Consensus or Controversy? Documenting and Discussing Investigators' Approaches to the Management of Relapsed/Refractory Multiple Myeloma

Monday, June 1, 2026
7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)

Faculty

Melissa Alsina, MD
Hans Lee, MD
Paul G Richardson, MD

Moderator

Sagar Lonial, MD, FACP, FASCO

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Dr Mikhael — Disclosures
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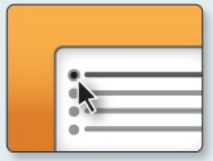

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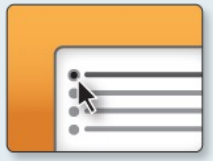

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- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based program. An email will be sent to all attendees when the activity is available.

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Agenda

Module 1: Integrating Bispecific Antibodies into the Management of Relapsed/Refractory (R/R) Multiple Myeloma (MM) — Dr Lee

Module 2: Current Utility of Antibody-Drug Conjugates for MM — Dr Lonial

Module 3: Potential Role of Cereblon E3 Ligase Modulators in Therapy for MM — Dr Richardson

Module 4: Chimeric Antigen Receptor T-Cell Therapy for R/R MM — Dr Alsina

Agenda

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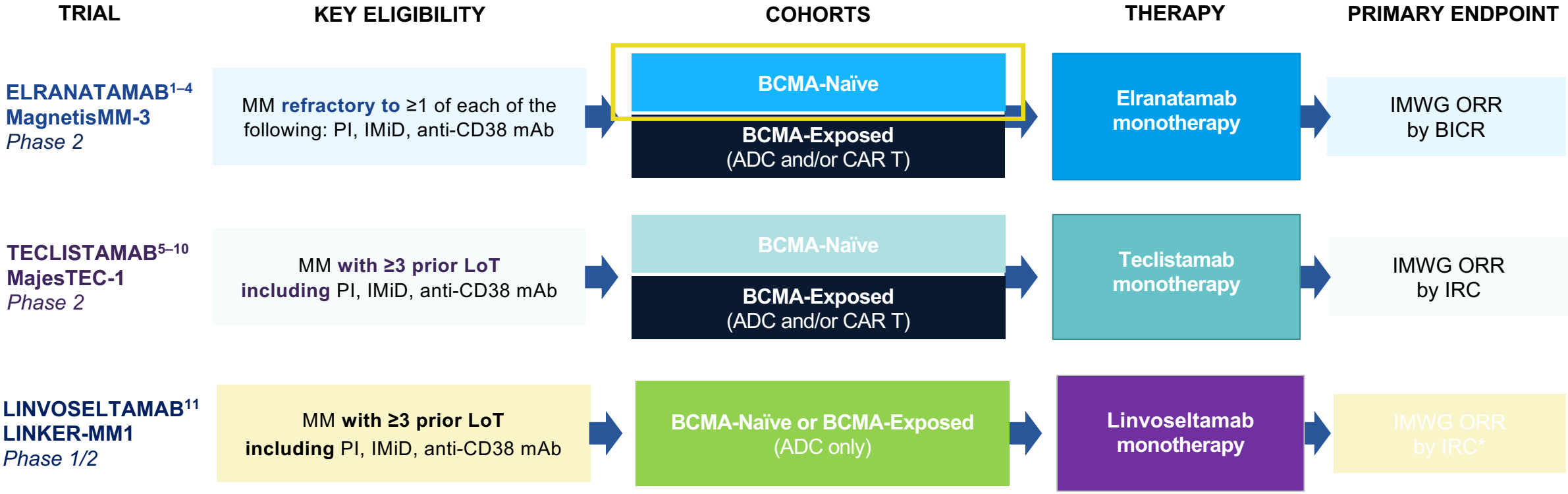
Integrating Bispecific Antibodies into the Management of Relapsed/Refractory Multiple Myeloma

June 1, 2026

Hans Lee, MD
Director, Multiple Myeloma Research
Sarah Cannon Research Institute

BCMA-directed BsAbs for RRMM: Registrational trials



Linvoseltamab is not approved by the EMA

*Primary endpoint for Phase 2 of trial.

ADC, antibody-drug conjugate; BCMA, B-cell maturation antigen; BICR, blinded independent committee review; BsAb, bispecific antibody; CAR T, chimeric antigen receptor T-cell; CD, cluster of differentiation; EMA, European Medicines Agency; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; IRC, independent review committee; LoT, lines of therapy; mAb, monoclonal antibody; MM, multiple myeloma; ORR, overall response rate; PI, proteasome inhibitor.

1. Clinicaltrials.gov. https://clinicaltrials.gov/study/NCT04649359. Accessed 21 August 2024. 2. ELREXFIO™ (elranatamab-bcmm) [prescribing information]. New York, NY. Pfizer Inc; August 2023. 3. ELREXFIO® (elranatamab) Summary of Product Characteristics. Bruxelles Belgium: Pfizer Europe; 2024. 4. ELREXFIO® (elranatamab). Sao Paulo, Brazil: Pfizer Brazil; 2024. 5. Clinicaltrials.gov. https://clinicaltrials.gov/study/NCT04557098. Accessed 21 August 2024. 6. Moreau P et al. *N Engl J Med*. 2022;387:495–505. 7. TECVAYLI® (teclistamab-cqyv) [prescribing information]. Horsham, PA. Janssen Biotech, Inc; February 2024. 8. TECVAYLI® (teclistamab) Summary of Product Characteristics. Beerse Belgium: Janssen-Cilag International; 2024. 9. TECVAYLI™ (teclistamab) Sao Paulo, Brazil: Janssen-Cilag Farmacêutica Ltda; 2024. 10. Touzeau C et al. ASCO 2022. Abstract 8013 (poster presentation). 11. Bumma N et al. *J Clin Oncol.* 2024;42:2702–2712.

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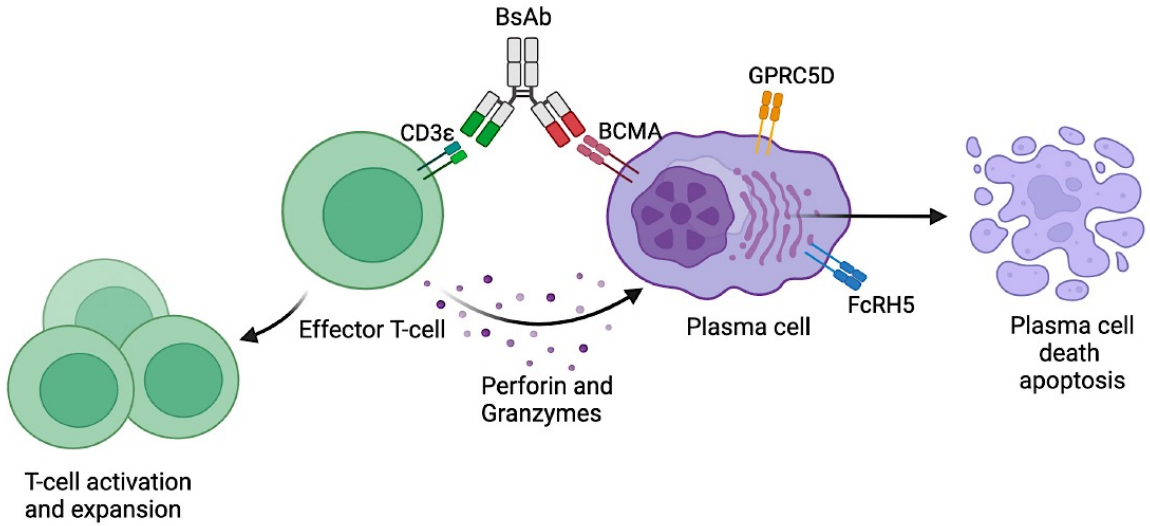
Content Courtesy of Noopur Raje, MD

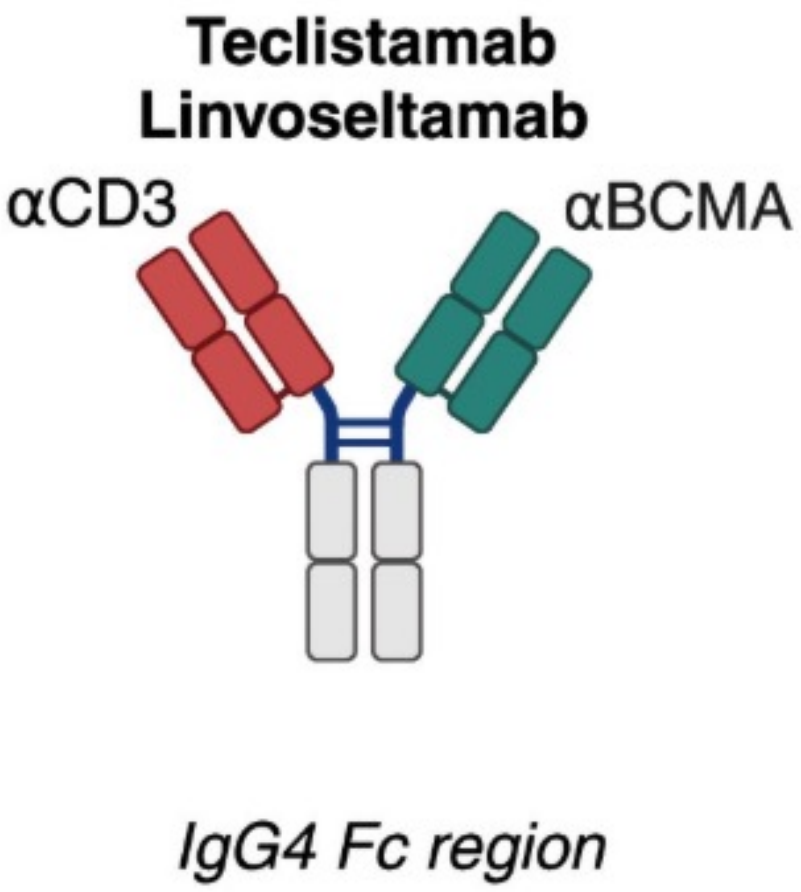
Bispecific Antibody Targets and Mechanism of Action

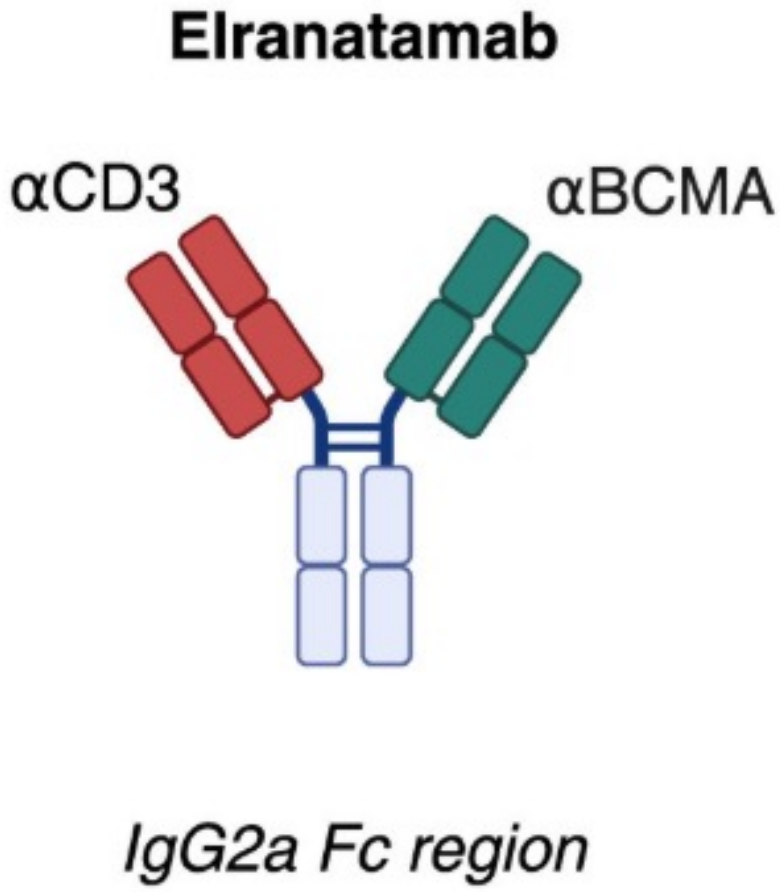


	BCMA	GPRC5D	FcRH5
Expression	Plasma cells, plasmablasts	Plasma cells, hair follicles, eccrine glands, filiform papillae of tongue	B-cell lineage cells, including plasma cells
Biological significance	Survival/growth of plasma cells	Unclear	Unclear
Location	16p13	12p13	1q21
Extracellular shedding?	Yes	No	Yes

Rees M, et al. *Front Immunol*. 2024;15:1424925; Yu B, et al. *J Hematol Oncol.* 2020;13:125; Rodrigueze-Otero P, et al. *Blood Cancer J.* 2024;14:24; Li J, et al. *Cancer Cell.* 2017;31:383-395; Ise T, et al. *Leukemia.* 2007;21:169-174.

BCMA Bispecific T-Cell Antibodies





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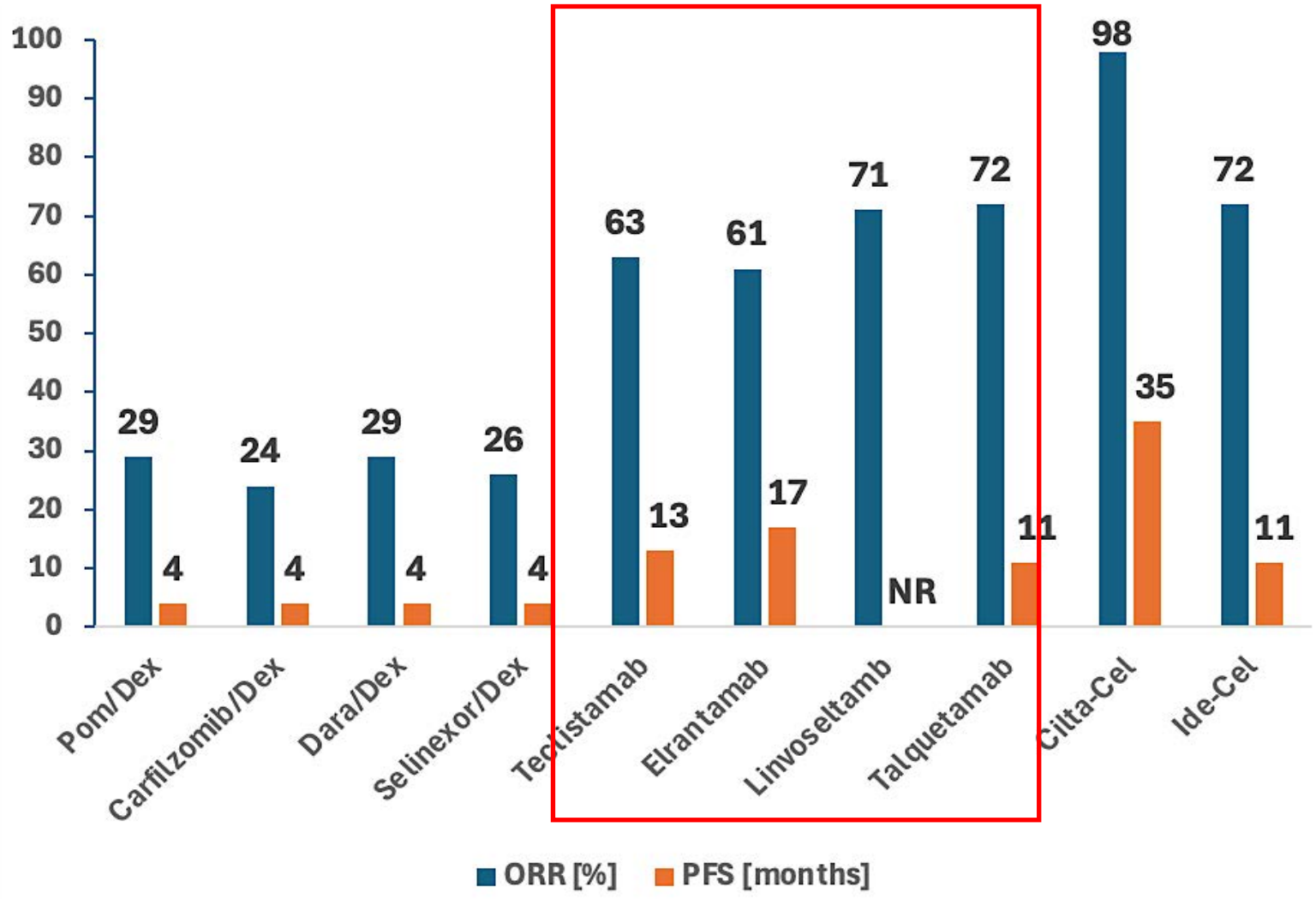
Waldschmidt et al. Clin Lymphoma Myeloma Leuk 2025

Overall Response Rate (ORR) and Progression Free Survival (PFS) of Recently Approved Drugs in Relapsed/Refractory Myeloma



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Moreau P, et al. *N Engl J Med.* 2022;387:495-505; Lesokhin AM, et al. *Nat Med.* 2023;29:2259-2267; Bumma N, et al. *J Clin Oncol.* 2024;42:2702-2712; Chari A, et al. *N Engl J Med.* 2022;12:e269-e281.

BCMA Bispecific T-Cell Antibodies Clinical Data

Drug	N	Route/Schedule	ORR at RP2D or Higher Doses Tested to Date	CRS	Comments
Teclistamab FDA/EC approved, 2022	165	SC q week, then q2 weeks if ≥CR for 6 months	63%, 59% ≥VGPR, N = 165	All grade (72%), grade 2 (21%), grade 3–4 (1%)	Median PFS 11.4 months Median DOR 24 months
Elranatamab FDA/EC approved, 2023	123	SC q week, then q2 weeks after 6 cycles with ≥PR for ≥2 months, then q4 weeks starting week 49	61%, 56% ≥VGPR (76 mg SC, N = 123)	All grade (56%), grade 2 (14%); grade 3–4 (0%)	Median PFS: 17.2 months 18-month DOR: 68.8%
Linvoseltamab FDA/EC approved, 2025	117	IV q week, then q2 weeks starting week 16, then q4 weeks starting week 24 if ≥VGPR	71%, 63% ≥VGPR (200-mg cohort, N = 117)	All grade (46%), grade 2 (10%), grade 3 (1%), (200-mg cohort)	Median DOR: 29.4 months 12-month median PFS: 70%
Ententamig (ABBV-383) (in clinical development)	75	IV q3 (40 mg) or q4 (60 mg) weeks	66%, 54% ≥VGPR (N = 146)	All grade (30%), grade 3–4 (0%)	12-month PFS 55%; 2 BCMA binding domains with attenuated CD3 binding domain

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Garfall A, et al. ASCO 2024. Abstract 7540; Bumma N, et al. *J Clin Oncol.* 2024;42:2702-2712; Lesokhin A, et al. *Nat Med.* 2023;29:2259-2267; Tomasson M, et al. ASH 2023. Abstract 3385; Baljevic M, et al. ASCO 2025. Abstract 7527.

MajesTEC-3: Teclistamab + Dara vs. SOC in RRMM

Key inclusion criteria

- RRMM
- 1-3 prior LOTs including a PI and lenalidomide
  - Patients with only 1 prior LOT must have been lenalidomide refractory per IMWG criteria
- ECOG PS score of 0-2

Key exclusion criteria

- Prior BCMA-directed therapy
- Refractory to anti-CD38 mAbs[a]

1:1 randomization N=587

22 Oct 2021 to 29 Sept 2023[b]

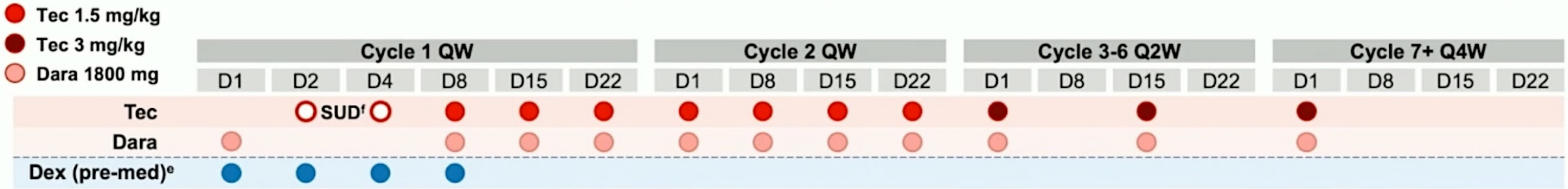
Tec-Dara
N=291
SC dosing following Dara schedule

DPd/DVd
N=296 (91% DPd)
by investigator's choice[c]

Primary endpoint
- PFS per IRC

Key secondary endpoints
- ≥CR[d] and ORR[d]
- MRD negativity (10^{-5})
- OS
- MySIm-Q Total Symptom score

Other secondary endpoints
- Safety
- PK and immunogenicity



SC dosing aligned with Dara schedule, with monthly dosing after 6 cycles; steroid sparing after Cycle 1 Day 8

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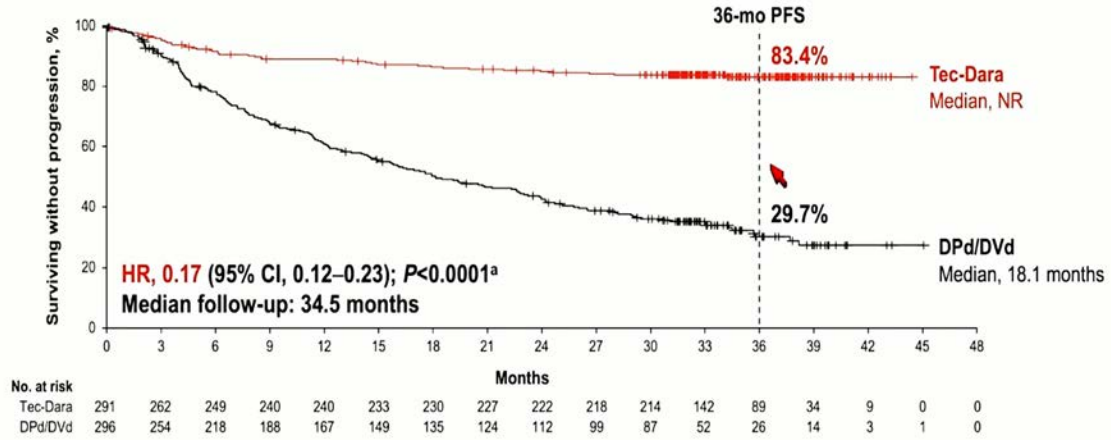
Mateos et al, *Blood* 2025; 146 (Supplement 2): 94.

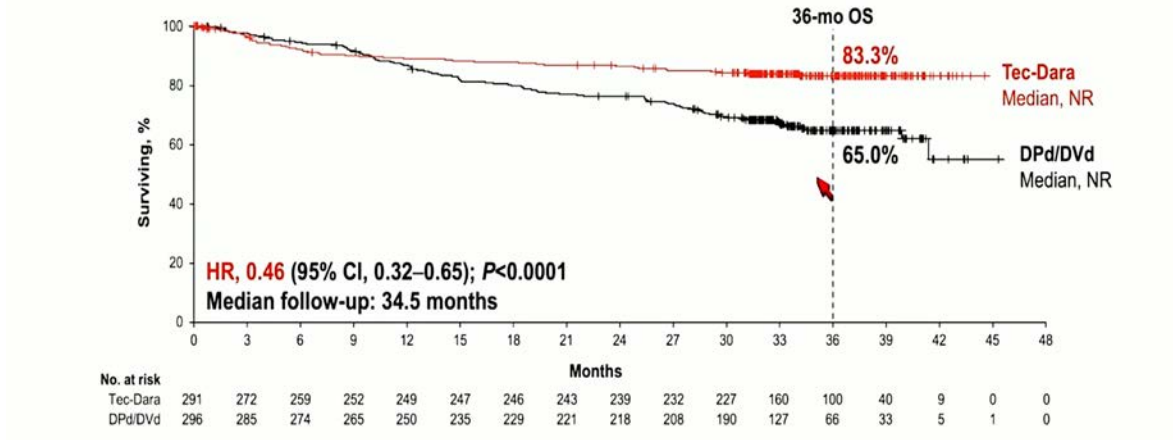
MajesTEC-3: Teclistamab + Daratumumab vs. Standard Therapies (1-3 prior lines of therapy)

MajesTEC-3: PFS (Primary Endpoint)



Tec-Dara significantly improved PFS, with a plateauing curve after ~6 months and >90% of patients progression-free at 6 months sustaining such a benefit at 3 years

MajesTEC-3: OS



Tec-Dara significantly improved OS versus DPd/DVd, with 83% of patients alive at 3 years

Teclistamab + Daratumumab combination significant longer survival compared to conventional therapies!

FDA Approved on March 5, 2026

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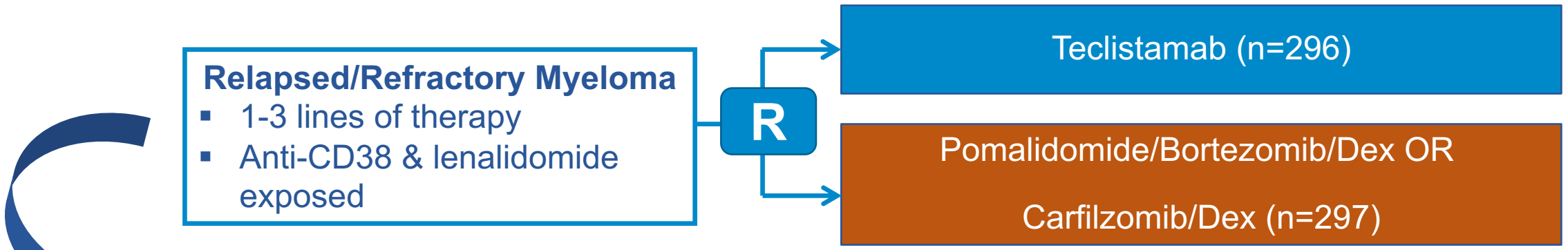
Ho et al, *ASH* 2025

MajesTEC-9: Teclistamab vs Standard Therapies (1-3 prior lines of therapy)



Len refractory: 80%
anti-CD38 refractory: 85%

Efficacy Tec vs. SOC
- **≥ CR rate:** 65.9% vs 16.8%; *P*<0.0001
- **Median PFS:** NR vs 8.2 months; HR 0.29
- **18-month PFS**: 69.8% vs 26.9%
- **Significant OS** benefit of Tec vs SOC; HR 0.60

Safety (Tec vs. SOC)
- Gr≥3 TEAEs: 85% vs 76%
- Gr≥3 Infections: 42% vs 29%

Tec arm:
- CRS: 66% (G1/2 48.8% and 16.5%)
- ICANS: 4%

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Mina et al. *ASCO Annual Meeting.* 2026.

