QUADRUPLETS VERSUS TRIPLETS FOR ELDERLY NEWLY DIAGNOSED MYELOMA

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EMORY MYELOMA PHYSICIAN TEAM PRIOR TO 2024

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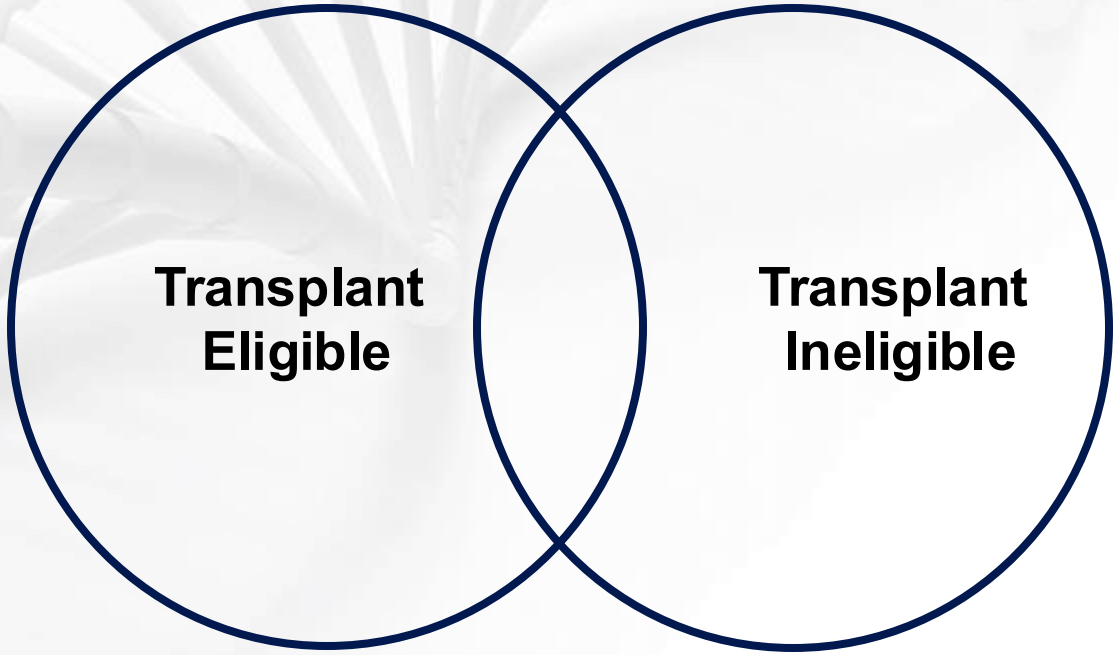
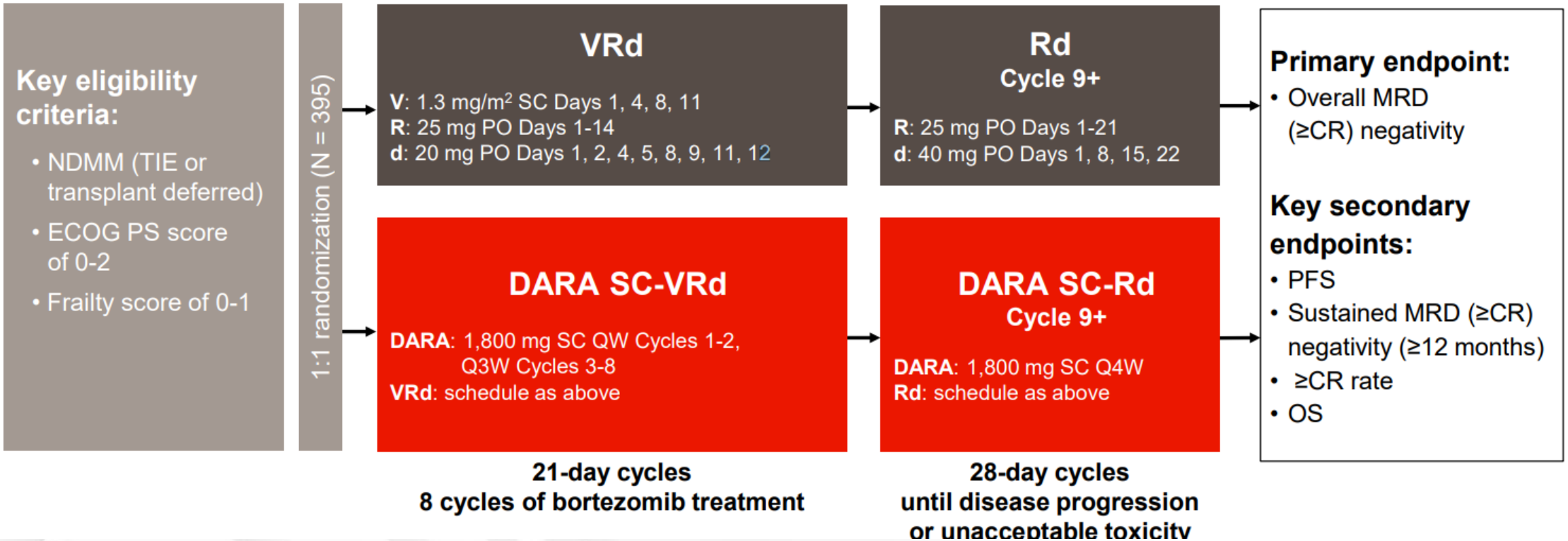
PLEASE GIVE EXAMPLES OF MEN THINKING MORE IS BETTER…

