Sequencing of Therapies for Multiple Myeloma

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Sequencing Therapy in MM:

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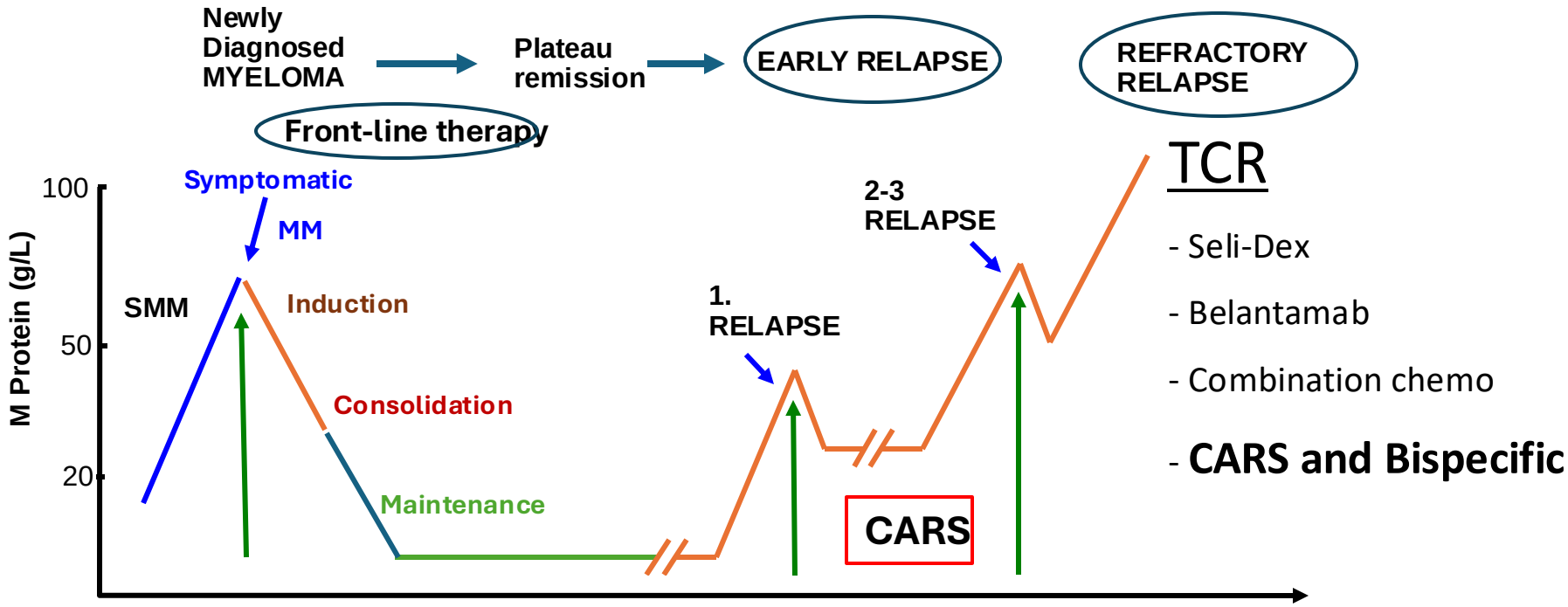
How should we sequence all these agents?



Frontline
Triplets: VRd/KRd
Quads: CD38 + VRd/KRd

Early Relapse
(1-3 Prior Line):
Triplets
CAR T-cell

Late Relapse
Recycle agents,
Immunotherapy

UCSF

AGENTS APPROVED for MULTIPLE MYELOMA

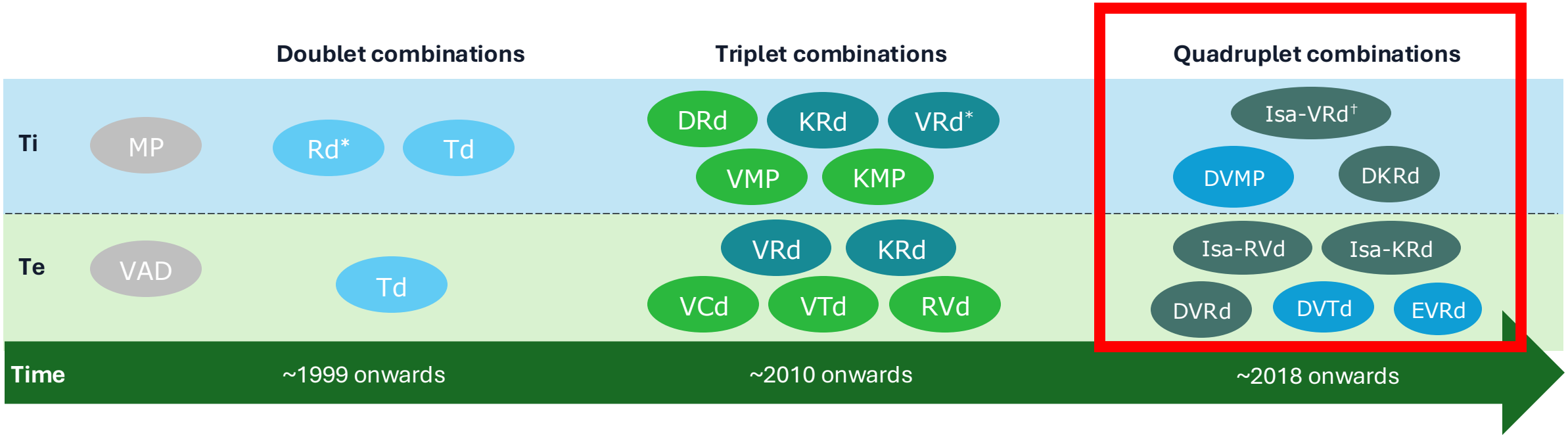
Proteasome Inhibitors	IMiDs	Alkylating Agents	Monoclonal Antibodies	Targeted Agents	Bispecific Antibodies	CAR T-cells BCMA-directed
Bortezomib	Lenalidomide	Melphalan	Daratumumab	Selinexor	Teclistamab	Idecabtagene vicleucel
Carfilzomib	Pomalidomide	Doxorubicin (liposomal)	Isatuximab	*Venetoclax*	Elranatamab	Ciltacabtagene autoleucel
Ixazomib	Thalidomide	Cyclophosphamide	Elotuzumab		Talquetamab	
		PACE/CVAD				

Almost an infinite # of combinations of these agents: with the inclusion of corticosteroids in all (Dex)

Where and When to use these agents ➔ **Sequencing**

Options for initial myeloma treatment have evolved significantly over time

Therapeutic regimens explored in Phase III NDMM trials over time[1–4]



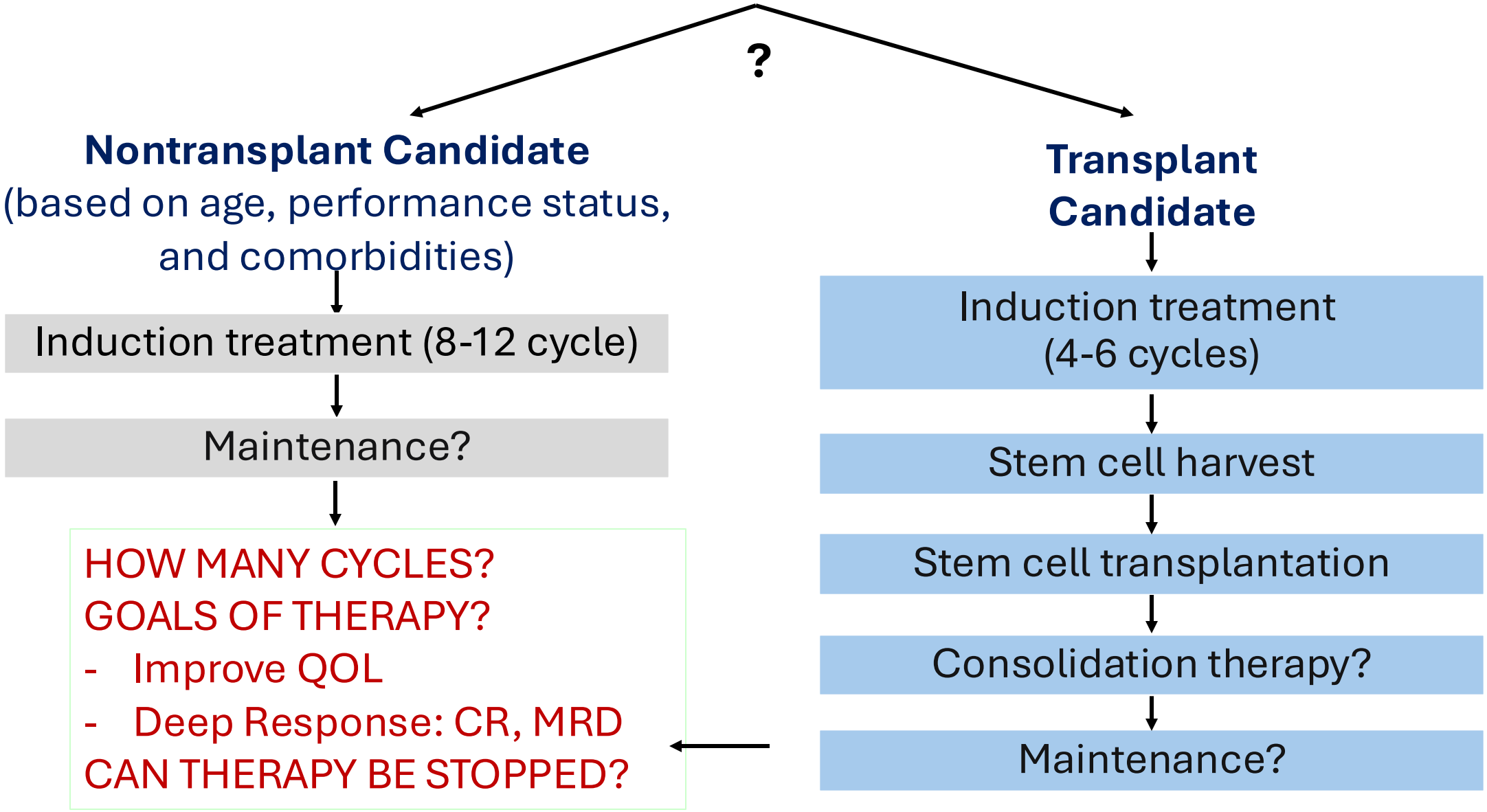
*Including transplant-deferred. †Twice-weekly and once-weekly V dosing are being explored in the IMROZ and BENEFIT studies, respectively

The emergence of newer agents and novel combination treatment strategies has improved patient outcomes

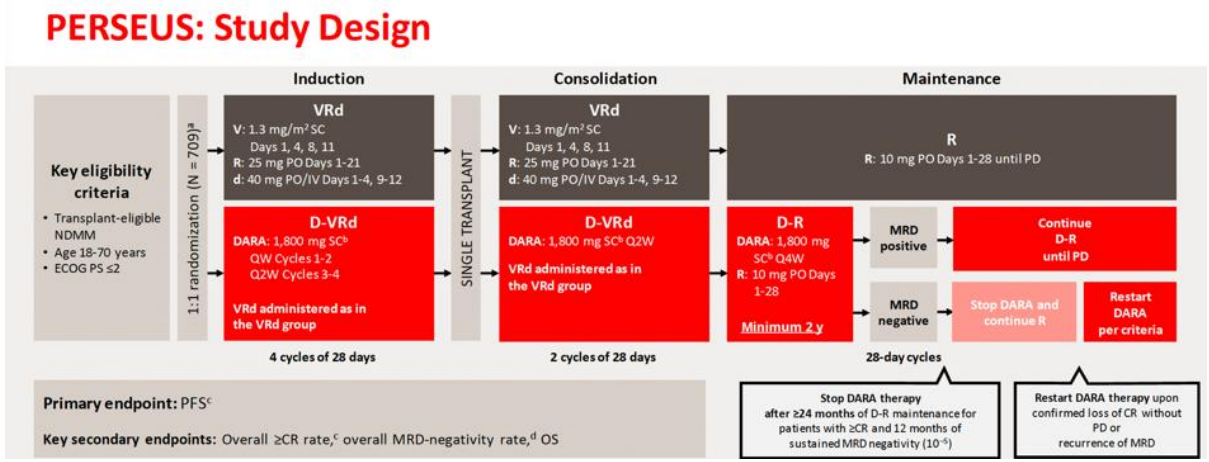
C, cyclophosphamide; d, dexamethasone; D, daratumumab; E, elotuzumab; Isa, isatuximab; K, carfilzomib; M, melphalan; P, prednisone; R, lenalidomide; T, thalidomide; Te; transplant eligible; Ti, transplant ineligible; V, bortezomib

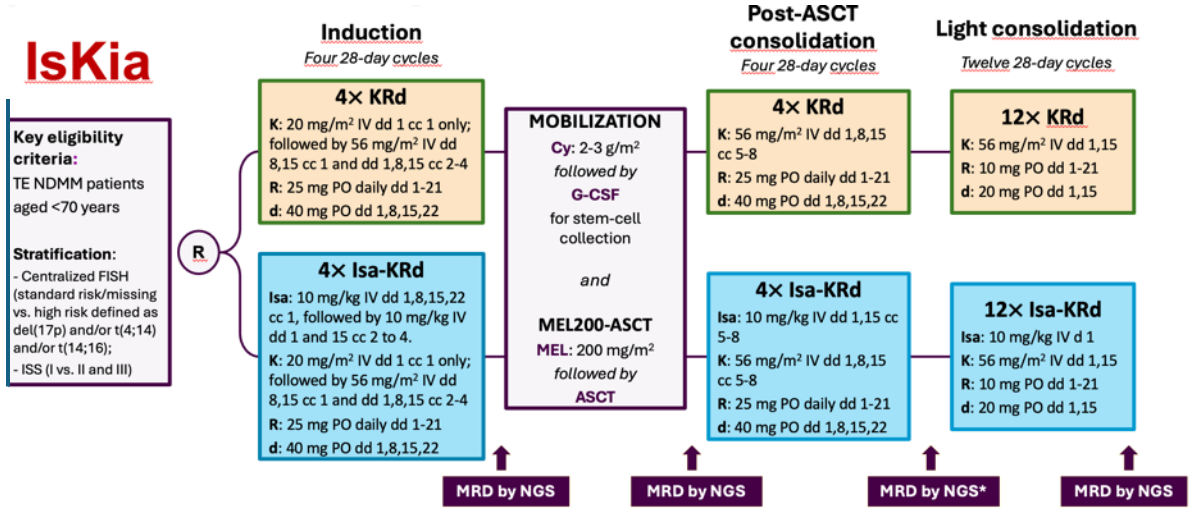
1. Bal S, et al. Am J Hematol 2021;96:367–78; 2. Gay F, et al. ASH 2023; Presentation 4; 3. Mateos MV, et al. ASH 2023; Presentation 209; 4. Mai EK, et al. Leukemia 2015;29:1721–9

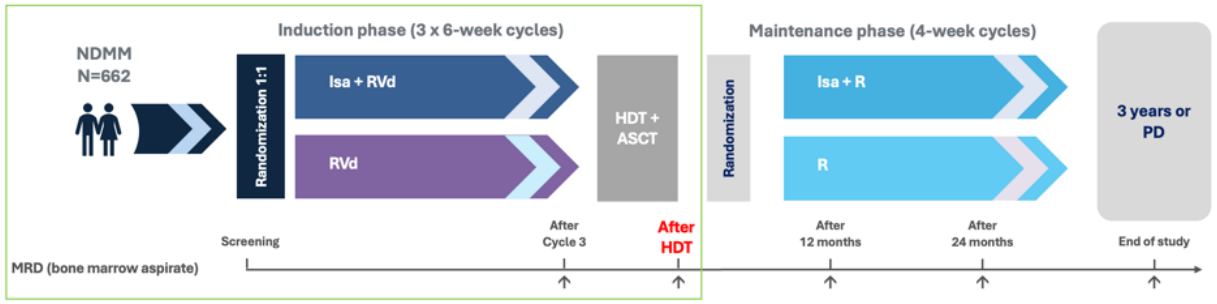
Initial Approach to Treatment of Myeloma

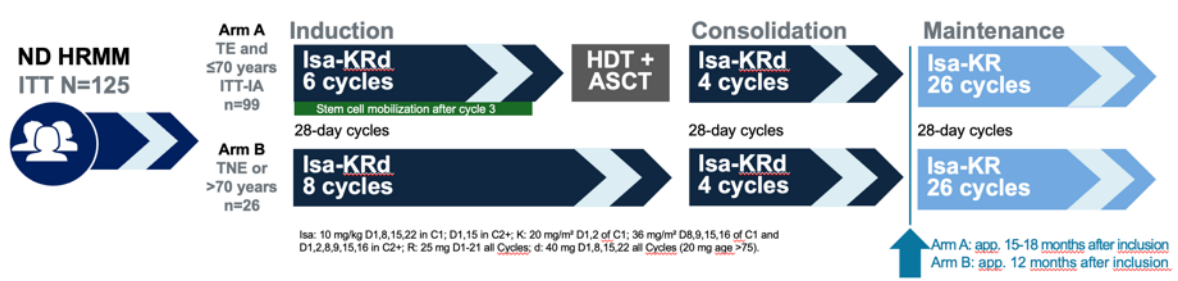


Frontline for TE: Quads vs. Triplets (CD38 for ALL?)