MagnetisMM-5: Elranatamab vs. Dara/Pom/Dex (≥ 1 line of prior therapy)

PRESS RELEASE on April 29, 2026

- Primary endpoint met at the interim analysis in MagnetisMM-5 trial with significant improvement in progression-free survival with elranatamab monotherapy
- Trial remains ongoing to assess overall survival (key secondary endpoint), which was not yet mature at the time of interim analysis

https://www.pfizer.com/news/press-release/press-release-detail/pfizers-elrexfio-significantly-improves-progression-free

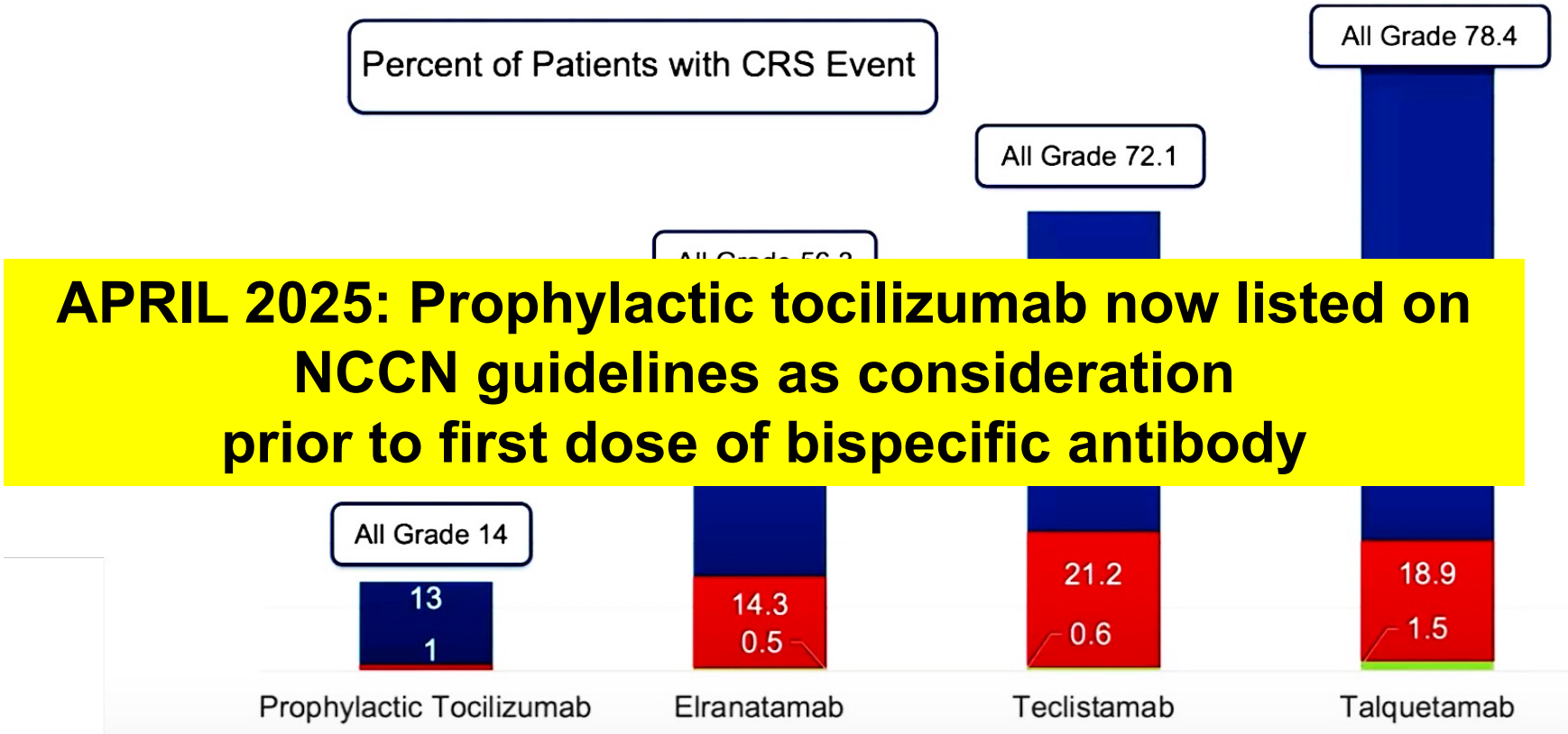
BCMA Bispecific Step-up Dosing Comparison

	Teclistamab	Elranatamab	Linvoseltamab
Step-up dosing (SUD) schedule	Day 1: 0.06 mg/kg Day 4: 0.3 mg/kg Day 7: 1.5 mg/kg	Day 1: 12 mg Day 4: 32 mg Day 8: 76 mg	Day 1: 5 mg Day 8: 25 mg Day 15: 200 mg
Recommended Hospitalization	48-hours after each SUD1, SUD2, SUD3	48 hours after SUD1 24 hours after SUD2	24 hours after SUD1 and SUD2
Subsequent dosing	1.5 mg/kg one week after first treatment dose and weekly thereafter	76 mg one week after first treatment dose and weekly through week 24; week 25 and every 2 weeks through week 48, week 49 and every 4 weeks thereafter	200 mg one week after day 15 and once weekly from week 4 to 13 for 10 doses

Hospitalization requirements can limit access to bispecifics!

teclistamab US PI; elranatamab US PI; linvoseltamab US PI

Tocilizumab Prophylaxis with Bispecific Step-up Dosing



APRIL 2025: Prophylactic tocilizumab now listed on NCCN guidelines as consideration prior to first dose of bispecific antibody

Prophylactic tocilizumab significantly reduces rates of CRS

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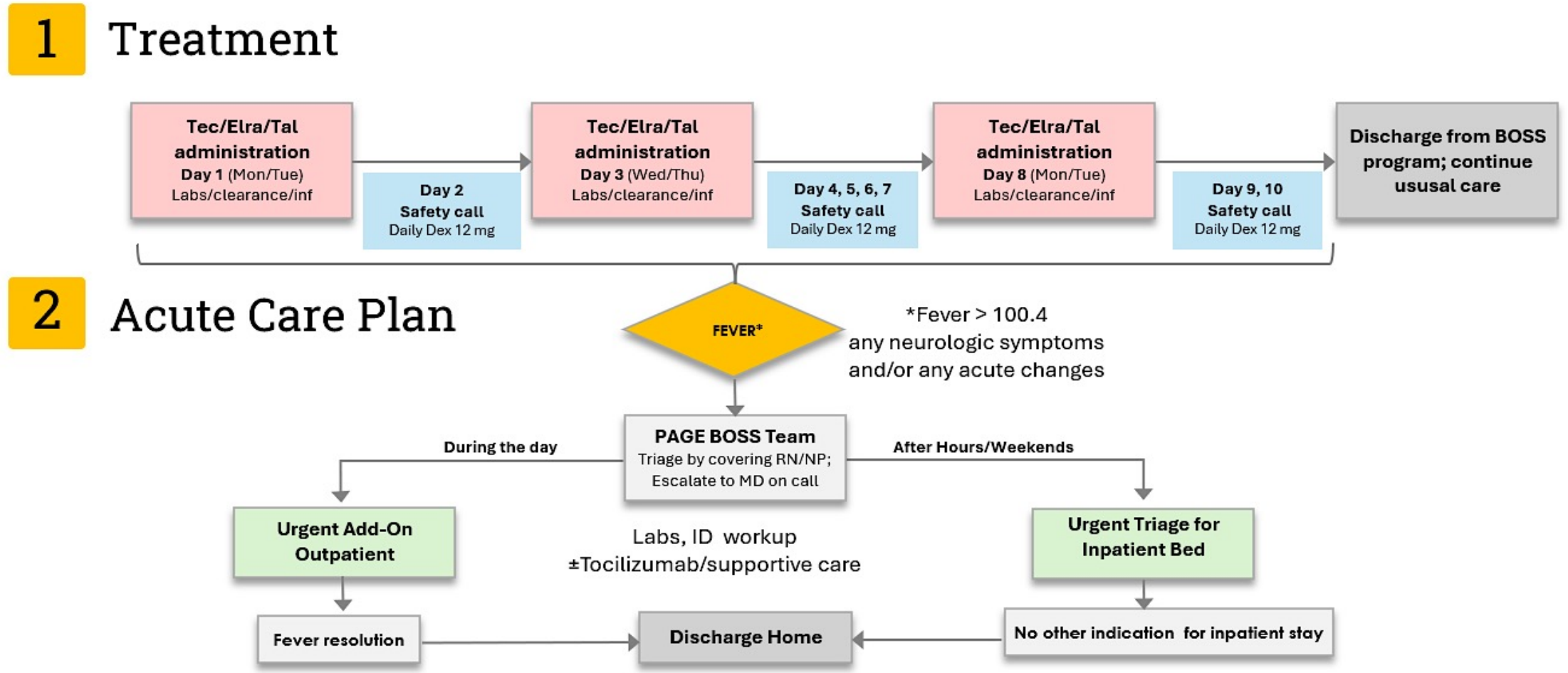
Kowalski A. et al., *ASH 2024*, Abstract 932; Kowalski A et al, *Blood Advances*, 2025

BISPECIFIC OUTPATIENT STEP-UP DOSING WITH PROPHYLACTIC DEXAMETHASONE: THE BOSS PROGRAM EXPERIENCE at MGH



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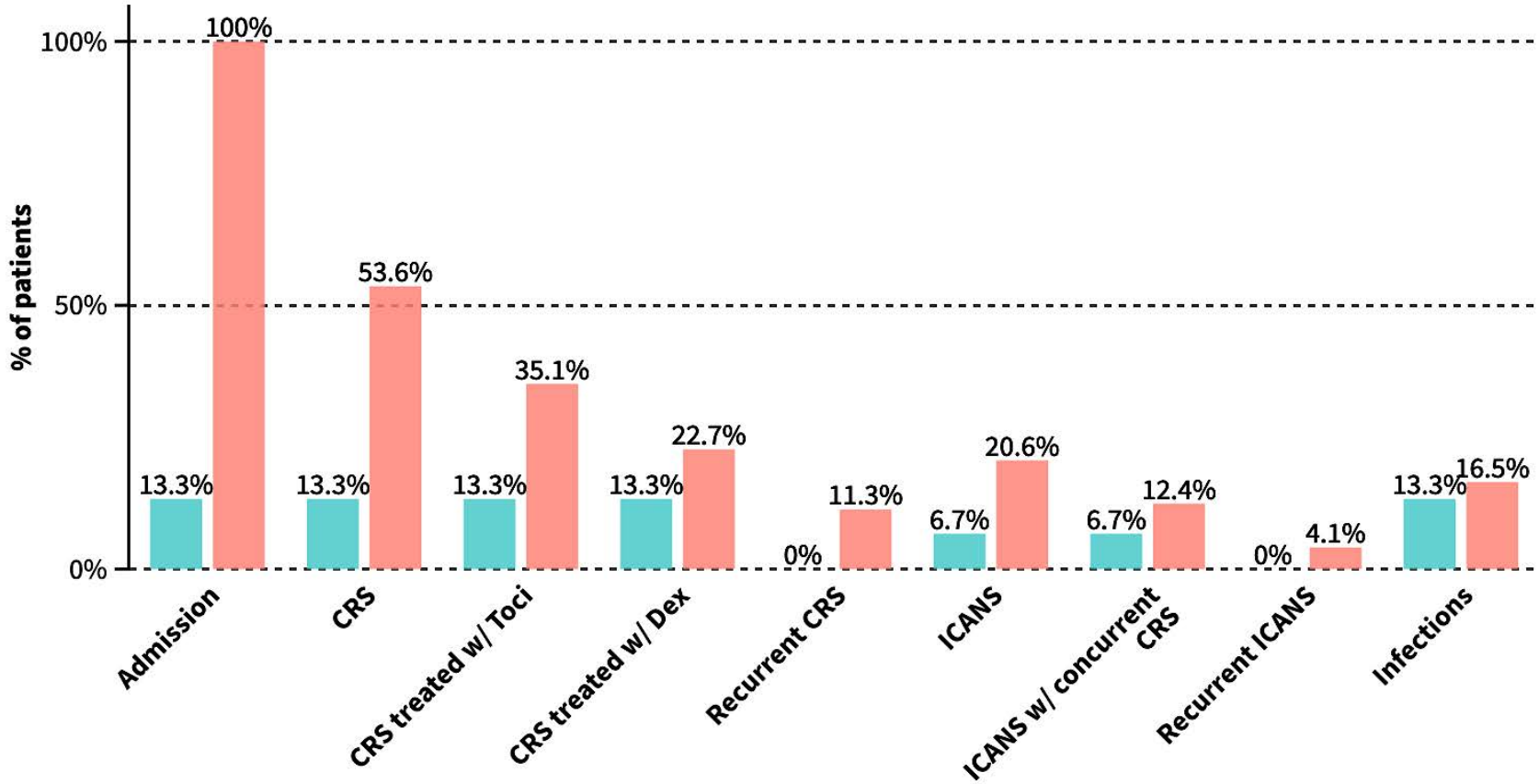
Cirstea et al IMS 2025

Toxicities and Management Among BOSS and iSUD Cohorts



Abbreviations: BOSS, bispecific outpatient safe step-up; iSUD, inpatient step-up dosing; CRS, cytokine release syndrome; ICANS, Immune effector cell-associated neurotoxicity syndrome; Toci, tocilizumab; Dex, dexamethasone

Figure 1: Grouped column chart illustrating percentage of patients experiencing CRS, ICANS, recurrent events, requiring admission or treatment with tocilizumab or dexamethasone across BOSS (n=15) and iSUD (n=97) cohorts

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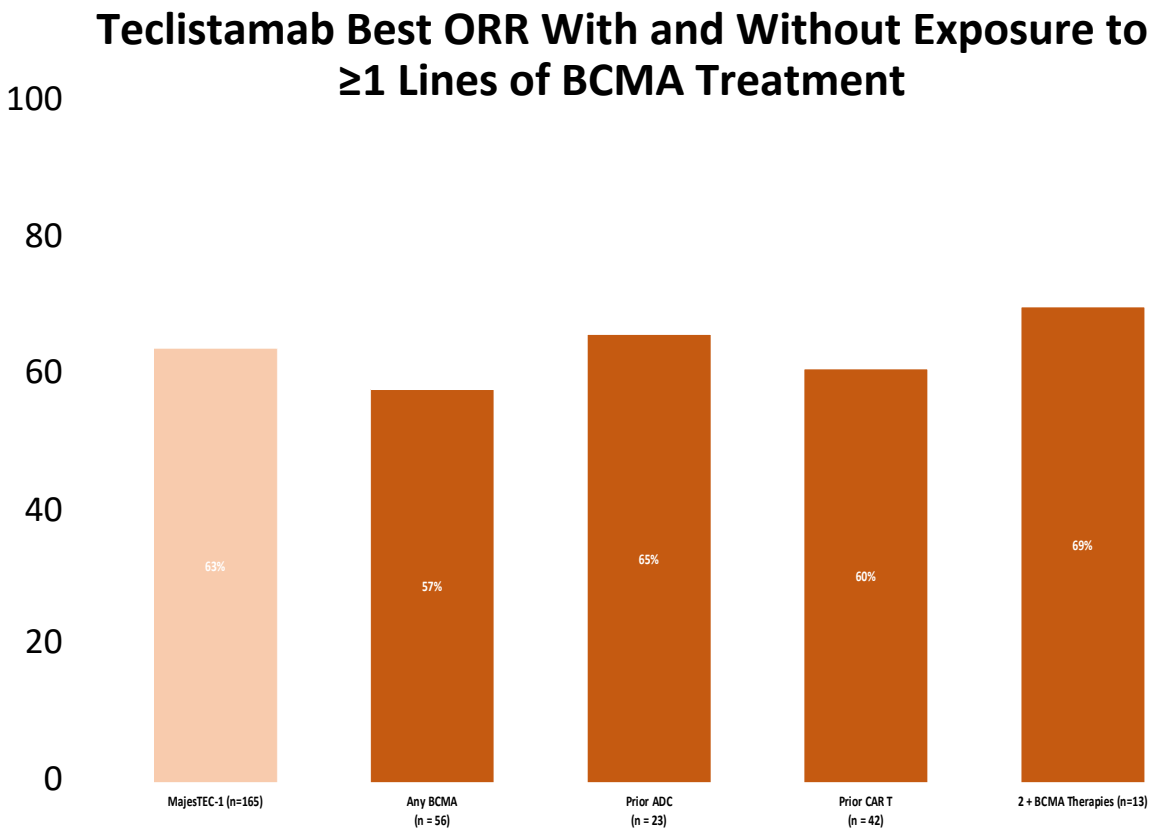
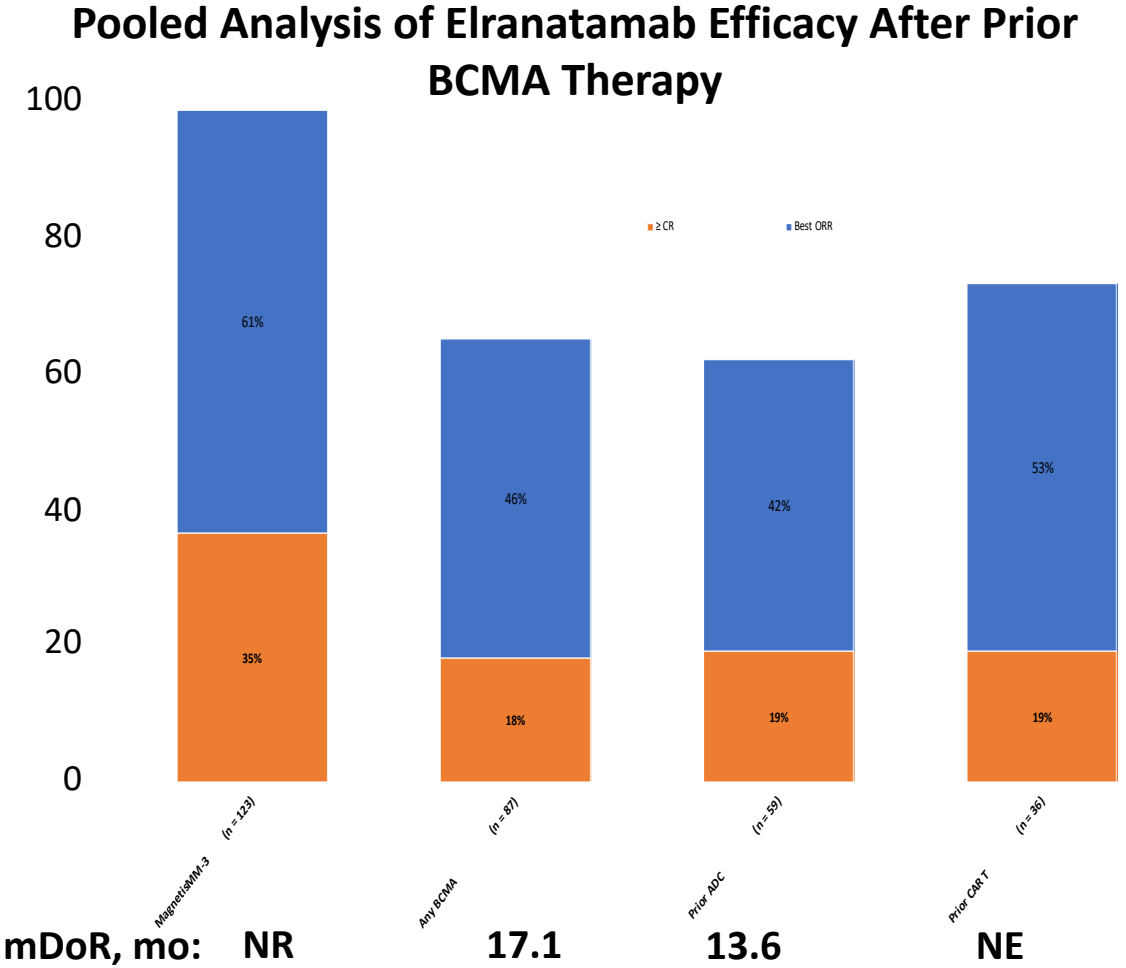
Content Courtesy of Noopur Raje, MD

Outcomes With Bispecific Antibodies After Prior BCMA-Directed Therapy





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Moreau. NEJM. 2022;387:495. Dima. ASH 2023. Abstr 91.
Lesokhin. Nat Med. 2023;29;2259-2267. Nooka. ASCO 2023. Abstr 8008.

Content Courtesy of Noopur Raje, MD

Non-BCMA Bispecific T-Cell Antibodies in Clinical Development

Drug	N	Route/Schedule	ORR at RP2D or Higher Doses Tested to Date	CRS	Comments
Talquetamab (GPRC5D × CD3) **FDA approved August 2023**	74	SC q week SC q2 weeks	74%, 59% ≥VGPR (0.4 mg/kg q week, N = 143) 73%, 57% ≥VGPR (0.8 mg/kg q2 weeks, N = 145)	79% all grade, 2% grade 3–4 (0.4 mg/kg q week, N = 143) 72% all grade, 1% grade 3–4 (0.8 mg//kg q2 weeks, N = 145)	Other unique AEs: dysgeusia, skin exfoliation, nail disorders
Cevostamab (FcRH5 × CD3)	16 7	IV q3 weeks × 17 cycles **(fixed duration)**	43% (160-mg target dose) No prior BCMA: 61% Prior BCMA: 30%	All grade (74%) grade 3–4 (2%)	57% prior BCMA 24% prior bispecific

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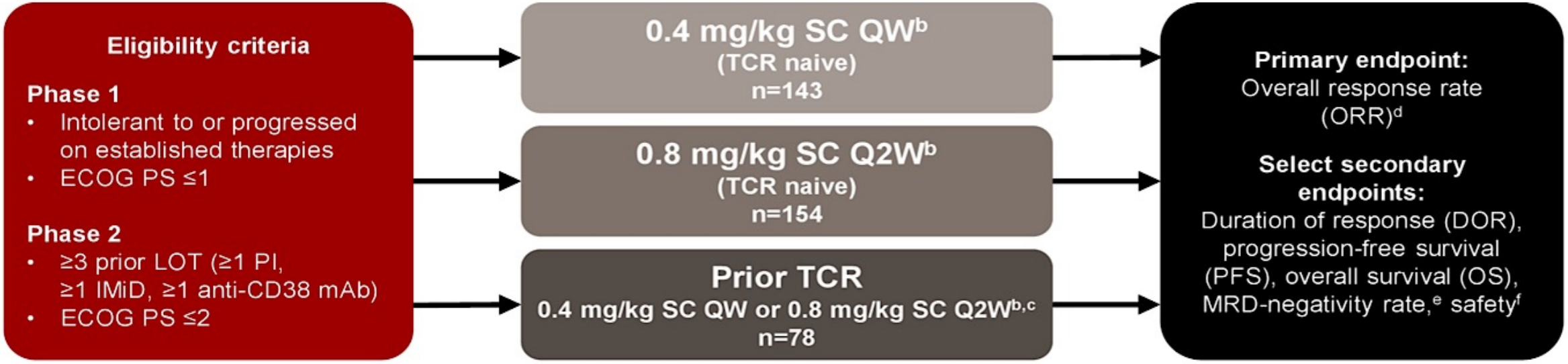
Chari A, et al. *N Engl J Med.* 2019;381:727-738; Chari A, et al. ASH 2022; Richter et al. ASH 2024.