HOW DO WE DEFINE FRAILTY?



CEPHEUS: PHASE 3 TRIAL OF D-RVD VS RVD IN TIE OR TRANSPLANT-DEFERRED



Usmani et al, IMS 2024

CEPHEUS: BASELINE DEMOGRAPHIC & CLINICAL CHARACTERISTICS

	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)

No patients over 80 years

45% are under 70 years

90% have an ECOG PS 0-1

No frail pts by IMWG

25% of pts were deferred ASCT

Usmani et al, IMS 2024

CEPHEUS: SAFETY

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

IMROZ SAFETY

Safety Summary (Safety Population)

Preferred term, n (%)	Isa-VRd (n=263)		VRd (n=181)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Hematologic laboratory abnormalities				
Neutropenia	230 (87.5)	143 (54.4)	145 (80.1)	67 (37.0)
Nonhematologic adverse events				
Infections	240 (91.3)	118 (44.9)	157 (86.7)	69 (38.1)
Pneumonia	79 (30.0)	53 (20.2)	35 (19.3)	23 (12.7)
Upper respiratory tract infection	90 (34.2)	2 (0.8)	61 (33.7)	2 (1.1)
Diarrhea	144 (54.8)	20 (7.6)	88 (48.6)	15 (8.3)
Peripheral sensory neuropathy	143 (54.4)	19 (7.2)	110 (60.8)	11 (6.1)
Cataract	100 (38.0)	41 (15.6)	46 (25.4)	20 (11.0)
Invasive second primary malignancies				
Solid tumors	22 (8.4)	14 (5.3)	8 (4.4)	6 (3.3)
Hematologic	3 (1.1)	1 (0.4)	2 (1.1)	2 (1.1)
Event rate per patient-year[a]				
Infections	1.181	-	1.166	-
Secondary primary malignancies[b]	0.041	-	0.026	-

