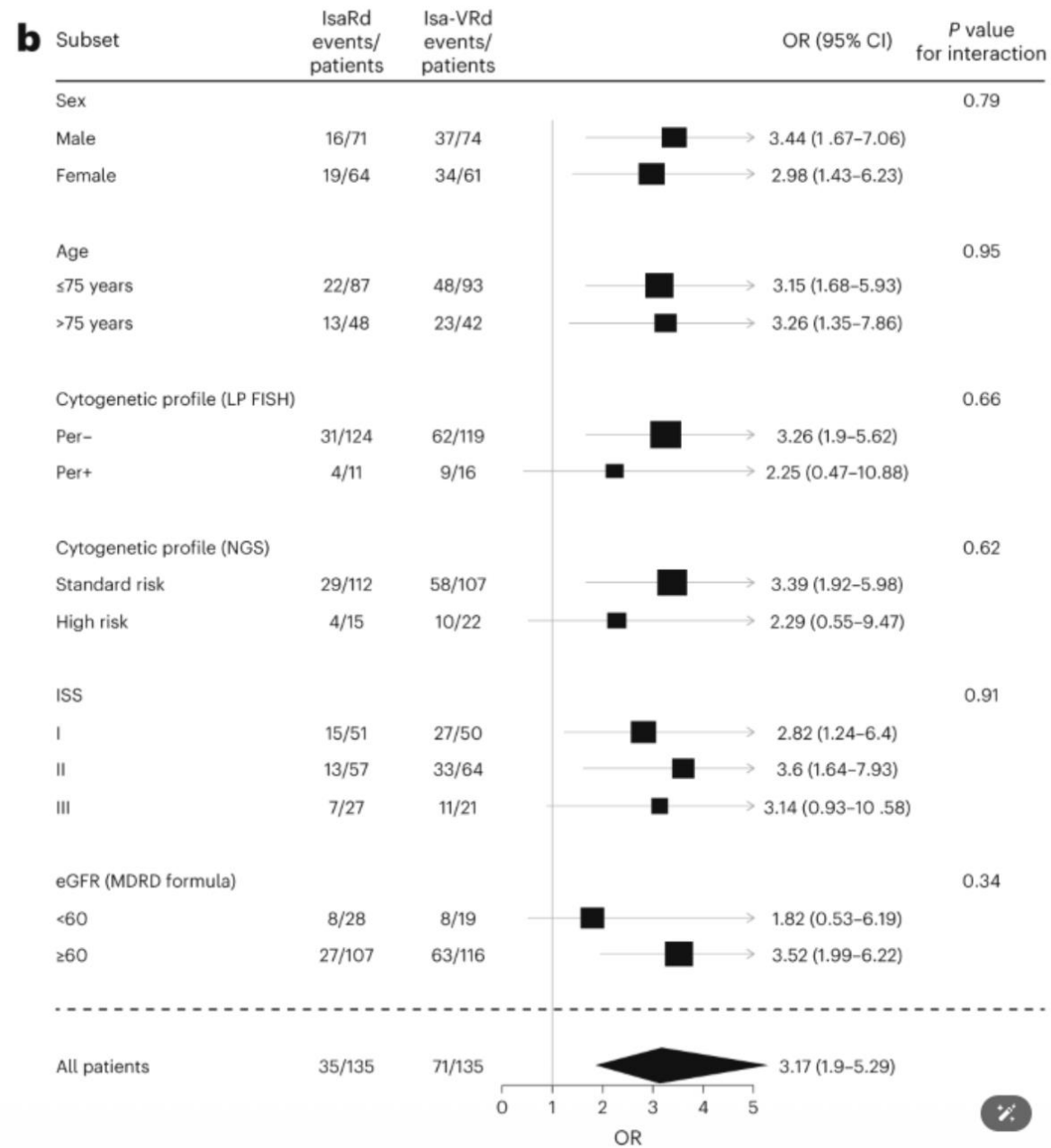
Baseline characteristics

	Non-HR (n=198)	HR* (n=72)
Randomisation arm		
Isa-VRd	93 (47)	42 (58)
IsaRd	105 (53)	30 (42)
Sex – no. (%)		
Female	87 (44)	38 (53)
Male	111 (56)	34 (47)
Median age (IQR) – yr	73.5 (71–76)	73 (71–76)
Age category, yr – no. (%)		
<70	39 (20)	14 (19)
[70–75[	94 (47)	33 (46)
≥75	65 (33)	25 (35)
ECOG performance status – no. (%) [†]		
0 or 1	181 (91)	63 (87.5)
>1	17 (9)	9 (12)
eGFR <60 ml/min/1.73 m ² (MDRD) – no. (%)	38 (19)	9 (12)
Median time between diagnosis of multiple myeloma and randomization (range) – months	1 (0.7–1.7)	0.9 (0.7–1.5)
Type of myeloma at baseline – no. (%)		
IgG	118 (62)	43 (63)
IgA	42 (22)	20 (29)
Light chain only (κ and/or γ)	28 (15)	4 (6)