Phase I/II MonumenTAL-1 Study: Design



As of Sept 2024, 17, 27, and 18 patients remained on talquetamab in the QW, Q2W, and prior TCR QW and Q2W cohorts, respectively. All were responders (≥VGPR, most ≥CR), and 2 subsequently progressed during this time

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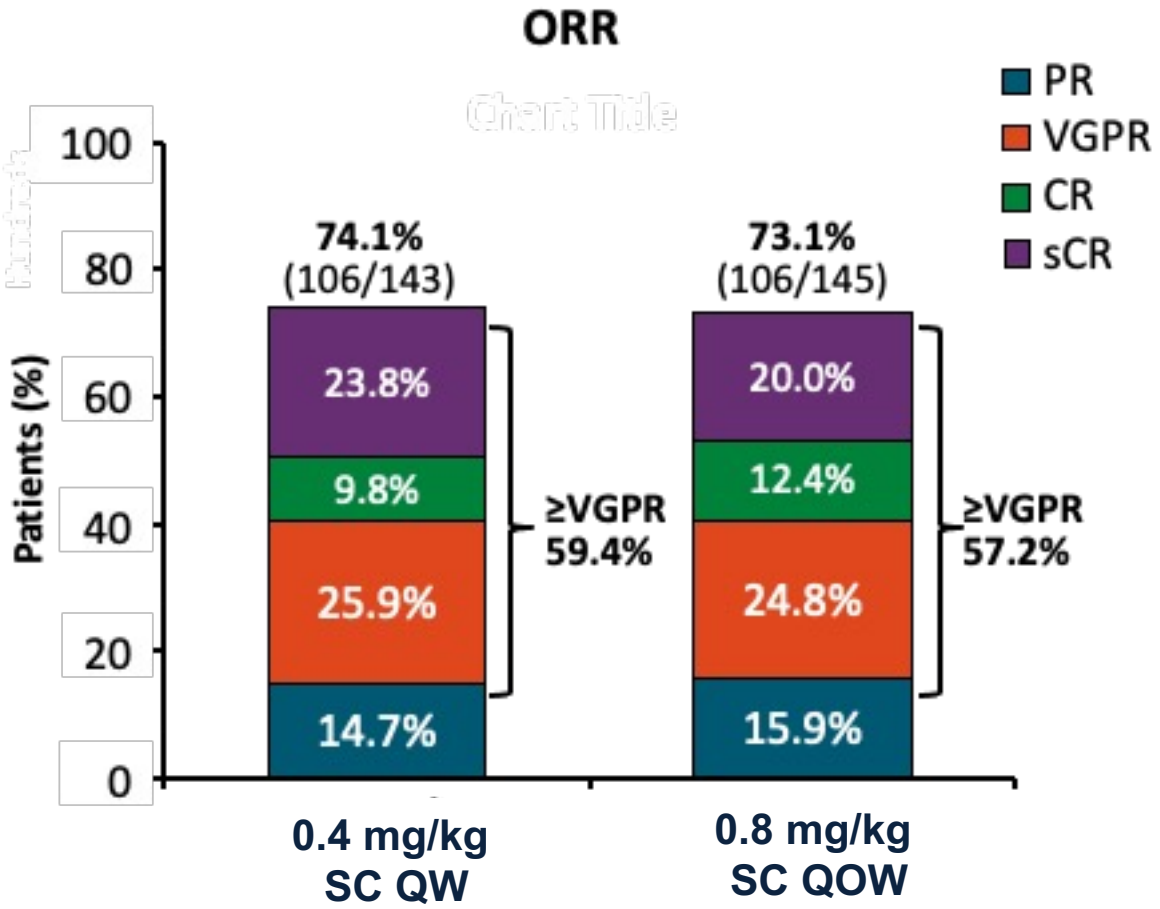
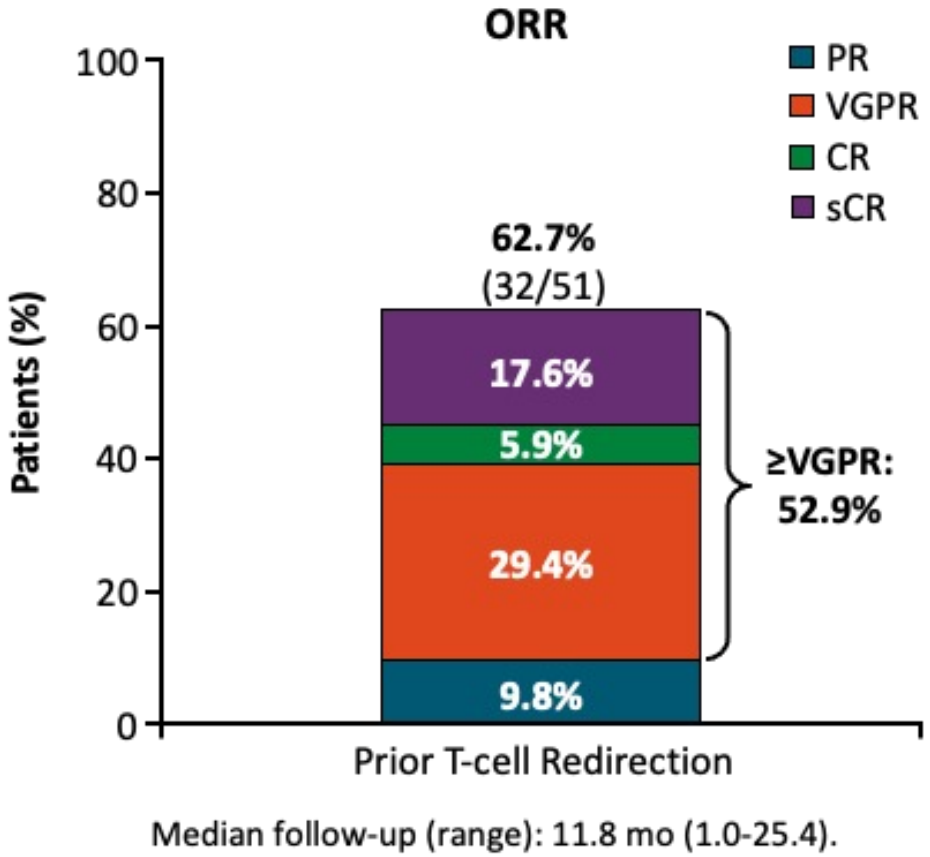
Content Courtesy of Noopur Raje, MD

Rasche L et al. ASCO 2025

Talquetamab (MonumenTAL-1) – Efficacy





Median follow-up (range): 11.8 mo (1.0-25.4).

71% received CAR T therapy, 35% received a BsAb, and 6% received both

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Chari A, et al. ASH 2022; Chari A, et al. *N Engl J Med.* 2019;381:727-738.

Phase I/II MonumenTAL-1 Study: Additional Efficacy Outcomes*

Outcome	QW (n=100)	Q2W (n=90)	Prior TCR QW and Q2W[a] (n=58)
ORR, %	73.0	71.1	72.4
≥CR	35.0	43.3	50.0
VGPR	22.0	17.8	8.6
PR	16.0	10.0	13.8
Median time to best response of ≥CR,[b] mo (range)	2.27 (1.1–12.7)	6.24 (1.2–16.8)	2.66 (1.2–17.5)
Median time to best response of VGPR,[c] mo (range)	1.97 (1.1–6.2)	3.06 (0.3–18.9)	2.04 (1.2–2.1)
Median time to best response of PR,[d] mo (range)	1.28 (1.1–2.9)	2.07 (1.2–2.8)	1.13 (1.1–3.0)
Median DOR, mo (95% CI)[e]	10.2 (6.6–15.7)	17.9 (12.5–26.0)	19.2 (6.7–NE)
≥CR[b]	28.8 (18.9–NE)	26.1 (18.0–NE)	24.7 (19.2–NE)
VGPR[c]	6.4 (4.4–9.5)	9.3 (7.4–15.2)	4.8 (2.1–NE)
PR[d]	3.0 (1.9–5.6)	5.5 (0.9–6.5)	2.4 (1.9–4.6)
Median PFS (95% CI), mo	6.8 (5.5–10.4)	12.4 (9.6–18.2)	11.3 (4.8–21.4)
36-mo PFS, %	17.6 (10.7–26.0)	NE (NE–NE)	28.2 (16.0–41.7)
Median OS (95% CI), mo	NR (21.7–NE)	NR (33.2–NE)	30.6 (20.2–NE)
36-mo OS, %	50.5 (40.0–60.0)	NE (NE–NE)	46.4 (29.2–61.9)

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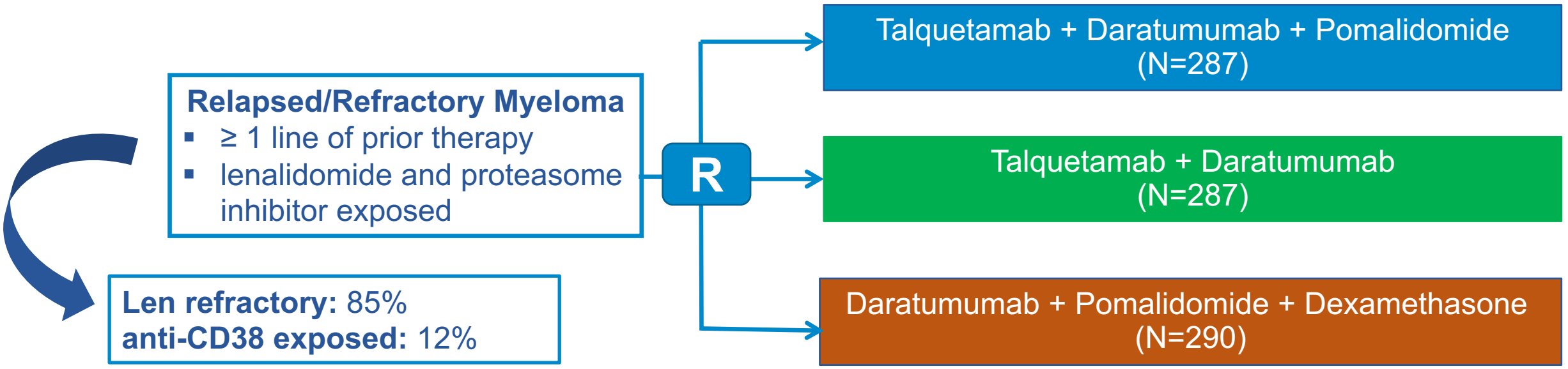
Content Courtesy of Noopur Raje, MD

Data reported from phase 2 only*
Rasche L et al. ASCO 2025

Phase I/II MonumenTAL-1 Study: AEs

AE (≥30% in any cohort), n (%)	QW (n=143)		Q2W (n=154)		Prior TCR QW and Q2W (n=78)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Hematologic AE						
Anemia	65 (45.5)	46 (32.2)	67 (43.5)	39 (25.3)	38 (48.7)	22 (28.2)
Neutropenia	50 (35.0)	44 (30.8)	44 (28.6)	33 (21.4)	40 (51.3)	37 (47.4)
Thrombocytopenia	39 (27.3)	29 (20.3)	46 (29.9)	28 (18.2)	30 (38.5)	22 (28.2)
Nonhematologic AE						
CRS	113 (79.0)	3 (2.1)	116 (75.3)	1 (0.6)	57 (73.1)	1 (1.3)
Dysgeusia[a]	103 (72.0)	NA	111 (72.1)	NA	59 (75.6)	NA
Infections[b]	87 (60.8)	33 (23.1)	109 (70.8)	33 (21.4)	61 (78.2)	20 (25.6)
Skin related[c]	85 (59.4)	0	113 (73.4)	1 (0.6)	53 (67.9)	0
Nail related[d]	80 (55.9)	0	84 (54.5)	0	47 (60.3)	0
Weight decreased	59 (41.3)	3 (2.1)	64 (41.6)	9 (5.8)	29 (37.2)	1 (1.3)
Rash related[e]	57 (39.9)	2 (1.4)	48 (31.2)	8 (5.2)	25 (32.1)	2 (2.6)
Pyrexia	57 (39.9)	4 (2.8)	44 (28.6)	2 (1.3)	27 (34.6)	0
Dry mouth	38 (26.6)	0	60 (39.0)	0	34 (43.6)	0
Fatigue	36 (25.2)	5 (3.5)	44 (28.6)	1 (0.6)	25 (32.1)	1 (1.3)

MONUMENTAL-3: Tal + Dara + Pom vs. Tal + Dara vs. Dara + Pom + Dex



Efficacy: Tal/Dara/Pom vs. Tal/Dara vs. Dara/Pom/Dex

- **MRD neg ≥ CR rate:** 52.3% vs. 46.3% vs. 15.9%
- **Significant PFS** benefit of Tal/Dara/Pom and Tal/Dara vs Dara/Pom/Dex; HRs 0.28 and 0.33, respectively
- **24-month PFS**: 81.3% vs 77.6% vs. 51.2%.

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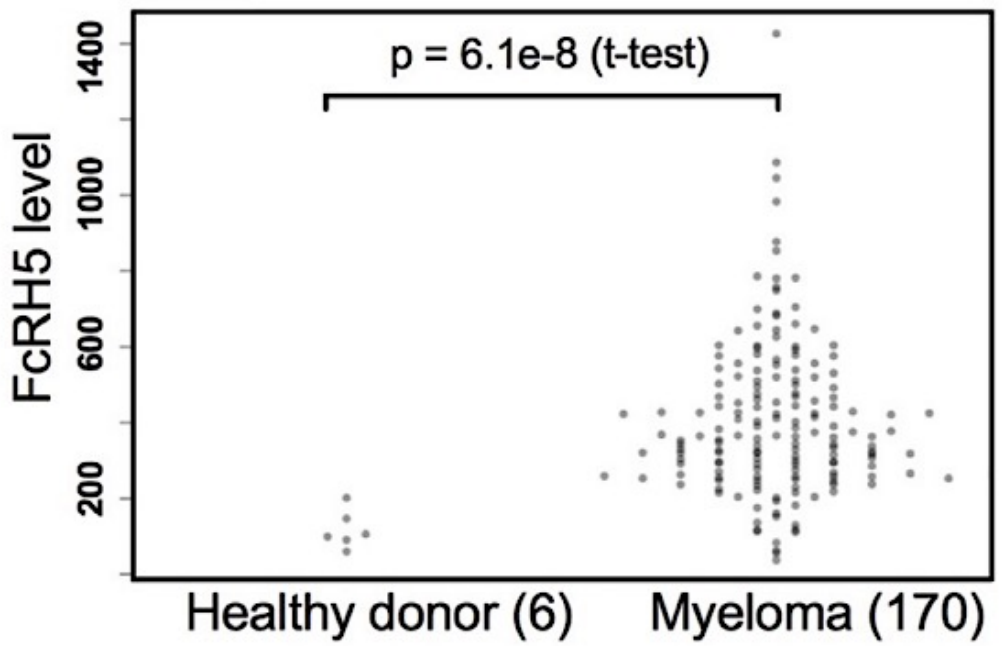
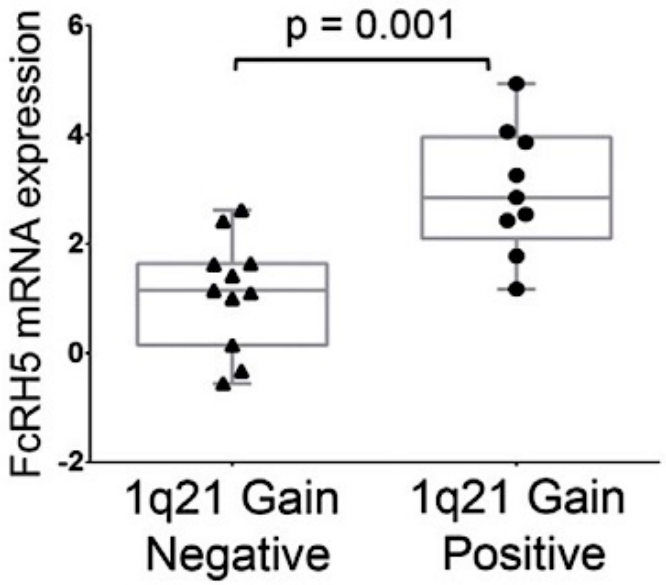
Voorhees et al. *EHA*. 2026.

FcRH5 as a Target in Multiple Myeloma





- Fc receptor-homolog 5 (FcRH5) located in the chromosomal breakpoint in 1q21
- Increased and near exclusive expression on B cells and plasma cells
- Increased expression in +1q21 multiple myeloma

Li et al, Cancer Cell, 2017

CAMMA 1: Randomized dose-expansion of cevostamab, pomalidomide, and dexamethasone

Patients

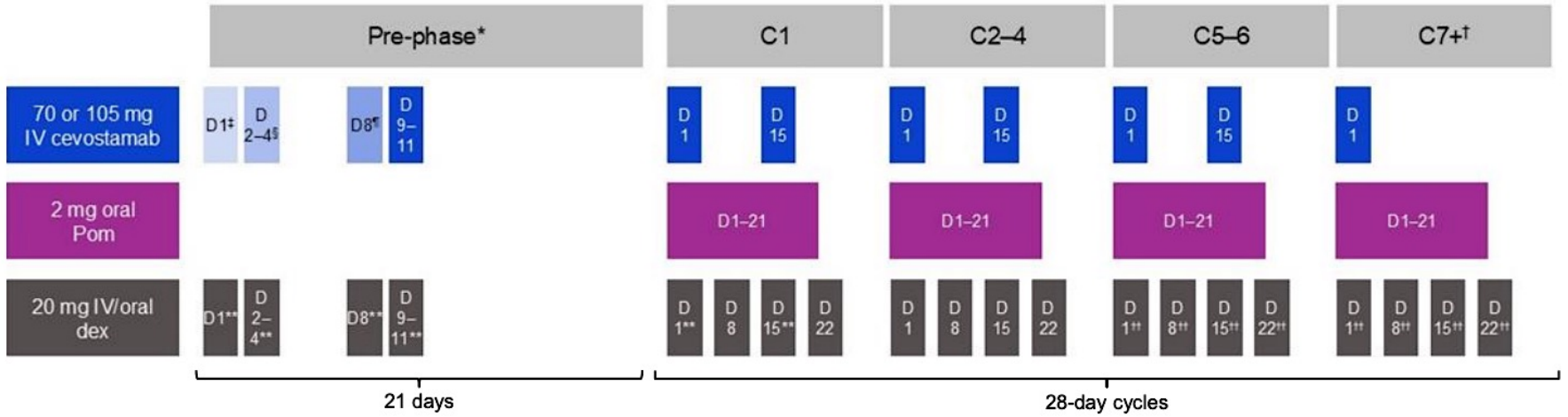
- RRMM with ≥1 prior line including an IMiD and a PI
- Pom-refractory patients excluded

Objectives

- **Primary**: Safety and tolerability, RP2D
- **Secondary**: PK, PD, anti-tumour activity

Arm B3E randomised dose-expansion schedule **(triple step-up dosing)**

- Subsequent expansion cohort with limited follow-up
- Patients randomised 1:1 to 70 mg or 105 mg cevostamab target dose
- Cevostamab initiated with **triple step-up dosing** (0.3/1.2/3.6 mg)



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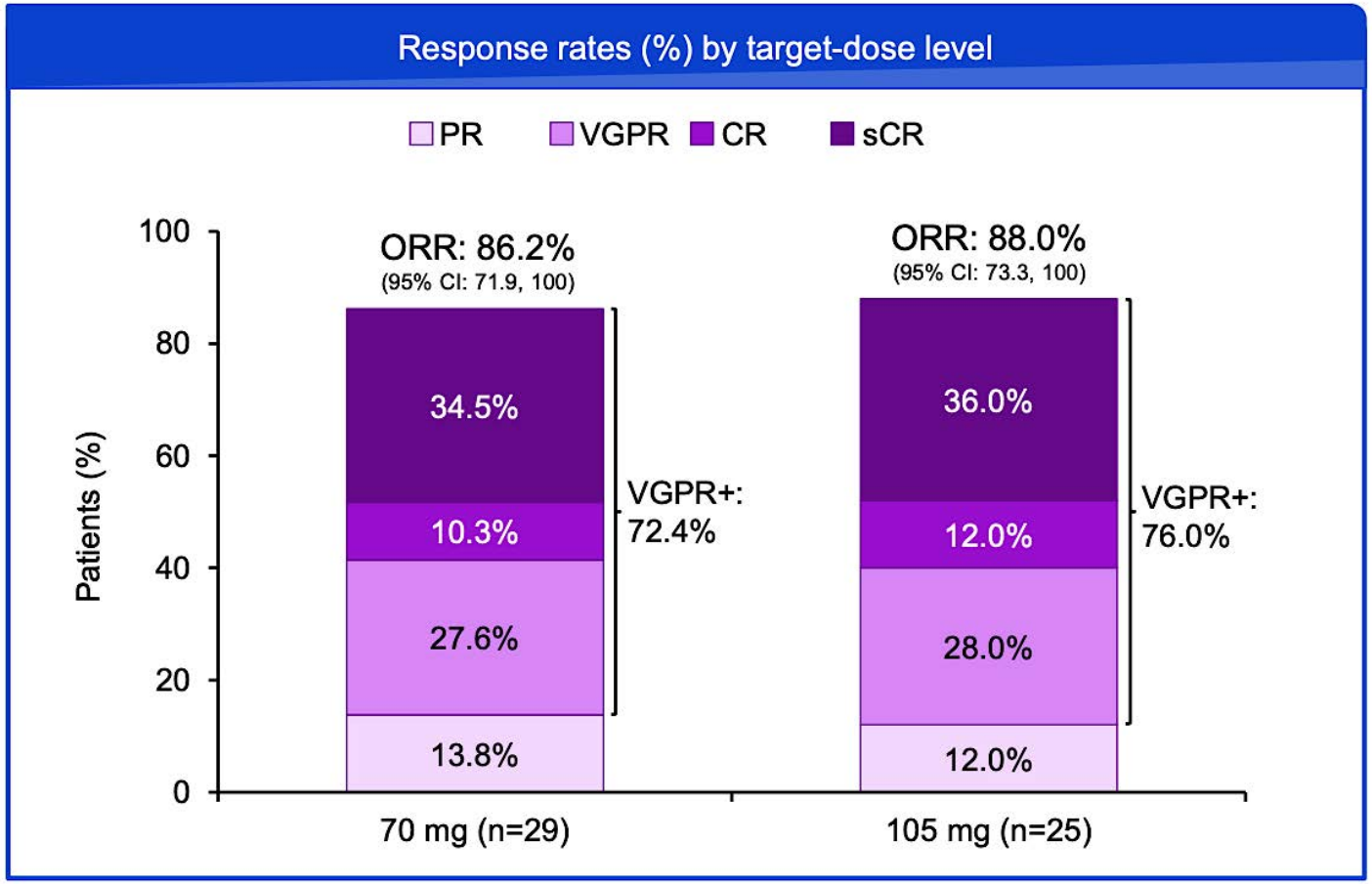
Mian et al, *IMS* 2025

CAMMA 1: Randomized dose-expansion of cevostamab, pomalidomide, and dexamethasone



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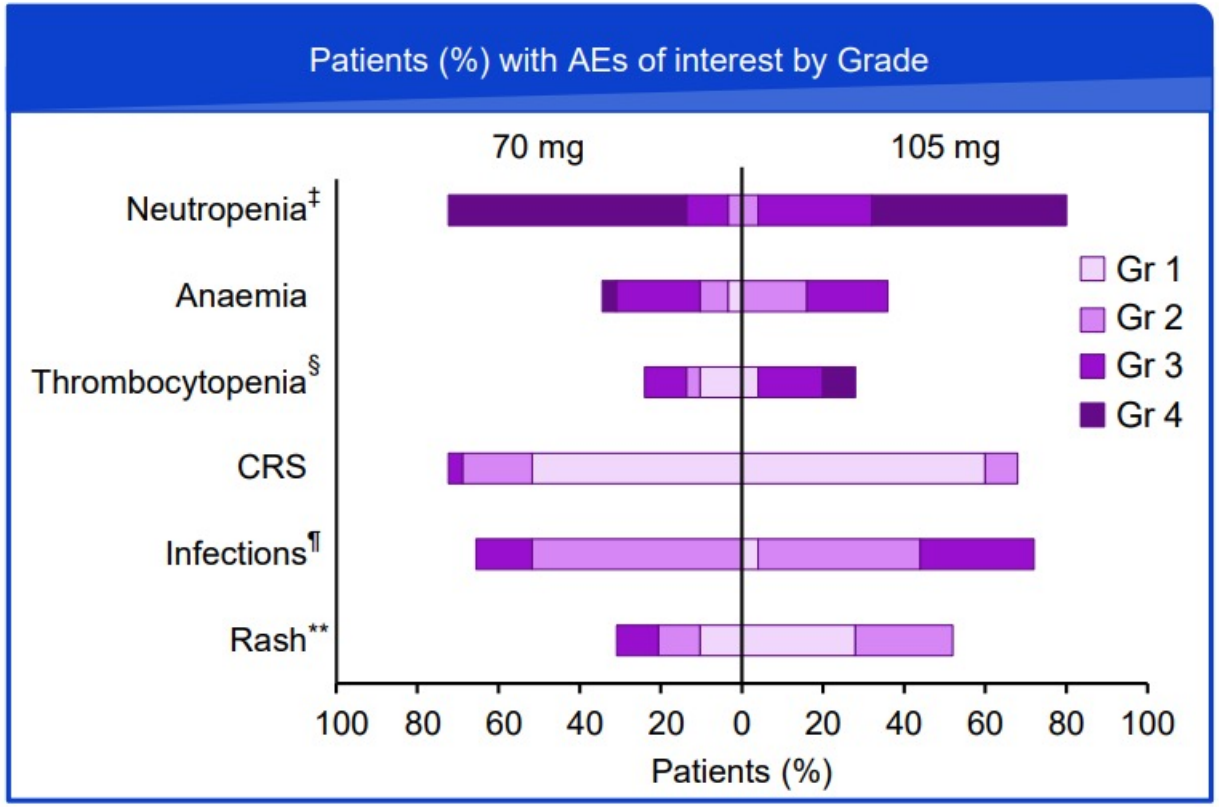
Mian et al, *IMS* 2025

CAMMA 1: Safety summary by target dose level

n (%) unless stated	70 mg (N=29)	105 mg (N=25)
Median time on study, months (range)	10.4 (6.3–15.5)	8.3 (3.3–15.7)
AE	29 (100)	25 (100)
Gr 3–4 AE	26 (89.7)	24 (96.0)
SAE	16 (55.2)	15 (60.0)
Gr 5 (fatal) AE excluding PD	0	1 (4.0)
AE leading to discontinuation		
Cevostamab	1 (3.4)*	1 (4.0)†
Pom	6 (20.7)	6 (24.0)
Dex	0	2 (8.0)



Reversible cytopenias, CRS, infections and rash were frequently reported and were frequently managed with dose delays. AEs leading to discontinuation of cevostamab were infrequent.

Data cut-off: 11 June 2025; *clear cell renal cell carcinoma; †diffuse large B-cell lymphoma; ‡group term: neutropenia, neutrophil count decreased, febrile neutropenia; §group term: thrombocytopenia, platelet count decreased; ¶MedDRA System Organ Class Infections and Infestations; **MedDRA high-level terms: rashes, eruptions and exanthems NEC, exfoliative conditions, dermatitis ascribed to specific agent, acnes, dermatitis and eczema, bullous conditions; AE, adverse event; Gr, Grade; SAE, serious AE.