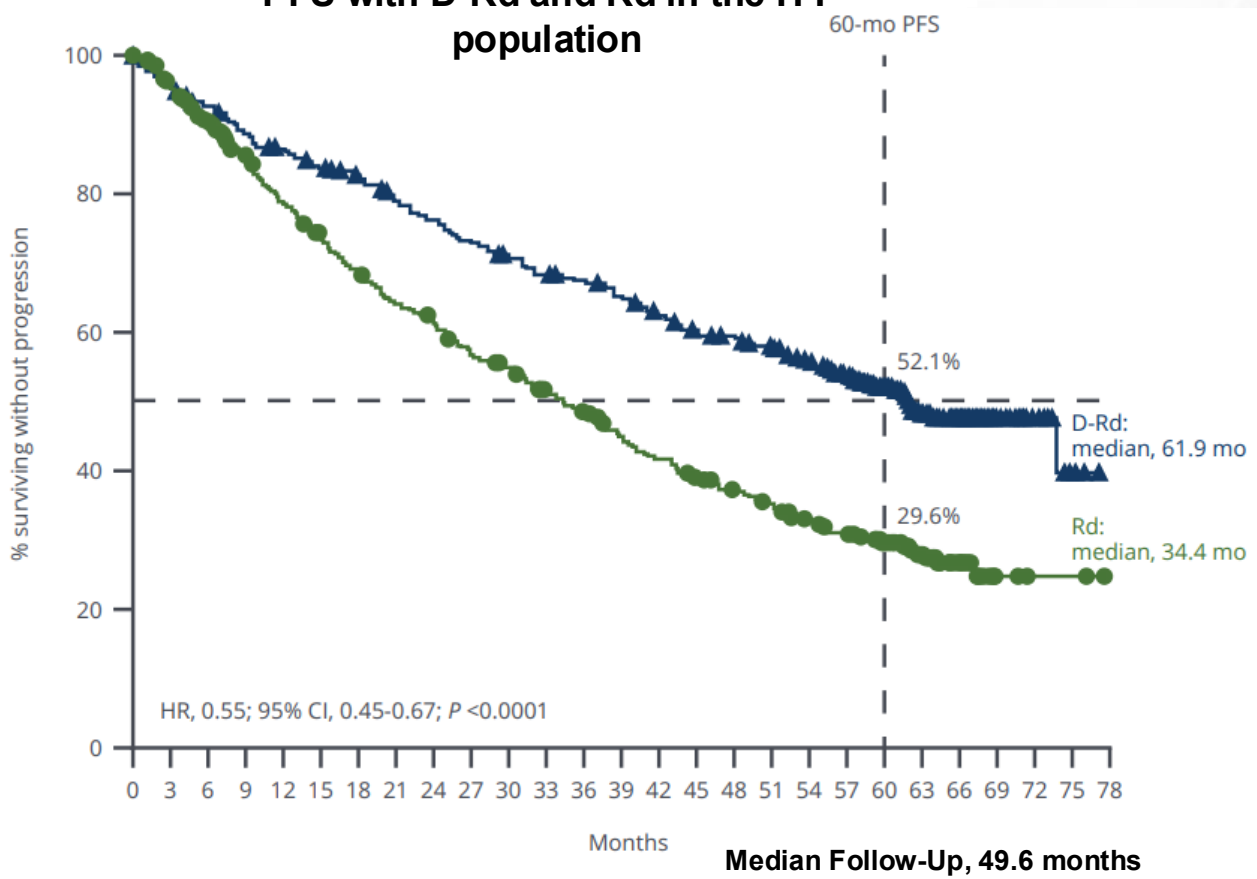
Isa-VRd was well tolerated, and the safety profile remains consistent with the known safety profiles of each agent

a. Calculated as number of patients with an event divided by total patient-years. Patients were followed yearly; b. Included non-melanoma skin cancer.

Facon T, et al. J Clin Oncol. 2024;42(suppl 16):7500.