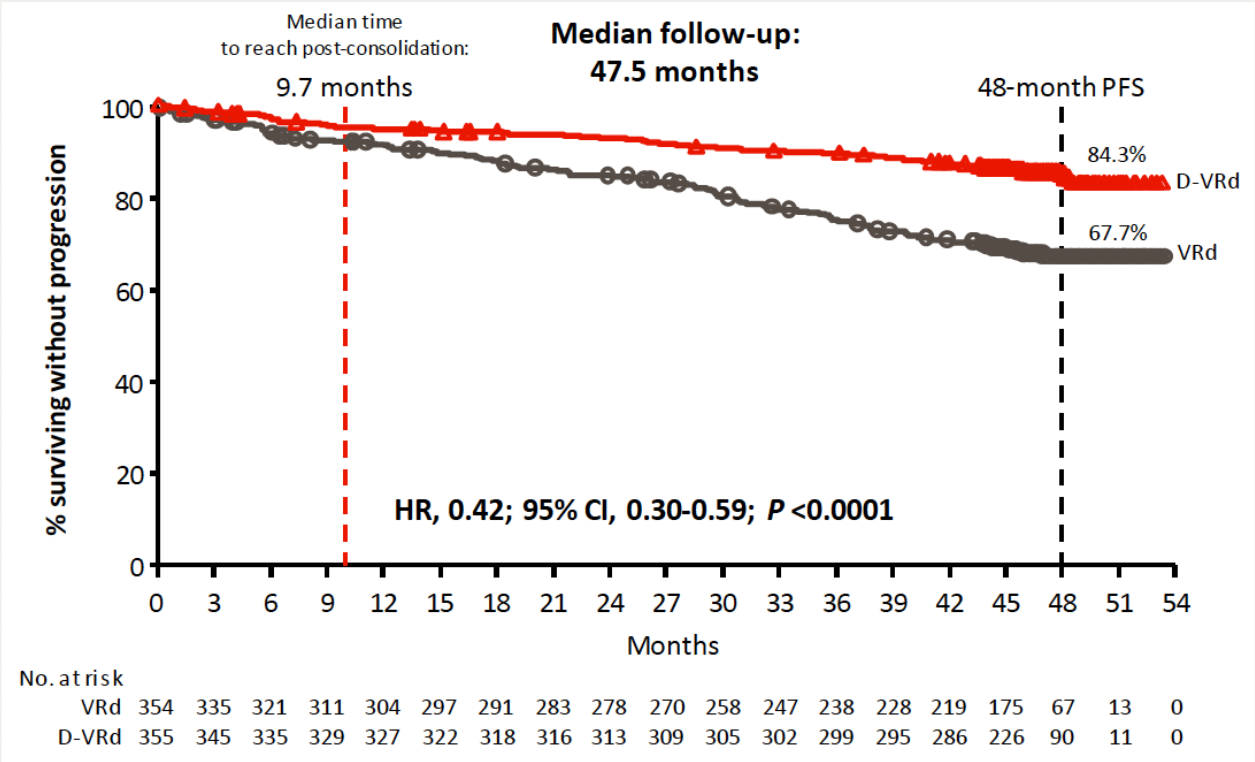


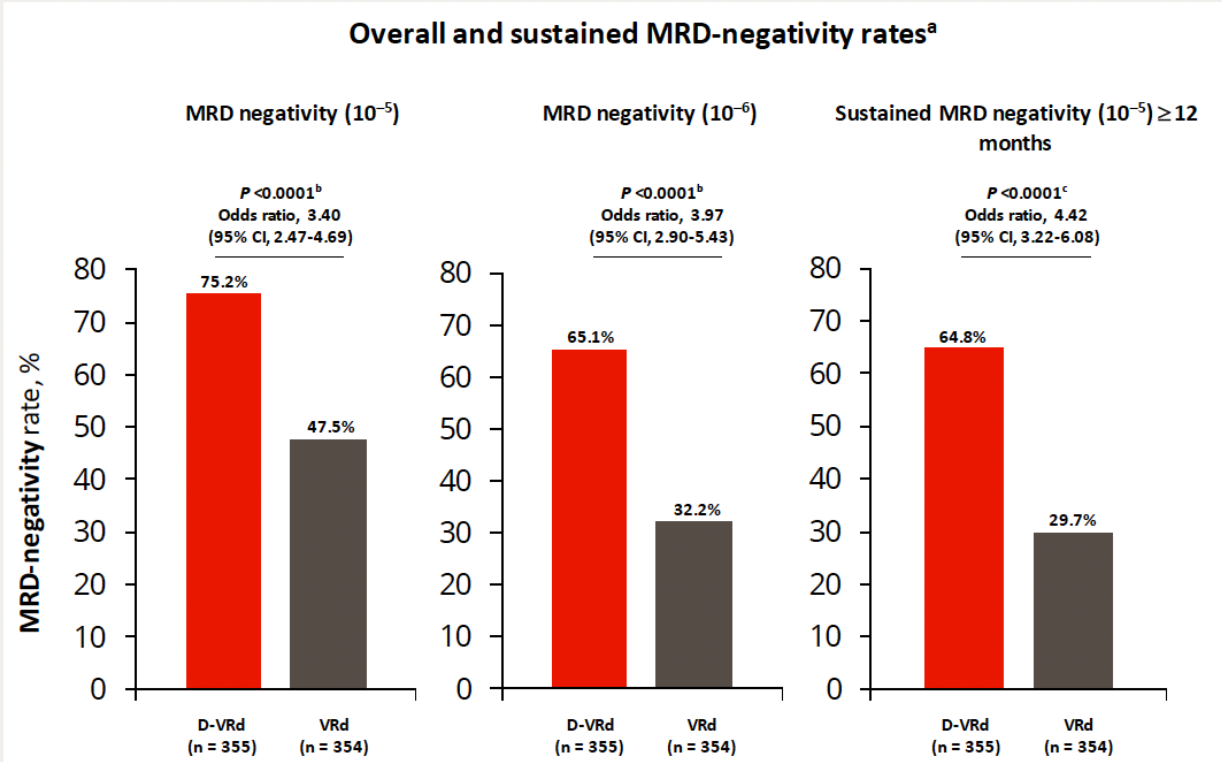




Sonneveld P, et al. EHA 2024; Raab M, et al. EHA 2024; Gay F, et al. ASH 2023; Leypoldt LB, et al, IMS 2023

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

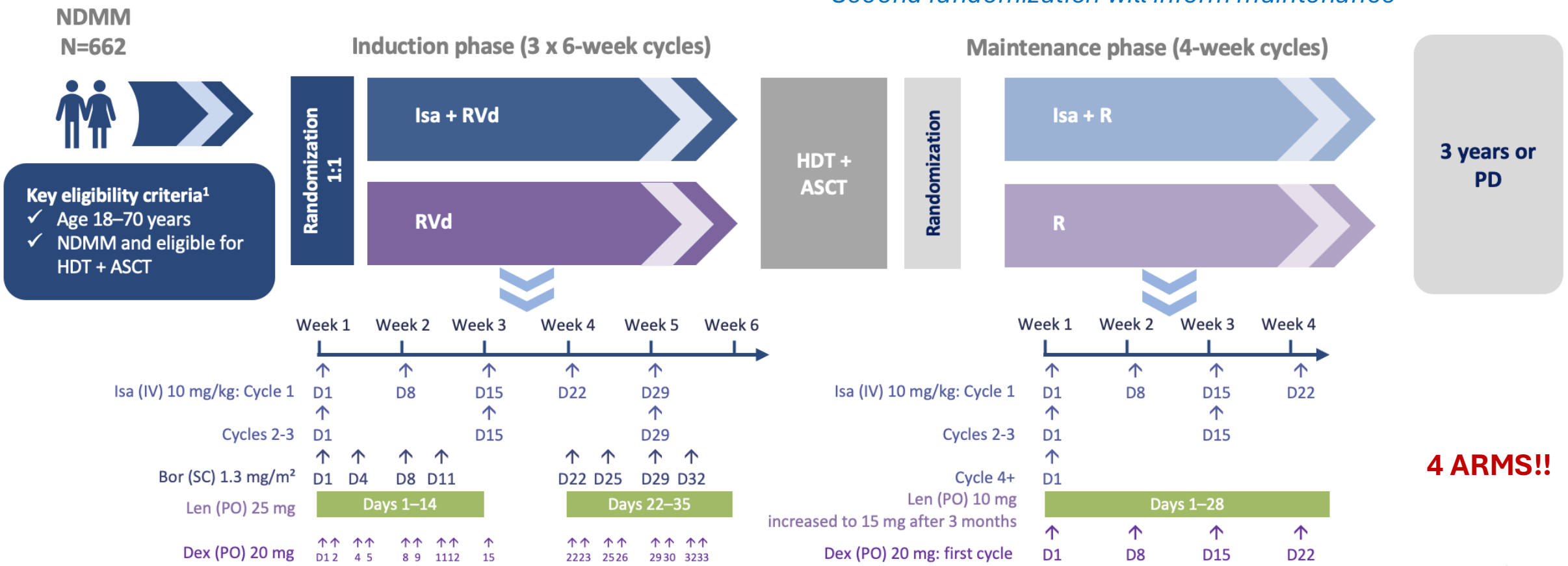
HR, hazard ratio; CI, confidence interval. [a]MRD-negativity rate was defined as the proportion of patients who achieved both MRD negativity and ≥CR. MRD was assessed using bone marrow aspirates and evaluated via NGS (clonoSEQ assay, version 2.0; Adaptive Biotechnologies, Seattle, WA, USA). [b]*P* values 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.

1. Sonneveld P, et al. *N Engl J Med*. 2024;390(4):301-313.

GMMG-HD7: The first phase 3 study evaluating Isa + RVd for induction and maintenance in patients with Te NDMM

HD7

Second randomization will inform maintenance



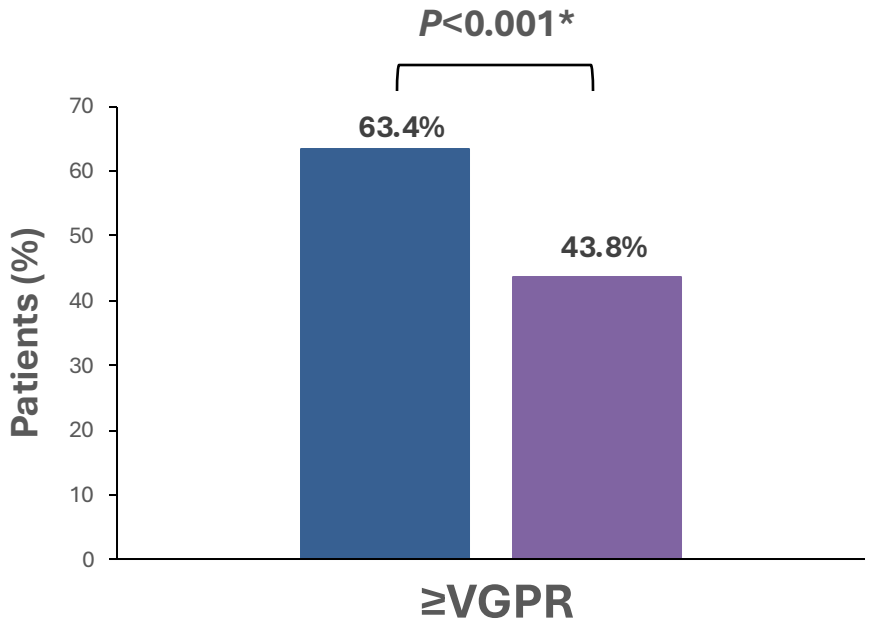
4 ARMS!!

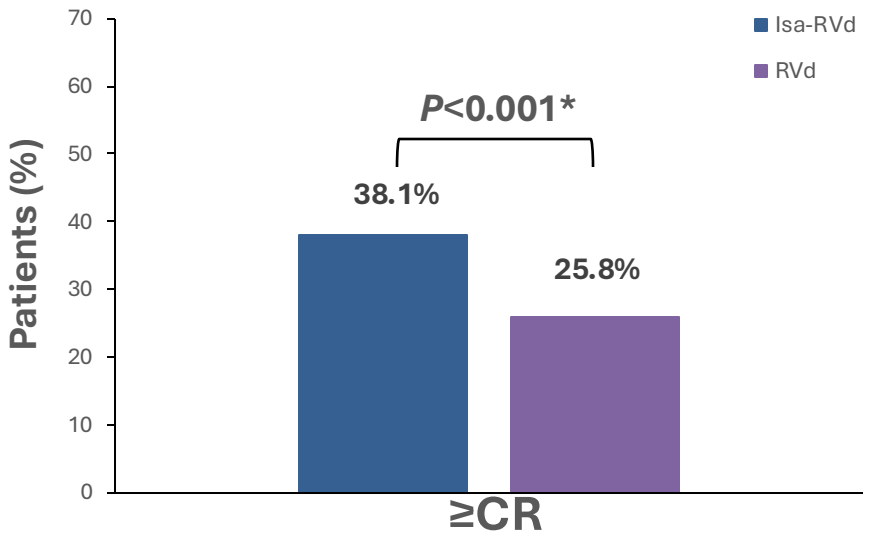
**Primary Endpoint: MRD (-); Secondary PFS

The use of RVd is off-label in some countries, according to the lenalidomide summary of product characteristics.
ASCT, autologous stem cell transplant; D, day; d/Dex, dexamethasone; HDT, high-dose therapy; Isa, isatuximab; IV, intravenous; NDMM, newly diagnosed multiple myeloma; PD, progressive disease; PO, oral; R/Len, lenalidomide; SC, subcutaneous; Te, transplant eligible; V/Bor, bortezomib.
1. ClinicalTrials.gov identifier: NCT03617731. Updated May 12, 2023. Accessed June 5, 2024. https://clinicaltrials.gov/study/NCT03617731?term=NCT03617731&rank=1

GMMG-HD7 interim analysis: MRD negativity by NGF (10^{-5}) after intensification (ITT; by response)

Patients with MRD negativity and indicated response status



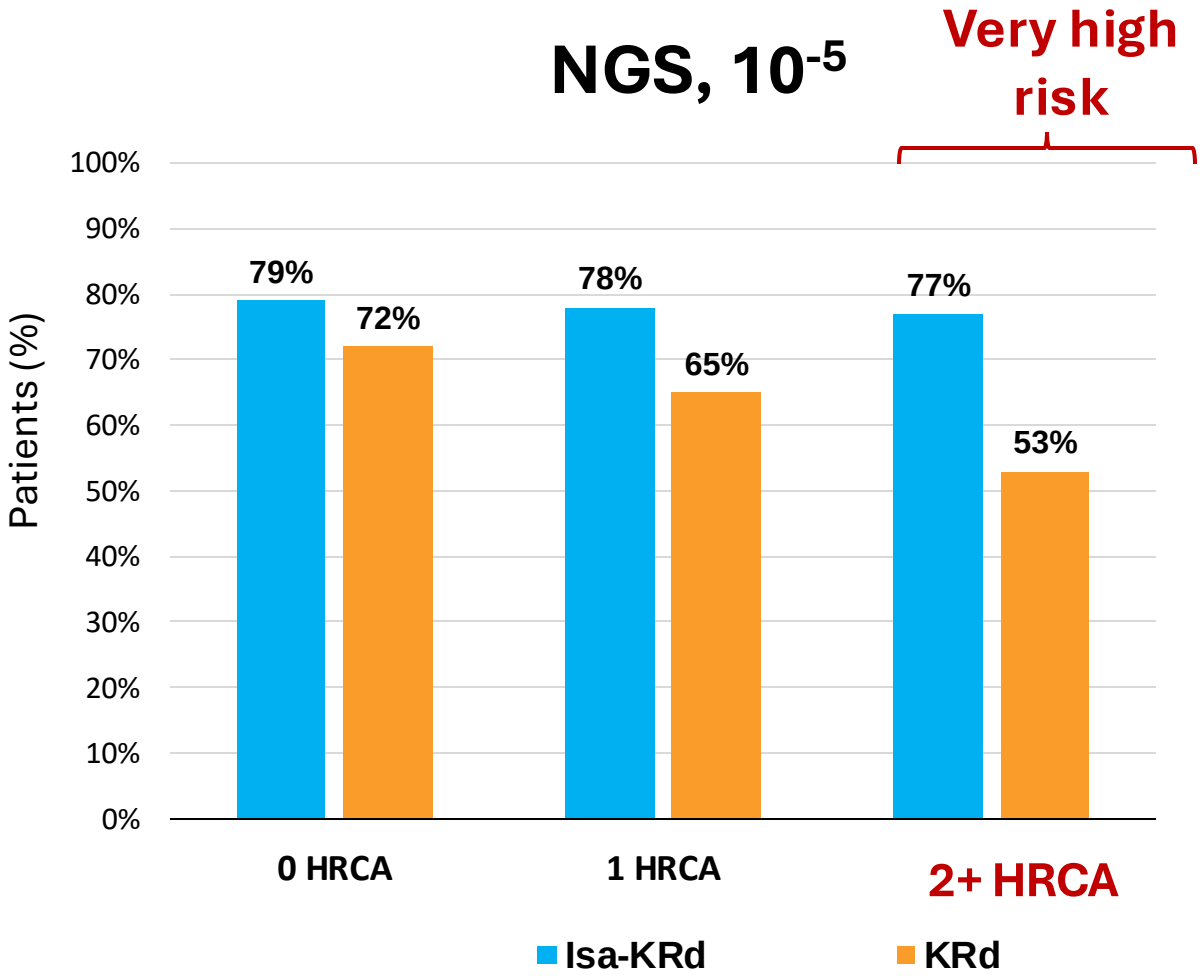


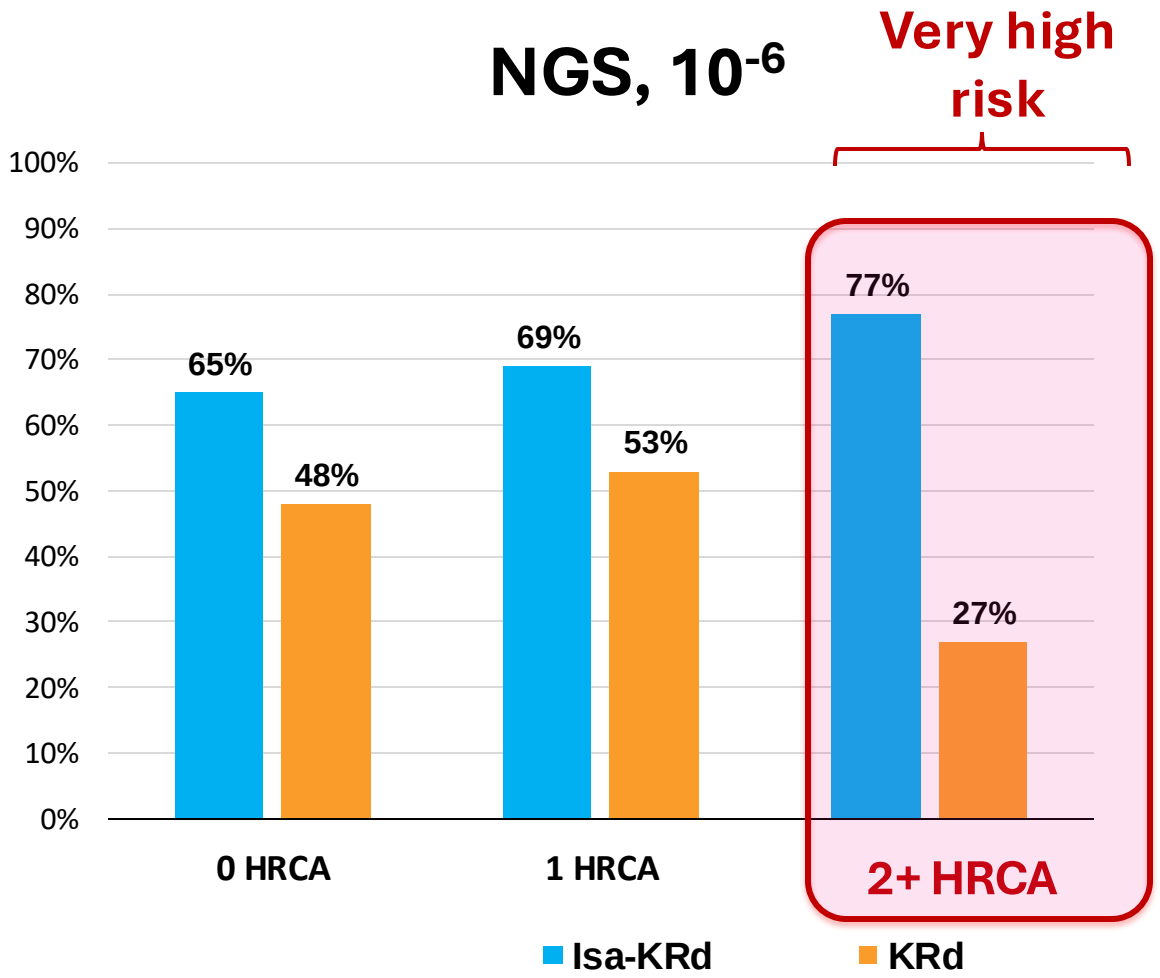
Isa-RVd led to significantly higher MRD negativity/VGPR and MRD negativity/CR rates (per IMWG) compared with RVd after intensification

*P value derived from stratified conditional logistic regression analysis.
CR, complete response; d, dexamethasone; Isa, isatuximab; ITT, intent to treat; MRD, minimal residual disease; NGF, next-generation flow; R, lenalidomide; V, bortezomib; VGPR, very good partial response.

IsKia - Post-consolidation MRD negativity by NGS

Subgroup analysis by cytogenetic risk



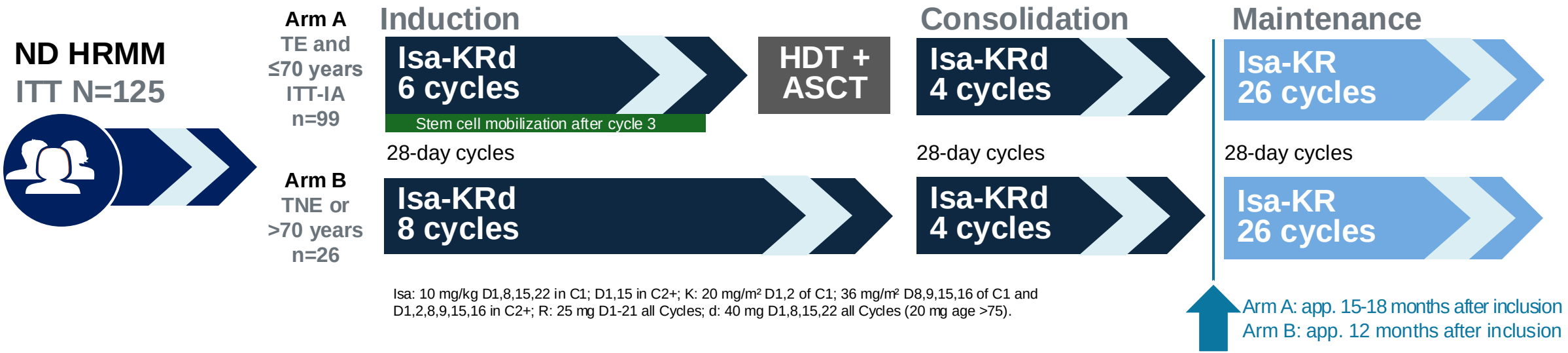


1 HRCA was defined as the presence of one of the following high-risk cytogenetic abnormalities: del(17p13.1), t(4;14) (p16.3;q32.3), t(14;16) (q32.3;q23), gain(1q21), or amp(1q21); 2+ HRCA was defined as the presence of at least two high-risk cytogenetic abnormalities.