Mian et al, *IMS* 2025

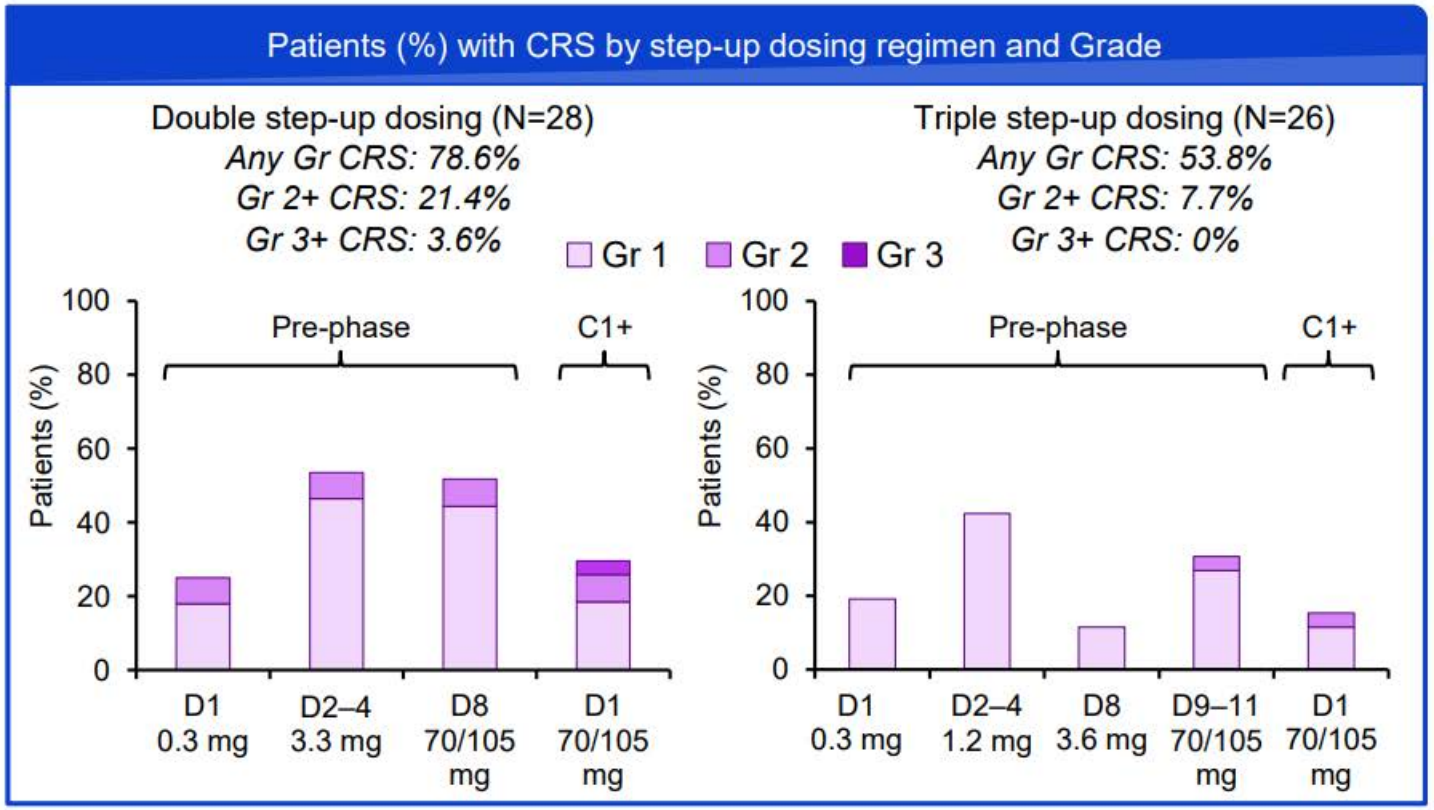
CAMMA 1: Infection summary by target dose level

n (%)	70 mg (N=29)	105 mg (N=25)
AE of infection*†	19 (65.5)	18 (72.0)
URTI	8 (27.6)	4 (16.0)
Pneumonia	3 (10.3)	4 (16.0)
COVID-19	3 (10.3)	2 (8.0)
UTI	2 (6.9)	3 (12.0)
Rhinitis	3 (10.3)	0
Gr 3–4 AE of infection†	4 (13.8)‡	7 (28.0)‡
SAE of infection†	5 (17.2)	9 (36.0)
Gr 5 (fatal) AE of infection†	0	0
AE of infection† leading to discontinuation of cevostamab, pom or dex	0	0
Ig administration	18 (62.1)	17 (68.0)

No Gr 4+ AEs of infection occurred and no AE of infection led to discontinuation of cevostamab, pom or dex

Data cut-off: 11 June 2025; *MedDRA System Organ Class Infections and Infestations; †MedDRA Preferred Terms in ≥3 patients at either target-dose level; ‡all Gr 3; Ig, immunoglobulin; URTI, upper respiratory tract infection; UTI, urinary tract infection.

CAMMA 1: CRS by step-up dosing regimen



n (%) of patients with CRS medication	Double step-up dosing (N=28)	Triple step-up dosing (N=26)
Tocilizumab	10 (35.7)	2 (7.7)
Corticosteroids	12 (42.9)	1 (3.8)
Tocilizumab and corticosteroids	6 (21.4)	1 (3.8)

<10% Gr 2+ CRS and <10% tocilizumab use with the triple step-up dosing regimen

Data cut-off: 11 June 2025.

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Mian et al, *IMS* 2025

CAMMA 1: Randomized dose-expansion of cevostamab, pomalidomide, and dexamethasone

Randomized Phase 3 ”CEVOLUTION” study to start in 2026 (NCT07555938)

- RRMM with 1-3 prior lines of therapy and prior anti-CD38 & lenalidomide exposure
- Cevostamab, pomalidomide, dexamethasone vs. SOC investigator’s choice (dara/pom/dex, elo/pom/dex or carfilzomib/dex)
- **Primary end points:** MRD neg CR at 9 months and PFS

Mian et al, *IMS* 2025

Myeloma Bispecific Antibody Summary

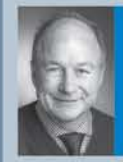
- Bispecific antibodies represent a highly effective accessible “off-the-shelf” approach for the treatment of relapsed/refractory myeloma
- Multiple clinically validated targets (BCMA, GPRC5D, FCRH5)
- Randomized phase 3 studies reported to-date with BCMA and GPRC5D bispecific antibodies showing unprecedented results in early relapsed/refractory myeloma (≥ 1 line of prior therapy).
- Side effect profile manageable so that most patients can receive them
- Will form backbone of treatments across the myeloma disease spectrum for the foreseeable future

Regulatory and reimbursement issues aside, which next line of therapy would you most likely recommend for an 80-year-old patient with standard-risk MM who received initial treatment with Rd/daratumumab and experienced disease progression after 5 years of maintenance therapy?

 Dr Alsina	Teclistamab/daratumumab
 Dr Lee	Teclistamab
 Dr Lonial	Teclistamab
 Dr Richardson	Belantamab mafotodin/bortezomib/dexamethasone
 Dr Fonseca	Elranatamab
 Dr Mikhael	Teclistamab

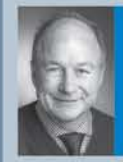
RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, which next line of therapy would you most likely recommend for an 80-year-old patient with high-risk (del[17p]) MM who received initial treatment with Rd/daratumumab and experienced disease progression after 3 years of maintenance therapy?

 Dr Alsina	Ciltacabtagene autoleucel
 Dr Lee	Ciltacabtagene autoleucel
 Dr Lonial	Teclistamab/daratumumab
 Dr Richardson	Belantamab mafotodin/bortezomib/dexamethasone
 Dr Fonseca	Elranatamab
 Dr Mikhael	Ciltacabtagene autoleucel

RTP RESEARCH TO PRACTICE

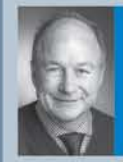
In general, how would you sequence a BCMA-targeted bispecific antibody and talquetamab for a patient with R/R MM who had experienced disease progression after BCMA-targeted CAR T-cell therapy?

 Dr Alsina	BCMA-targeted bispecific antibody → talquetamab (depending on DOR)
 Dr Lee	DOR >12 months: BCMA-targeted bispecific antibody → talquetamab; DOR <12 months talquetamab → BCMA-targeted bispecific antibody
 Dr Lonial	Talquetamab → BCMA-targeted bispecific antibody
 Dr Richardson	Talquetamab → BCMA-targeted bispecific antibody
 Dr Fonseca	Talquetamab → BCMA-targeted bispecific antibody
 Dr Mikhael	Talquetamab → BCMA-targeted bispecific antibody

DOR = duration of response to BCMA-targeted CAR T-cell therapy

RTP RESEARCH TO PRACTICE

In general, how would you sequence a BCMA-targeted bispecific antibody and talquetamab for a patient with R/R MM who had not previously received BCMA-targeted CAR T-cell therapy?

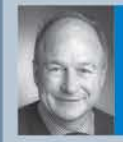
 Dr Alsina	BCMA-targeted bispecific antibody → talquetamab
 Dr Lee	BCMA-targeted bispecific antibody → talquetamab
 Dr Lonial	BCMA-targeted bispecific antibody → talquetamab
 Dr Richardson	BCMA-targeted bispecific antibody → talquetamab
 Dr Fonseca	BCMA-targeted bispecific antibody → talquetamab
 Dr Mikhael	BCMA-targeted bispecific antibody → talquetamab

RTP RESEARCH TO PRACTICE

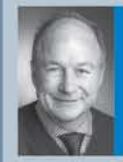
Based on early evidence, how would you indirectly compare the global efficacy of the FcRH5-directed bispecific antibody cevostamab to that of BCMA-targeted bispecific antibodies and talquetamab for R/R MM?

	BCMA-targeted bispecific antibodies	Talquetamab
 Dr Alsina	Not enough data are available to tell	Not enough data are available to tell
 Dr Lee	Efficacy is about the same	Efficacy is about the same
 Dr Lonial	Not enough data are available to tell	Not enough data are available to tell
 Dr Richardson	Not enough data are available to tell	Not enough data are available to tell
 Dr Fonseca	BCMA-targeted bispecific antibodies are more efficacious	Talquetamab is more efficacious
 Dr Mikhael	BCMA-targeted bispecific antibodies are more efficacious	Talquetamab is more efficacious

Based on early evidence, how would you indirectly compare the global and tolerability of cevostamab to that of BCMA-targeted bispecific antibodies and talquetamab for R/R MM?

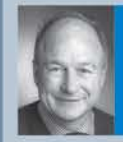
	BCMA-targeted bispecific antibodies	Talquetamab
 Dr Alsina	Not enough data are available to tell	Not enough data are available to tell
 Dr Lee	Cevostamab is more tolerable	Cevostamab is more tolerable
 Dr Lonial	Tolerability is about the same	Cevostamab is more tolerable
 Dr Richardson	Cevostamab is more tolerable	Cevostamab is more tolerable
 Dr Fonseca	Tolerability is about the same	Tolerability is about the same
 Dr Mikhael	Tolerability is about the same	Cevostamab is more tolerable

If cevostamab were to become available, how would you most likely sequence it relative to BCMA- and GPRC5D-targeted bispecific antibodies?

 Dr Alsina	BCMA bispecific → GPRC5D bispecific → cevostomab
 Dr Lee	BCMA bispecific → cevostomab → GPRC5D bispecific
 Dr Lonial	BCMA bispecific → cevostomab → GPRC5D bispecific
 Dr Richardson	BCMA bispecific → GPRC5D bispecific → cevostomab
 Dr Fonseca	BCMA bispecific → GPRC5D bispecific → cevostomab
 Dr Mikhael	BCMA bispecific → cevostomab → GPRC5D bispecific

RTP RESEARCH TO PRACTICE

Do you believe that bispecific antibodies can be safely and effectively administered in community cancer centers?
Would you recommend preemptive tocilizumab before administering a bispecific antibody to a patient with R/R MM?

	Administered in community setting?	Preemptive tocilizumab?
 Dr Alsina	Yes	Yes, for all patients
 Dr Lee	Yes	Yes, for all patients
 Dr Lonial	Yes	Yes, for all patients
 Dr Richardson	No	Yes, for all patients
 Dr Fonseca	Yes	Yes, for select patients
 Dr Mikhael	Yes	Yes, for all patients

Agenda

Module 1: Integrating Bispecific Antibodies into the Management of Relapsed/Refractory (R/R) Multiple Myeloma (MM) — Dr Lee

Module 2: Current Utility of Antibody-Drug Conjugates for MM — Dr Lonial

Module 3: Potential Role of Cereblon E3 Ligase Modulators in Therapy for MM — Dr Richardson

Module 4: Chimeric Antigen Receptor T-Cell Therapy for R/R MM — Dr Alsina

EMORY WINSHIP CANCER INSTITUTE

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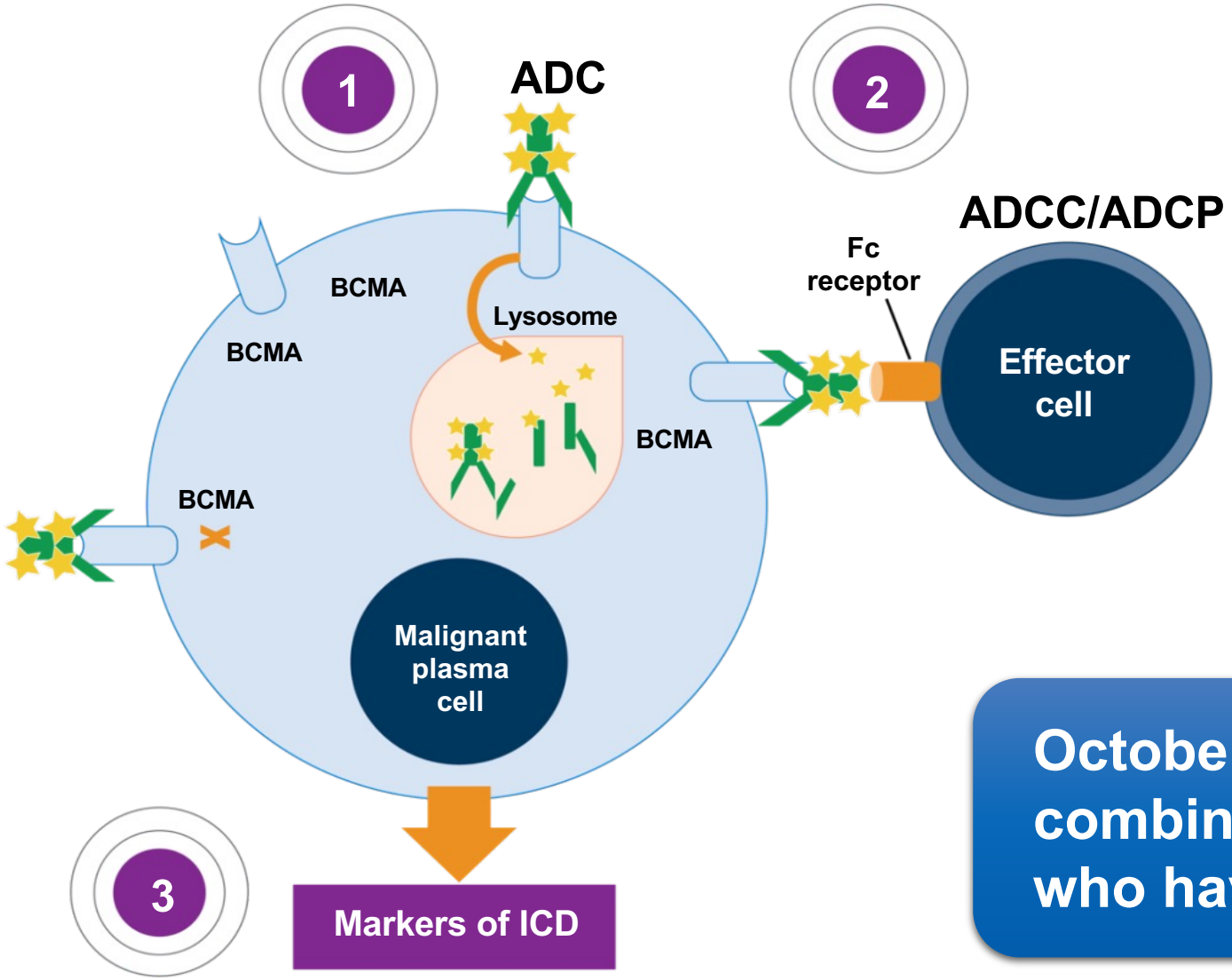
EMORY UNIVERSITY SCHOOL OF MEDICINE

BCMA ADC in MM

Sagar Lonial, MD
Professor and Chair
Department of Hematology and Medical Oncology
Anne and Bernard Gray Professor in Cancer
Chief Medical Officer, Winship Cancer Institute
Emory University School of Medicine

Belamaf Is an Immunoconjugate Targeting BCMA With a Multimodal MOA[1]



BCMA-targeting antibody conjugated with a cytotoxic payload (MMAF)

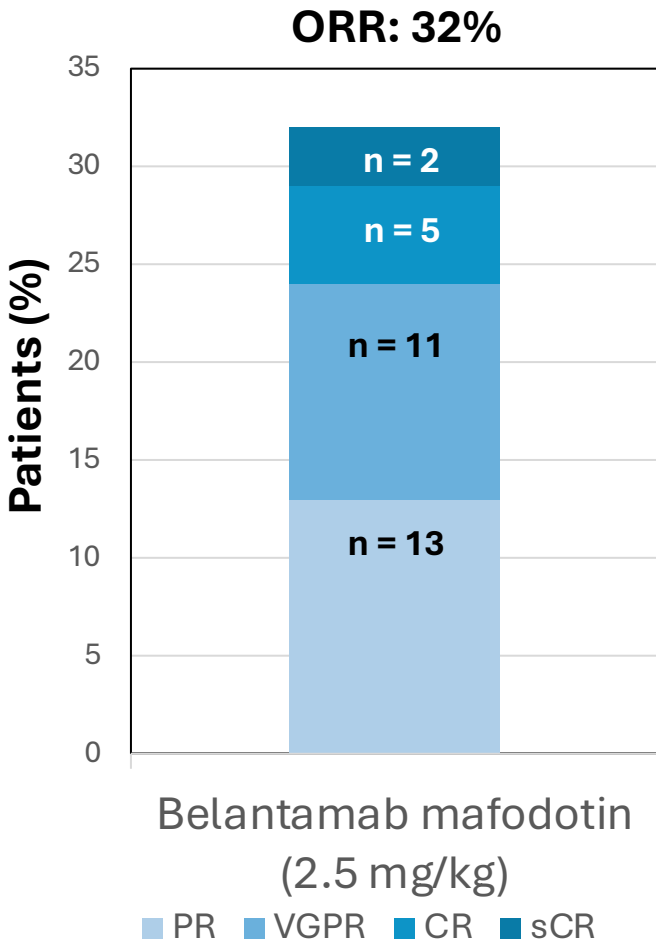
- Payload induced direct cell death
- Antibody engineered to have ADCC, while MMAF induces immunogenic cell death, eliciting an immune response

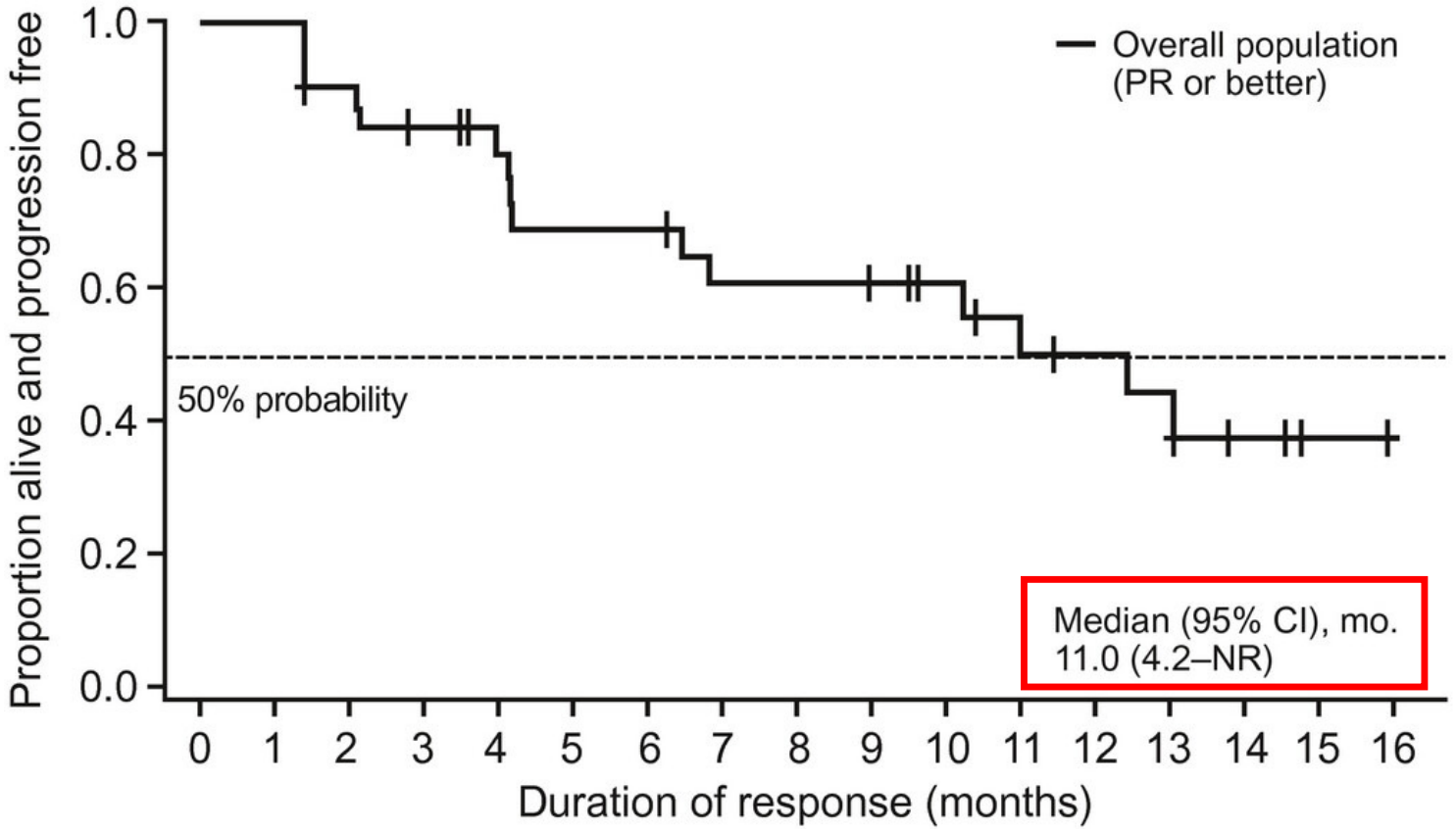
An "off-the-shelf" BCMA option useful for patients unable to receive CAR-T (eg, due to frailty or mobility issues)

October 2025: FDA-approved in combination with Vd for patients who have received ≥2 prior LOT[2]

1. Lonial S et al. *Lancet Oncol*. 2020;21:207-221.
2. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-belantamab-mafodotin-blmf-relapsed-or-refractory-multiple-myeloma.

Phase II DREAMM-2: Response and DoR 13 mo Follow-up





Lonial S et al. Cancer. 2021 Nov 15;127(22):4198-4212.

In Current Guidelines, BCMA ADC Therapy Is Recommended for Early-Relapse MM[1,a]

Therapy for Previously Treated RRMM After One to Three Prior Therapies

Preferred

CAR-T cell therapy

After one prior LOT, including an IMiD and a PI, and refractory to lenalidomide

- **Ciltacabtagene autoleucel (category 1)**

After two prior LOT, including an IMiD, a PI, and an anti-CD38 mAb

- **Idecabtagene vicleucel (category 1)**

Other Recommended

Supported by DREAMM-7

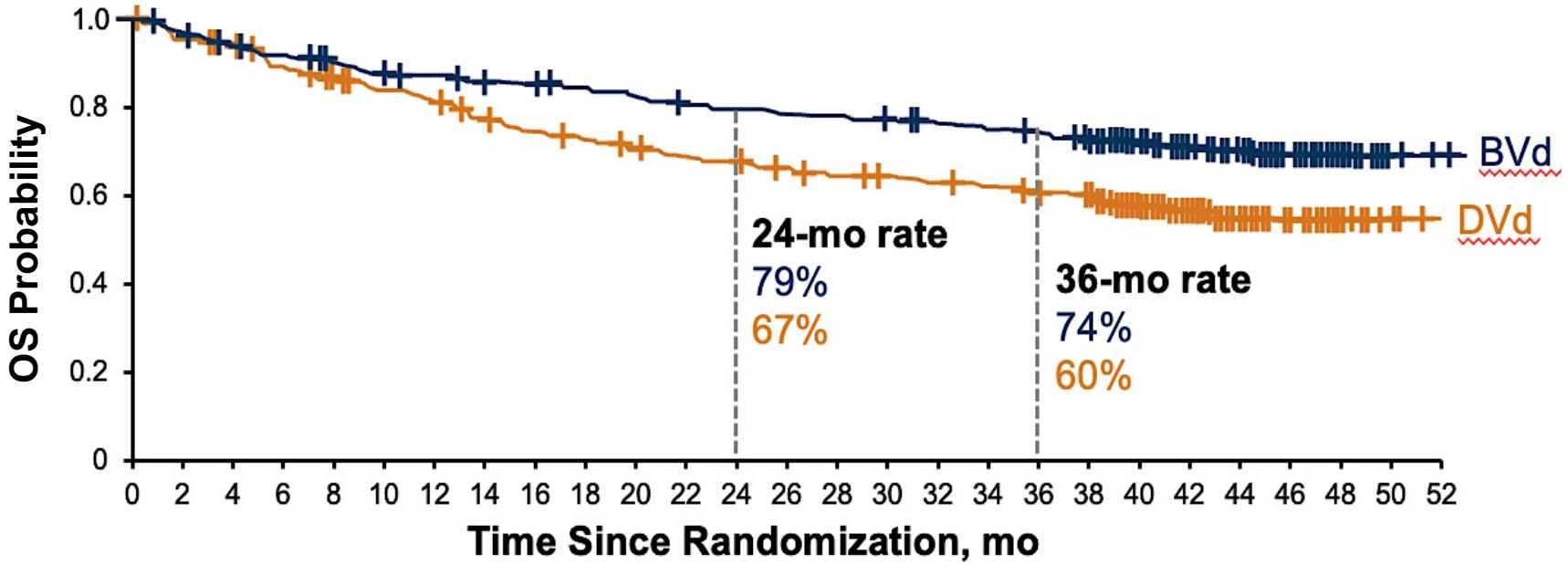
After two prior LOT, including an IMiD and a PI

- **Belantamab mafodotin-blmf/Bortezomib/Dexamethasone (category 1)**

[a] Please consult guidelines for complete list; this table lists BCMA-targeting cellular and antibody options.

1. NCCN Clinical Practice Guidelines in Oncology. Multiple Myeloma. Version 4.2026. https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf.