MAIA: PFS AND OS

PFS with D-Rd and Rd in the ITT population

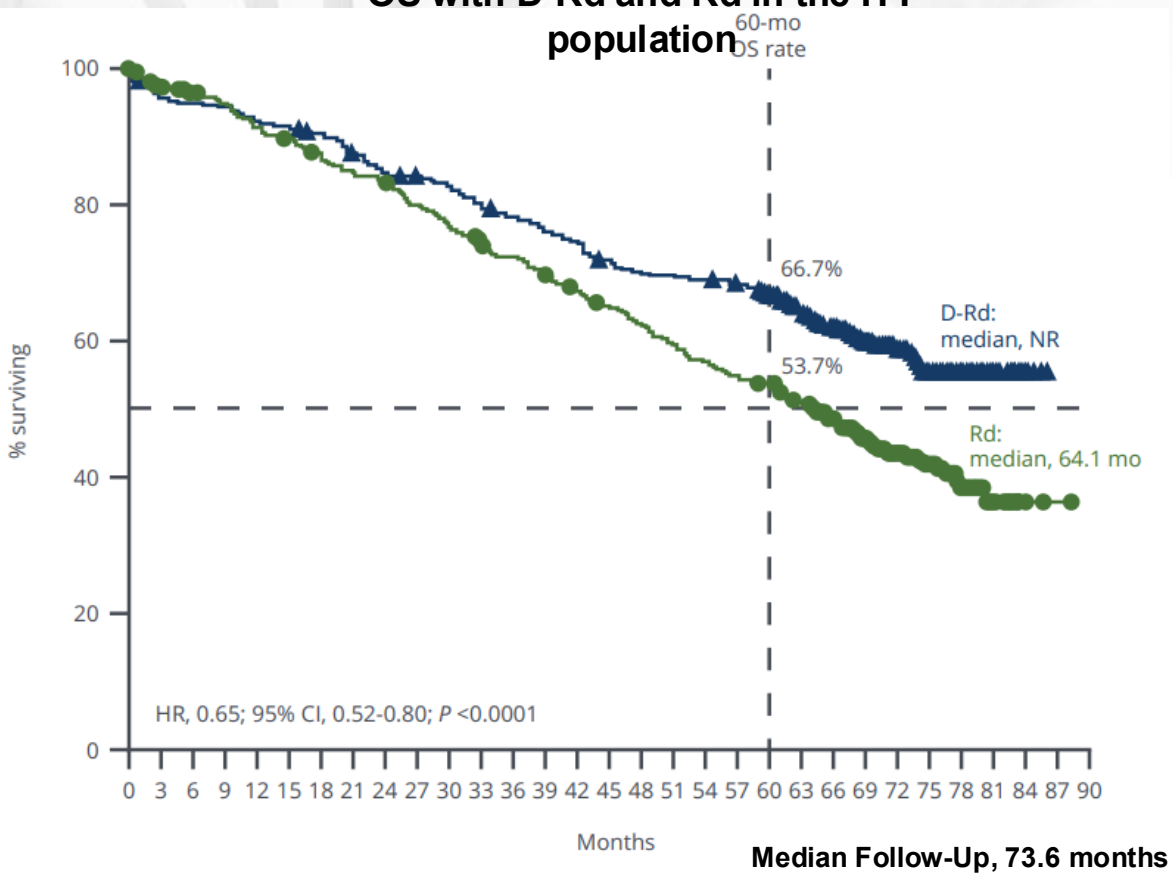


Median Follow-Up, 49.6 months

No. at risk

Rd	369	333	307	280	255	237	220	205	196	179	172	156	147	134	124	114	106	99	88	81	64	47	20	4	2	2	0
D-Rd	368	347	335	320	309	300	290	276	266	256	246	237	232	223	211	200	197	188	177	165	132	88	65	28	11	3	0