	Non-HR (n=198)	HR* (n=72)
ISS stage at baseline – no. (%) [§]		
Stage I	85 (43)	16 (22)
Stage II	88 (44)	33 (46)
Stage III	25 (13)	23 (32)
R-ISS stage at baseline – no. (%) [‡]		
Stage I	63 (32)	3 (4)
Stage II	125 (63)	56 (78)
Stage III	10 (5)	13 (18)
Bone marrow plasma cells (%, IQR)	25 [15;43]	33 [18.5;48]

Depth of response at 12, 18 and 24 months - ITT Population

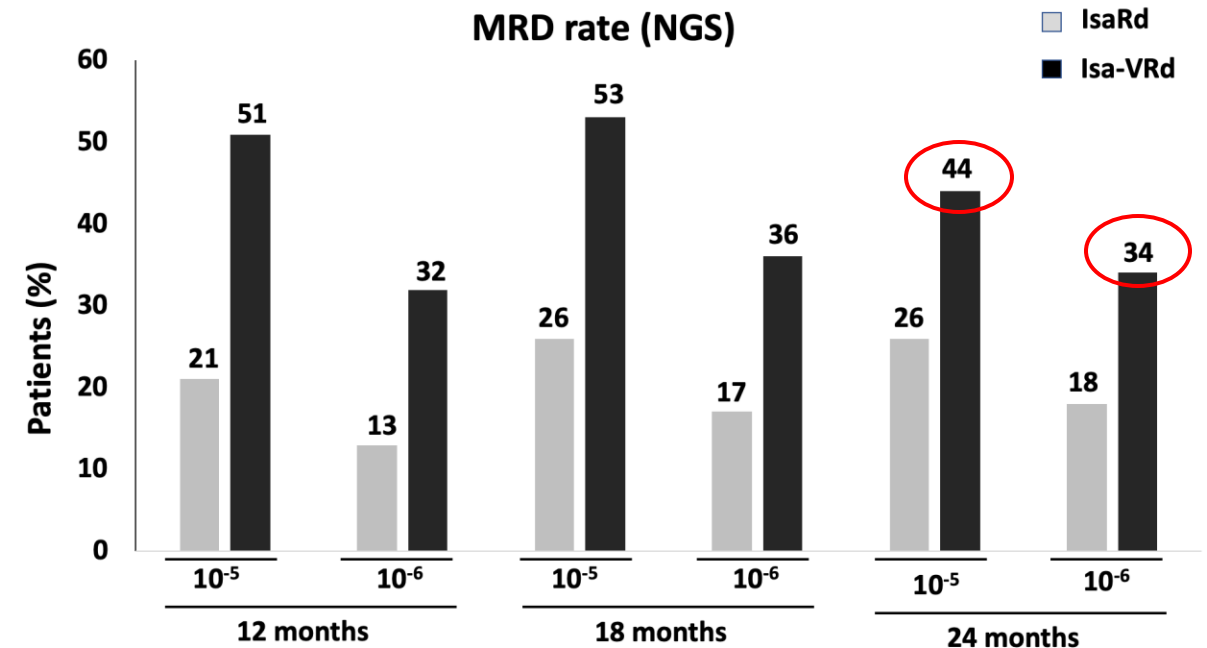




Event, no. of patients (%)	IsaRd (N = 135)	Isa-VRd (N = 135)		
Nonhematologic AE				
	Any grade	≥Grade 2	Any grade	≥Grade 2
Diarrhea	65 (48)	30 (22)	66 (49)	39 (29)
Constipation	41 (30)	19 (14)	52 (39)	30 (22)
Nausea	21 (16)	7 (5)	18 (13)	6 (4)
Nervous system disorders 10% patients discontinued bortezomib related to nervous system disorders ≥grade 2				
Peripheral neuropathy	38 (28)	13 (10)	70 (52)	37 (27)
Other	41 (30)	17 (13)	38 (28)	19 (14)
Psychiatric disorders	32 (24)	17 (13)	33 (24)	22 (16)
Eye disorders	19 (14)	12 (8)	20 (15)	10 (7)
Hepatobiliary disorders	19 (14)	13 (9)	—	—