DREAMM-7 Showed Greater and Sustained PFS and OS Benefit With Belamaf Plus Vd Compared With DVd[1]



Median Follow-Up: 39.4 mo	BVd (N = 243)	DVd (N = 251)
Median PFS, mo	36.6	13.4
OS at 24 mo, %	79	67
OS at 36 mo, %	74	60
Median OS, mo	NR, HR = 0.58; *P* = .0002	
ORR, %	83	71
≥CR, %	36	18

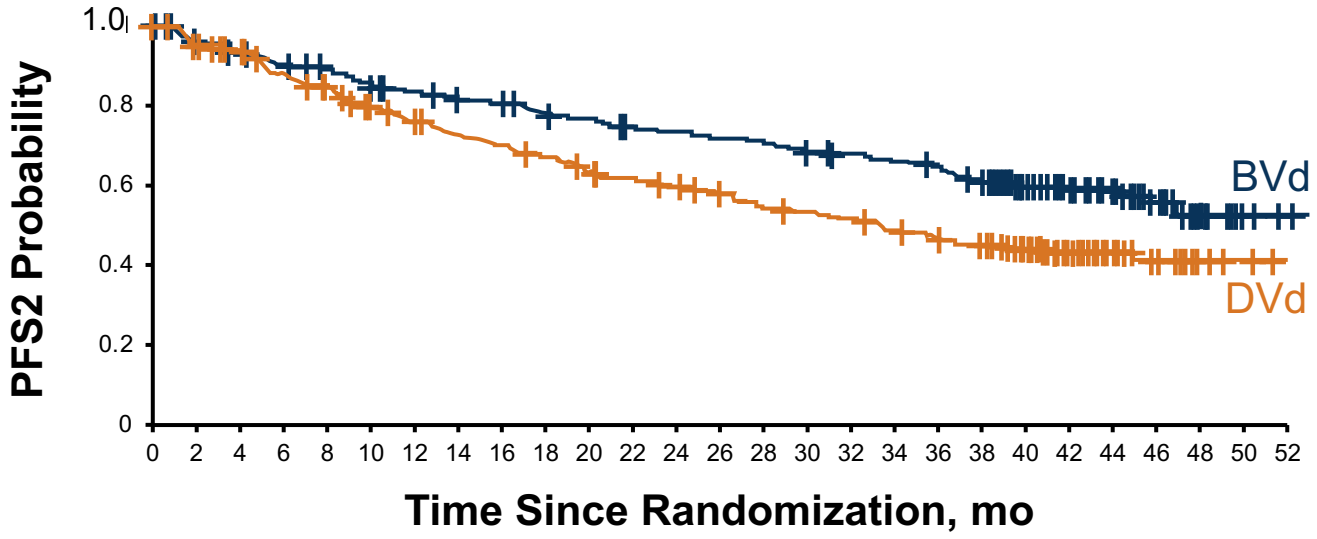
1. Hungria V et al. *Lancet Oncol*. 2025;26:1067-1080.

Additional Outcomes Show Maintained Treatment Benefit After BVd And Encouraging MRD-Negativity Rates

PFS2 showed maintained treatment benefit with BVd vs DVd following subsequent antimyeloma therapy[1]

	Median PFS2, mo	Events, n (%)
BVd	NR (45.6-NR)	93 (38)
DVd	33.4 (26.7-44.9)	126 (50)

HR for disease progression or death = 0.59 (95% CI, 0.45-0.77)



BVd showed greater overall MRD negativity rates compared with DVd[2]

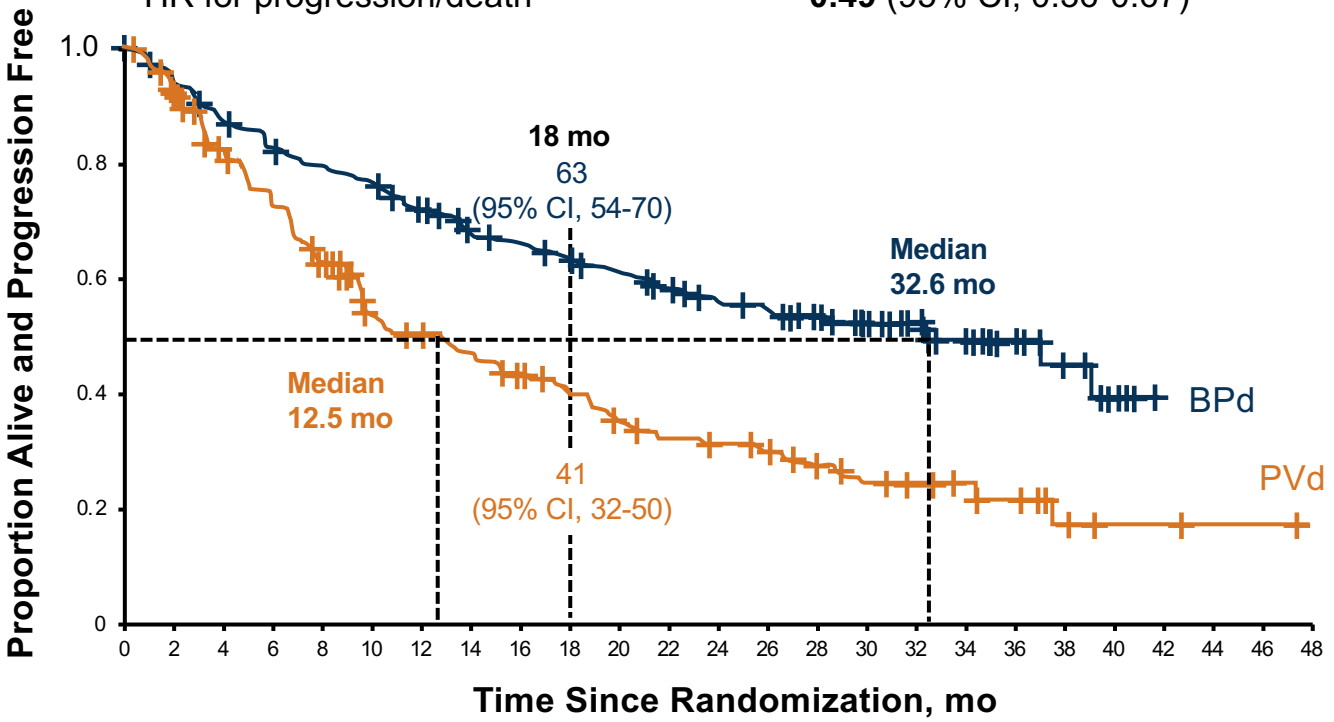
Responses, % (n/N)	BVd (N = 243)	DVd (N = 251)
≥CR	36 (87/243)	18 (44/251)
≥CR and MRD negativity (10^{-5})	70 (61/87)	59 (26/44)
≥CR and MRD negativity (10^{-6})	45 (39/87)	23 (10/44)
Sustained ≥CR MRD negativity for ≥12 mo	57 (35/61)	42 (11/26)

1. Hungria V et al. *Lancet Oncol*. 2025;26:1067-1080. 2. Mateos MV et al. ASH 2025. Poster Abstract 2265.

DREAMM-8: Adding Belamaf to Pd Improved PFS in Patients With RRMM and ≥1 Prior LOT[1]

In patients with ≥1 high-risk cytogenetic abnormality, responses were more frequent and deeper with BPd[2]

	BPd (N = 155)	PVd (N = 147)
Events, n (%)	68 (44)	89 (61)
PFS, median (95% CI), mo	32.6 (21.2-NR)	12.5 (9.1-17.6)
HR for progression/death	**0.49** (95% CI, 0.36-0.67)	

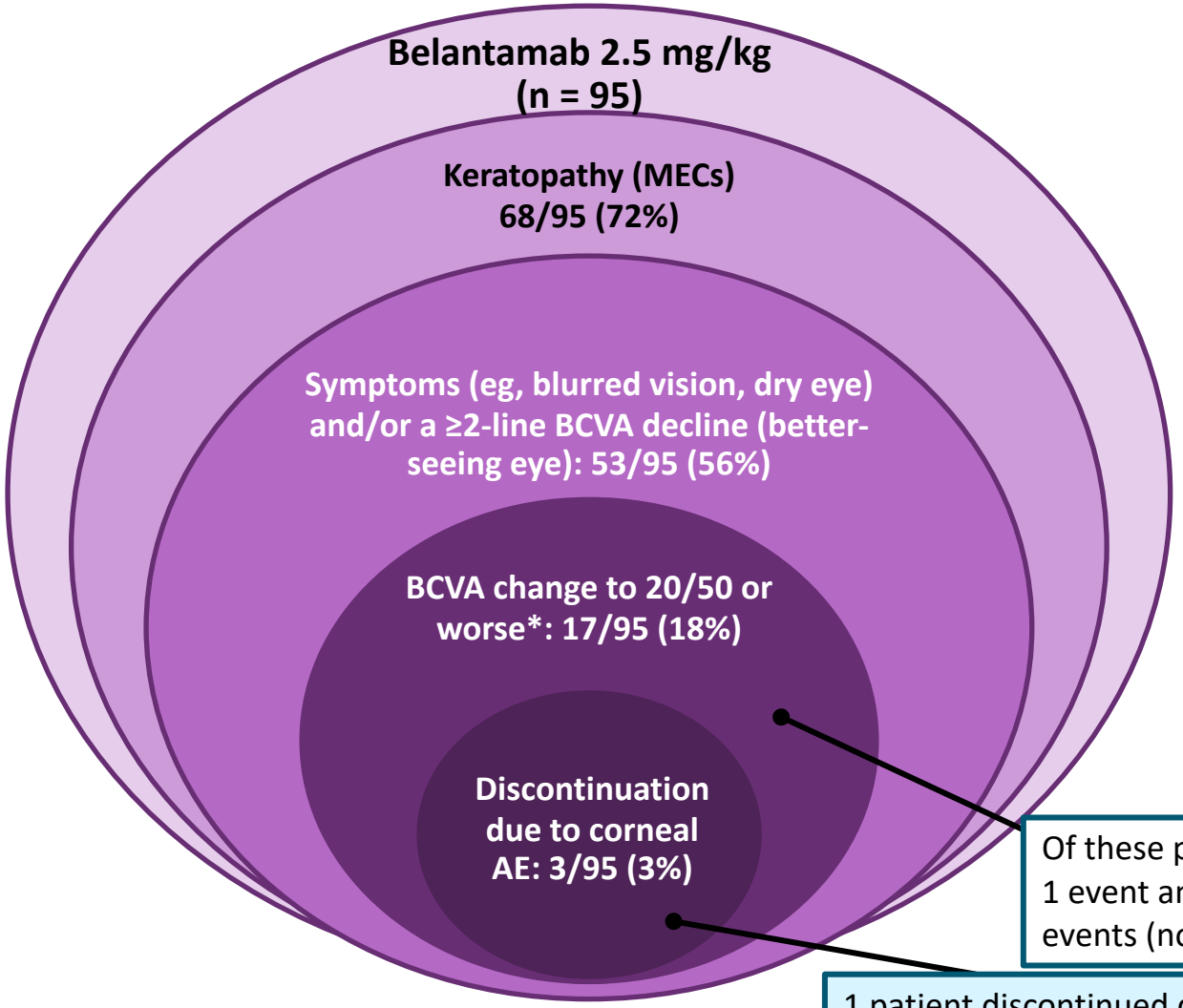


Longer follow-up (median 35.8 mo) show depth and durability of response with BPd[3]

Responses	BPd (N = 155)	PVd (N = 147)
≥CR, % (n/N)	43 (67/155)	17 (25/147)
≥CR MRD negativity, % (n/N)	28 (43/155)	6 (9/147)
≥CR MRD negativity for ≥ 12 mo, % (n/N)	15 (24/155)	3 (4/147)
Median DOR (≥PR; 95% CI), mo	NR (29.5-NR)	16.4 (11.1-22.5)
PFS2, mo	47.1 (28.4-NR)	21.7 (13.8-28.6)

1. Dimopoulos MA et al. EHA 2025. Abstract PF728. 2. Trudel S et al. *J Clin Oncol*. 2025;43(suppl 16):7533-7533. 3. Trudel S et al. ASH 2025. Poster Abstract 2264.

Keratopathy Can Occur With or Without Symptoms



*Better-seeing eye; represents threshold at which ADL (eg, driving) are affected.

Lonial. ASH 2020. Abstr 3224.

Responses after Dose Interruptions	2.5 mg/kg (n = 16)
Maintained clinical benefit, n (%)	14 (88)
▪ Deepened response	6 (38)
▪ Maintained same response category	6 (38)
▪ Did not meet progression criteria	2 (13)
Developed PD, n (%)	2 (13)

Of these patients, 76% (13/17) had 1 event and 24% (4/17) had 2 events (no patients had >2 events)

1 patient discontinued due to keratopathy (MECs), 1 due to blurred vision, and 1 due to reduced BCVA

Under investigation

Can we safely utilize BM

@lower doses

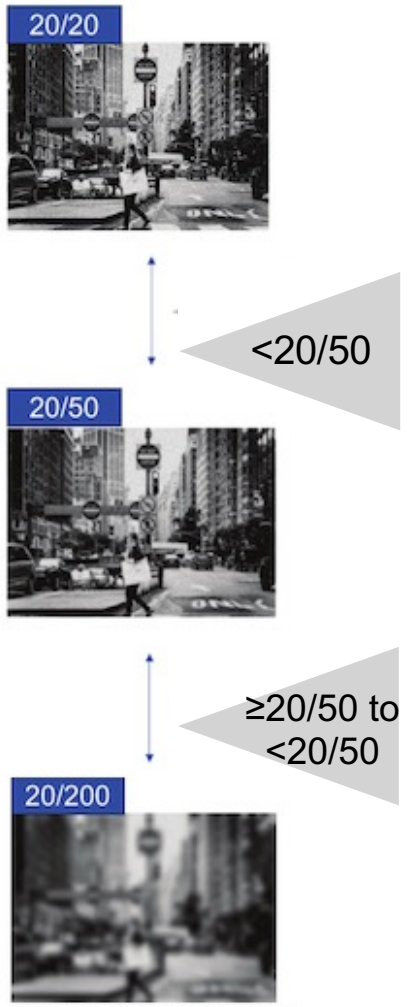
with less frequent ophtho visits [use Sxs + BCVA]

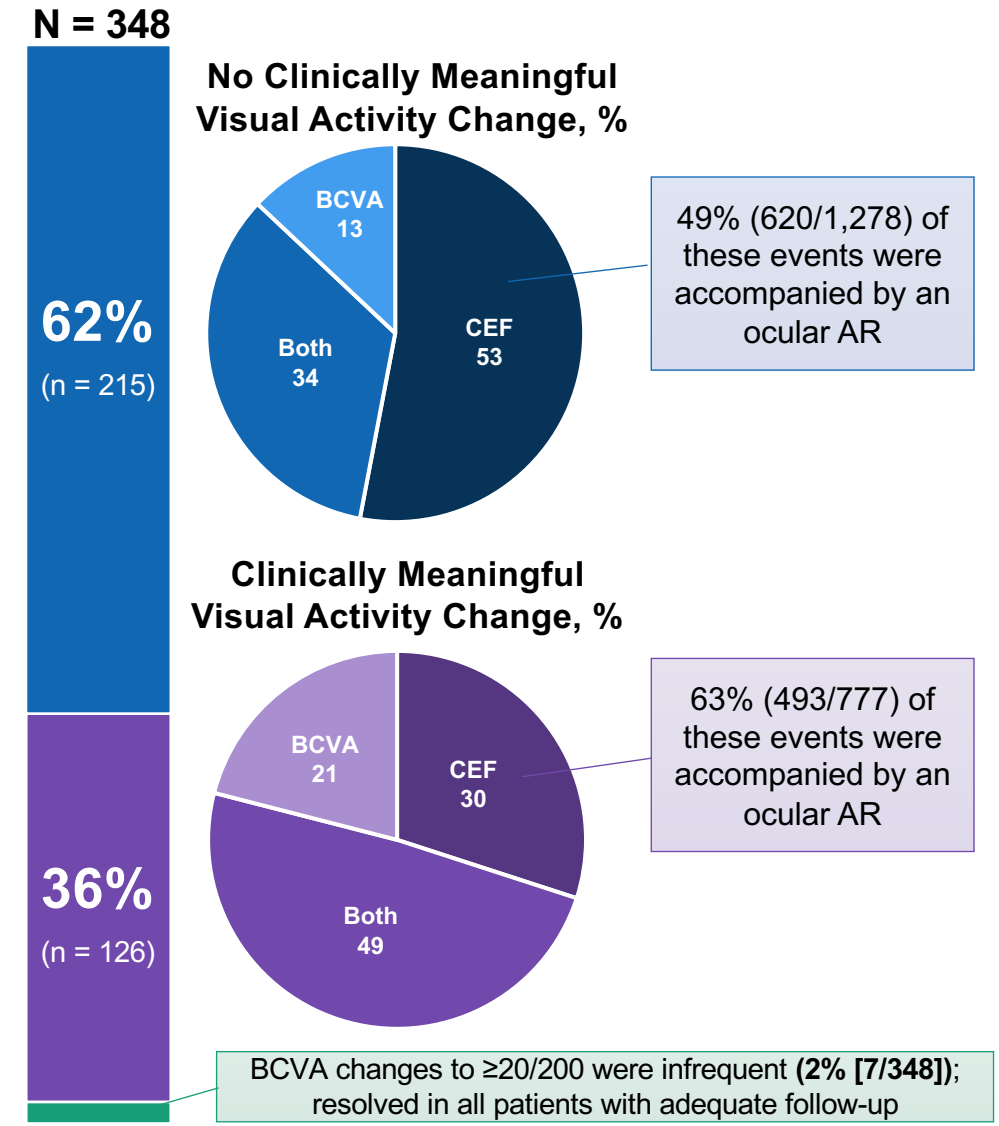
Characterization of Ocular Toxicities With Belamaf-Based Regimens[1-3]

392 patients treated with belamaf-based regimens in DREAMM-7 (N = 242) and DREAMM-8 (N = 150)

Overall grade ≥2 OEFs was 86% and 87% with BVd and BPd, respectively

- Common ocular AEs included blurred vision, dry eye, photophobia, foreign body sensation, and eye irritation or pain
- Majority of grade ≥2 OEFs were associated with no clinically meaningful change in visual acuity
- Majority of patients did not have to stop reading or driving



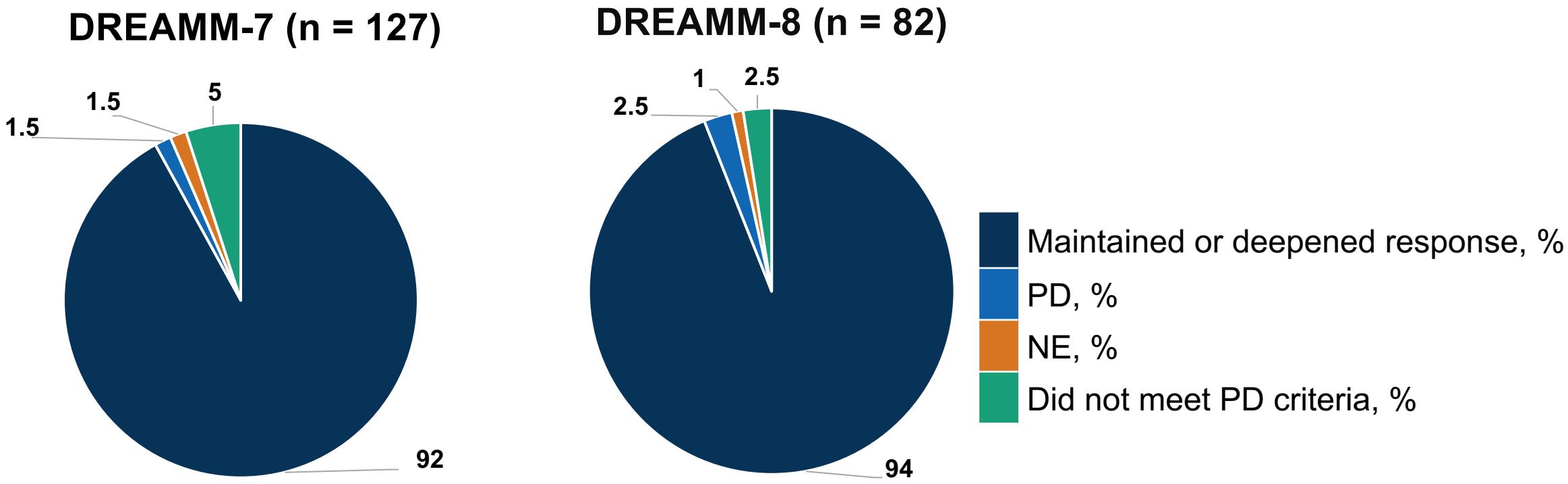


1. Hájek R et al. EHA 2025. Abstract PS1761. 2. Mateos MV et al. *Blood Adv.* 2025;9:5708-5719.
3. Shi C et al. *J Vis*. 2020;20:29.

Dose Modifications of Belamaf Were Common and Didn't Impact Efficacy[1]

In DREAMM-7 and DREAMM-8, 92% and 94% of patients, respectively, sustained or deepened their response during their first extended dose delay

Last Assessed Response During First Extended Belamaf Dose Delay of >9 Weeks



1. Hájek R et al. EHA 2025. Abstract PS1761.

Dose Modifications Guided by Standard Assessments Can Manage and Reverse Ocular Events With Belamaf[1]

Regimen	Severity of OEF	DREAMM-7 BVd (cycle length: 3 wk)	DREAMM-8 BPd (cycle length: 4 wk)
Standard schedule	No finding Grade 1	2.5 mg/kg Q3W	2.5 mg/kg once in cycle 1 followed by 1.9 mg/kg Q4W from cycle 2
Reduced dose level 1	Grade 2 Grade 3	Dose delay until resolution to grade ≤1, then resume at same dose (2.5 mg/kg Q3W or 1.9 mg/kg Q3W) after grade 2 finding or 1.9 mg/kg Q3W after grade 3 finding	Dose delay until resolution of both components to grade ≤1, then 1.9 mg/kg Q8W
	Grade 4	Discontinuation or 1.9 mg/kg Q3W rechallenge after improvement and sponsor approval	–
Reduced dose level 2	Grade 4	NA	Dose delay until KVA grade ≤1, then 1.4 mg/kg Q8W

Standard-assessment guided dose modification can manage and reverse the emergence of ocular event (based on DREAMM-7 and -8 experience)[2]

1. Mateos MV et al. *Blood Adv.* 2025;9:5708-5719. 2. Lonial S et al. ASH 2025. Poster Abstract 4055.

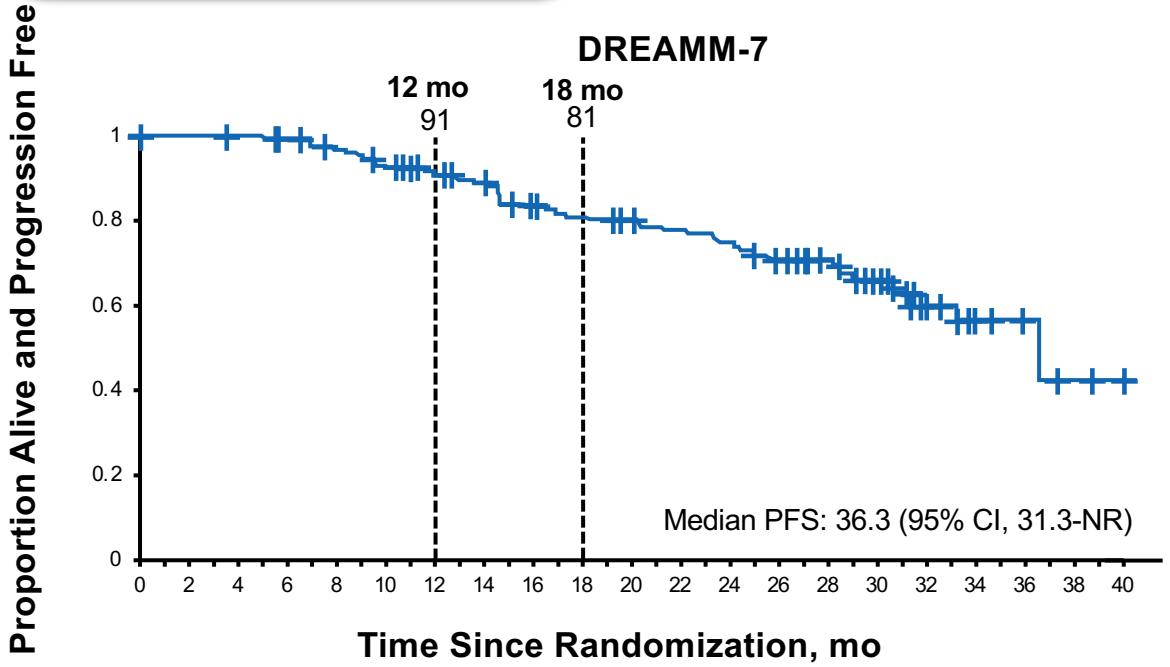
Sustained, Deepened Responses With Dose-Modified Belamaf[1]