Is K better than V in HRMM

MRD, minimal residual disease; NGS, next-generation sequencing; HRCA, high-risk cytogenetic abnormalities; Isa, isatuximab; K, carfilzomib; R, lenalidomide; d, dexamethasone; del, deletion; t, translocation; amp, amplification

GMMG CONCEPT TRIAL: Study Design

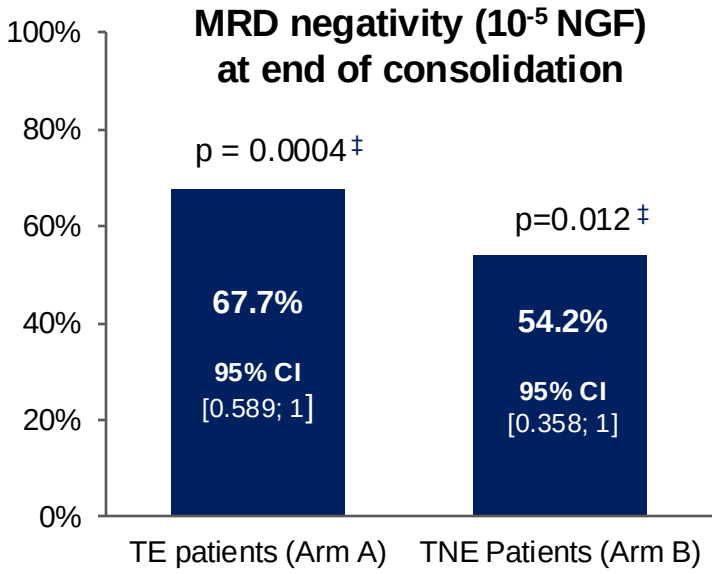


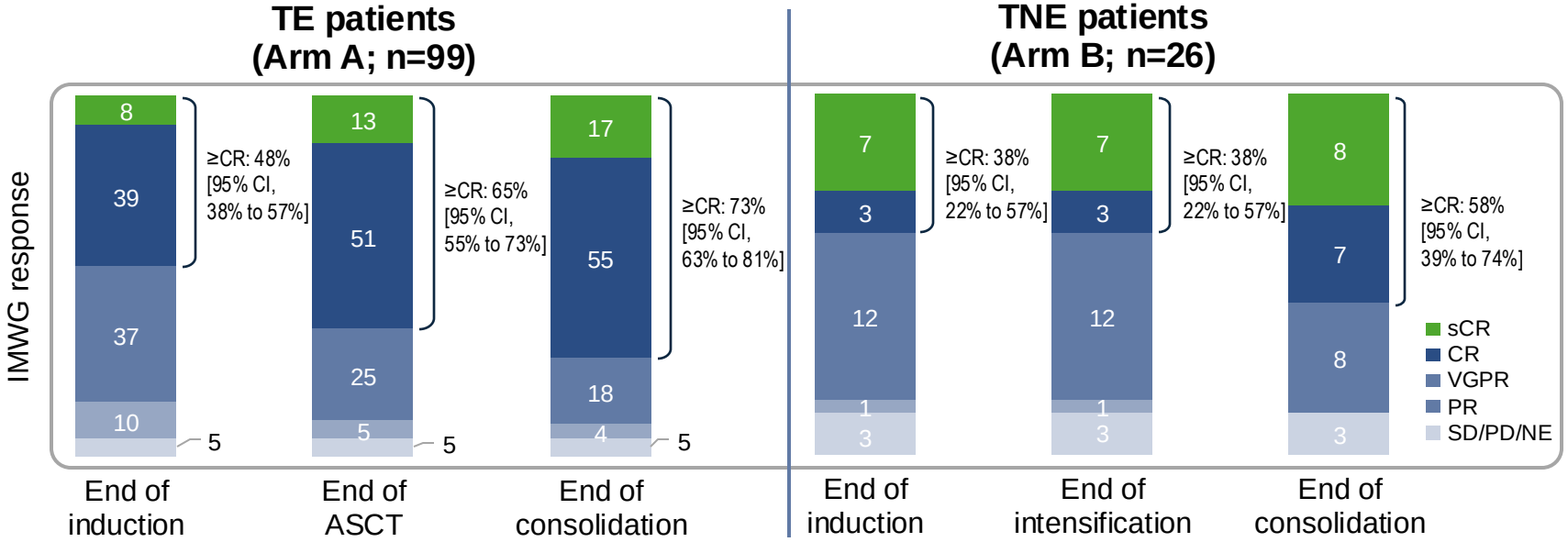
HRMM criteria: ISS stage II or III **PLUS** ≥1 of: del(17p), t(4;14), t(14;16) and/or >3 copies 1q21 (amp1q21)
Primary objective: MRD negativity after consolidation (NGF, 10^{-5})
Secondary objective: PFS; Key tertiary objectives: ORR, OS, safety

HR: Focus has been on duration of therapy and #of agents

Leypoldt LB, et al, IMS 2023

CONCEPT Trial: MRD Negativity and IMWG Response





MRD status, n (%)	TE patients (Arm A) (n=93*)	TNE patients (Arm B) (n=24†)
Negative	**63 (67.7)**	**13 (54.2)**
Positive	3 (3.2)	0 (0)
Not done/missing	2 (2.2)	0 (0)
Time point not reached	25 (27.0)	11 (45.8)

6 TE and 2 TNE patients were not assessable

Footnotes

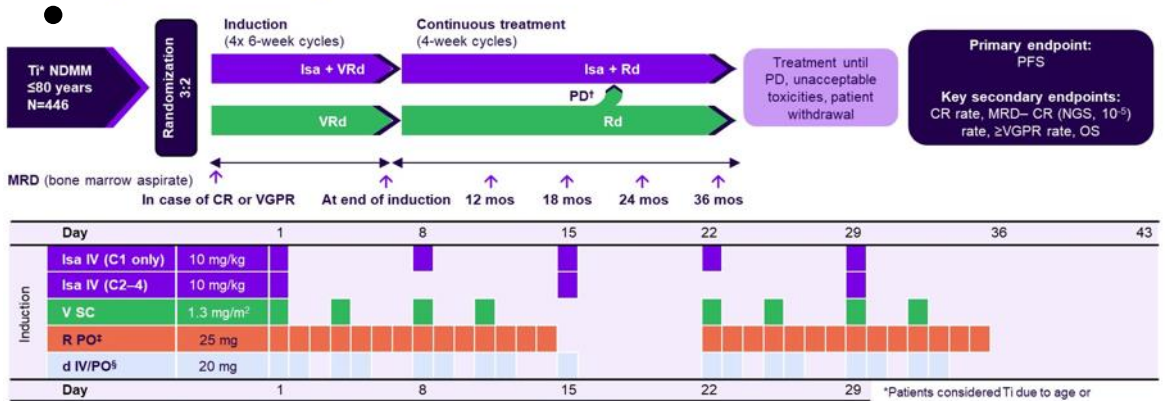
- **The trial met its primary endpoint with MRD negativity rates of 67.7% (TE) and 54.2% (TNE) at the end of consolidation**
- Responses deepened over time with ≥CR-rates of 72.7% (TE) and 57.7% (TNE) as best response

Leypoldt LB, et al, IMS 2023

Frontline for TI: Quads vs. Triplets (CD38 for ALL?)

Study design: Isa-VRd vs VRd in transplant-ineligible NDMM

IMROZ



CEPHEUS

Key Eligibility Criteria
- NDMM (transplant ineligible or deferred)
- ECOG PS 0-2; frailty score of 0-1

1:1 Randomization (N=395)

SUBQ Dara-VRd
Dara: 1800 mg SUBQ
Cycles 1-2: qw; cycles 3-8 q3w
VRd: Schedule as below

→ **SUBQ Dara-Rd**
Cycles 9+
Dara: 1800 mg SUBQ q4w
Rd: Schedule as below

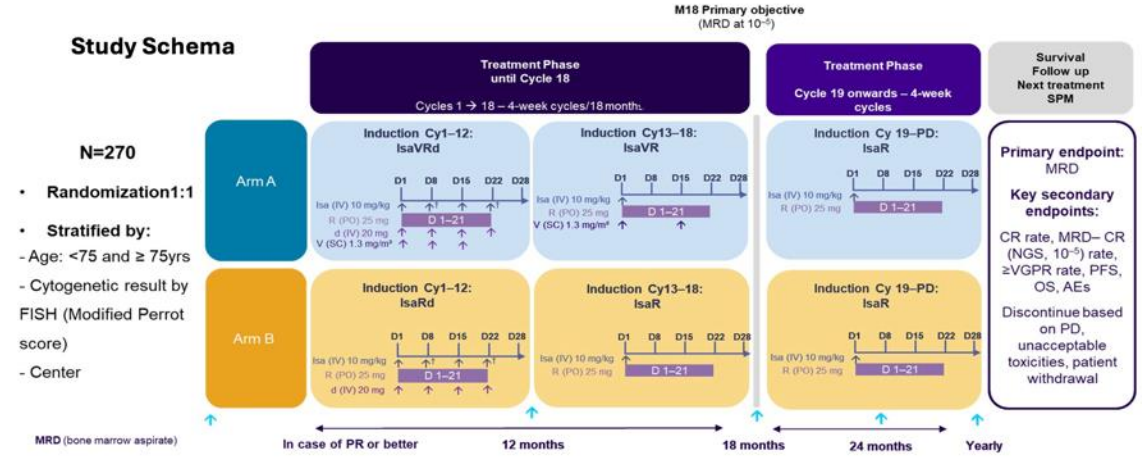
VRd
V: 1.3 mg/m² SUBQ, days 1, 4, 8, 11
R: 25 mg PO, days 1-14
d: 20 mg PO, days 1, 2, 4, 5, 8, 9, 11, 12

21-day cycles; 8 cycles of V

→ **Rd**
Cycles 9+
R: 25 mg PO, days 1-21
d: 40 mg PO, days 1, 8, 25, 22

28-day cycles until PD or unacceptable toxicity

BENEFIT Trial: Isa-VRd vs. Isa-RD in TI NDMM



MAIA Study Design

– Patients were enrolled in MAIA from March 2015 through January 2017

Key eligibility criteria
- TIE NDMM
- ECOG PS score 0-2
- CrCl ≥30 mL/min

1:1 randomisation

D-Rd
D: 16 mg/kg IV
QW Cycles 1-2, Q2W Cycles 3-6, then Q4W thereafter until PD
R: 25 mg PO
Days 1-21 until PD
d[a]: 40 mg[b] PO or IV
Days 1, 8, 15, 22 until PD

Rd
R: 25 mg PO Days 1-21 until PD
d: 40 mg PO
Days 1, 8, 15, 22 until PD

Cycles: 28 days

→ End-of-treatment visit (30 days after last dose)

→ Long-term follow-up

Primary endpoint
- PFS

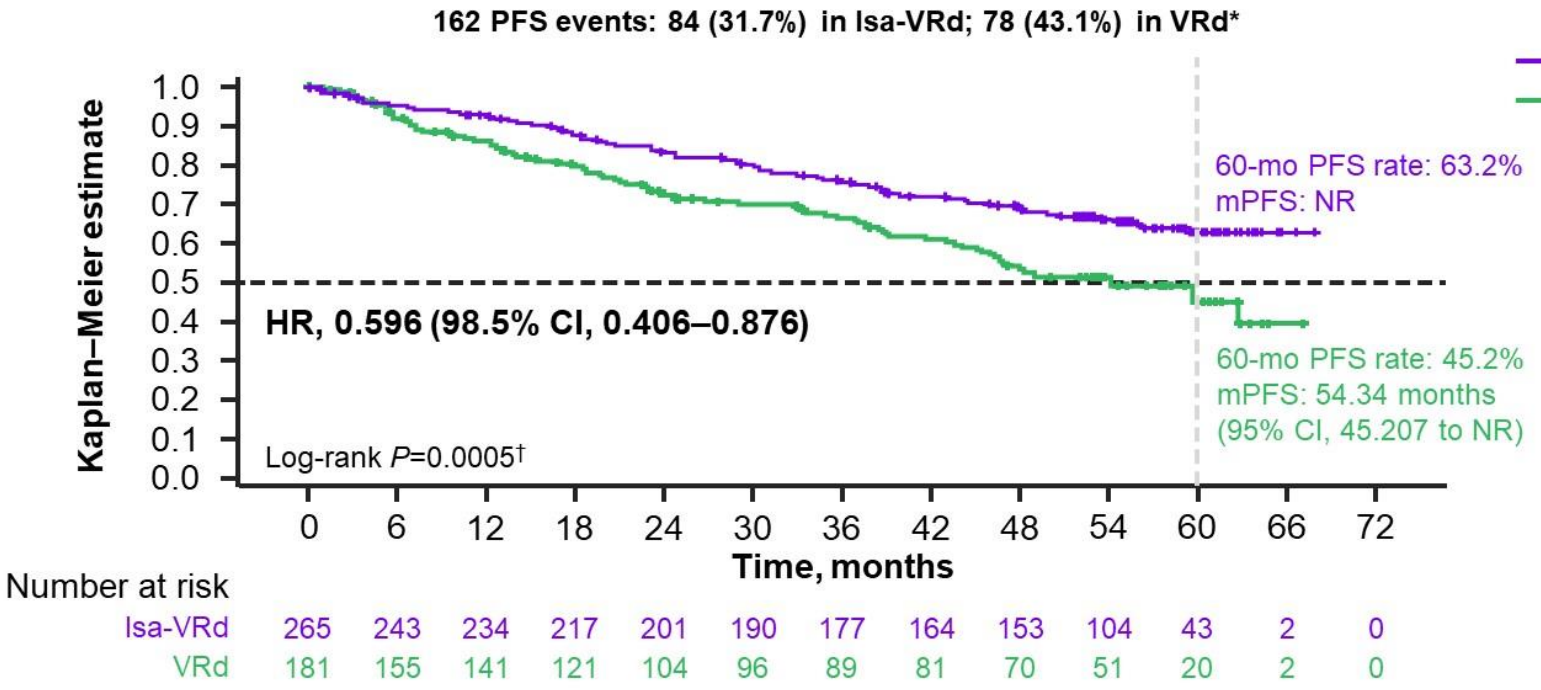
Key secondary endpoints
- OS
- PFS2
- ORR
- CR/sCR rate
- MRD (NGS; 10^{-5})

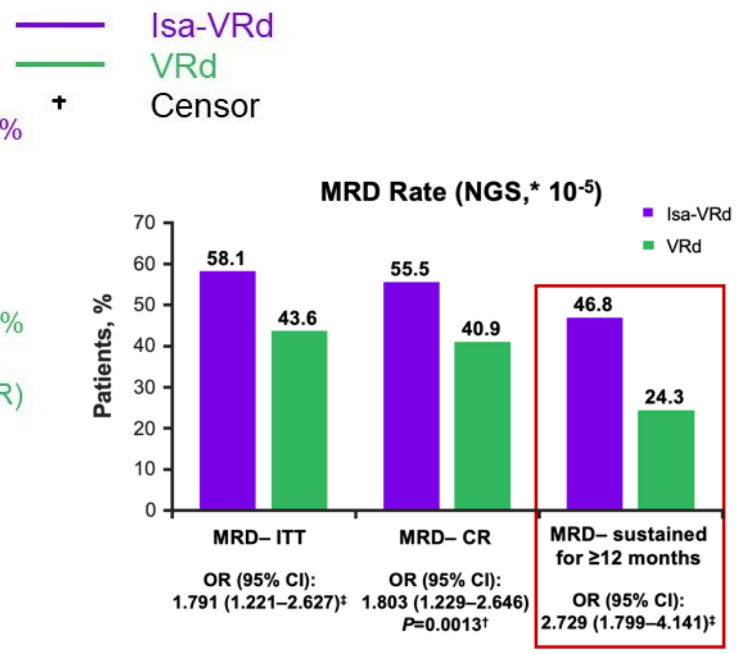
Facon T, et al. EHA 2024; LeLeu X, et al. EHA 2024; Facon T, et al. EHA 2024; Usmani S, et al. IMS 2024

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

IMROZ

Isa-VRd vs. VRd





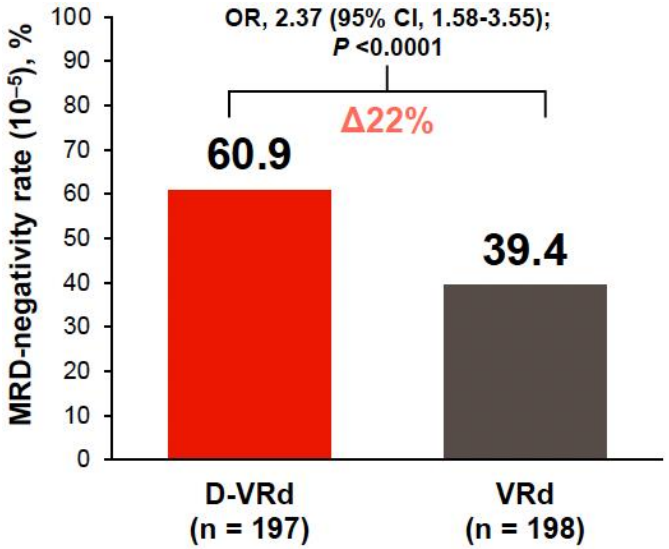
At a median follow-up of 5 years (59.7 months), Isa-VRd followed by Isa-Rd led to a statistically significant reduction in the risk of progression or death by 40.4%

*Cutoff date for PFS analysis: September 26, 2023 (median follow-up, ~5 years). †Nominal one-sided *P* value.
NR, not reached.