OS with D-Rd and Rd in the ITT population

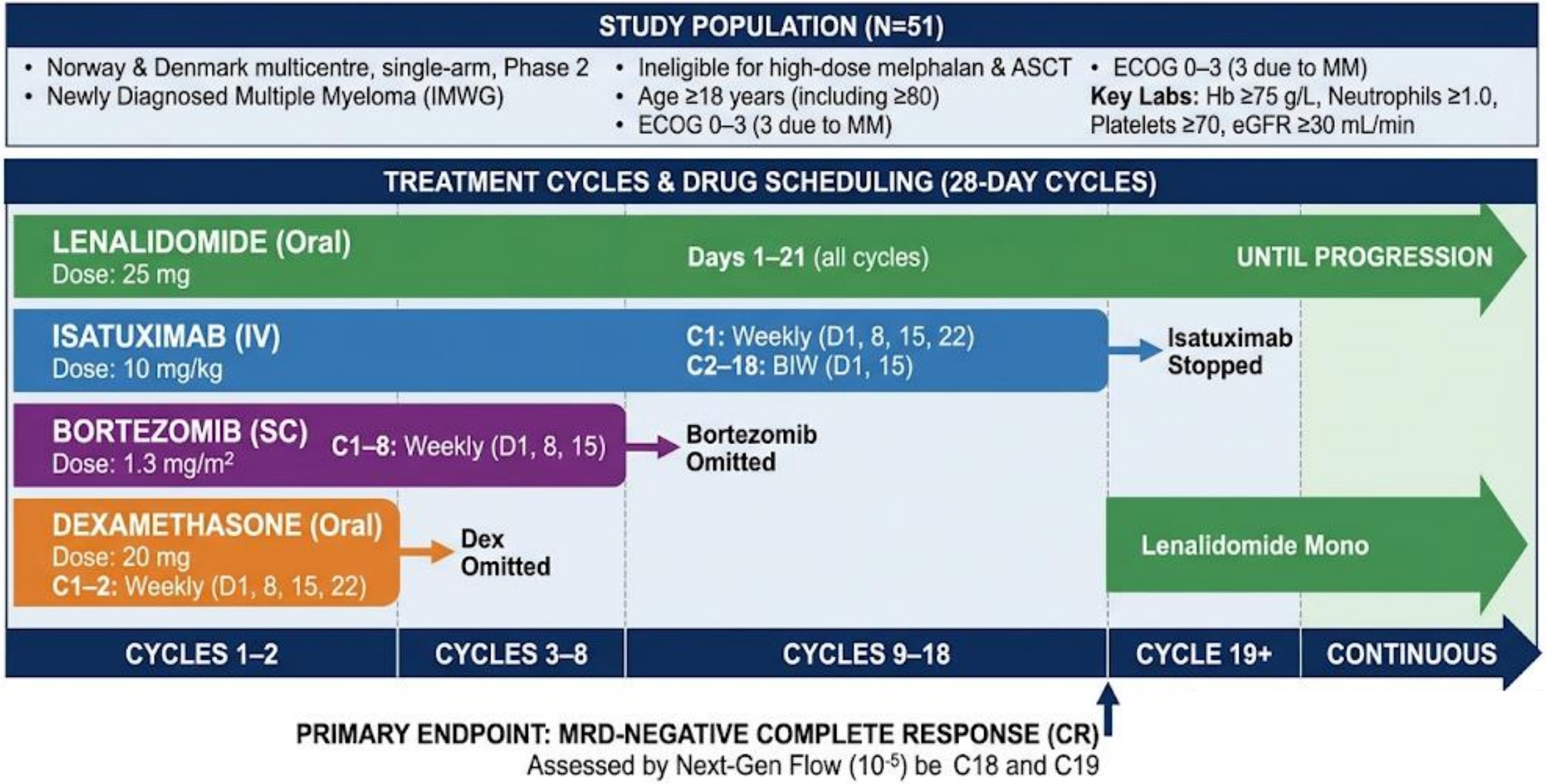


Median Follow-Up, 73.6 months

No. at risk

Rd	369	351	343	336	324	317	308	300	294	281	270	258	251	241	232	223	214	204	195	188	183	170	154	134	97	68	35	11	3	1	0
D-Rd	368	350	346	344	338	334	328	316	305	302	297	286	280	273	266	255	249	248	246	241	228	206	190	163	128	82	56	26	10	0	0