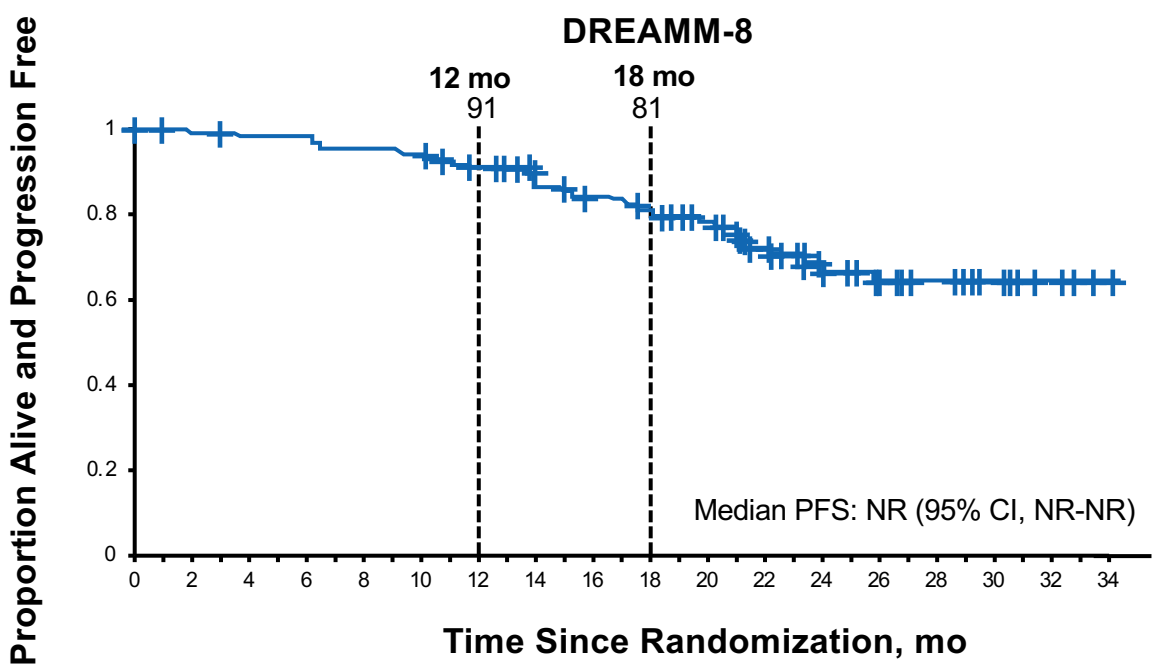
Responses were maintained or deepened during/after the first extended dose delay (>2 cycles)

Patients with ≥1 extended delay (≥12 weeks) showed robust long-term PFS

Rates of VGPR or better increased markedly after the first delay

- DREAMM-7: 45% → 75%
- DREAMM-8: 55% → 87%





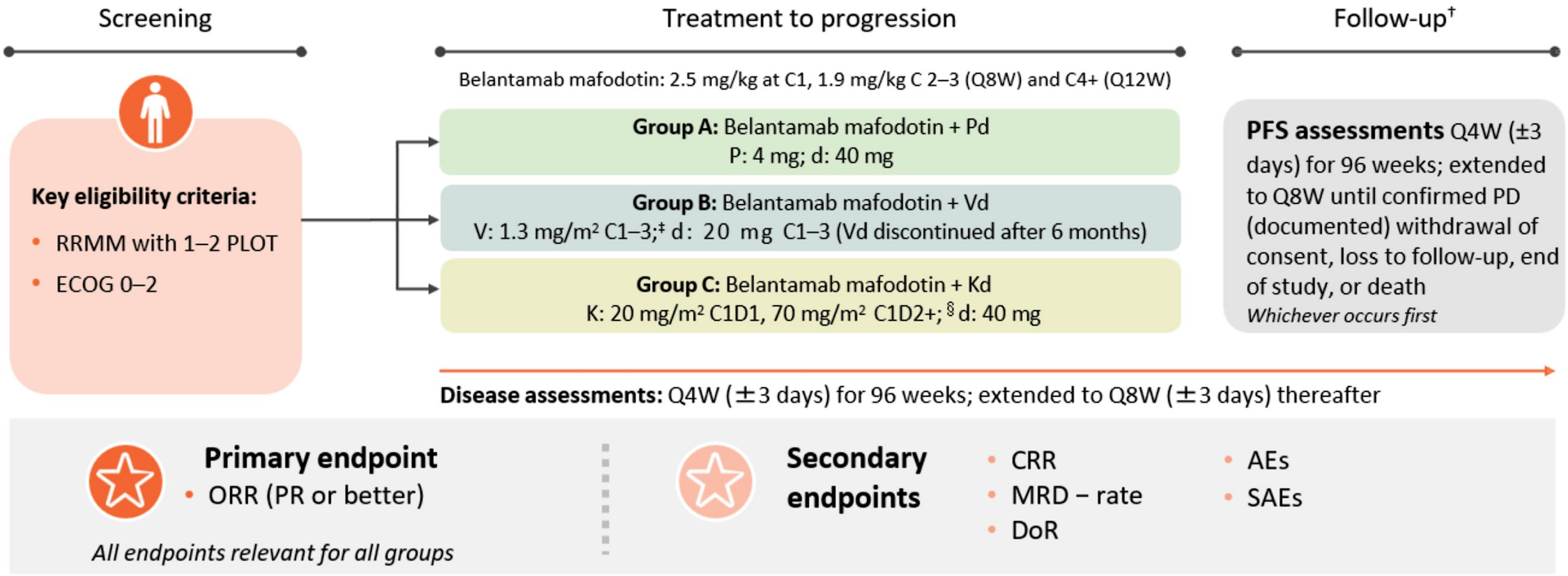
1. Mateos MV et al. *Blood Adv.* 2025;9:5708-5719.

Extended Dosing of Belantamab Mafodotin: Phase II DREAMM-15 Trial to Be Presented at EHA 2026

Figure: Study Design (Global n=200; US n=50)*

NCT07227311

Phase 2, Multicenter, Open-Label, Non-Randomized Study



Sborov D et al. EHA 2026;Abstract PB3225.

Patient Monitoring and Dosing Principles With Belamaf-Containing Regimens[1]

Before Cycle 1

Eye specialist

Baseline ophthalmic evaluation

Cycles 2-4

Eye specialist

Evaluation before each dose

Treating physician

Dose adjustment may be necessary

Cycles 5+

Eye specialist

Use KVA scale to inform whether dose modification is necessary

Treating physician

Administer VRA tool before each subsequent dose

1. Terpos E et al. *Am J Hematol.* 2025;100:1839-1850.

DREAMM-7 Study: Safety Profile

	BVd group (n=242)				DVd group (n=246)			
	Grade 1–2	Grade 3	Grade 4	Grade 5	Grade 1–2	Grade 3	Grade 4	Grade 5
Any adverse event	11 (5%)	83 (34%)	122 (50%)	26 (11%)	50 (20%)	108 (44%)	68 (28%)	20 (8%)
Blood and lymphatic system disorders								
Thrombocytopenia†	34 (14%)	52 (21%)	83 (34%)	0	35 (14%)	44 (18%)	43 (17%)	0
Anaemia‡	27 (11%)	20 (8%)	1 (<1%)	0	40 (16%)	19 (8%)	6 (2%)	0
Neutropenia	6 (2%)	18 (7%)	12 (5%)	0	12 (5%)	13 (5%)	3 (1%)	0
Infections and infestations								
Pneumonia	18 (7%)	22 (9%)	1 (<1%)	7 (3%)	13 (5%)	6 (2%)	2 (1%)	2 (1%)
Other adverse events (occurring in ≥15% of patients in either treatment group)								
Diarrhoea	70 (29%)	10 (4%)	0	0	68 (28%)	10 (4%)	0	0
Platelet count decreased	8 (3%)	13 (5%)	30 (12%)	0	14 (6%)	16 (7%)	10 (4%)	0
Peripheral sensory neuropathy	59 (24%)	2 (1%)	0	0	50 (20%)	1 (<1%)	0	0
Neuropathy peripheral	47 (19%)	3 (1%)	0	0	45 (18%)	10 (4%)	0	0
Constipation	47 (19%)	2 (1%)	0	0	55 (22%)	1 (<1%)	0	0
Fatigue	40 (17%)	9 (4%)	0	0	42 (17%)	6 (2%)	0	0
Insomnia	35 (14%)	3 (1%)	0	0	48 (20%)	2 (1%)	0	0
Alanine aminotransferase increased	34 (14%)	14 (6%)	0	0	26 (11%)	4 (2%)	0	0
Pyrexia	46 (19%)	1 (<1%)	0	0	22 (9%)	3 (1%)	0	0
Cough	34 (14%)	0	0	0	37 (15%)	0	0	0
Nausea	37 (15%)	2 (1%)	0	0	31 (13%)	0	0	0
Back pain	21 (9%)	3 (1%)	0	0	32 (13%)	5 (2%)	0	0
Gamma-glutamyltransferase increased	15 (6%)	23 (10%)	1 (<1%)	0	7 (3%)	4 (2%)	0	0
Aspartate aminotransferase increased	33 (14%)	3 (1%)	1 (<1%)	0	13 (5%)	0	0	0
Infusion-related reaction	7 (3%)	1 (<1%)	0	0	38 (15%)	4 (2%)	0	0

Data are n (%). BVd=belantamab mafodotin, bortezomib, and dexamethasone. DVd=daratumumab, bortezomib, and dexamethasone. *Each patient could have more than one event and multiple occurrences of each event; however, each patient was only counted once for each row; the maximum toxicity grade was selected for each patient and each adverse event; percentages were calculated, with the number of patients in each group as the denominator; graded using the National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0; a table showing grade 1 or 2 adverse events occurring in ≥10% of patients and all grade 3-5 adverse events can be found in the appendix (pp 34-43). †If platelet count decrease is also included, the percentage of thrombocytopenia events for all grades was 88% and 65% with BVd and DVd, respectively, and for grade 3 or 4 was 73% and 46% with BVd and DVd, respectively. ‡Red blood cells decreased was not reported.

Table 3: **Non-ocular adverse events of clinical interest***

Hungria V et al. Lancet Oncol. 2025

DREAMM-8 Study: Safety Profile

Table 3. Adverse Events Reported in at Least 20% of Patients in Either Group (Safety Population).

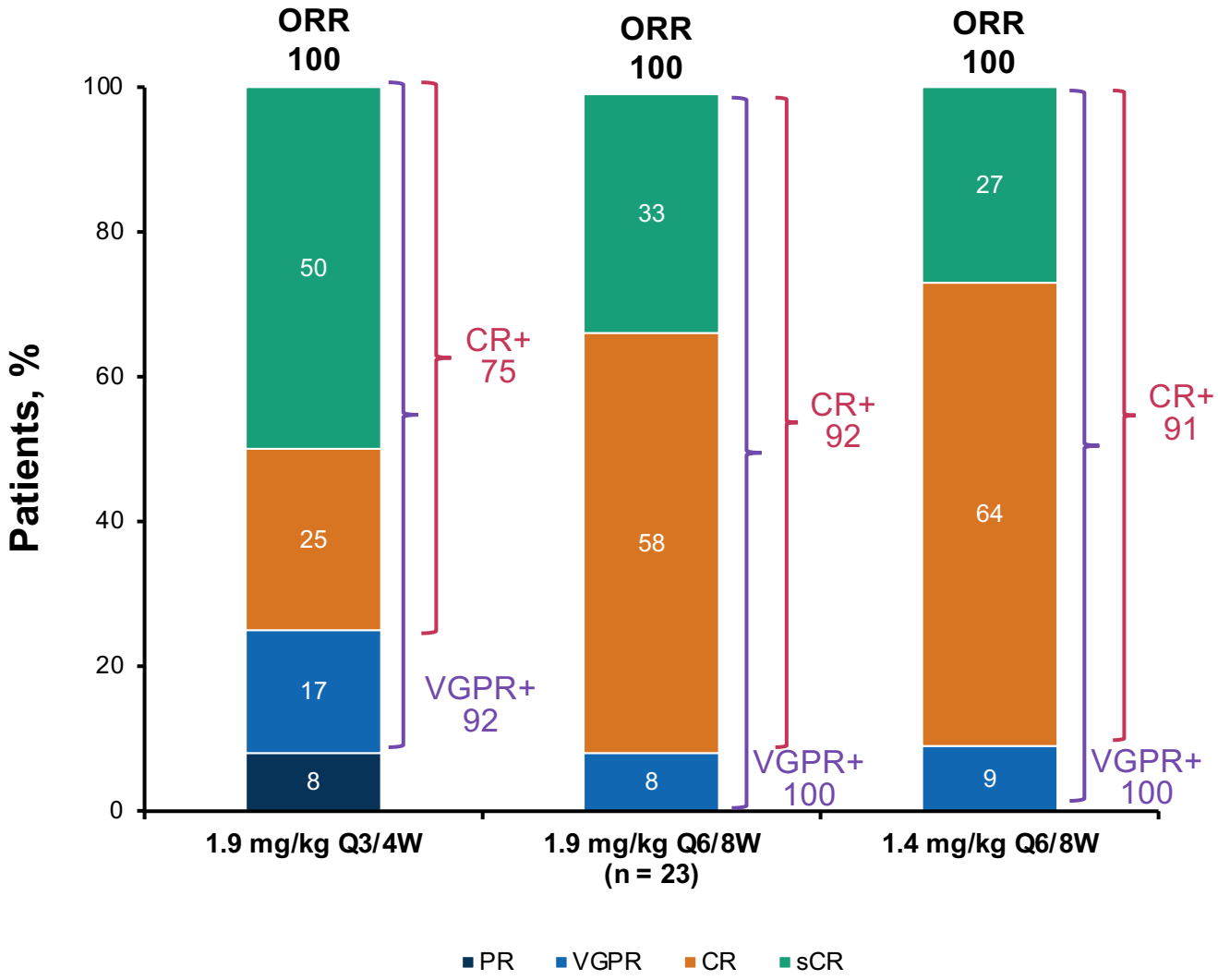
Event*	BPd (N=150)		PVd (N=145)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
	number (percent)			
Any adverse event	149 (99)	141 (94)	139 (96)	110 (76)
Blurred vision	119 (79)	26 (17)	22 (15)	0
Dry eye	91 (61)	12 (8)	14 (10)	0
Foreign-body sensation in eyes	91 (61)	9 (6)	9 (6)	0
Eye irritation	75 (50)	6 (4)	13 (9)	0
Neutropenia	72 (48)	63 (42)	50 (34)	41 (28)
Photophobia	66 (44)	5 (3)	6 (4)	0
Coronavirus disease 2019	56 (37)	10 (7)	31 (21)	3 (2)
Thrombocytopenia	54 (36)	36 (24)	44 (30)	29 (20)
Eye pain	49 (33)	3 (2)	7 (5)	0
Cataract	40 (27)	9 (6)	15 (10)	6 (4)
Fatigue	40 (27)	9 (6)	32 (22)	7 (5)
Upper respiratory tract infection	40 (27)	2 (1)	25 (17)	0
Pneumonia	36 (24)	26 (17)	17 (12)	11 (8)
Anemia	35 (23)	15 (10)	38 (26)	19 (13)
Diarrhea	35 (23)	2 (1)	33 (23)	10 (7)
Corneal epithelial microcysts	34 (23)	12 (8)	0	0
Punctate keratitis	34 (23)	9 (6)	1 (1)	1 (1)
Reduced visual acuity	34 (23)	20 (13)	8 (6)	1 (1)
Decreased neutrophil count	31 (21)	31 (21)	19 (13)	18 (12)
Decreased platelet count	30 (20)	22 (15)	22 (15)	18 (12)
Constipation	23 (15)	2 (1)	33 (23)	2 (1)
Peripheral neuropathy	11 (7)	1 (1)	34 (23)	4 (3)

Dimopoulos MA et al. NEJM 2024

DREAMM-9: Can We Move BCMA ADC Combinations Even Earlier in Myeloma Care?[1]

DREAMM-9 is evaluating belamaf plus VRd (BVRd) in transplant ineligible (TI) NDMM

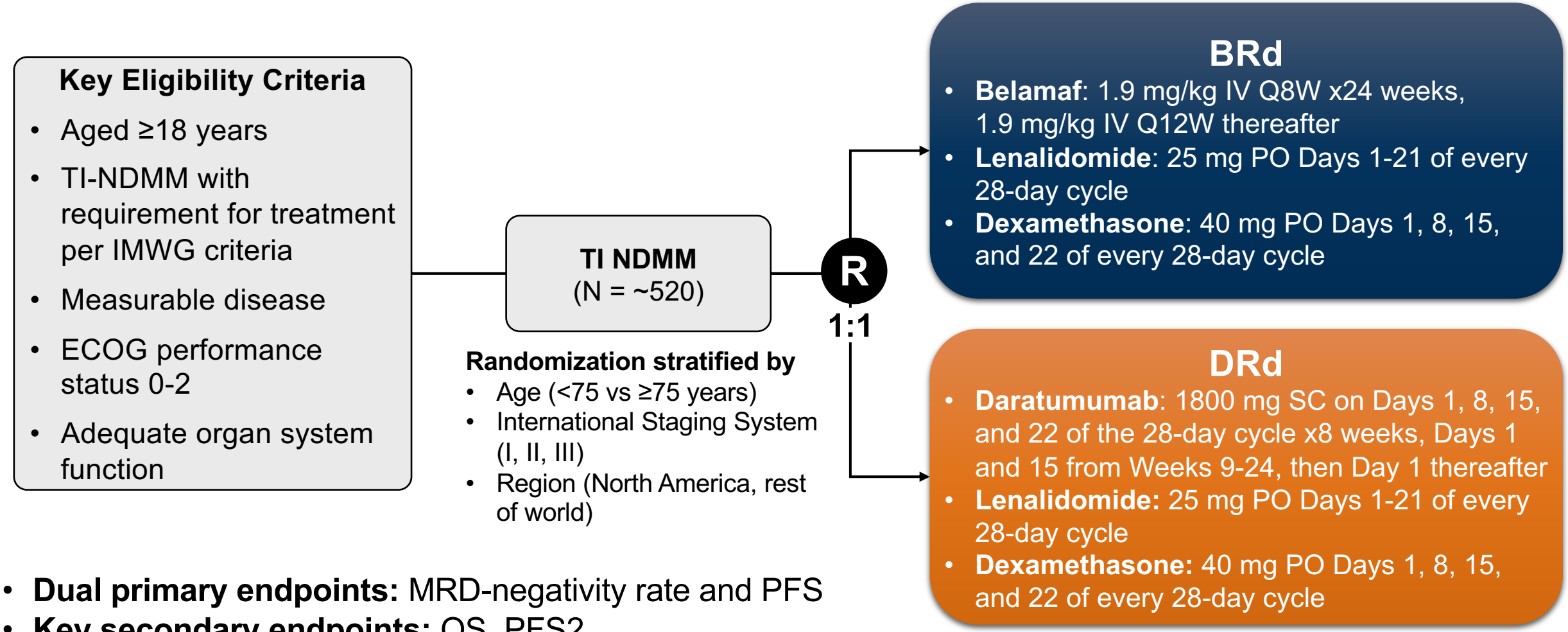
- **ORR:** 100% with 1.9 mg/kg belamaf
- **MRD negativity:** ≥73% in patients with CR+
- Using a stretched dosing schedule (Q6/8W) reduced rates of any grade ≥3 belamaf-related AEs, supporting the use of a 1.9 mg/kg starting dose with extended intervals to achieve an improved efficacy–safety profile in TI NDMM



1. Usmani SZ et al. IMS 2025. Abstract PA-416.

DREAMM-10: Belamaf Triplet Regimen in Transplant-Eligible MM[1]

- **DREAMM-10 is evaluating belamaf plus Rd (BRd) in TI NDMM**



- **Dual primary endpoints:** MRD-negativity rate and PFS
- **Key secondary endpoints:** OS, PFS2

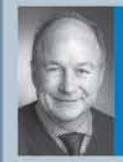
1. Lonial S et al. EHA 2025. Abstract PS1793.

Regulatory and reimbursement issues aside, what is the earliest timepoint in the treatment algorithm that you would administer belantamab mafodotin to patients with MM?

 Dr Alsina	Third or fourth relapse
 Dr Lee	First relapse
 Dr Lonial	Second relapse
 Dr Richardson	First relapse
 Dr Fonseca	Fourth relapse
 Dr Mikhael	First relapse

RTP RESEARCH TO PRACTICE

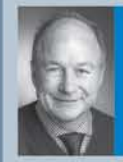
If a patient with R/R MM were to ask you to estimate the likelihood that their disease would respond to belantamab mafodotin-based combination therapy, how would you respond?

 Dr Alsina	If no prior BCMA-targeted therapy, it could be very effective with PFS around 3 years
 Dr Lee	80% ORR
 Dr Lonial	In combination over 80% ORR with predicted median PFS of 3 years
 Dr Richardson	Greater that 80% response rate
 Dr Fonseca	Greater than 60% depending on prior BCMA-targeted agent exposure
 Dr Mikhael	Greater than 80% response rate

PFS = progression-free survival

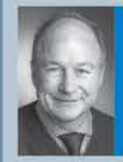
RTP RESEARCH TO PRACTICE

Do you believe belantamab mafodotin has greater efficacy when used earlier in the treatment course?

 Dr Alsina	Yes
 Dr Lee	Yes
 Dr Lonial	Yes
 Dr Richardson	Yes
 Dr Fonseca	Yes
 Dr Mikhael	Yes

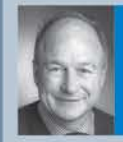
RTP RESEARCH TO PRACTICE

Outside of a clinical trial, would you combine belantamab mafodotin with agents other than bortezomib/dexamethasone under any circumstances?

 Dr Alsina	Yes, pomalidomide; carfilzomib for patients who cannot tolerate bortezomib
 Dr Lee	Yes, pomalidomide
 Dr Lonial	Yes, either pomalidomide or CELMoDs
 Dr Richardson	Yes, pomalidomide
 Dr Fonseca	Yes, pomalidomide
 Dr Mikhael	Yes, pomalidomide

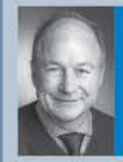
CELMoDs = cereblon E3 ligase modulators

In general, would you recommend belantamab mafodotin to patients who previously received …

	BCMA-directed CAR T-cell therapy	BCMA-directed CAR T-cell therapy and a BCMA-directed bispecific antibody
 Dr Alsina	Yes, but only after testing for serum BCMA	Yes, but only after testing for serum BCMA
 Dr Lee	Yes	Yes
 Dr Lonial	Yes, but only after testing for serum BCMA	Yes, but only after testing for serum BCMA
 Dr Richardson	Yes	Yes, but only after testing for serum BCMA
 Dr Fonseca	Yes, but after NGS for BCMA	Yes, but only after NGS for BCMA
 Dr Mikhael	Yes	Yes

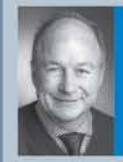
NGS = next-generation sequencing

What strategies do you generally recommend for mitigation of ophthalmic toxicities with belantamab mafodotin?

 Dr Alsina	Screening and frequent visits with ophthalmology as per PI
 Dr Lee	Start with reduced dose of 1.9 mg/kg and go to every 8-12-week dosing early when used in combination
 Dr Lonial	Dosing every 8-12 weeks based on side effects
 Dr Richardson	Dose reduction and schedule change, natural tears
 Dr Fonseca	Adjust dose and interval of administration
 Dr Mikhael	Adjust dosing to every 8-12 weeks, learn patient's "metabolism" for belantamab mafotodin, drug holds over dose reductions

PI = principal investigator

Do you adjust the dose or dosing frequency of belantamab mafodotin for patients with R/R MM who are experiencing a good response to treatment?