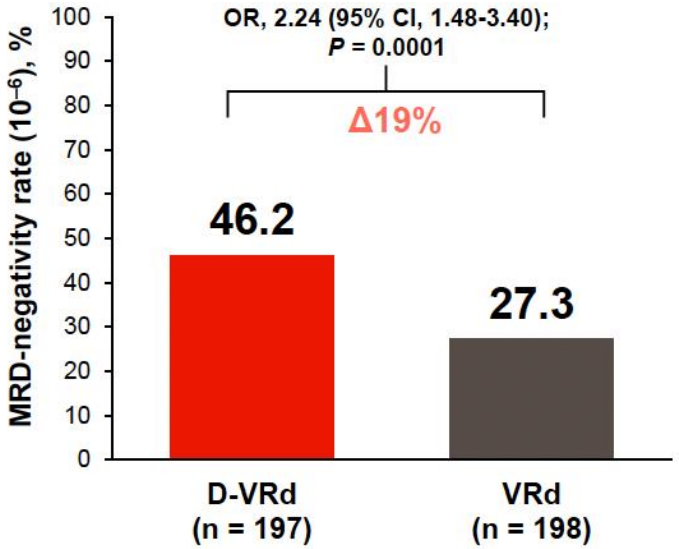
PRESENTED BY: Thierry Facon, MD

CEPHEUS Phase 3 Study of SUBQ Dara-VRd vs VRd in TI or –Deferred Patients With NDMM: MRD-Negative and Response Rates

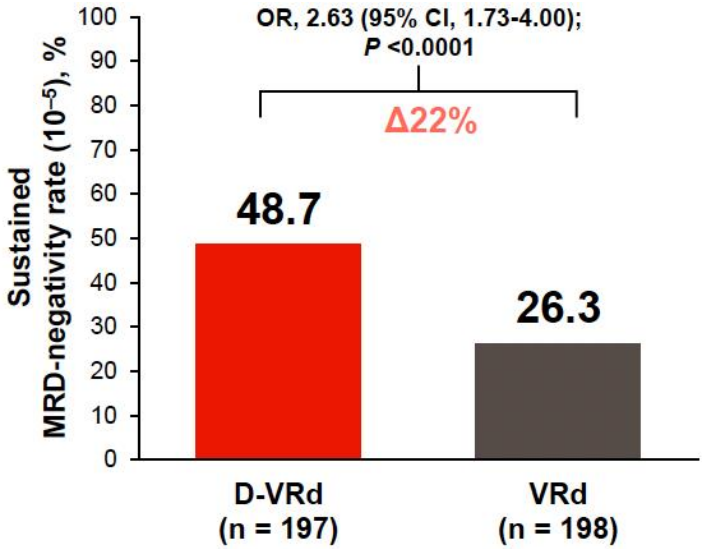
Overall MRD-Negative Rate (10^{-5})



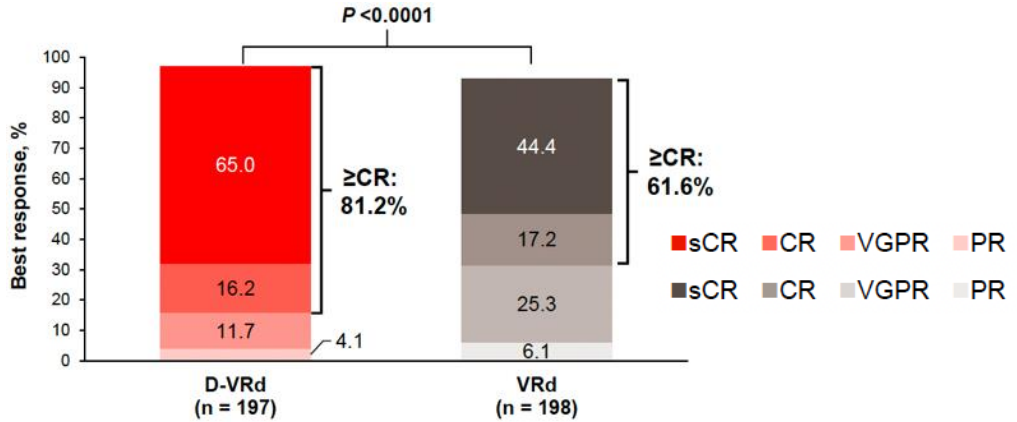
Overall MRD-Negative Rate (10^{-6})



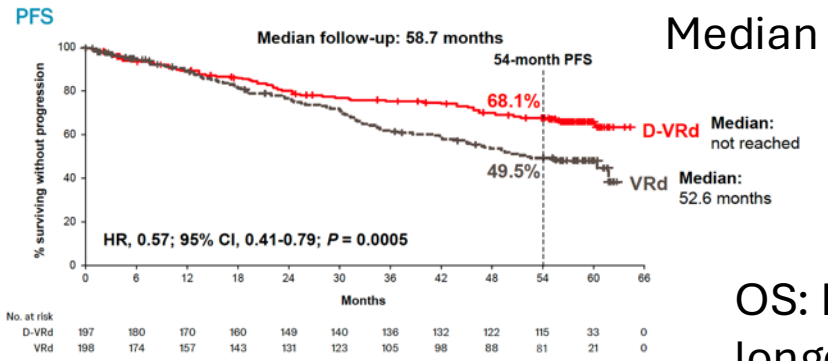
Sustained MRD-Negative Rate (10^{-5}) ≥12 Months



≥CR Rate



PFS



Median F/u 58.7m

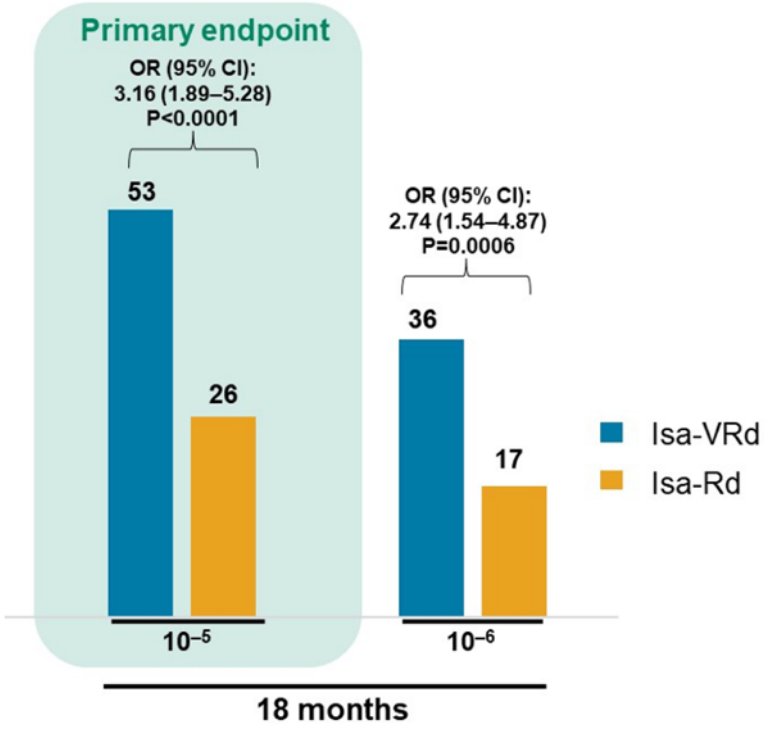
OS: Needs longer f/u

- Dara benefit was generally consistent across prespecified subgroups

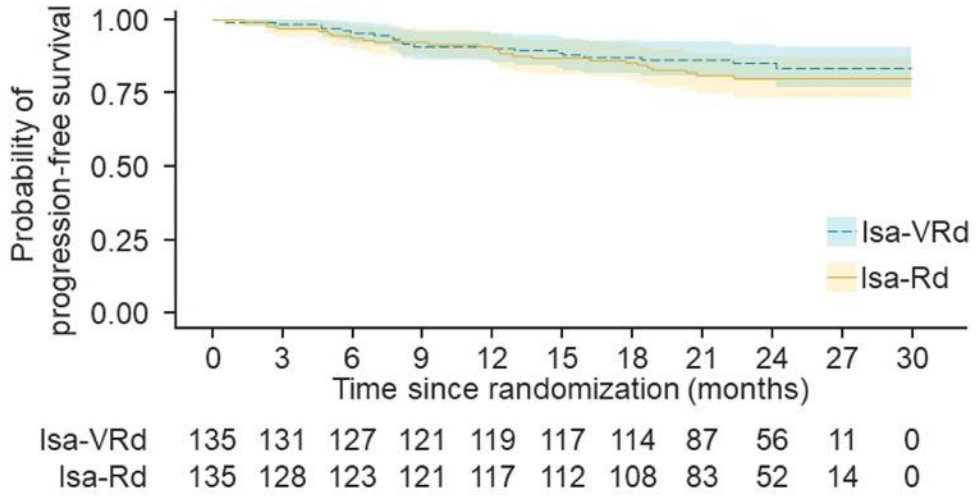
Usmani SZ et al. IMS 2024. Abstract OA-63.

BENEFIT Trial: Isa-VRd vs. Isa-RD in TI NDMM

Results: Primary Endpoint MRD(-)



Preliminary PFS (Median F/U 23.5 mos)



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

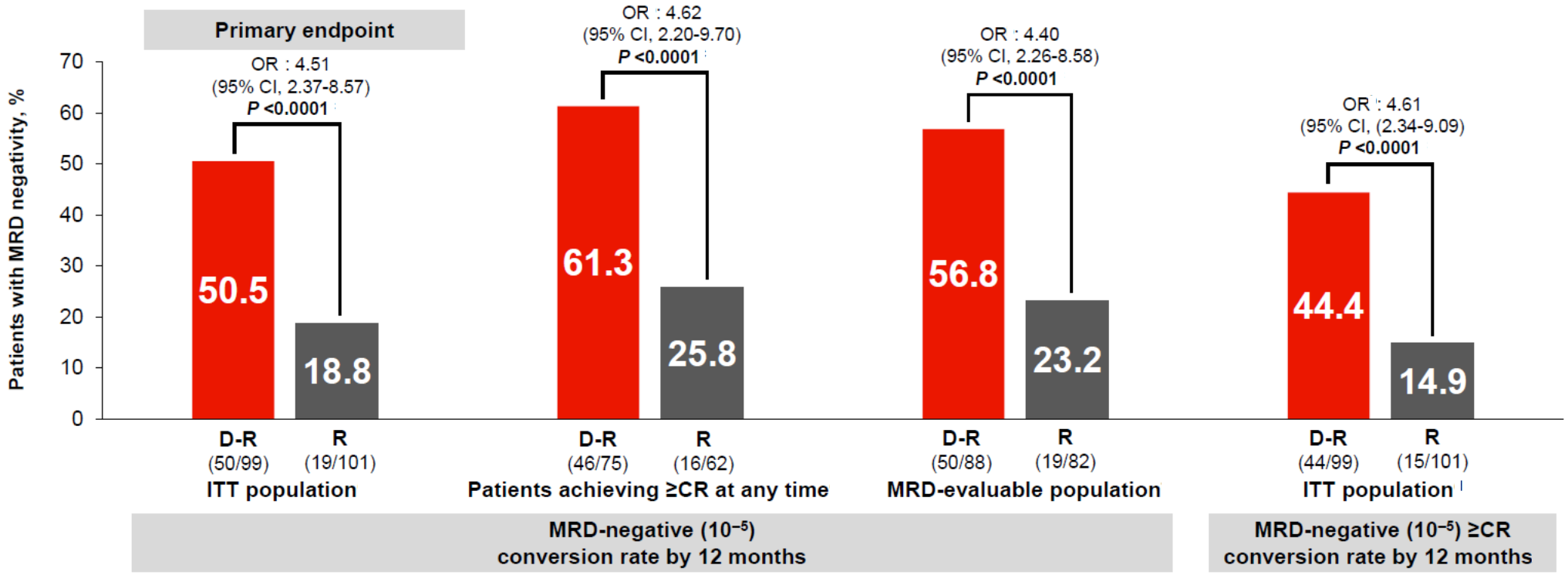
Isa-VRd resulted in deep response rates, particularly MRD(-) at 18 months and PFS is still immature

*MRD was assessed on the basis of IMWG recommendations.[1]
CI, confidence interval; CR, complete response; Isa, isatuximab; ITT, intent-to-treat; MRD–, minimal residual disease negativity; NGS, next generation sequencing; OR, odd ratio; R, lenalidomide; V, bortezomib.
1. Kumar S, et al. *Lancet Oncol* 2016;17:e328–e346.

Maintenance: AURIGA Phase 3 Study of SUBQ Dara-R vs R Post Transplant

Results From Maintenance: *MRD*

MRD-Negative (10^{-5}) Conversion Rates From Baseline to 12 Months of Maintenance Treatment



- MRD-negative (10^{-5}) conversion rates by 12 months were improved with Dara-R vs R across all clinically relevant subgroups

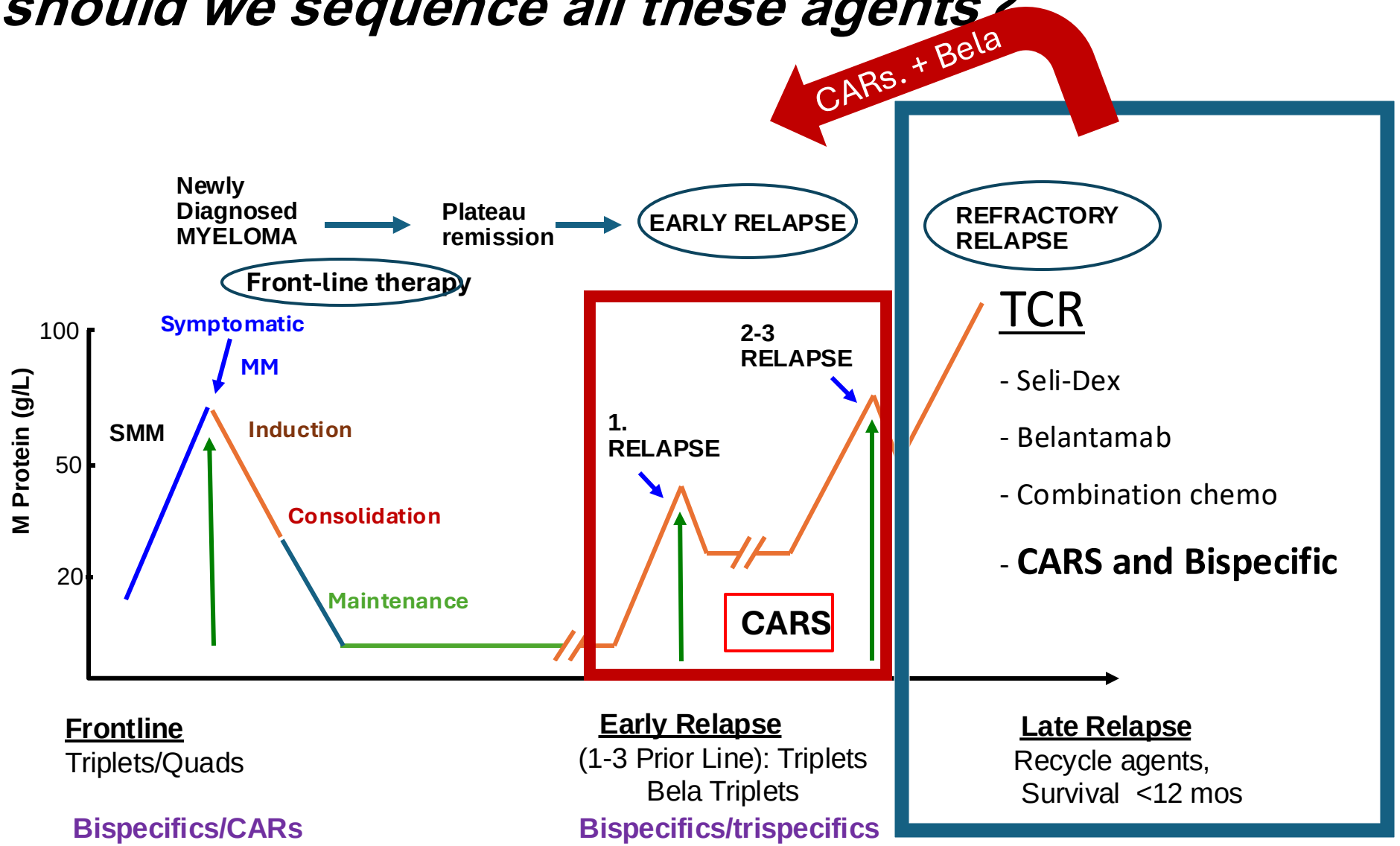
Median follow-up: 32.3 months.
Badros A, et al. IMS 2024. Abstract OA-45.

Conclusions for NDMM

- CD38 + VRd (QUAD therapy) – appears to be new SOC for TE and TI NDMM
- Results appear durable both in TE and TI – projected PFS >80-90 months
- In TI, (BENEFIT) – QWk bortezomib appears well-tolerated and effective
  - Unclear in TE
- High-risk NDMM appears to benefit from QUAD therapy
  - Dara-VRd subgroup looks good – need prolonged maintenance
  - Isa-KRd shows improved MRD- rates, especially in double hit subgroup
- MRD(–) CR will be the new "early" response metric for future trials
- CD38 in induction and maintenance appears important.
- Treatment adapted trials based on MRD, are needed to help guide treatment duration
- Will CART and bispecifics show even better results (response and TF)?

Sequencing Therapy in MM after Front-Line:

How should we sequence all these agents?

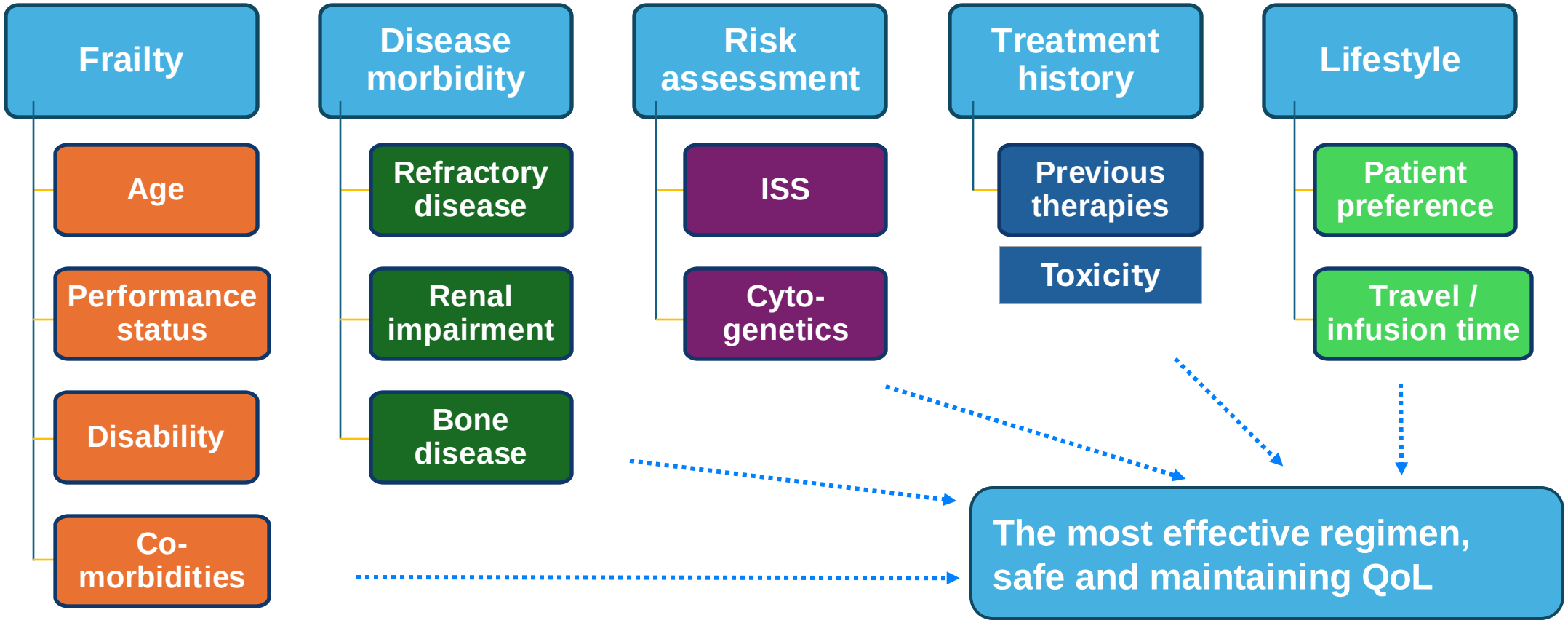


Trials:

Therapy: Approved and Experimental Products
Competitive Landscape for Triple Class Exposed/Refractory MM