THE PHASE 2 REST TRIAL: "REPLACING STEROIDS IN THE TRANSPLANT-INELIGIBLE"



REST TRIAL OUTCOMES IN OLDER AND FRAIL PATIENTS

Isatuximab + VRd in a dexamethasone-sparing fashion

(Once weekly bortezomib, discontinue dexamethasone at 2 months)

Demographics (N = 51)

- Median age 77
- 31% were over age 80
- 45% were considered frail[a]

Findings

- **Overall response rate 100%**
- **37% achieved MRD-negativity**
- **12-month PFS 86%**
- **Less than 10% discontinuation due to AE**

Adverse Events (> 15%)	Any Grade ≥ 2, n (%)	Grade 3/4, n (%)
Grade 3/4 Neutropenia	—	28 (55%)
Grade 3/4 Thrombocytopenia	—	11 (22%)
Any infection	39 (76%)	20 (39%)
Bone pain	16 (31%)	4 (8%)
Constipation	15 (29%)	—
Maculopapular rash	12 (24%)	2 (4%)
Oedema	12 (24%)	—
Diarrhea	8 (16%)	3 (6%)
Peripheral neuropathy	8 (16%)	2 (4%)

TEC-LILLE TRIAL (IFM2021-01)

Newly diagnosed transplant-ineligible MM

Teclistamab 3mg/kg q4w

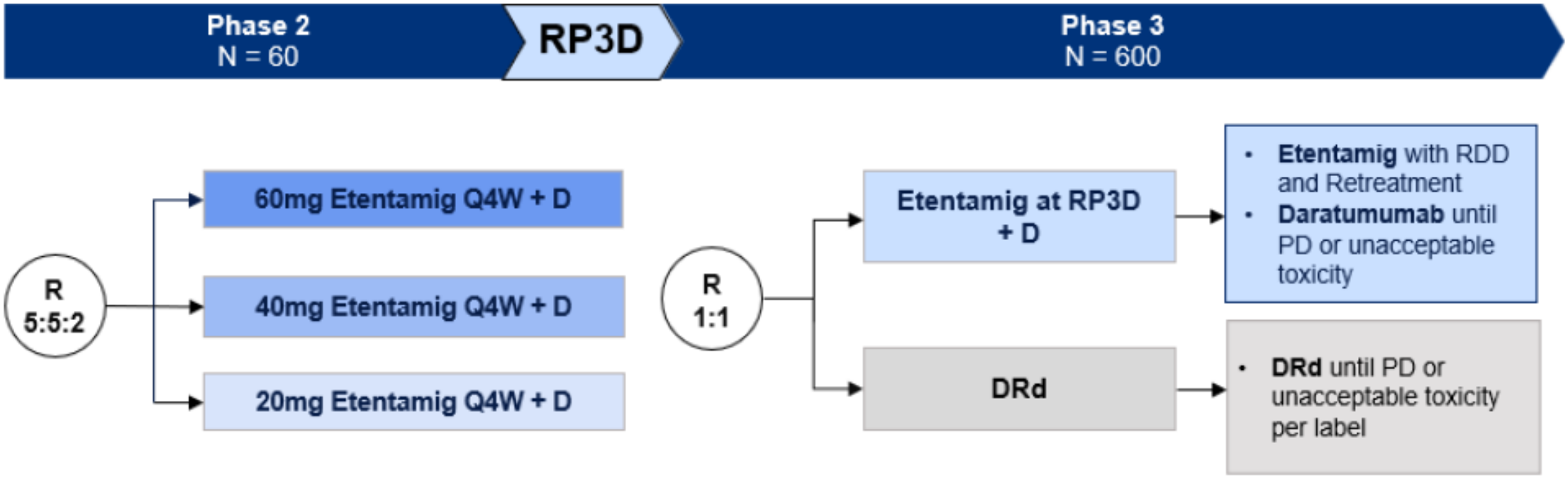
+

Daratumumab

- N = 37; median age was 73 years, 68% SR, 32% HR
- High response rates:
  - **ORR 100%**
  - **≥VGPR 78%.**
  - **MRD negativity (10-6) 51%** in the IIT population and **100%** in the 21 evaluable pts
- Median DOR, PFS, and OS were not reached.