 Dr Alsina	Yes, stop therapy if sustained CR, decrease frequency if toxicity with good response
 Dr Lee	Yes, dose every 8 or 12 weeks
 Dr Lonial	Yes, every 8 or 12 weeks after the first dose
 Dr Richardson	Yes, dose every 8-12 weeks
 Dr Fonseca	Yes, space out administration intervals
 Dr Mikhael	Yes, reduce frequency to achieve no eye toxicity, often to every 12 weeks or less frequently

CR = complete response

RTP RESEARCH TO PRACTICE

Agenda

Module 1: Integrating Bispecific Antibodies into the Management of Relapsed/Refractory (R/R) Multiple Myeloma (MM) — Dr Lee

Module 2: Current Utility of Antibody-Drug Conjugates for MM — Dr Lonial

Module 3: Potential Role of Cereblon E3 Ligase Modulators in Therapy for MM — Dr Richardson

Module 4: Chimeric Antigen Receptor T-Cell Therapy for R/R MM — Dr Alsina

Dana-Farber Cancer Institute

DANA-FARBER CANCER INSTITUTE

Research To Practice CME Symposium
Consensus or Controversy?
Documenting and Discussing Investigators' Approaches to the Management of Relapsed/Refractory Multiple Myeloma
ASCO 2026, Chicago, IL – Monday, June 1

Potential Role of Cereblon E3 Ligase Modulators (CELMoDs) in Therapy for Multiple Myeloma (MM)

Paul G. Richardson, MD
RJ Corman Professor of Medicine
Harvard Medical School

Clinical Program Leader, Director of Clinical Research
Jerome Lipper Multiple Myeloma Center
Dana-Farber Cancer Institute
Boston, Massachusetts, USA

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Treatment of MM in 2026: multiple therapies approved or under investigation

Backbone/standard-of-care agents

Additional RRMM/recent approvals

Emerging therapies for RRMM**

IMiDs	PIs	mAbs	HDACis	ADCs	Targeted therapies	CAR T cell therapies	BiTEs® / bispecifics	BiTEs® / bispecifics	CELMoDs®
Lenalidomide	Bortezomib*	Daratumumab (CD38)	Panobinostat‡	Belantamab mafodotin‡	Selinexor	Idecabtagene vicleucel	Teclistamab (BCMAxCD3)	Etentamig (ABBV-383)† (BCMAxCD3)	Iberdomide†
Pomalidomide	Carfilzomib	Isatuximab (CD38)	Vorinostat†,#	AZD0305†	Melflufen‡	Ciltacabtagene autoleucel	Elranatamab (BCMAxCD3)	Alnuctamab†# (BCMAxCD3)	Mezigdomide†
Thalidomide	Ixazomib	Elotuzumab (SLAMF7)		Belantamab†	Venetoclax†,#	CAR T cell therapies	Talquetamab (GPRC5DxCD3)	Forimtamig† (GPRC5DxCD3)	Others
	Marizomib†,#				Lisaftoclax†	Arlocabtagene autoleucel†	Linvoseltamab (BCMAxCD3)	Cevostamab† (FcRH5xCD3)	Cemsidomide, Inobrodib†
					Sonrotoclax†	Anitocabtagene autoleucel†			CAR NK cell therapies†
						Durcabtagene autoleucel†			ICIs, Immuno-cytokines†,#

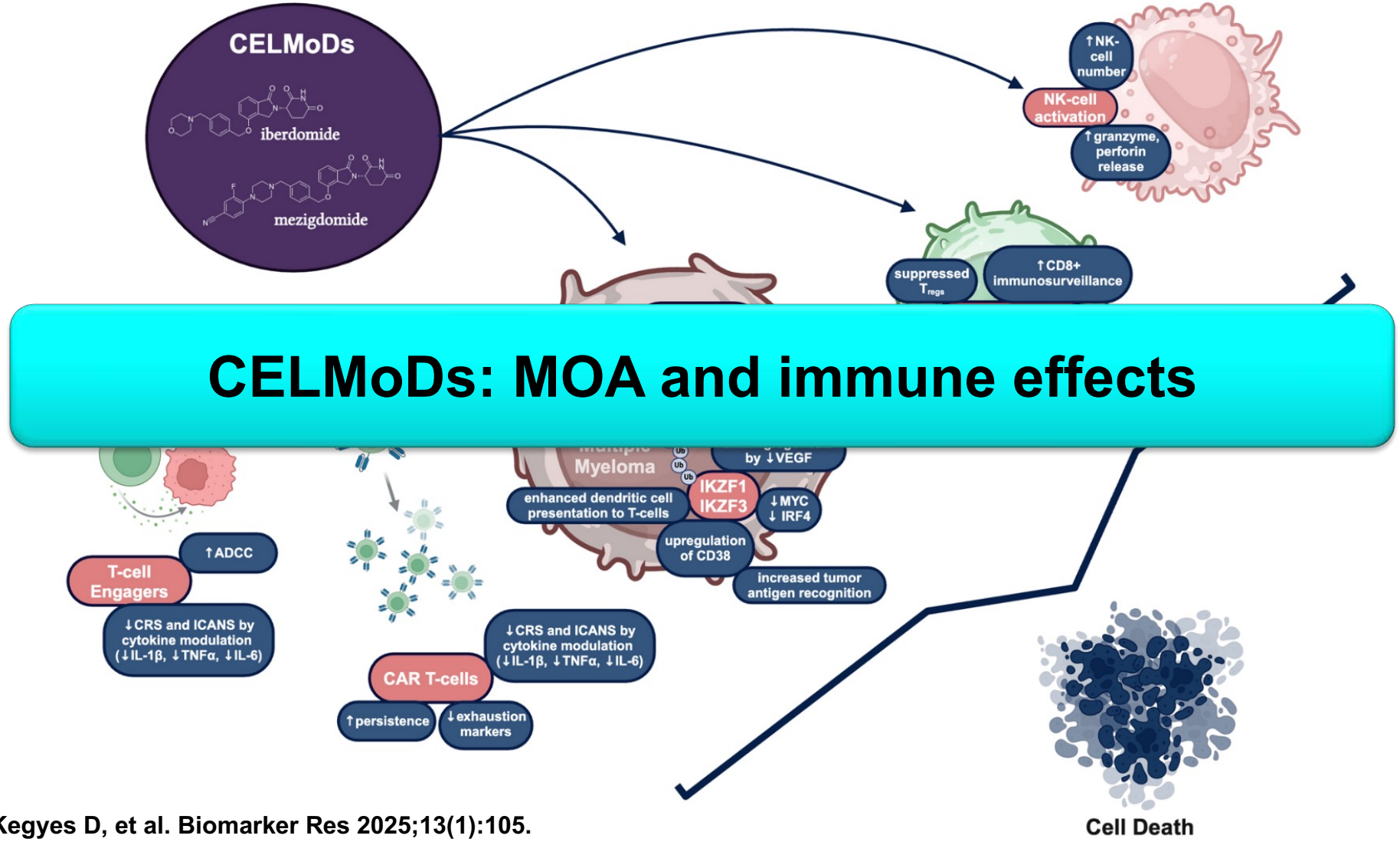
Strategies for managing MM, including doublet, triplet, and quadruplet combination regimens both upfront and in relapse, as well as treatment sequencing, are rapidly evolving in the context of this expanding therapeutic armamentarium

*Also approved in combination with l… n.
†Not currently approved in RRMM. ‡F…
ADCs, antibody–drug conjugates; BC… cell engagers; CAR, chimeric antigen… rs; CHMP, Committee for Medicinal Prod… le myeloma; EMA, European Medicines A… d and Drug Administration; GPRC5D, G protein-coupled receptor family C group 5 member D; ICIs, immune checkpoint inhibitors; IMiDs®, immunomodulatory drugs; mAbs, monoclonal antibodies; PIs, proteasome inhibitors; RRMM, relapsed/refractory multiple myeloma.

Adapted from Richardson PG. 5th Oxford Myeloma Workshop, January 30–31, 2025, Oxford, UK.

MOA of CELMoDs: iberdomide[1] and mezigdomide[2]

CELMoDs: overview of immunologic effects



Kegyes D, et al. Biomarker Res 2025;13(1):105.

1. Lonial S, et

Figures adapted from: (left) Sato T, et al. Front Cell Dev Biol 2021;9:629326; (right) D'Souza C, et al. Front Immunol 2021;12:632399.

CELMoDs: summary of pharmacodynamics

Enhanced effects seen with anti-MM agents, potential mechanisms of resistance

Sensitization/potentiation

- ↑ Cytotoxicity of BCMA-targeted BsAb alnuctamab, greater enhancement of activity with mezigdomide vs pom
- ↑ Alnuctamab antitumor activity … activation, tumor tissue infiltrati… …ll
- ↑ Adhesion molecules, T-cell-me…
- ↑ Regressions and PFS in vivo w… + GPRC5D-targeted BsAb forimt…
- ↑ Durable responses, favorable T-cell p…

Direct immune/antitumor effects

- ↑ Cytokine production
- ↑ T cell activation and proliferation
- ↑ NK cell cytotoxicity
- ↓ Exhausted/senescent T and NK cells

Enhanced/synergistic effects

- ↑ Tumor growth inhibition, synergistic cell killing – mezigdomide + V±dex
- Potent immunomodulation with mezigdomide + Vd
- ↑ Apoptotic activity vs pom with mezigdomide + V
- …0-fold lower concentration of …ide vs pom
- …lete regressions, prolonged survival in …ezigdomide + Vd vs pom-Vd

Enhanced viability/persistence

- ↑ Viability in IL-2-starved CAR T cells
- ↑ Activation markers HLA-DR, CD69
- ↑ Effector memory phenotype CAR T c…
- ↑ Production of IL-2, IL-17a, TNFα antig… specific cytokines by CD8+ and CD4+ CAR T cells against BCMA-expressing MM cells
- ↑ Antigen-specific toxicity

…priming, enhanced apoptosis

- …ell surface expression
- … ADCP with subsequent Dara
- …sis with mezigdomide + Dara
- …rative CD3+ T cells, effector …y CD4+ T cells, HLA-DR-expressing CD4+ T cell activation

CKS1B downregulation

- ↑ Apoptosis, ↓ cell proliferation with mezigdomide + bromodomain-containing protein 4 (BRD4) inhibitor
- Potential for activity in gain/amp 1q21 MM

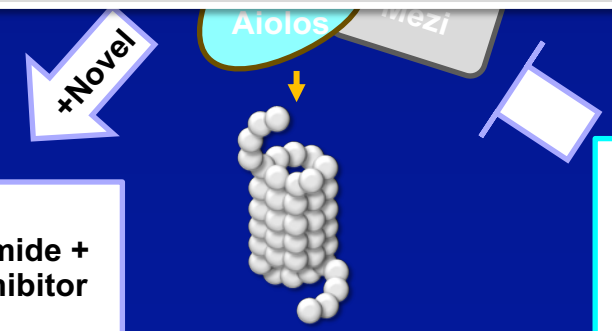
Potential resistance mechanisms

- *CRBN* alterations
- Monoallelic 3p26 loss
- ↓ Expression of COP9 signalosome protein complex
- ↑ USP15 expression
- Alterations in SREBP lipid synthesis pathway
- High baseline EZH2 expression → poorer PFS

Mezi overcomes *CRBN* mutations emerging post IMiD therapy

- Mezigdomide interacts with additional moieties outside of the thalidomide binding domain
- May affect the stabilization of cereblon or the CRL4CRBN E3 ligase complex
- May result in clinical responses
- Not seen with pomalidomide

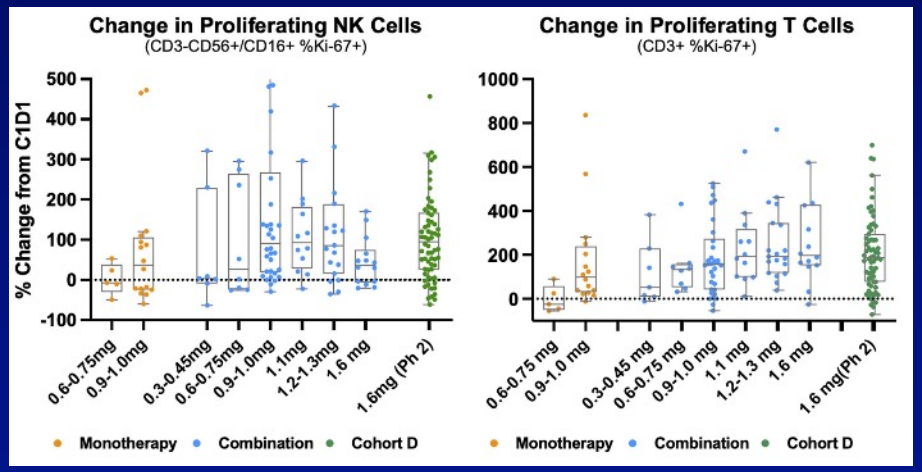
Watson E, et al. Blood 2025;146(Supplement 1):436.



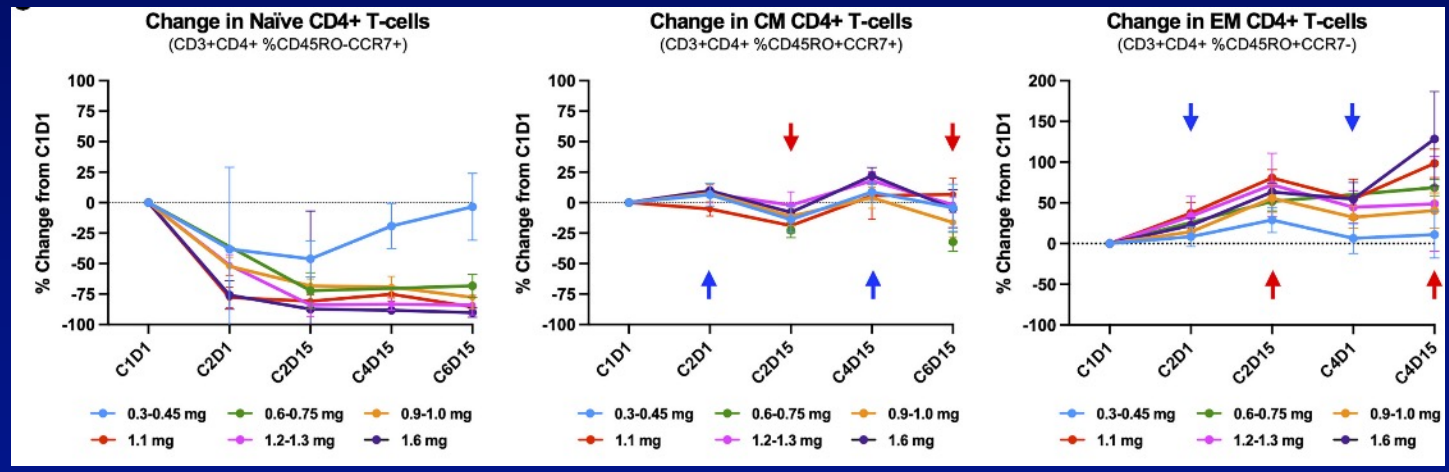
Mo CC, et al. Expert Opin Emerg Drugs 2025;30(3):209–19.

Iberdomide: immune cell responses

Immunostimulatory effects:[1] increased proliferating (Ki-67+) NK and T cells

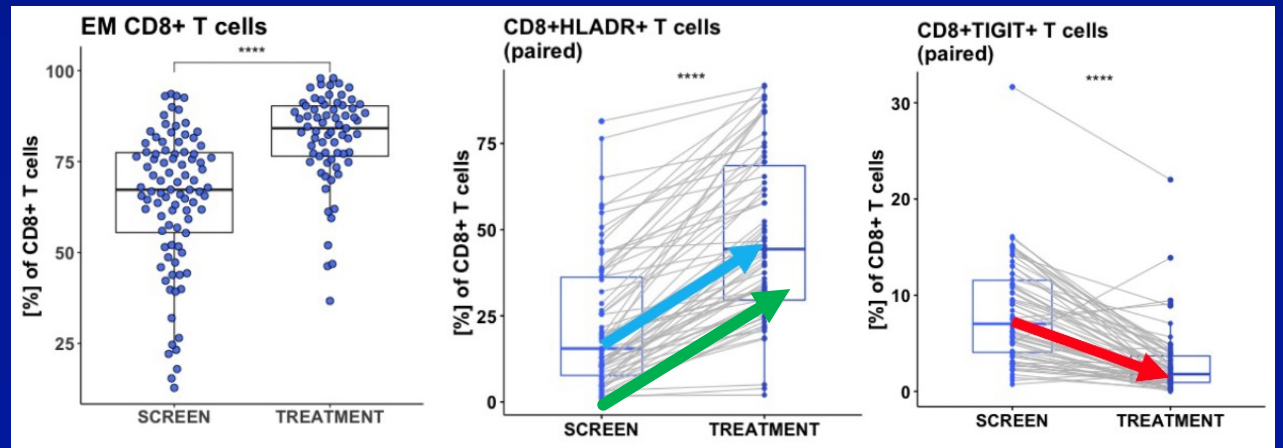


T-cell subset analysis:[1] shift from naïve to activated, effector-memory T cell phenotype with iberdomide, with decrease in naïve T cells and increase in effector-memory T cells



Paired BM sample analysis of iberdomide effects[2]

Increased effector cell abundance | **Increased activation** | **Decreased exhaustion**

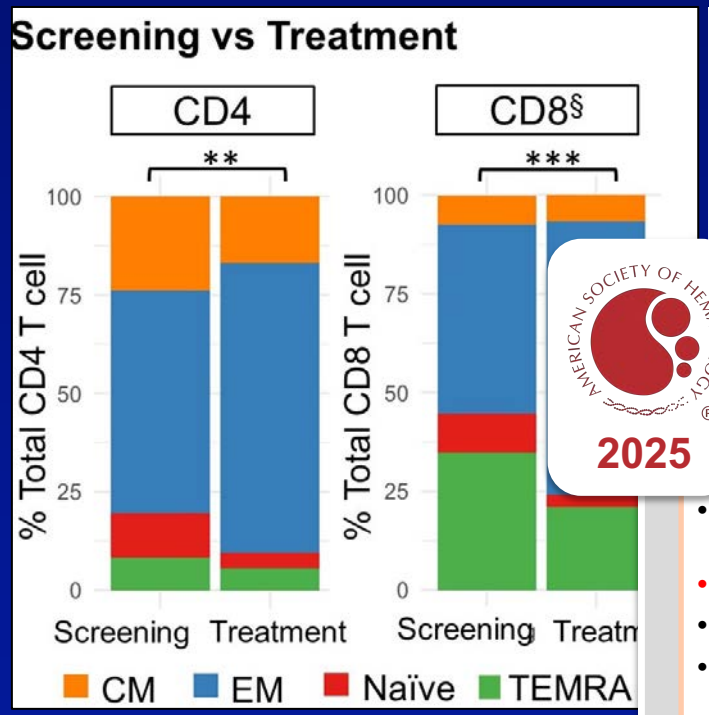


1. Amatangelo M, et al. Cell Rep Med 2024;5(6):101571.
2. Van Oekelen O, et al. Cell Rep Med 2024;5(6):101684.

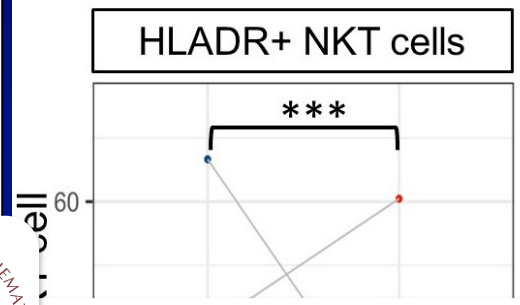
Mezigdomide: immune cell responses

Paired BM sample analysis of mezigdomide effects[1]

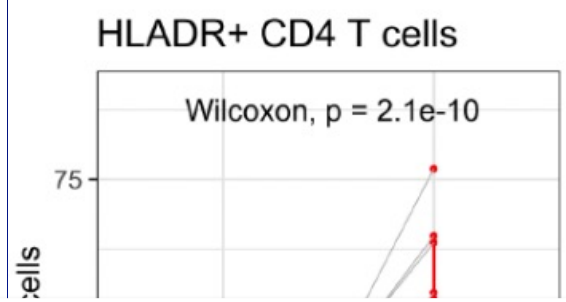
Shift towards effector T cell phenotype



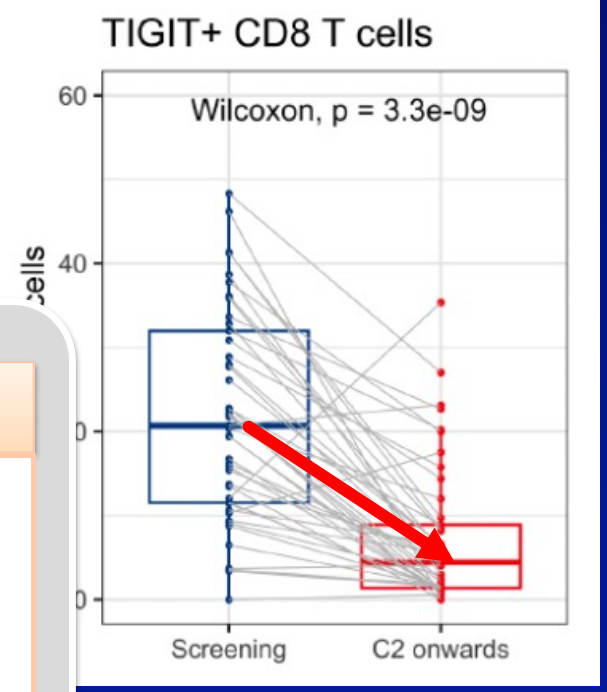
Increased activation



Increased activation



Decreased exhaustion



2025

Mechanistic rationale for enhanced antitumor immunity

- Mezigdomide and iberdomide significantly decrease induction of monocytic myeloid-derived suppressor cells (mMDSCs)
- Significant upregulation of inflammatory response genes in MM cells
- Reduced expression of key immunosuppressive mediators IL-10 and MIF
- Mechanisms contribute to remodelling tumor microenvironment towards an immune-permissive state

Niiyama-Uchibori Y, et al. Blood 2025;146(Supplement 1):7447.

Chen, LY et al. Blood 2023;142(Supplement 1):4686.

The NEW ENGLAND JOURNAL of MEDICINE

CELMoD doublet for later-relapse RRMM

Mezigdomide + dex: Phase 1/2 study, N=178

CC-92480-MM-001 first-in-human phase 1 trial: Mezigdomide + Dex

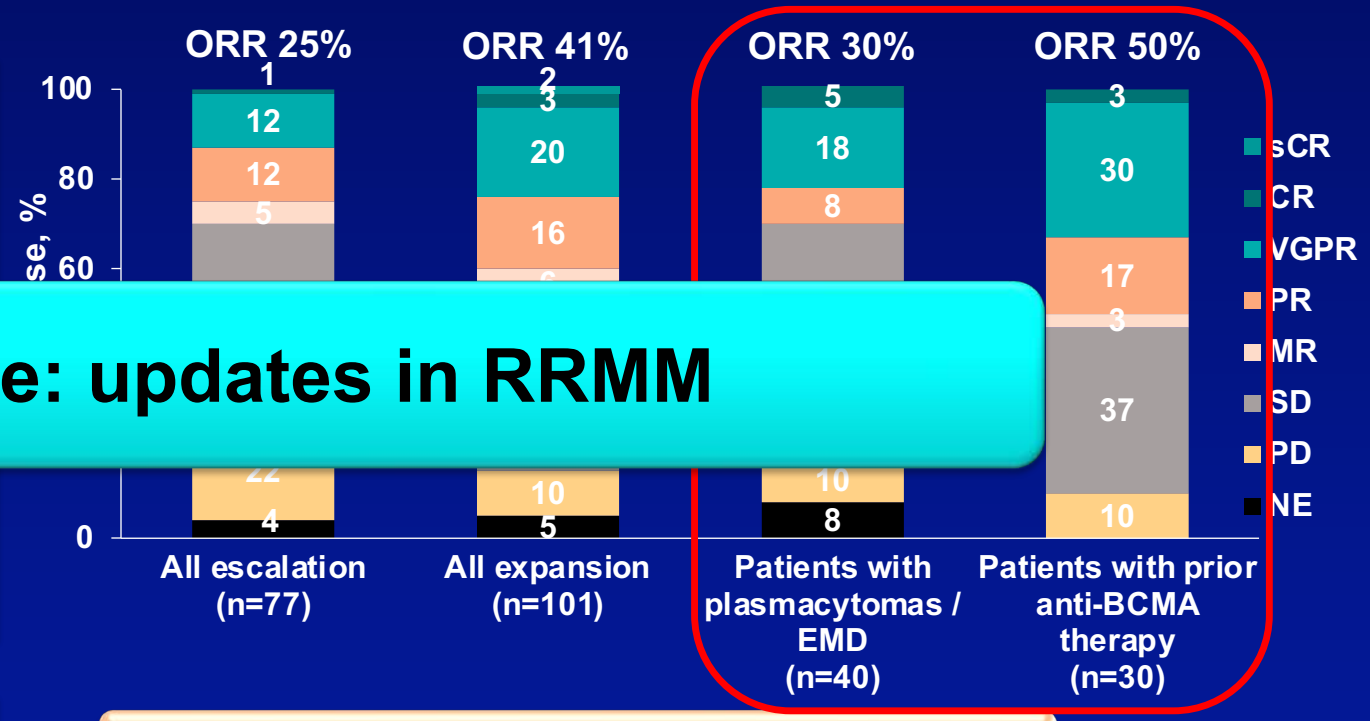
Dose escalation

- 77 heavily pretreated RRMM patients
- 30% high-risk cytogenetics, 35% EMD
- Median 6 prior therapies
- 56% triple-class-refractory

Dose expar

- 101 heavily [illegible]
- 37% high-risk cytogenetics, 40% EMD
- Median 6 prior therapies
- 100% triple-class-refractory

Mezigdomide: updates in RRMM



Efficacy in dose expansion cohort

- Median DOR 7.6 months
- Median PFS 4.4 months
- In patients with prior anti-BCMA therapy, median DOR 6.9 months and median PFS 5.4 months

Safety in dose escalation/expansion cohorts

- Grade 3/4 neutropenia 71%/76%, anemia 38%/36%, thrombocytopenia 24%/28%, febrile neutropenia 9%/15%
- Infections 74%/65% (Grade 3/4 40%/35%)
- Treatment discontinuation due to AEs NR/6%

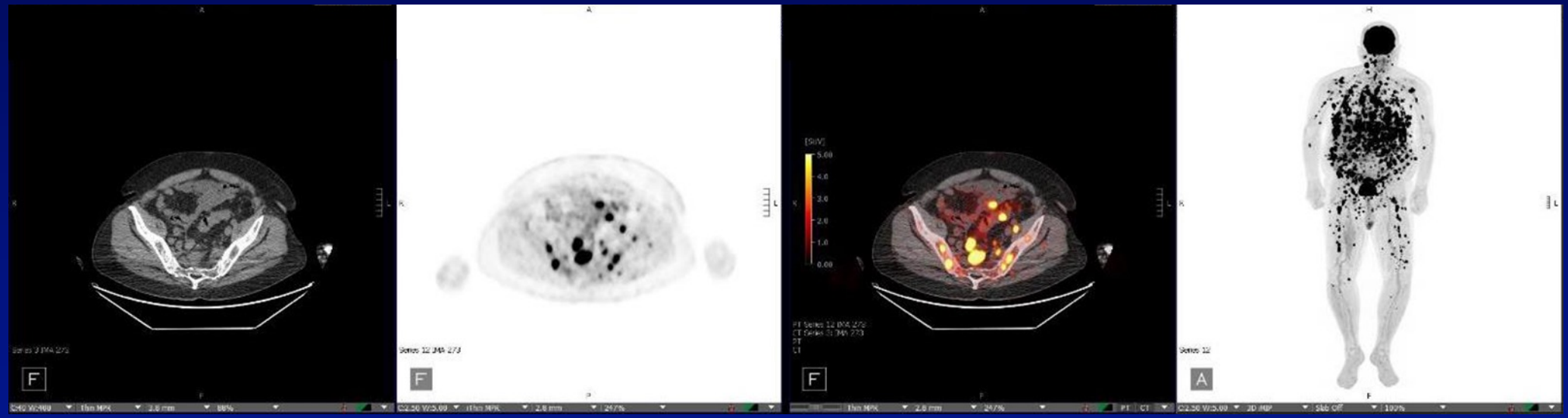
Richardson PG, et al. N Engl J Med 2023;389(11):1009–22.