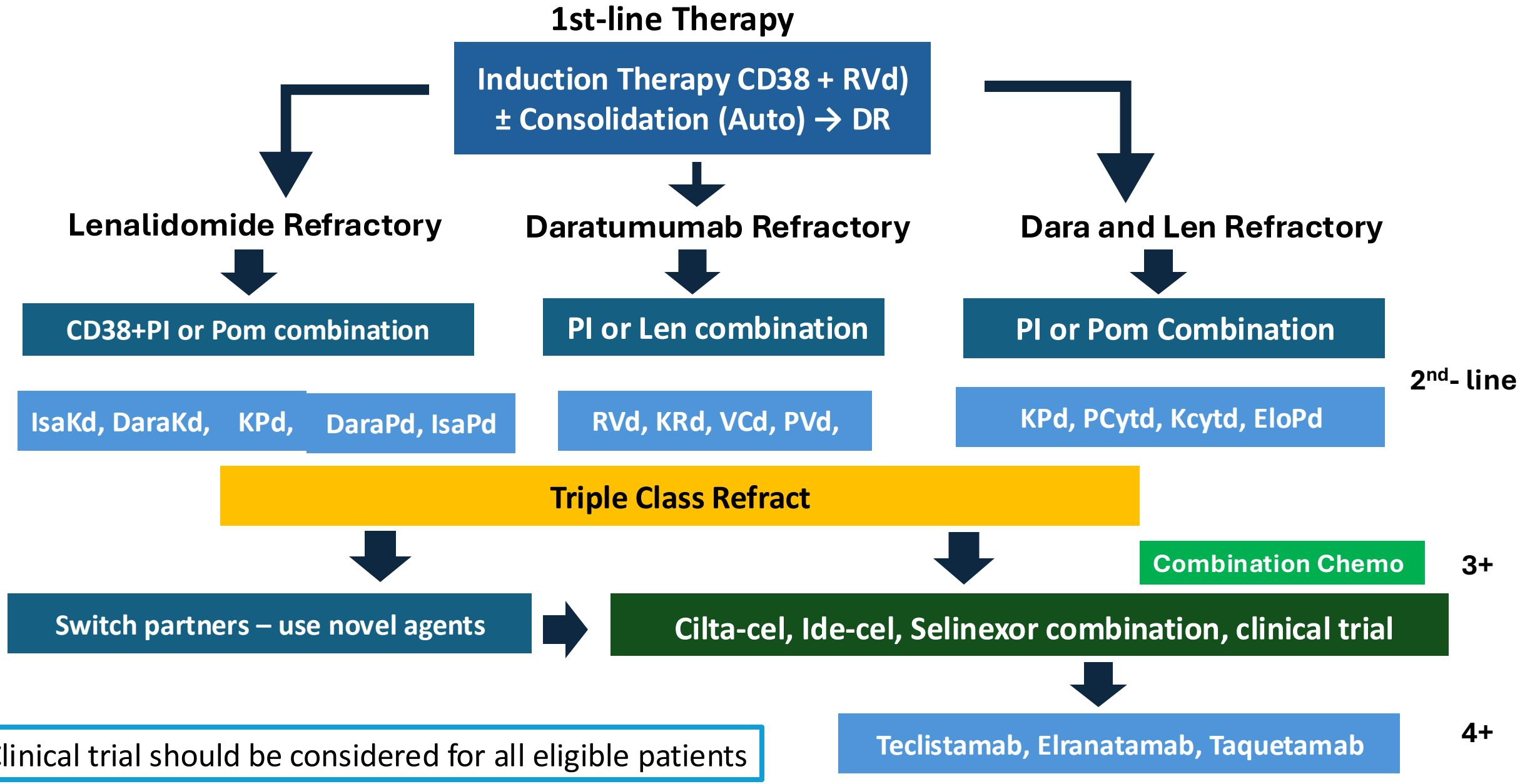
Novel Drugs	Novel Monoclonal Antibodies	ADCs	BCMA Bispecifics	Cellular Therapies BCMA CARs
Iberdomide, Mezigdomide	SAR442085 Hexabody-CD38 TAK-079	**Belantamab mafodotin**	**Teclistamab** **Elranatamab**	**Idecabtagene vicleucel** **Ciltacabtagene-autoleucel**
Selinexor Venetoclax	TAK-573 AMG-424 GBR-1343	CC-99712	ABBV-383 Linvoseltamab	Lummicar (CT053) Anitocabtagene FasT CAR (CD19/BCMA)
CFT7455	Immune – Toxin TAK-169 SEA-BCMA	AZD0305	Non-BCMA Cevostamab **Talquetamab**	Allo-CAR NK-CAR

Disease and Patient Factors Influence Treatment Choices in Relapsed Refractory MM



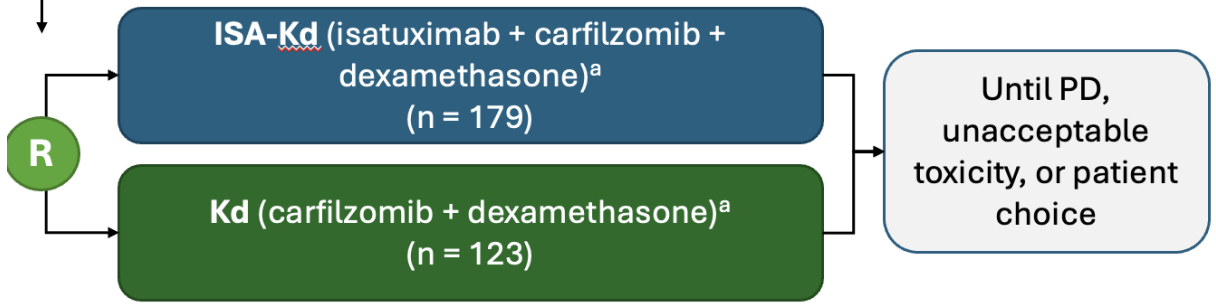
*__Attrition__ should be a consideration! With each line of therapy, 20-40% don't proceed to the next line .

Sequencing Therapy for Patients With R/R MM

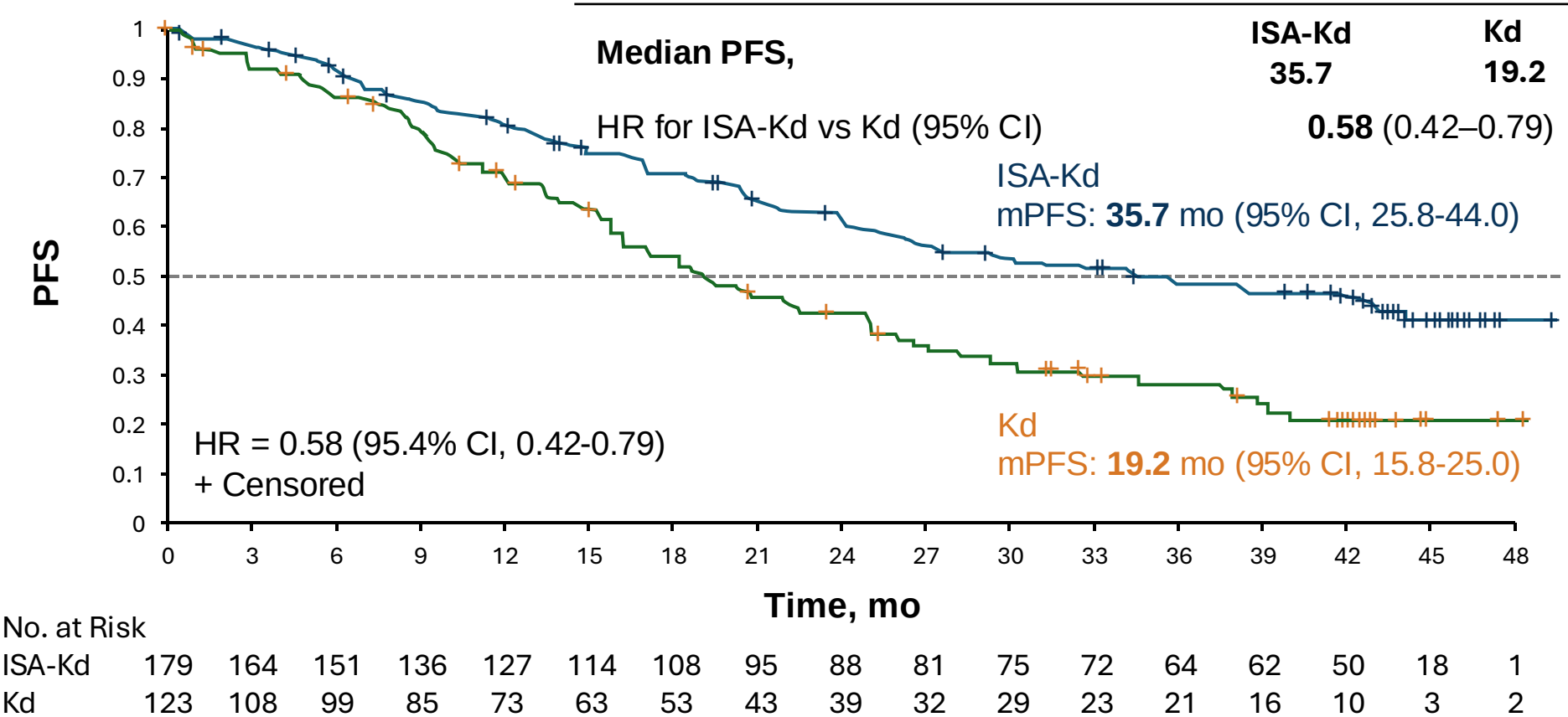


IKEMA: Randomized Phase3 Trial in RRMM 1-3 PLT

Study Design



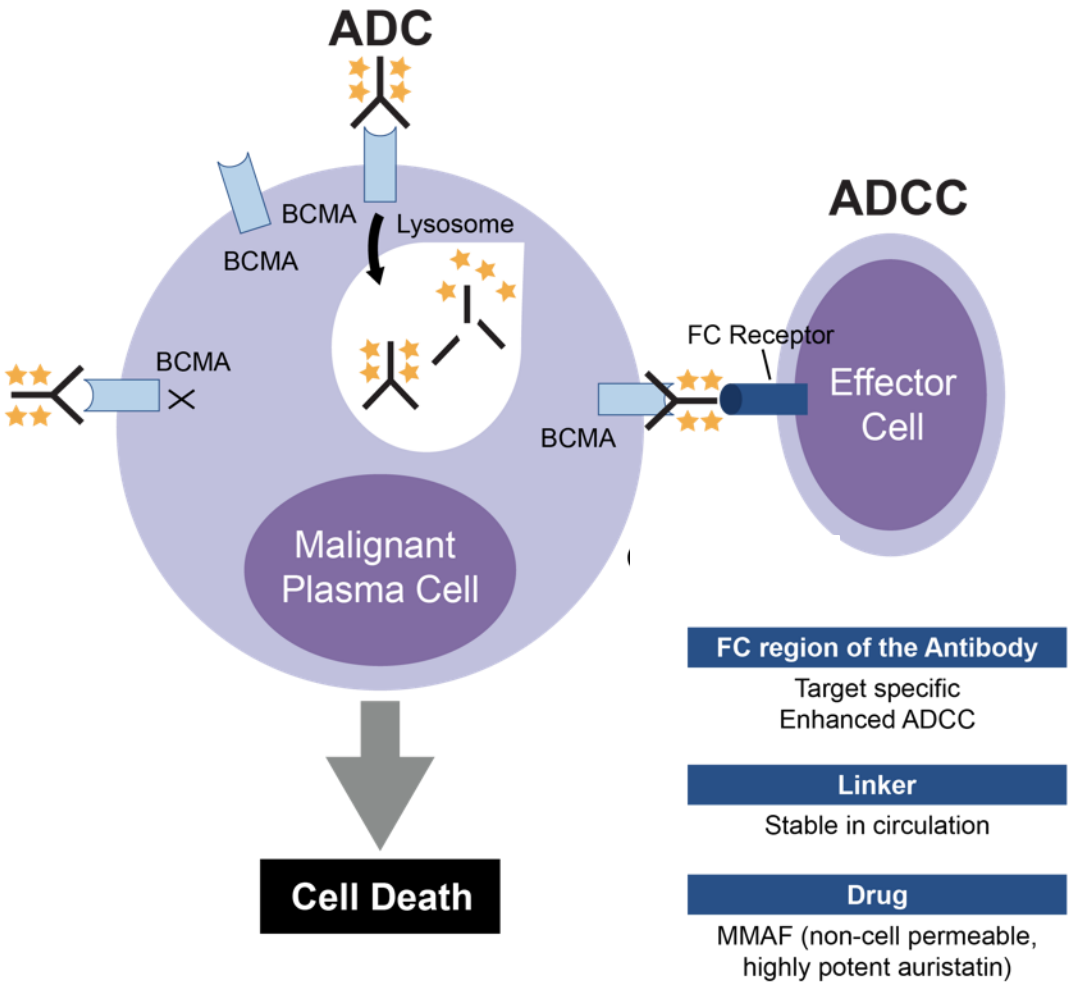
Results:



ISA-Kd showed the longest PFS on a PI-based backbone in RRMM, with 42% reduction vs Kd in the risk of progression or death

Analysis of OS is planned for 2023

Antibody-drug conjugate (ADC) - Belantamab



- Belantamab mafodotin is a humanized, afucosylated IgG1 anti-BCMA antibody conjugated to monomethyl auristatin (MMAF)
- FDA approved for patients previously treated with 4 ***prior therapies*** then withdrawn due to failed P3 trial B vs. Pd.

- DREAMM 7 – Phase 3: 494 patients
  - Randomized: BVd vs. DVd – RRMM 1-3 PLT
- DREAMM 8 – Phase 3:
  - Randomized P3: BPd vs. PVd

Single agent activity in RRMM => ORR 32%

- **Comeback-Kid of the year!!**

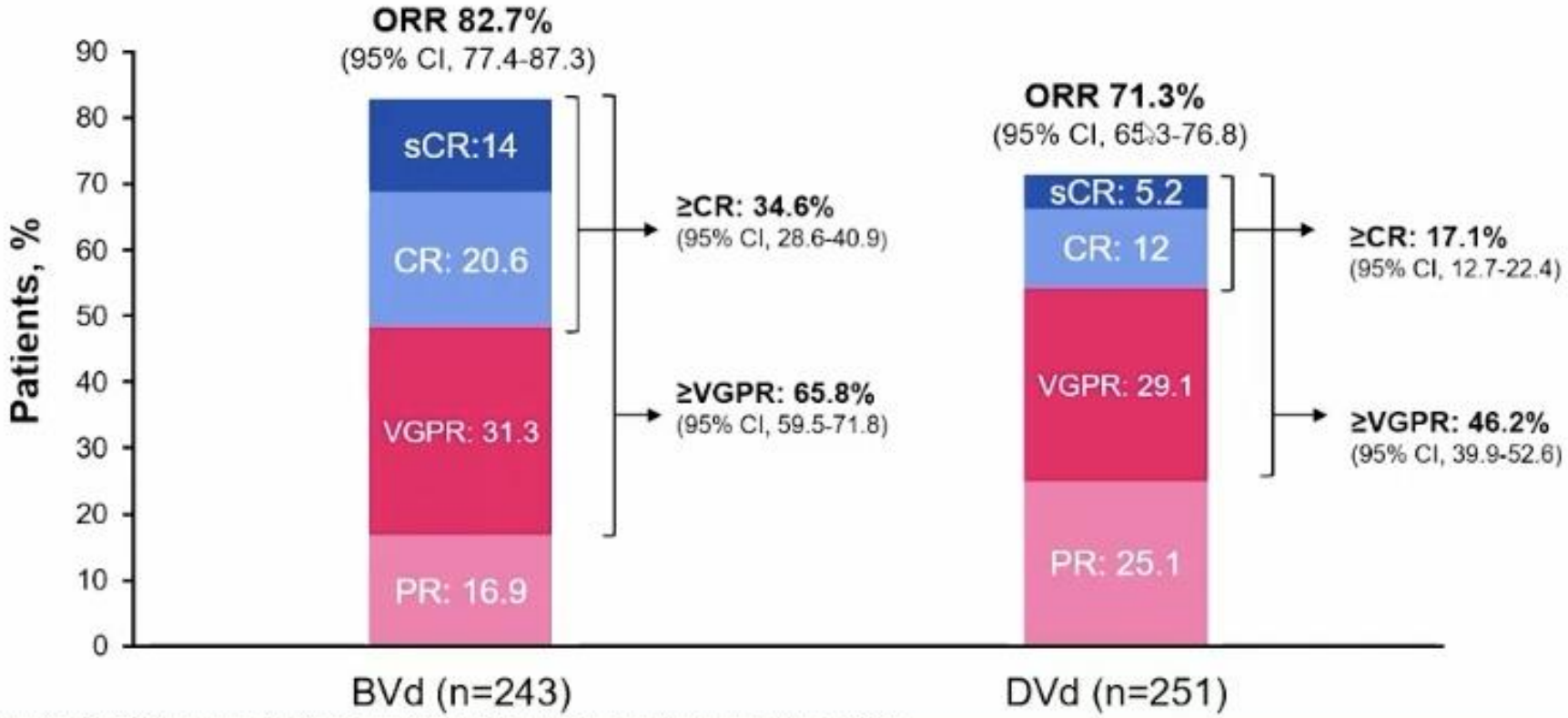
DREAMM-7: deeper responses with BVd vs DVd[a]

≥ CR MRD negativity[b]:

24.7% vs 9.6%
(95% CI, 19.4-30.6) (95% CI, 6.2-13.9)

≥ VGPR MRD negativity[b]:

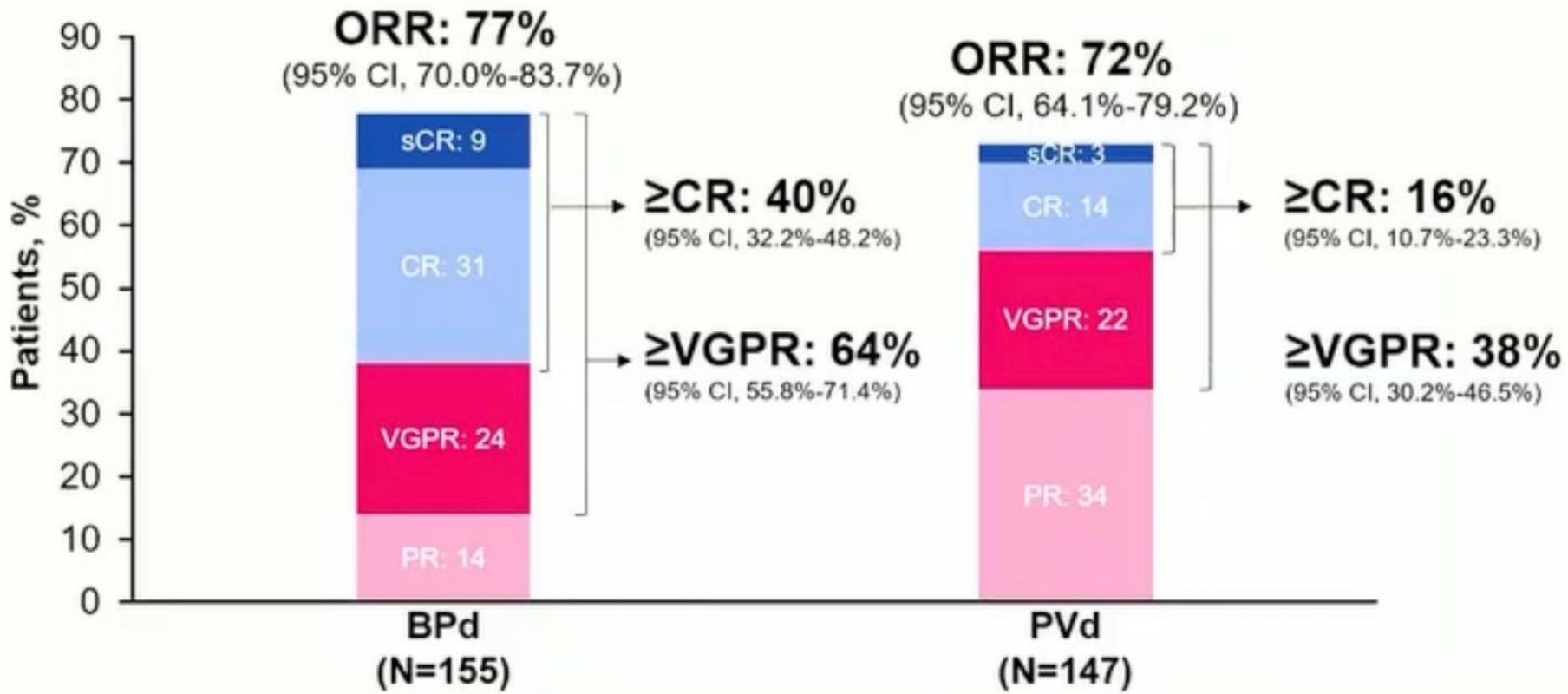
38.7% vs 17.1%
(95% CI, 32.5-45.1) (95% CI, 12.7-22.4)



BVd was associated with a greater depth of response with double the ≥CR rate and more than double the MRD negativity rates (sensitivity of 10^{-5}) of DVd (*P* value <.00001)[c]

BVd, belantamab mafodotin, bortezomib, and dexamethasone; CR, complete response; DVd, daratumumab, bortezomib, and dexamethasone; ITT, intent to treat; MRD, minimal residual disease; NGS, next-generation sequencing; PR, partial response; R-ISS, Revised International Staging System; sCR, stringent complete response; VGPR, very good partial response.
[a] CIs were based on the exact method. Two patients in the ITT population were randomized, not treated, rescreened, and rerandomized. They are counted as 4 unique patients in this output. [b] MRD negativity rate was defined as percentage of patients who were MRD negative by NGS based on a sensitivity of 10^{-5}. [c] Nominal *P* value. Cochran–Mantel–Haenszel test was used and adjusted for stratification factors, including number of prior lines of therapy (1 vs 2 or 3 vs ≥4), prior bortezomib, and R-ISS stage at screening (I vs II or III).