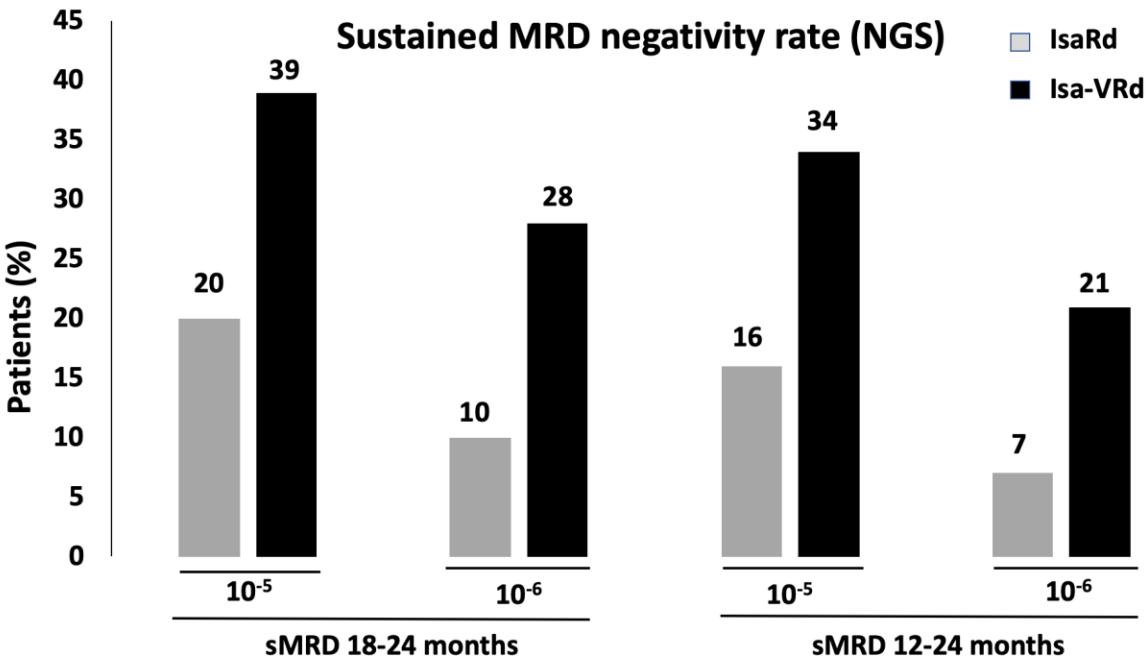
MRD– rate at 12, 18 and 24 months – ITT population

	IsaRd (n=135)	Isa-VRd (n=135)	OR (95%CI), p-value
At 12 months			
MRD- 10^{-5}	29 (21) [15-29]	69 (51) [42-60]	3.88 (2.27 - 6.62), <0.0001 ⁺
MRD- 10^{-6}	18 (13) [8-20]	43 (32) [24-40]	2.97 (1.6 - 5.5), 0.0005 ⁺
At 18 months			
MRD- 10^{-5}	35 (26) [19-34]	71 (53) [44-61]	3.16 (1.89 - 5.28), <0.0001
MRD- 10^{-6}	23 (17) [11-24]	49 (36) [28-45]	2.74 (1.54 - 4.87), 0.0006 ⁺
At 24 months			
MRD- 10^{-5}	35 (26) [19-34]	59 (44) [35-53]	2.26 (1.34 - 3.79), 0.002
MRD- 10^{-6}	24 (18) [12-25]	46 (34) [26-43]	2.39 (1.35 - 4.22), 0.003