- **Safety**
  - 28 (76%) of patients had grade ≥3 adverse events (AEs)
  - Overall, 5 (14%) patients had grade ≥3 infections.

BITES ARE COMING TO A NEWLY DIAGNOSED MYELOMA NEAR YOU



- MagnetisMM-6: **Elra-DR** vs DRD in TIE-NDMM
- MajesTEC-7: **Tec-DR** vs DRD in TIE-NDMM

  … and many more coming!

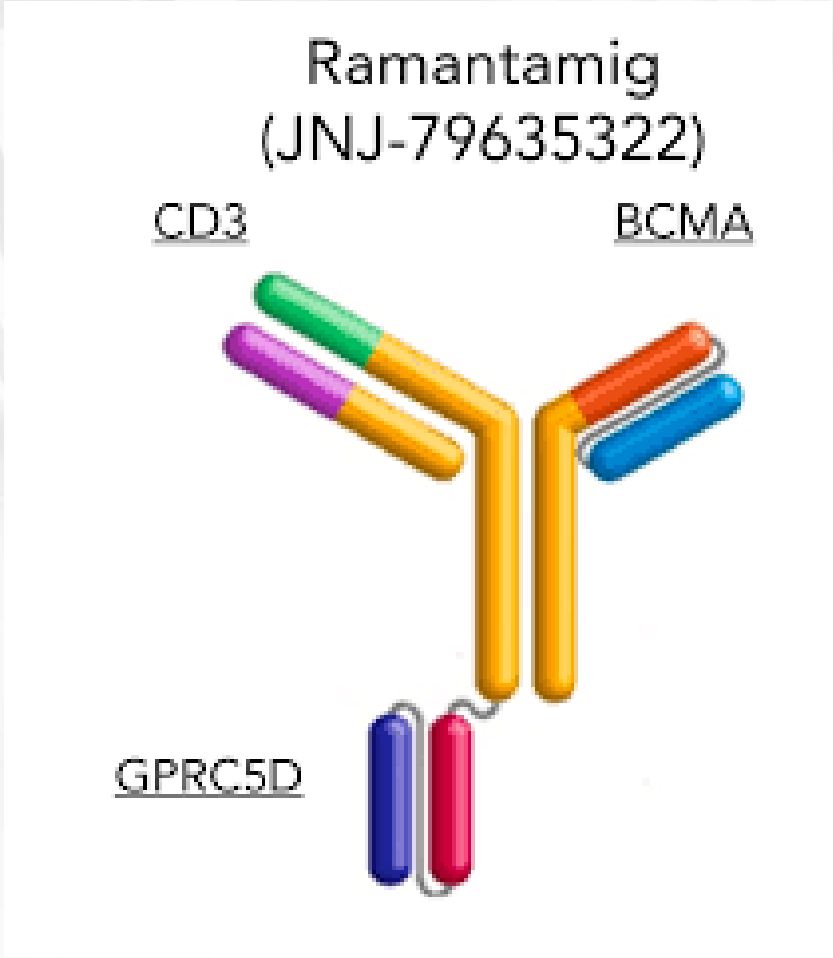
TRILOGY-7

Newly diagnosed transplant-ineligible/ deferred MM

Randomized

Ramantamig

Dara-RVD or DRD per physician's choice



IN SUMMARY

- MORE is not always BETTER
- Quads are current standard for fit TE and reasonable for fit TIE-NDMM but not for all TIE-NDMM
- Moving forward – quads will fade away for TIE/frail NDMM population…
  - Dex sparing regimens
  - Bispecifics
  - Trispecifics
  - CAR-T
  - Many more effective drug combinations on the horizon…