Deeper Responses With BPd vs PVd



The CR or better rate in the BPd arm was more than twice that in the PVd arm

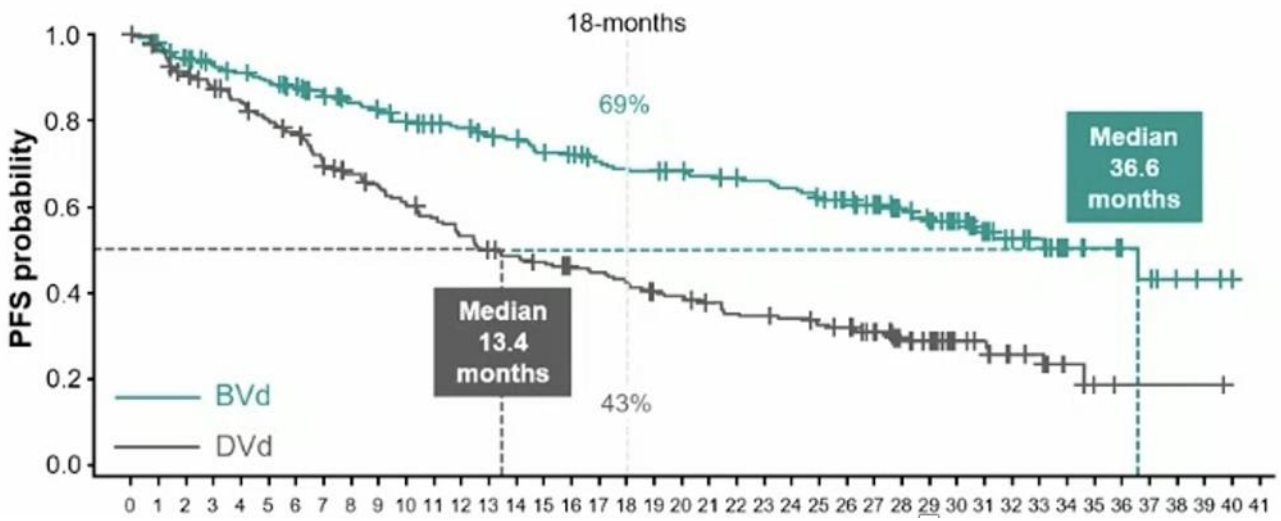
CIs were based on the exact method. All percents are based on the ITT population.
BPd, belamaf, pomalidomide, and dexamethasone; CR, complete response; ITT, intent to treat; ORR, objective response rate; PR, partial response; PVd, pomalidomide, bortezomib, and dexamethasone; sCR, stringent complete response; VGPR, very good partial response.

Both DreaMM-7 and -8 Show Significant PFS Benefit – No Blurriness Here

DREAMM

7

Mateous et al.
EHA2024

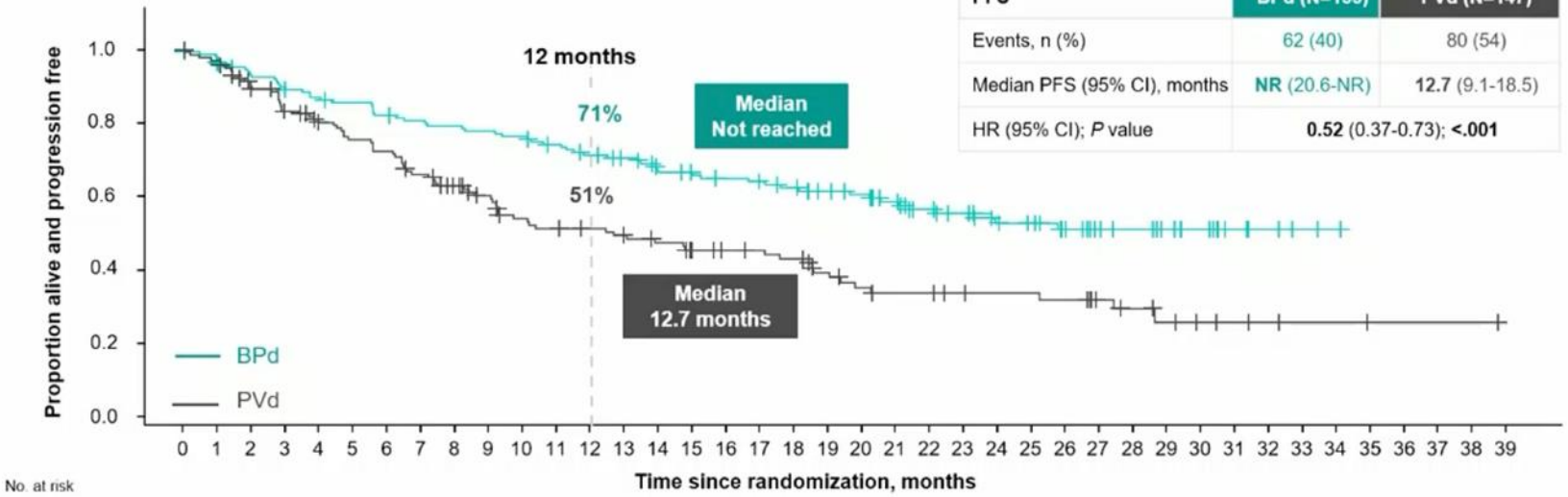


PFS[a]	BVd (N=243)	DVd (N=251)
Events, n (%)	91 (37)	158 (63)
PFS, median (95% CI),[b] months	36.6 (28.4-NR)	13.4 (11.1-17.5)
HR[c] (95% CI)	0.41 (0.31-0.53)	
P value[d]	<.00001	

Dimopoulos et al.
EHA2024

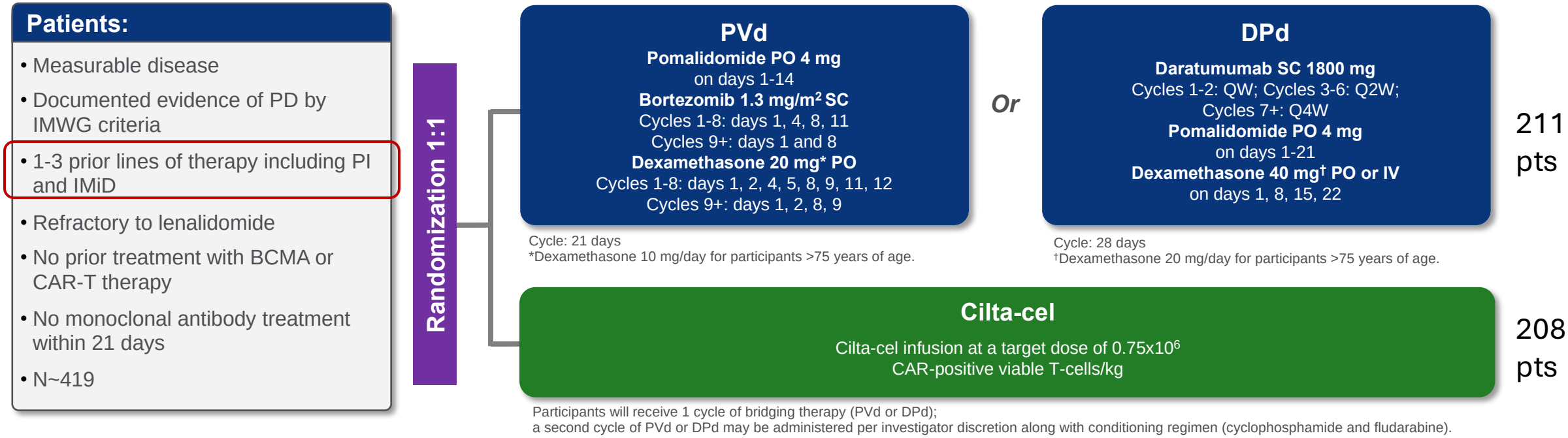
8

Significant PFS Benefit with BPd vs PVd



PFS	BPd (N=155)	PVd (N=147)
Events, n (%)	62 (40)	80 (54)
Median PFS (95% CI), months	NR (20.6-NR)	12.7 (9.1-18.5)
HR (95% CI); *P* value	0.52 (0.37-0.73); <.001	

CARTITUDE-4 (Phase 3) Study Design: 1-3 PLT



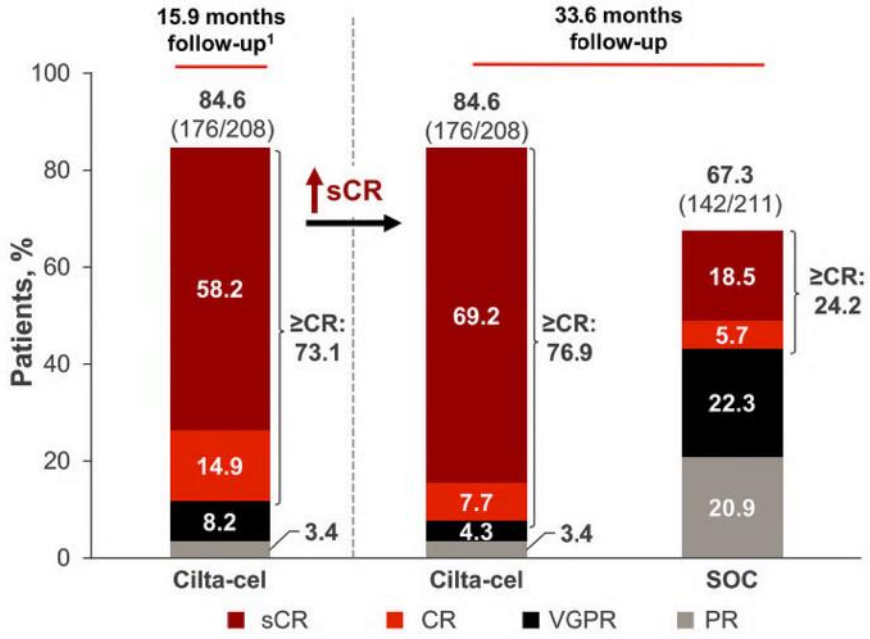
Primary Outcome:	Secondary Outcomes:	
• Progression-free survival	• CR or sCR • MRD negativity status • Sustained MRD negative rate	• HRQoL • OS, ORR, PFS2 • Safety

Primary endpoint of PFS was met and study now reported

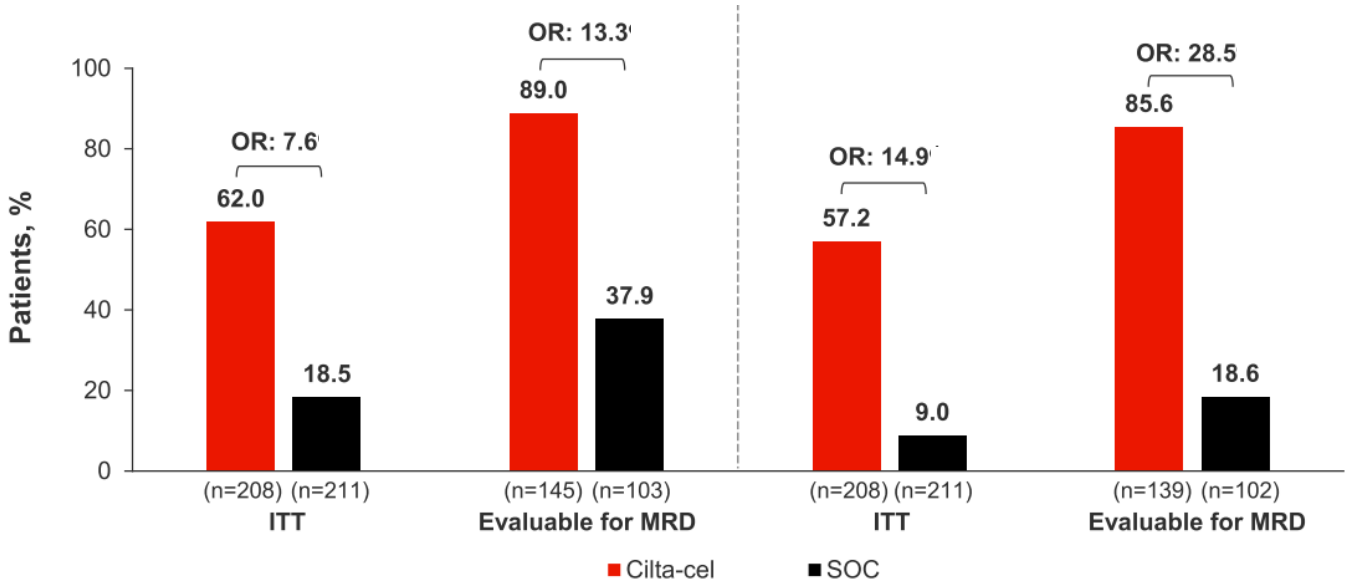
1. https://clinicaltrials.gov/ct2/show/NCT04181827 2. https://www.prnewswire.com/news-releases/janssen-announces-unblinding-of-phase-3-cartitude-4-study-of-carvykti-cilta-cel-as-primary-endpoint-met-in-treatment-of-patients-with-relapsed-and-refractory-multiple-myeloma-301732398.html. San Miguel j. et al. NEJM 2023

Long-term Update CARTITUDE-4 Phase 3 Trial: Response

ORR



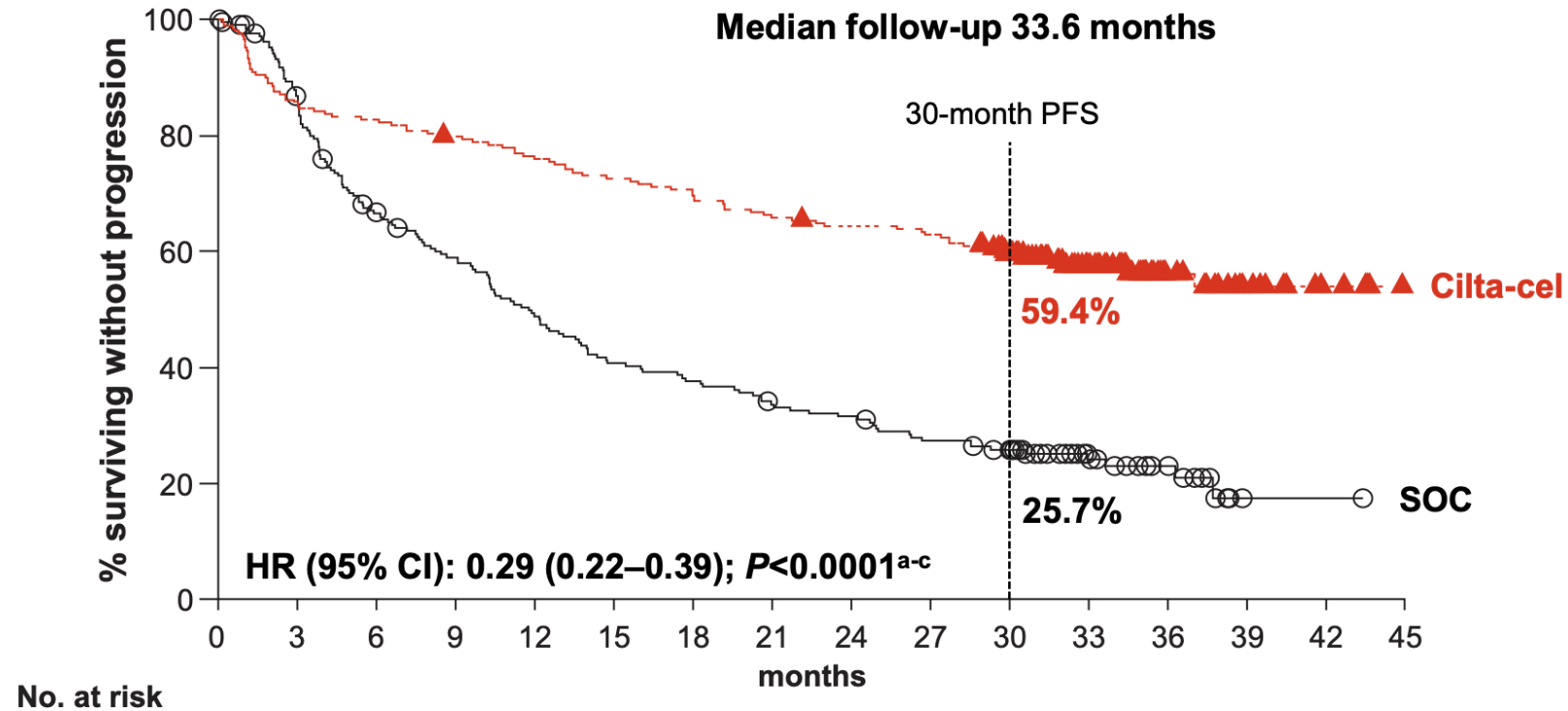
MRD Negativity at 10^{-5} (L) and 10^{-6} (R)



DOR	Cilta-Cel (n=208)	SOC (n=211)
Median, months (95% CI)	NR	18.7 (12.9-23.7)
30-month rate, % (95% CI)	67.4 (59.7-74.0)	35.5 (27.6-43.6)

Mateos, MV, et al. IMS 2024. Abstract OA-65.