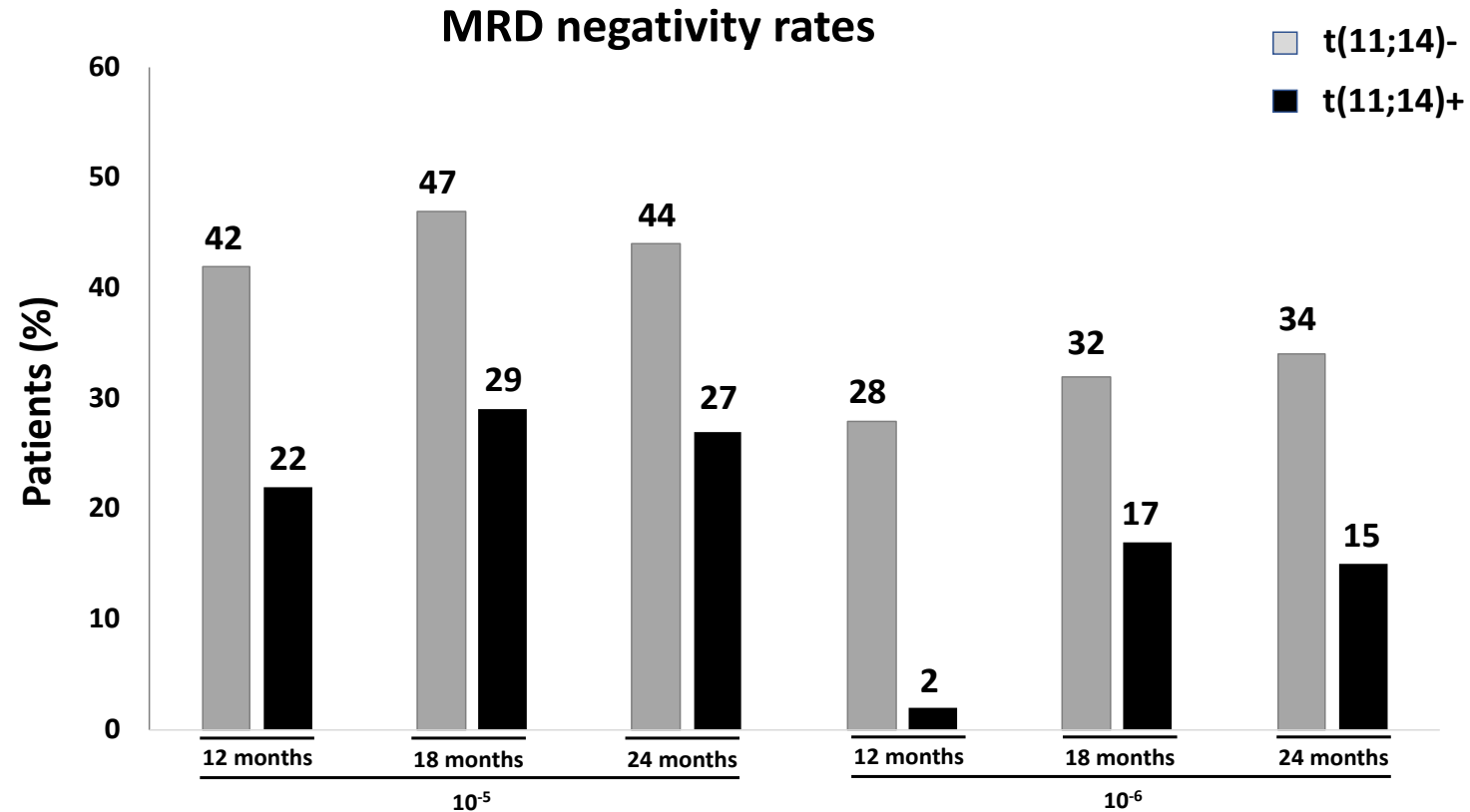


sMRD– rate ≥12 months – ITT population

	IsaRd (n=135)	Isa-VRd (n=135)	OR (95%CI), p-value
sMRD 18-24			
MRD- 10 ⁻⁵	27 (20) [14-28]	52 (39) [30-47]	2.55 (1.5 - 4.4), 0.0009 ⁺
MRD- 10 ⁻⁶	14 (10) [6-17]	38 (28) [21-37]	3.37 (1.7 - 6.6), 0.0004 ⁺
sMRD 12-24			
MRD- 10 ⁻⁵	22 (16) [11-24]	46 (34) [26-43]	2.73 (1.52 - 4.88), 0.0007 ⁺
MRD- 10 ⁻⁶	10 (7) [4-13]	28 (21) [14-29]	3.19 (1.48 - 6.88), 0.003 ⁺



MRD– rate at 12, 18 and 24 months according to t(11;14) – ITT population



Conclusions

- **Outcomes for patients with myeloma, including elderly, have improved with four drug induction**
- **Two randomized studies have shown clear benefit of four drug treatment compared to RVd**
- **Four drug induction is superior to Isa len dex as measured by improvement in MRD negativity.**
- **Age alone is only one component of frailty and should not be used as the sole determination of decision making**
- **Frail patients should have personalized treatment including consideration of two or three drug options**