Long-Term CARTITUDE-4 Update (34 Months): Cilta-cel Maintained Significant Improvement in Progression-Free Survival

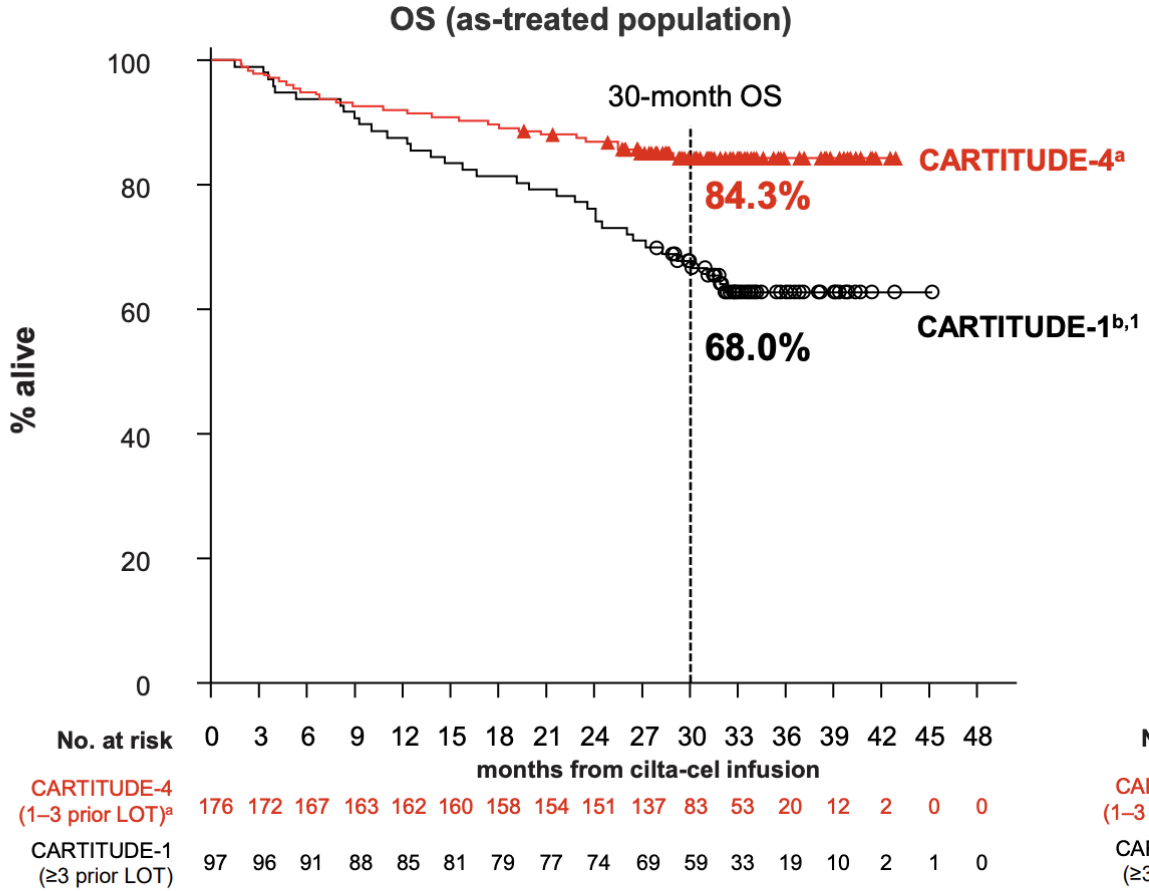


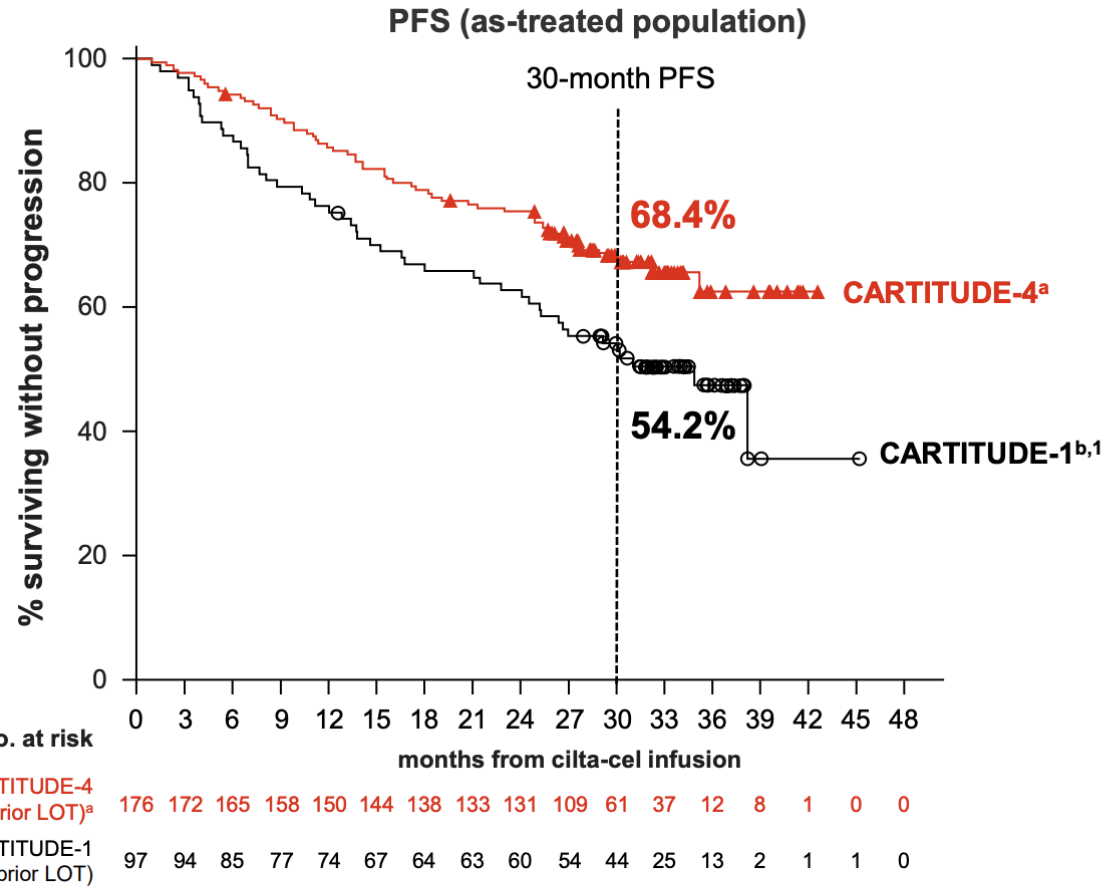
~70% reduction in the risk of progression or death in patients who received cilta-cel and mPFS has not been reached

[a]Constant piecewise weighted log-rank test. [b]HR and 95% CI from a Cox proportional hazards model with treatment as the sole explanatory variable, including only PFS events that occurred >8 weeks post randomization.
[c]Nominal *P* value.
Cilta-cel, ciltacabtagene autoleucel; HR, hazard ratio; mPFS, median progression-free survival; PFS, progression-free survival; SOC, standard of care.

Presented by M-V Mateos at the 21st International Myeloma Society (IMS) Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil

Long-Term CARTITUDE-4 Update (34 Months): Numerically Higher Overall and Progression-Free Survival Rates Versus CARTITUDE-1





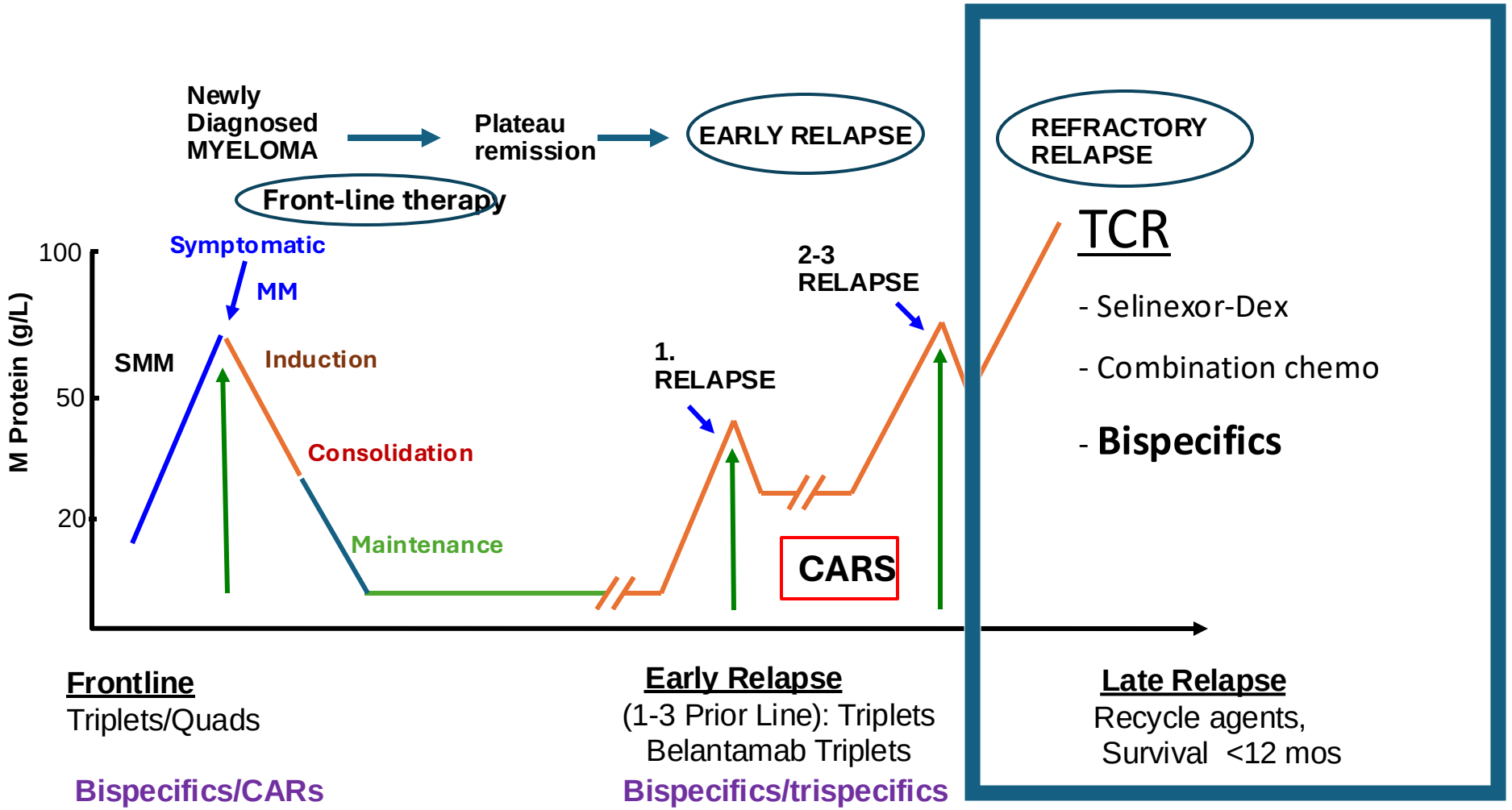
Cilta-cel use in earlier lines demonstrated numerically higher rates of overall and progression-free survival

[a]Re-baselined to begin at time of cilta-cel infusion for patients who received cilta-cel as study treatment, with median follow-up of 30.5 months. [b]33.4-month median follow-up.
Cilta-cel, ciltacabtagene autoleucel; LOT, line of therapy; OS, overall survival; PFS, progression-free survival; SOC, standard of care.
1. Lin et al. Abstract 8009, presented at ASCO; June 2–6, 2023; Chicago, IL, USA & Virtual.

Presented by M-V Mateos at the 21st International Myeloma Society (IMS) Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil

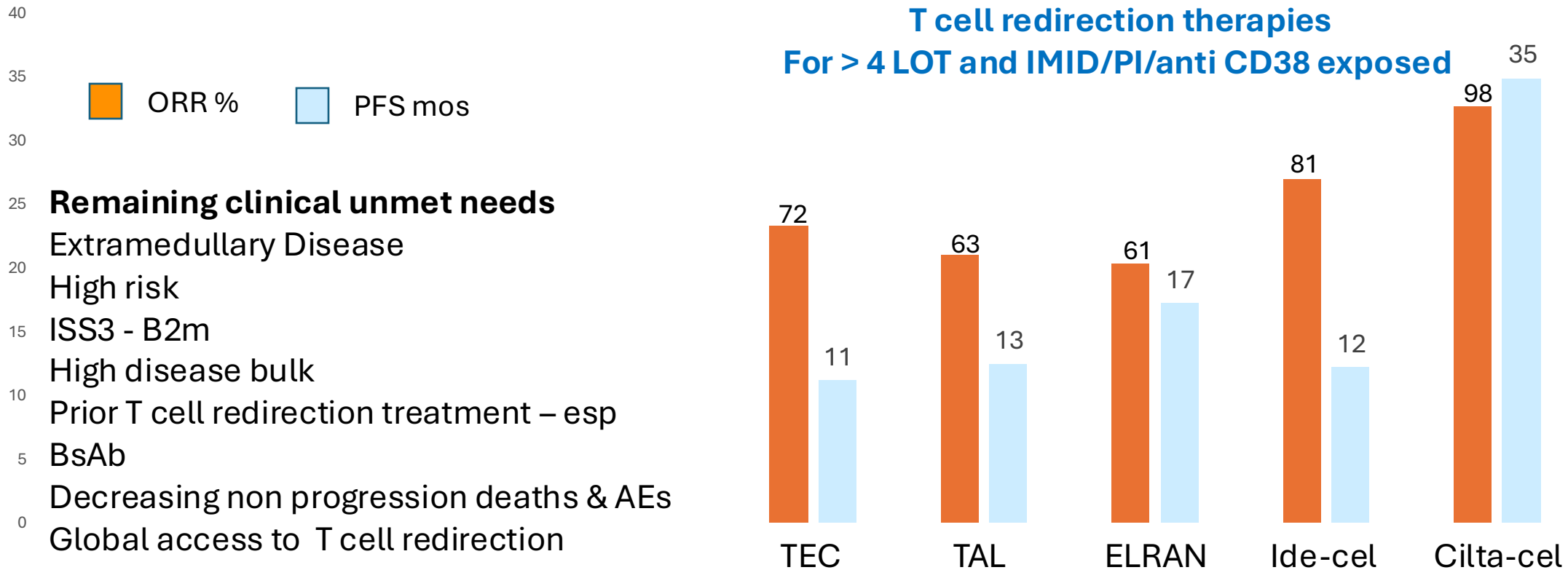
Sequencing Therapy in MM after Front-Line:

How should we sequence all these agents?



Trials:

Overall Response Rate (ORR) and Progression Free Survival (PFS) of Recently Approved Therapies in RRMM



Remaining clinical unmet needs

Extramedullary Disease

High risk

ISS3 - B2m

High disease bulk

Prior T cell redirection treatment – esp BsAb

Decreasing non progression deaths & AEs

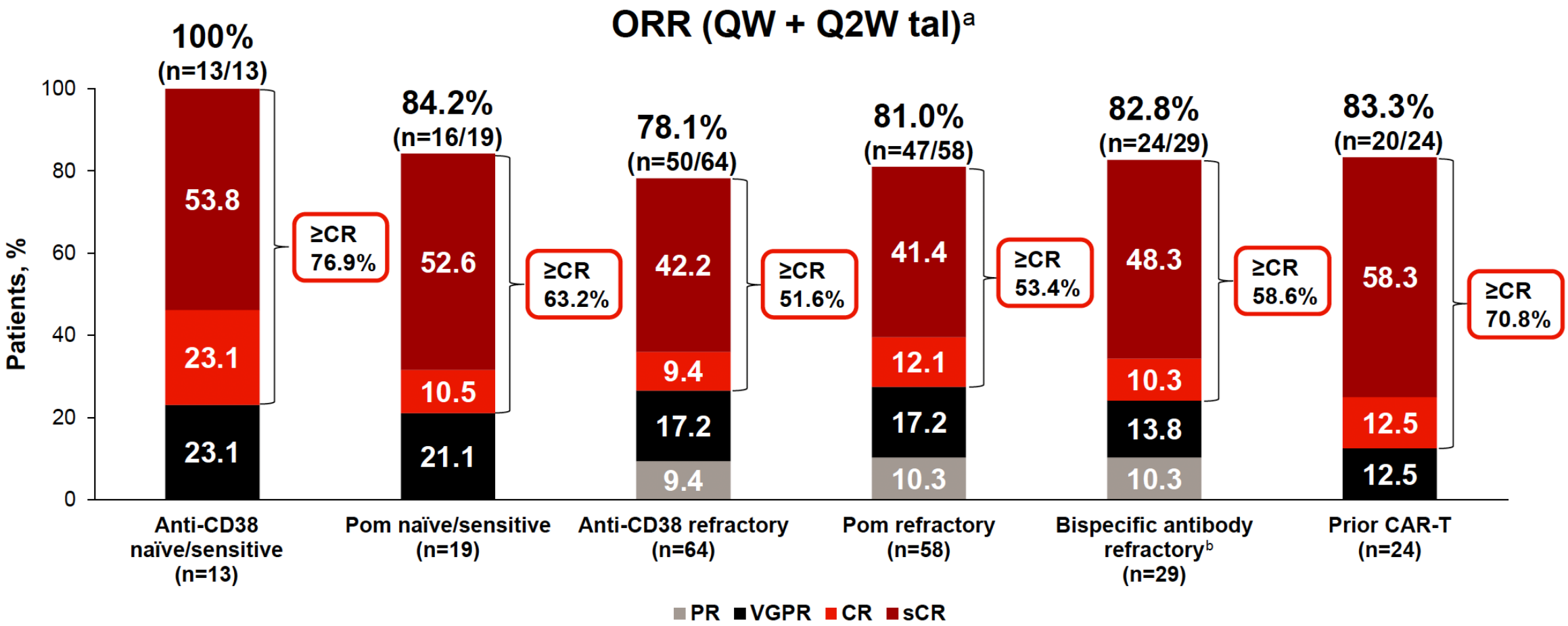
Global access to T cell redirection

Richardson P et al Blood 2014;123(12):1826-32
Siegel DS et al. Blood 2012;120(14): 2817–2825
Lonial S et al. Lancet 2016;387:1551-1560
Chari A et al. N Eng J Med 2019;381:727-738

Rasche et al EHA 2024
Van De Donk et al IMS 2023
Lesohkin et al Nat Med 2023
Anderson L et al. ASCO 2021;abstract 8016 (poster presentation)
Usmani S et al ASCO 2022;abstract 8028 (poster presentation)

This is not a head-to-head comparison and cross-trial comparisons should not be interfered from these data Data represent two populations, PFS includes all patients, DOR includes responding patients only

TRIMM-2 Tal + Dara + Pom Cohort: High ORRs in Prior Exposure Subgroups

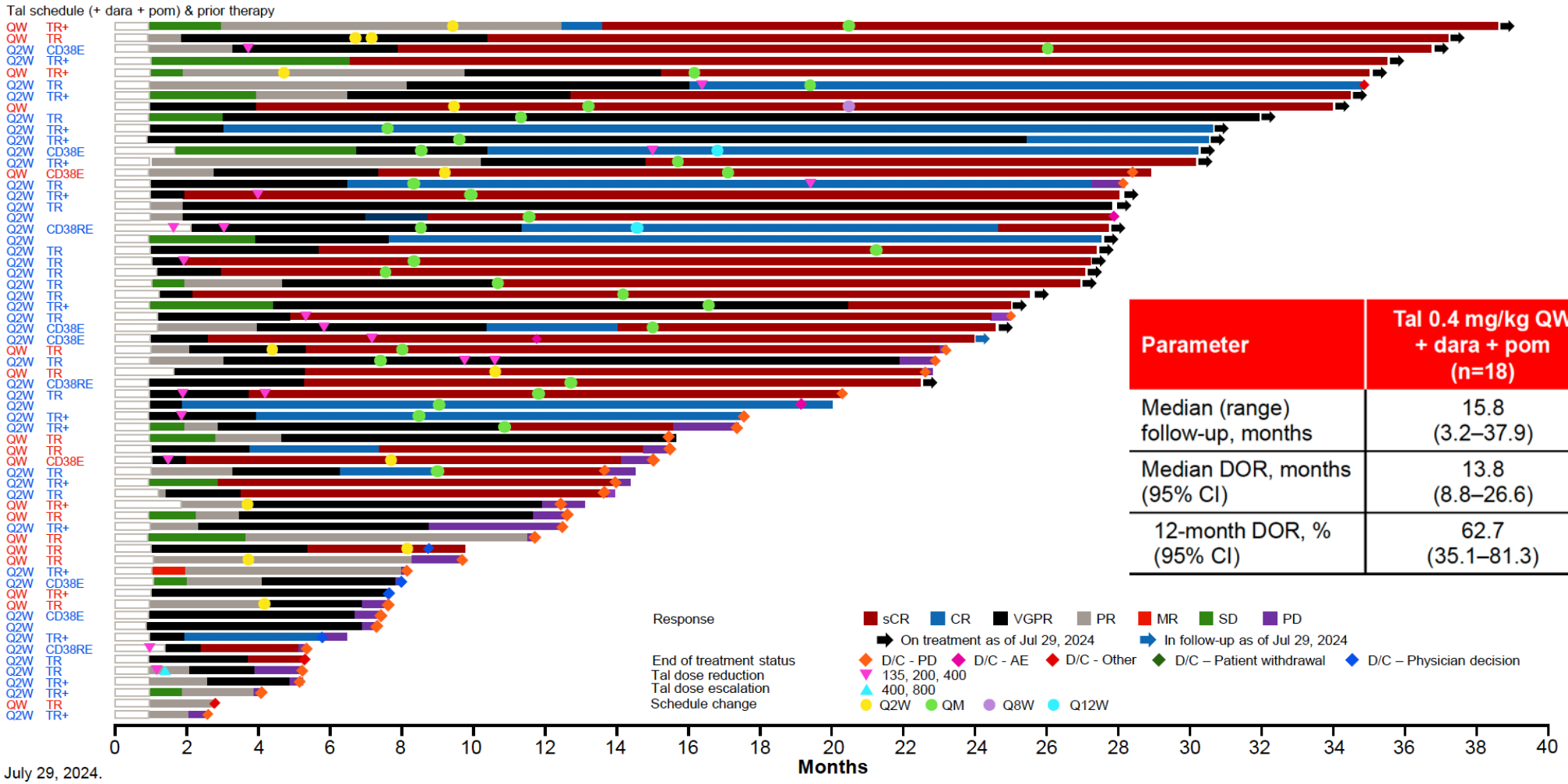


Data cut-off: July 29, 2024.

Anti-CD38 naïve = never received anti-CD38 therapy; anti-CD38 sensitive = minimal response or better during treatment; anti-CD38 refractory = best response of SD or PD during treatment or within 60 days of completing anti-CD38 therapy. [a]Response was assessed by investigators, based on IMWG criteria. Percentages are calculated with the number of patients in each group as denominator. [b]All 29 patients who received prior bispecific antibody therapy were refractory. CAR, chimeric antigen receptor; CR, complete response; dara, daratumumab; IMWG, International Myeloma Working Group; ORR, overall response rate; pom, pomalidomide; PD, progressive disease; PR, partial response; Q2W, every other week; QW, weekly; sCR, stringent complete response; SD, stable disease; tal, talquetamab; VGPR, very good partial response.

Presented by N Bahlis at the 21st International Myeloma Society (IMS) Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil

TRIMM-2 Tal + Dara + Pom Cohort: Responses Deepened Over Time, Irrespective of Dose Intensity Reductions



Parameter	Tal 0.4 mg/kg QW + dara + pom (n=18)	Tal 0.8 mg/kg Q2W + dara + pom (n=45)
Median (range) follow-up, months	15.8 (3.2–37.9)	17.5 (0.2–37.7)
Median DOR, months (95% CI)	13.8 (8.8–26.6)	26.4 (16.7–NE)
12-month DOR, % (95% CI)	62.7 (35.1–81.3)	73.1 (57.5–83.7)

Data cut-off: July 29, 2024.

+, penta-drug refractory; AE, adverse event; CD38E, anti-CD38 therapy exposed; CD38RE, anti-CD38 therapy refractory; CR, complete response; dara, daratumumab; D/C, discontinuation; MR, minimal response; Q2W, every other week; Q8W, every 8 weeks; Q12W, every 12 weeks; QM, monthly; QW, weekly; PD, progressive disease; PR, partial response; sCR, stringent complete response; SD, stable disease; TR, triple-class refractory; VGPR, very good partial response.

Presented by N Bahlis at the 21st International Myeloma Society (IMS) Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil

RedirecTT-1 Tal + Tec: Study Design

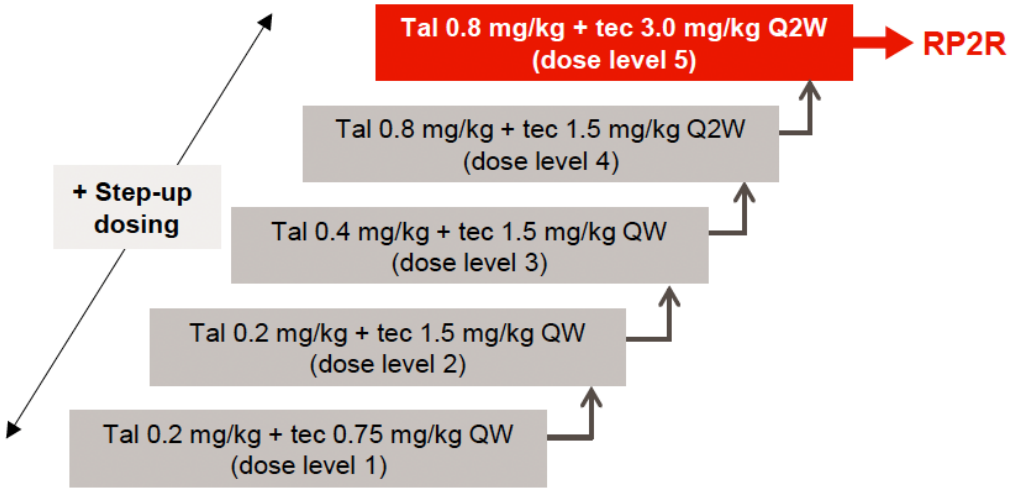
Key eligibility criteria

- Measurable MM
- EMD permitted (≥1 nonradiated, bone-independent lesion ≥2 cm)
- RR or intolerant to established therapies, including last LOT
- Triple-class exposed (prior PI, IMiD, anti-CD38)

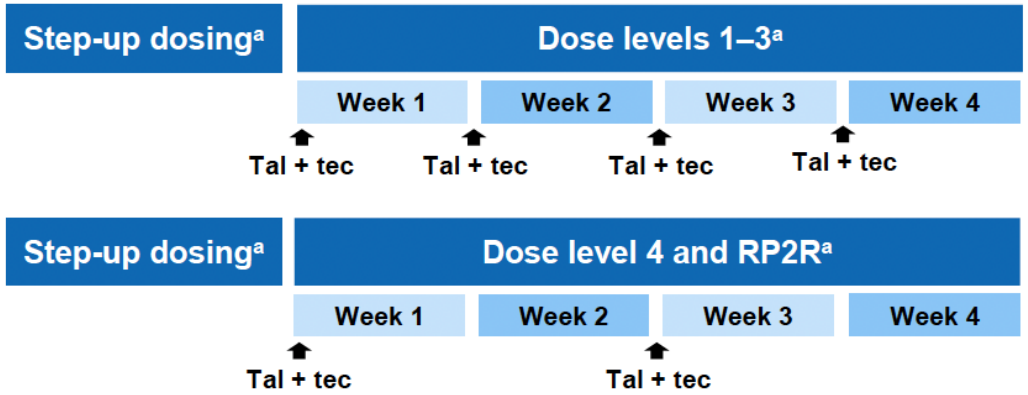
Key objectives

- Safety, including DLTs
- Identify RP2R(s)
- ORR, DOR, time to response, PK, immunogenicity
- PFS

Phase 1 dose escalation



Dosing schedule

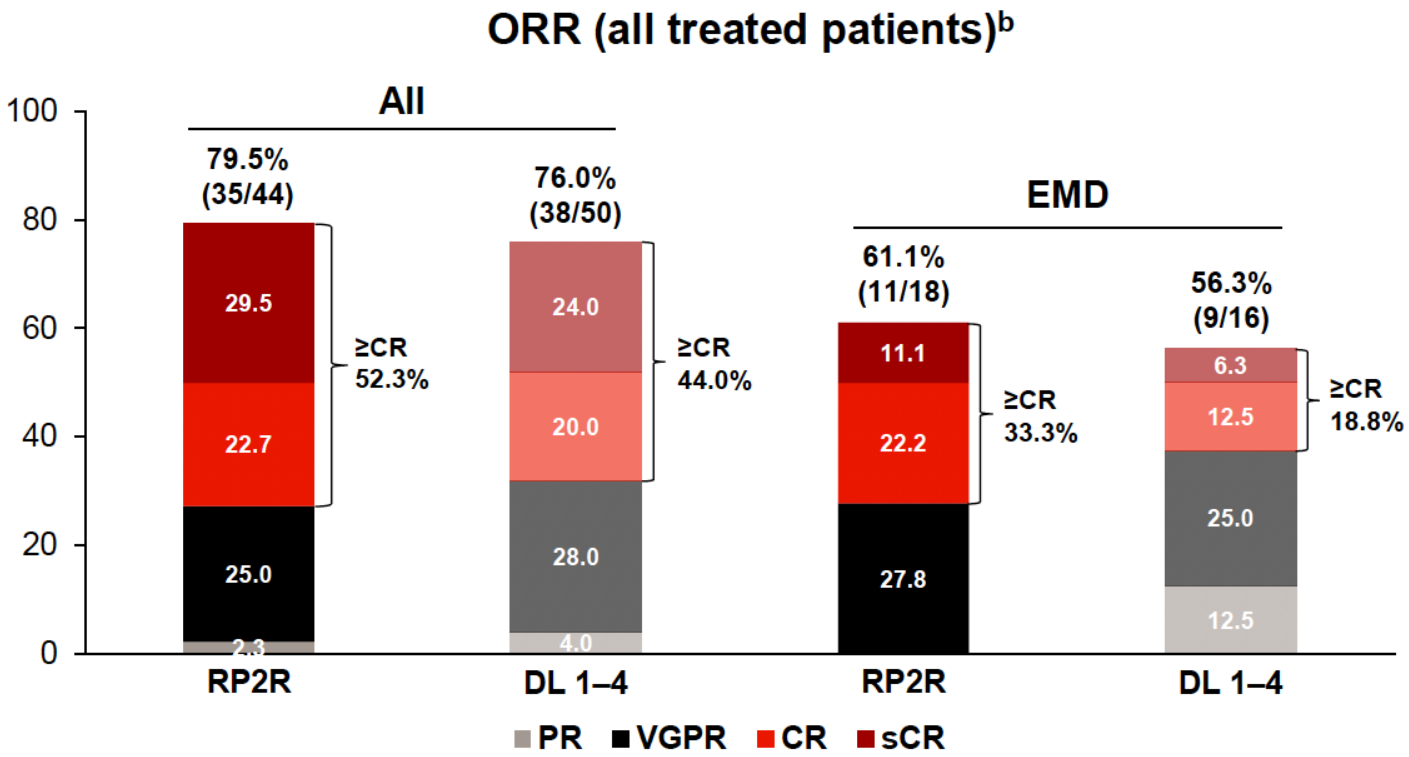


Patients could transition from QW to Q2W and from Q2W to Q4W dosing after achieving a ≥PR after cycle 4

[a]Tal and tec administered on the same day, 30 (±10) minutes apart, for all step-up and full treatment doses. DLT, dose-limiting toxicity; DOR, duration of response; EMD, extramedullary disease; IMiD, immunomodulatory drug; LOT, line of therapy; MM, multiple myeloma; ORR, overall response rate; PFS, progression-free survival; PI, proteasome inhibitor; PK, pharmacokinetics; PR, partial response; Q4W, monthly; Q2W, every other week; QW, weekly; RP2R, recommended phase 2 regimen; RR, relapsed/refractory; tal, talquetamab; tec, teclistamab.

Presented by YC Cohen at the 21st International Myeloma Society (IMS) Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil

RedirecTT-1 Tal + Tec: High ORR and Deep Responses, Including in EMD[a]



All patients	RP2R (n=44)	DL 1–4 (n=50)
Median (range) follow-up, months	18.2 (0.7–27.0)	29.0 (0.5[c]–37.1)
Median (range) time to first response, months	1.4 (0.3–5.1)	2.1 (1.1–7.7)
Median (range) time to best response, months	4.9 (1.4–19.8)	4.9 (1.1–30.6)

Patients with EMD	RP2R (n=18)	DL 1–4 (n=16)
Median (range) follow-up, months	13.6 (0.7–25.9)	18.7 (0.5[c]–33.8)
Median (range) time to first response, months	3.0 (1.4–5.1)	2.6 (2.1–3.8)
Median (range) time to best response, months	6.3 (3.0–10.7)	3.9 (2.1–10.7)

ORR 79.5% (61.1% in EMD) at RP2R with rapid and deep responses

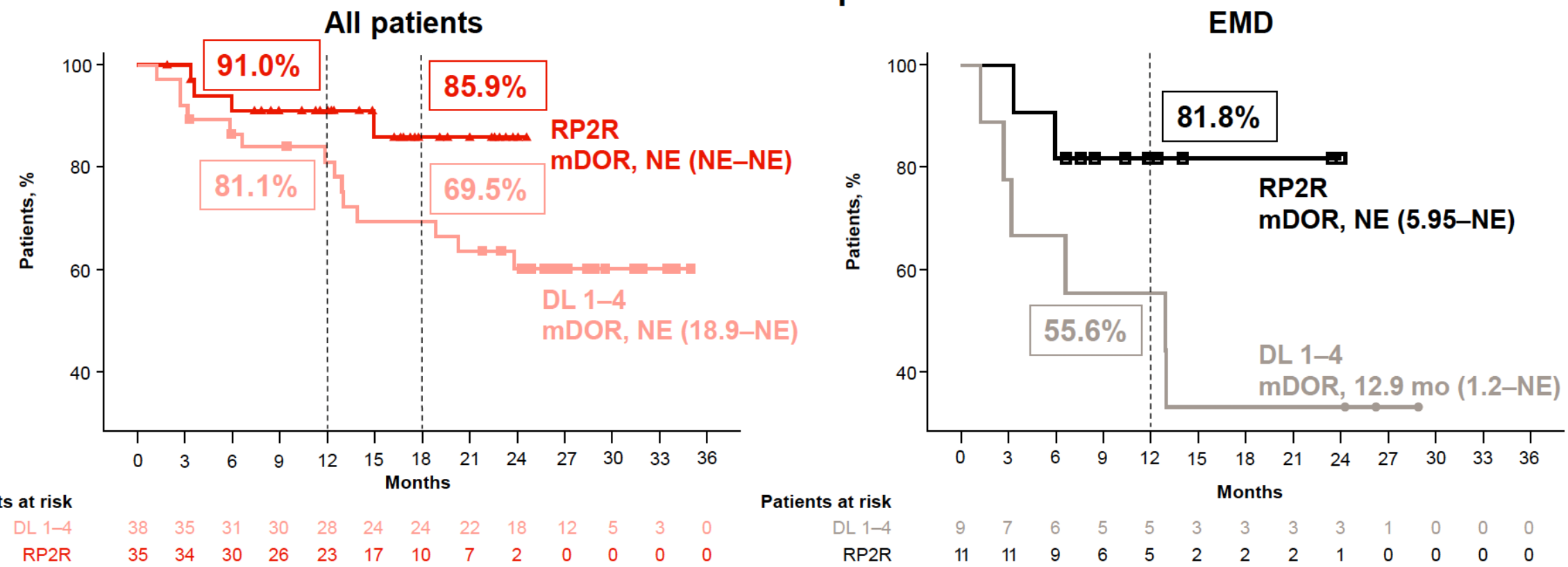
Data cut-off date: March 15, 2024.

[a]EMD defined as ≥1 nonradiated, bone-independent lesion ≥2 cm. [b]Responses were investigator-assessed per IMWG 2016 criteria. Data shown are confirmed responses and calculated in all treated patients. [c]Denotes patients who died. CR, complete response; DL, dose level; EMD, extramedullary disease; IMWG, International Myeloma Working Group; ORR, overall response rate; PR, partial response; RP2R, recommended phase 2 regimen; sCR, stringent complete response; tal, talquetamab; tec, teclistamab; VGPR, very good partial response.

Presented by YC Cohen at the 21st International Myeloma Society (IMS) Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil

RedirecTT-1 Tal + Tec: Highly Durable Responses, Including in EMD[a]

Duration of response



18-mo DOR of 85.9% at RP2R (81.8% 12-mo rate in EMD)

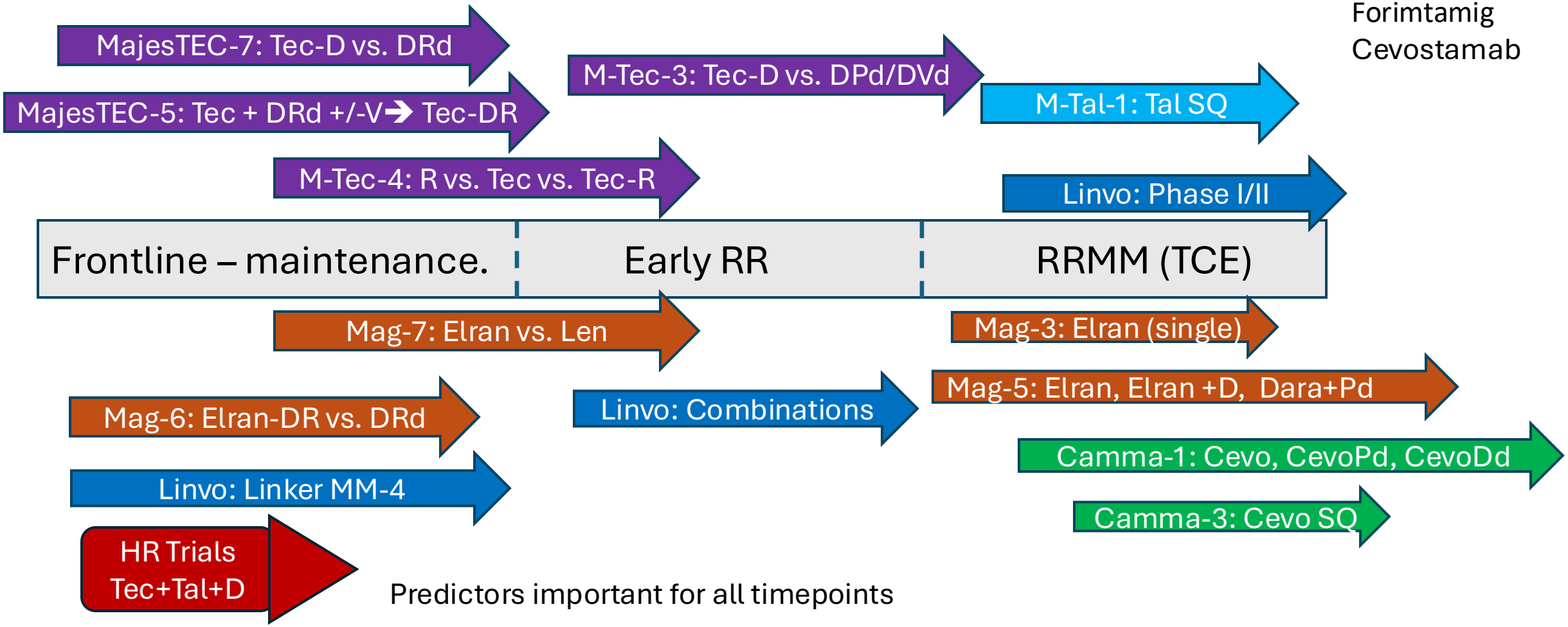
Data cut-off date: March 15, 2024. Median follow-up: 18.2 months (RP2R) and 29.0 months (dose levels 1–4). **Eighteen-month DOR rate at the RP2R was 81.8% in EMD patients.** [a]EMD defined as ≥1 nonradiated, bone-independent lesion ≥2 cm. DL, dose level; EMD, extramedullary disease; mDOR, median duration of response; NE, not evaluable; RP2R, recommended phase 2 regimen; tal, talquetamab; tec, teclistamab.

Presented by YC Cohen at the 21st International Myeloma Society (IMS) Annual Meeting; September 25–28, 2024; Rio de Janeiro, Brazil

Immunotherapy Bispecific Trials

Current and planned (not inclusive of all trials)

- Myeloma Treatment Paradigm



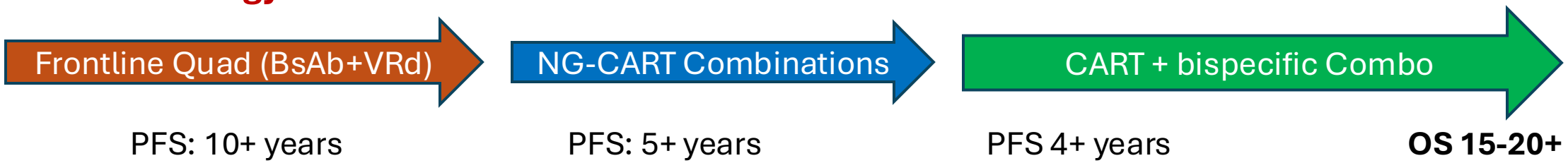
BCMA
Teclistamab
Elranatamab
Linvoseltamab
ABBV-383
Non-BCMA
Talquetamab
Forimtamig
Cevostamab

Summary: Sequencing in Multiple Myeloma

- Myeloma Treatment Paradigm

Current Strategy:

Future Strategy:



GOAL: Time-limited therapy!!!! At each Line of therapy; Chronic illness => CURE