The NEW ENGLAND JOURNAL of MEDICINE

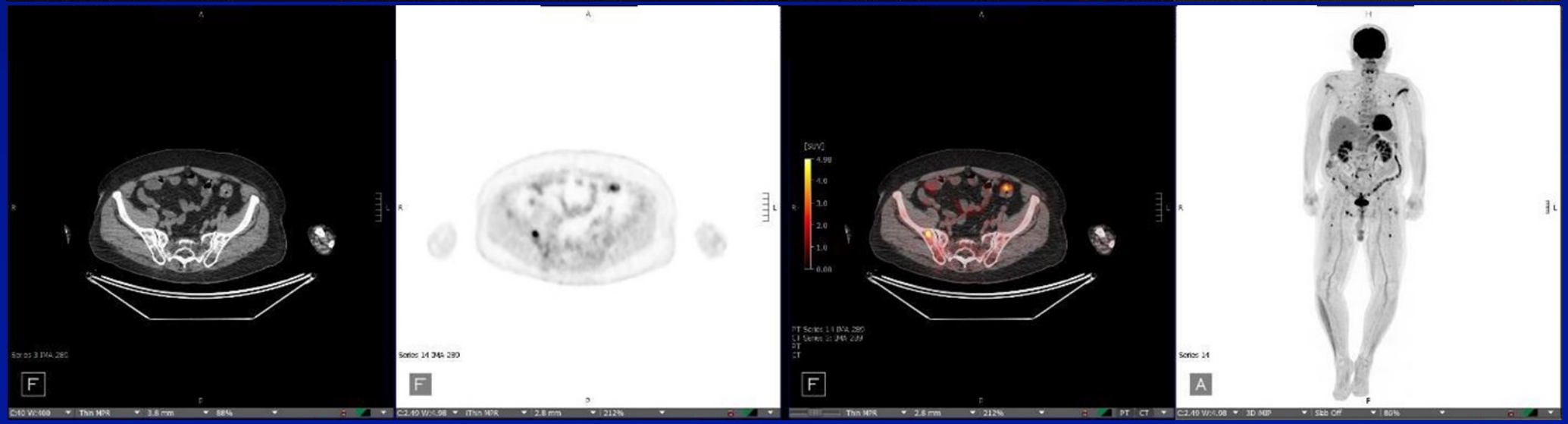
CELMoD doublet for later-relapse RRMM

Mezigdomide + dex induces responses in patients with EMD

At start of treatment (study entry)



After 4 months of treatment with Mezi 1.0 mg, D1–21 every 28 days, + Dex



Richardson PG, et al. Blood 2022;140(Supplement 1):1366–8. Richardson PG, et al. N Engl J Med 2023;389(11):1009–22.

CELMoD triplets for RRMM: mezigdomide–PI regimens

Mezigdomide + Vd or Kd

CC-92480-MM-002 Phase 1/2 Study: Mezigdomide + Vd / Kd[1,2]

Mezigdomide + Vd (N=28)

- 42.9% high-risk cytogenetics
- Median 3 prior therapies
- 82.1% R-refractory
- 50.0% PI-refractory
- 50.0% CD38 mAb-refractory
- Median duration of treatment: 12.5 cycles

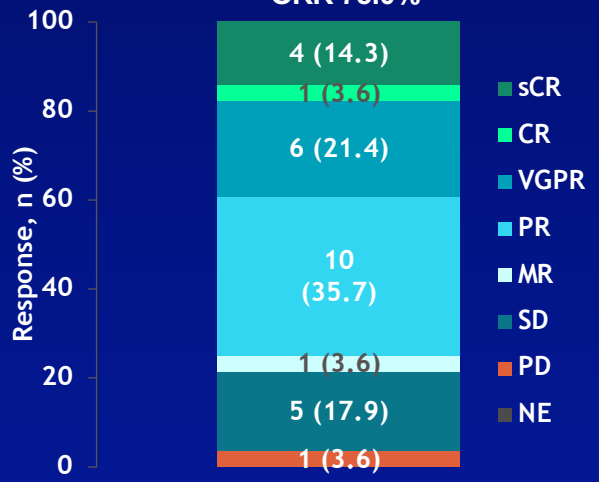
Mezigdomide + Vd 1.0mg (N=38) / 0.6 mg (N=11)

- 53.1% high-risk cytogenetics
- Median 1 prior therapy
- 63.3% R-refractory
- 16.3% PI-refractory
- 34.7% CD38 mAb-refractory
- Median duration of treatment: 15 cycles

Mezigdomide + Kd (N=27)

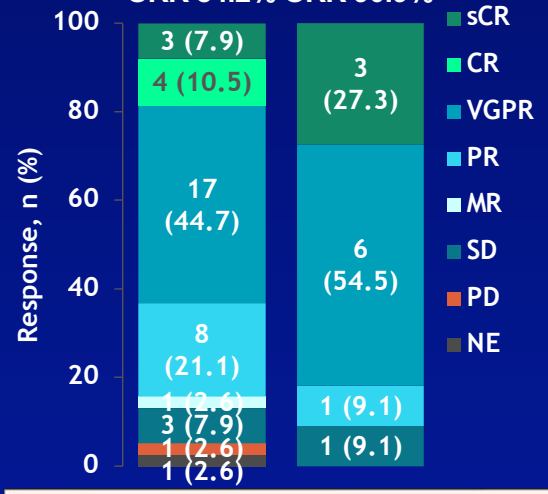
- 59.3% high-risk cytogenetics
- Median 2 prior therapies
- 77.8% R-refractory
- 51.9% PI-refractory
- 74.1% CD38 mAb-refractory
- Median duration of treatment: 12 cycles

Mezigdomide + Vd (N=28, dose escalation)



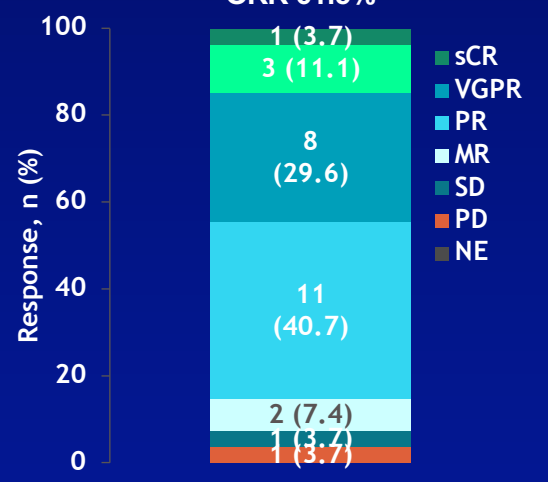
- Median DOR 10.9 months
- Median PFS 11.2–13.4 months
- Grade 3/4 neutropenia 35.7%
- Grade 3/4 thrombocytopenia 21.4%
- Grade 3 anemia 14.3%
- Infections 71.4% (Grade 3/4 17.9%)
- Grade 3/4 pneumonia 10.7%

Mezigdomide + Vd (1.0 mg, N=38 / 0.6 mg, N=11)



- Median DOR 19.4 months
- Median PFS 16.6 / 20.8 months
- Grade 3/4 neutropenia 63.3%
- Grade 3/4 thrombocytopenia 26.5%
- Grade 3 anemia 6.1%
- Infections 79.6% (Grade 3/4 32.7%)
- Grade 3/4 pneumonia 22.4%

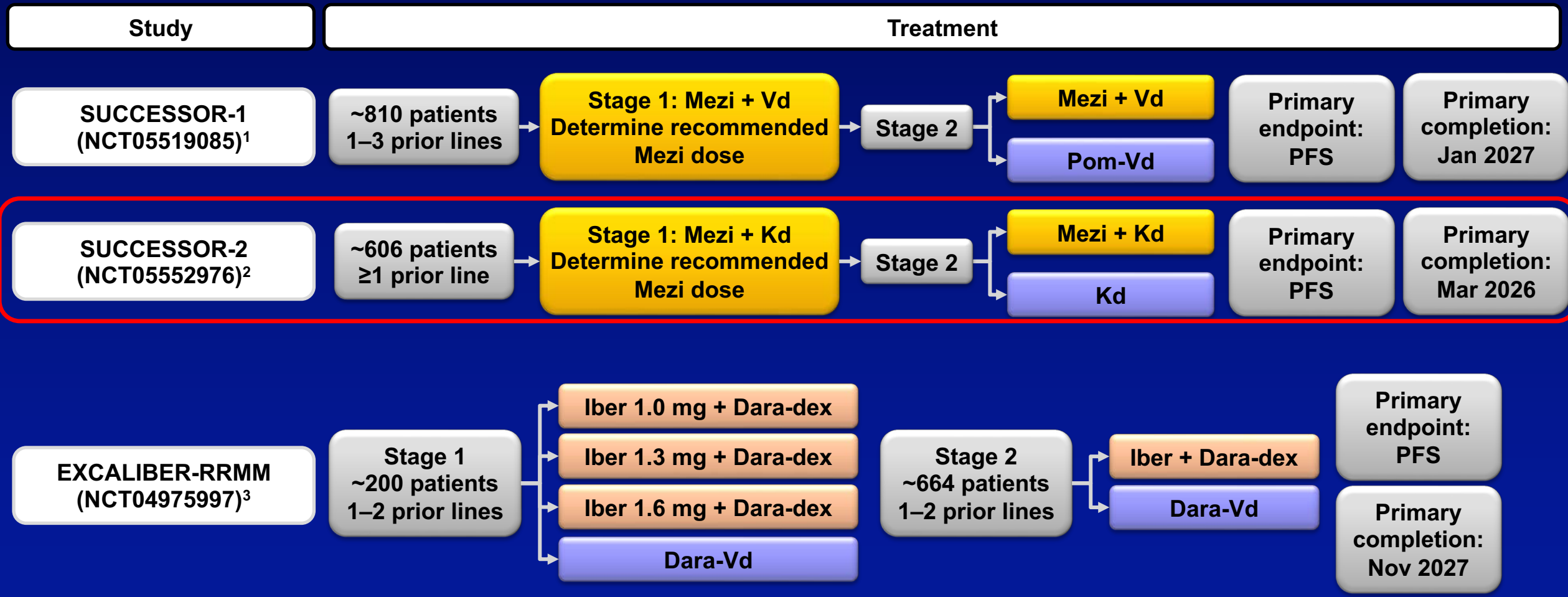
Mezigdomide + Kd (N=27)



- Median DOR 11.9 months
- Median PFS 11.7–13.8 months
- Grade 3/4 neutropenia 44.4%
- Grade 3/4 thrombocytopenia 14.8%
- Grade 3/4 anemia 14.8%
- Infections 70.4% (Grade 3/4 33.3%)
- Grade 3/4 pneumonia 3.7%

1. Oriol A, et al. Clin Lymphoma Myeloma Leukemia 2023;23(Suppl 2):S31.
2. Sandhu A, et al. Blood 2024;144(supplement 1):1025.

Phase 3 studies of CELMoD triplets in RRMM: combination with SOC mAbs or PIs



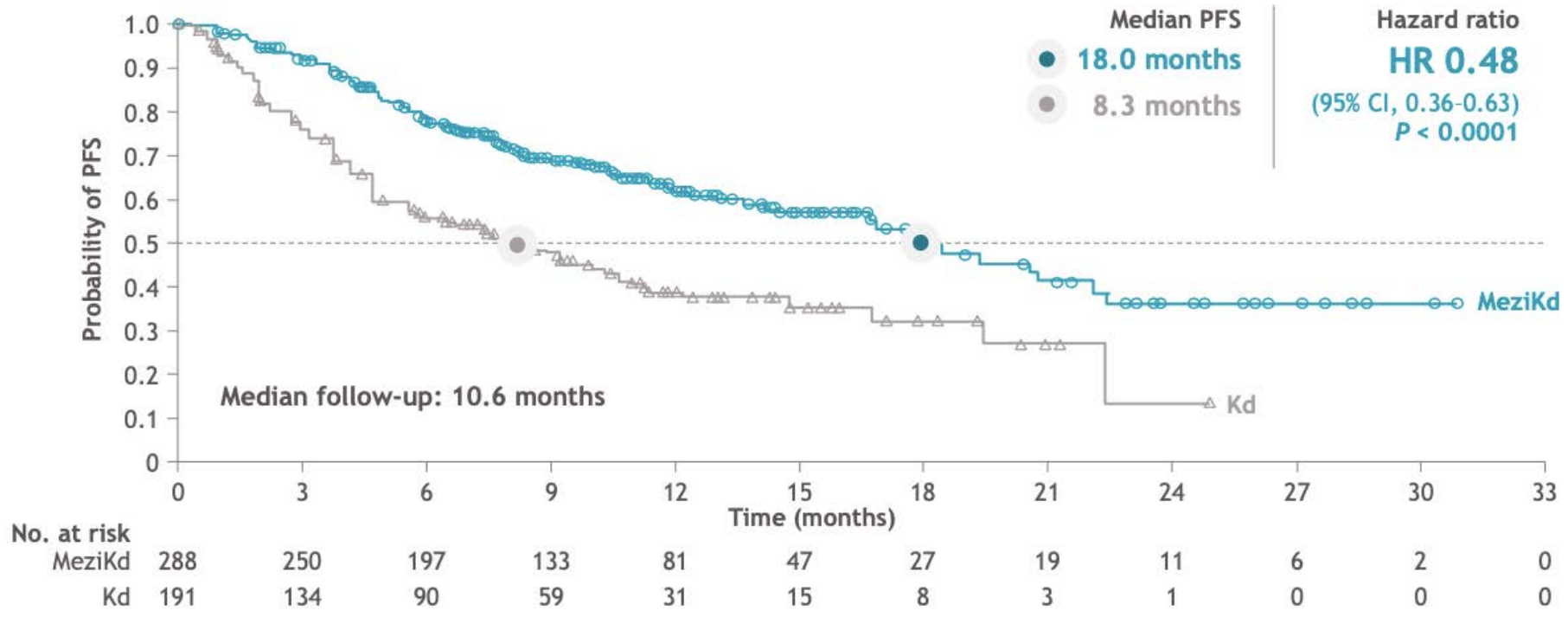
1. Richardson PG, et al. Clin Lymphoma Myeloma Leuk 2023;23(Supplement 1):S495–6, abstract MM-372.
2. Richardson PG, et al. J Clin Oncol 2023;41(16_suppl):abstract TPS8070.
3. Lonial S, et al. Future Oncol 2025;21(14):1761–9.

CELMoD triplets for RRMM: mezigdomide–PI regimen

Phase 3 SUCCESSOR-2 trial of mezigdomide + Kd vs Kd

N= 606; Stage 1 ~ dose optimization n=235, Stage 2 ~ efficacy and safety n=372, with total confirmatory analysis by ITT in 479 patients

PFS: Primary Endpoint

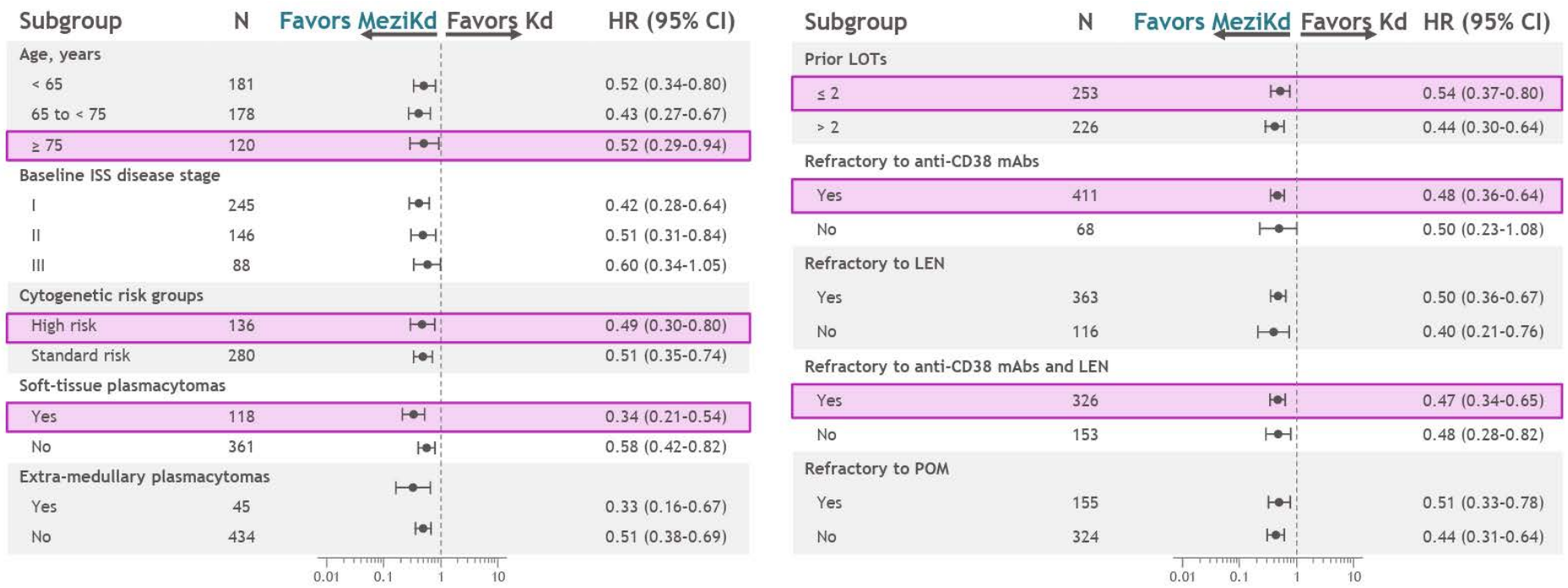


In anti-CD38 mAb- and LEN-exposed patients who had received ≥ 1 prior LOT (range 1-9), MeziKd significantly reduced risk of progression or death by 52%.

Richardson PG, et al. J Clin Oncol 2026;44(16_suppl):LBA7506.

CELMoD triplets for RRMM: mezigdomide–PI regimen
Phase 3 SUCCESSOR-2 trial of mezigdomide + Kd vs Kd
Confirmatory analysis group by ITT(n = 479)

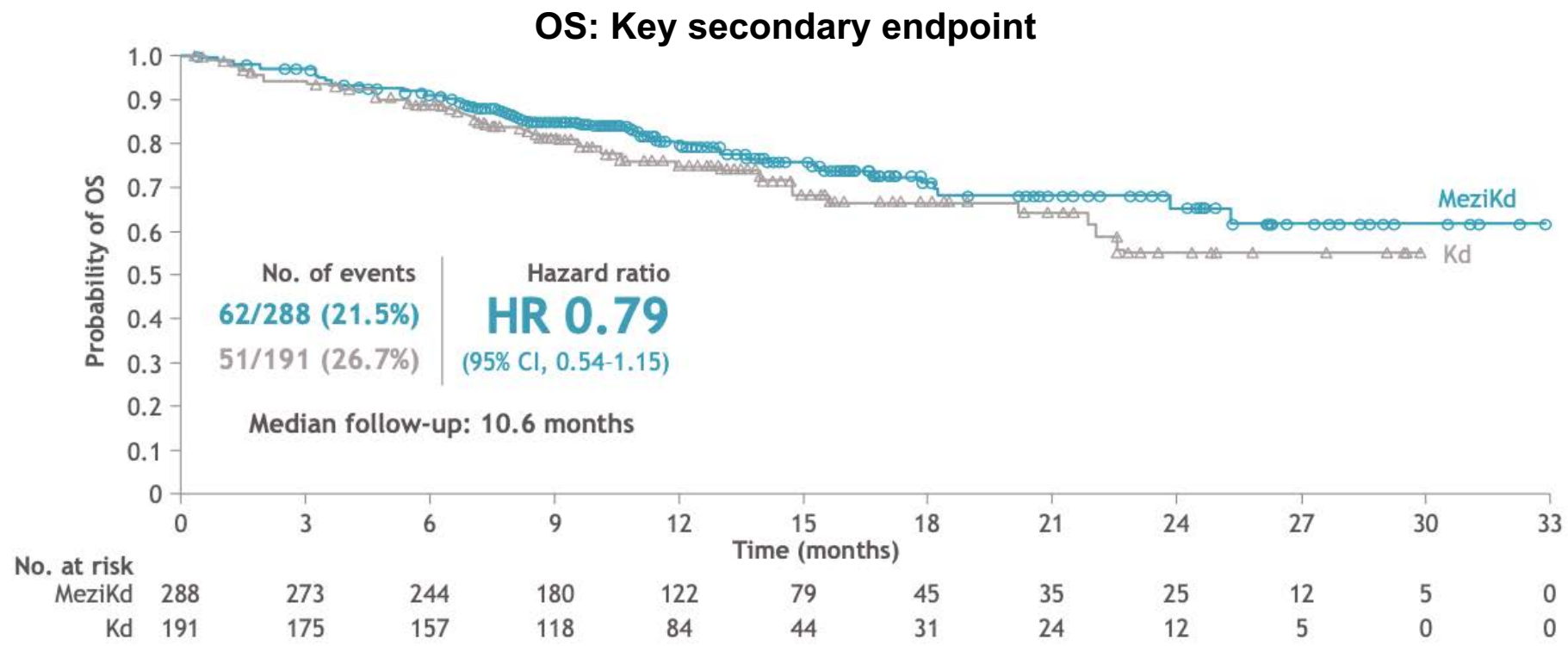
PFS Subgroup Analyses



PFS survival benefit with MeziKd superior across all prespecified subgroups.

Richardson PG, et al. J Clin Oncol 2026;44(16_suppl):LBA7506.

CELMoD triplets for RRMM: mezigdomide–PI regimen
Phase 3 SUCCESSOR-2 trial of mezigdomide + Kd vs Kd
Confirmatory analysis group by ITT (n = 479)

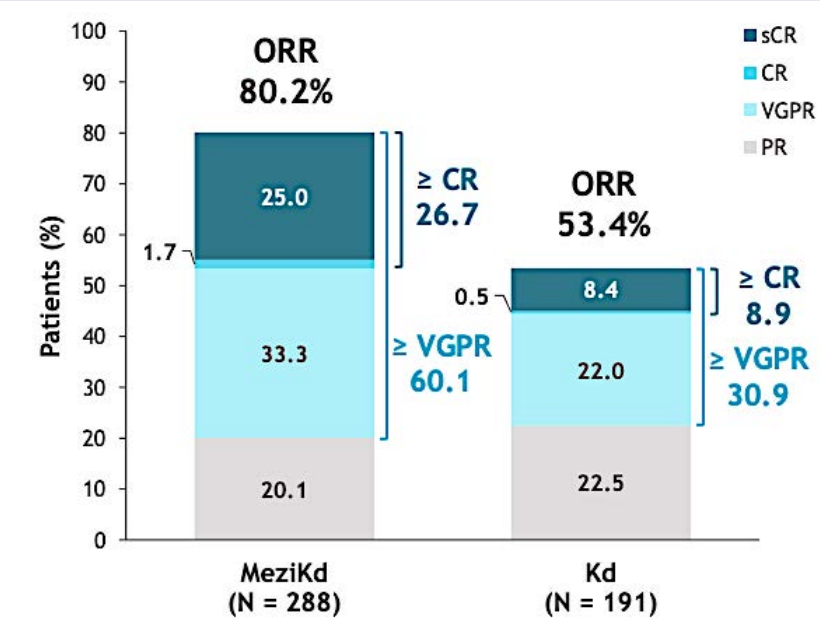


Planned futility analysis demonstrates a positive OS trend favoring MeziKd with no cross over of the curves.

Richardson PG, et al. J Clin Oncol 2026;44(16_suppl):LBA7506.

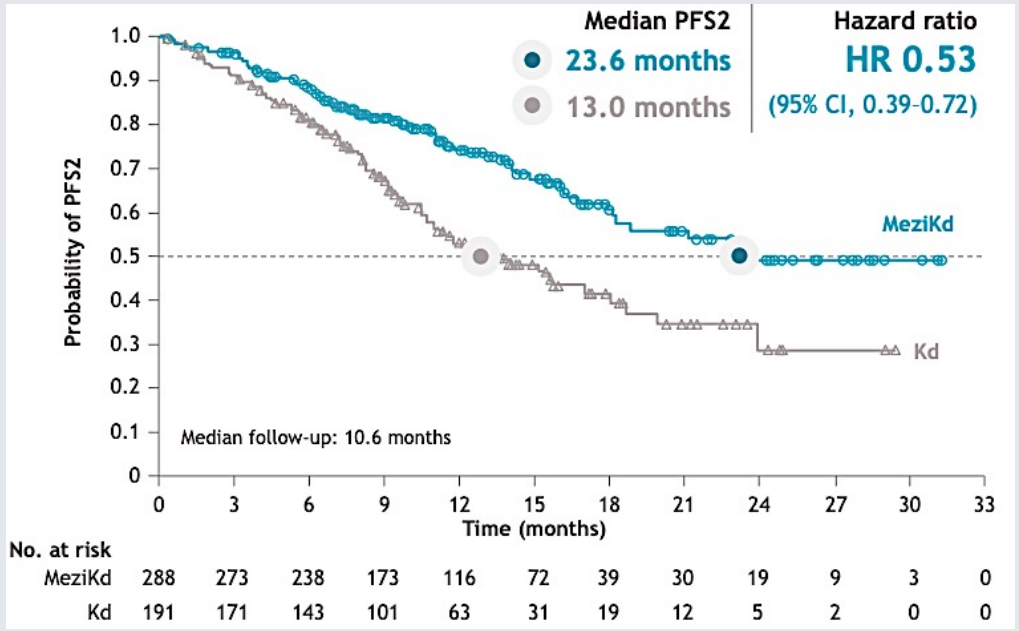
CELMoD triplets for RRMM: mezigdomide–PI regimen
Phase 3 SUCCESSOR-2 trial of mezigdomide + Kd vs Kd
Confirmatory analysis group by ITT (n = 479)

Treatment response



Time to response	1.1 mos	1.1 mos
12-month DoR	72%	54%

PFS2



Richardson PG, et al. J Clin Oncol 2026;44(16_suppl):LBA7506.

CELMoD triplets for RRMM: mezigdomide - PI regimen
Phase 3 SUCCESSOR-2 trial of mezigdomide + Kd vs Kd
Confirmatory analysis group for safety (n = 474)

Most common TEAEs

TEAE,[a] n (%)	MeziKd (N = 288)		Kd (N = 186)[b]	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Any TEAE	286 (99.3)	241 (83.7)	178 (95.7)	105 (56.5)
Hematological				
Neutropenia[c]	199 (69.1)	176 (61.1)	32 (17.2)	17 (9.1)
Febrile neutropenia	24 (8.3)	23 (8.0)	0	0
Thrombocytopenia[d]	174 (60.4)	113 (39.2)	77 (41.4)	42 (22.6)
Anemia	149 (51.7)	75 (26.0)	66 (35.5)	28 (15.1)
White blood cell count decrease	67 (23.3)	54 (18.8)	23 (12.4)	7 (3.8)
Nonhematological				
Diarrhea	112 (38.9)	10 (3.5)	33 (17.7)	1 (0.5)
URTI	79 (27.4)	13 (4.5)	31 (16.7)	3 (1.6)
Fatigue	67 (23.3)	9 (3.1)	39 (21.0)	7 (3.8)
Cough	66 (22.9)	1 (0.3)	22 (11.8)	0
Pneumonia	58 (20.1)	45 (15.6)	21 (11.3)	11 (5.9)
Dyspnea	58 (20.1)	11 (3.8)	26 (14.0)	5 (2.7)
Hypertension	31 (10.8)	11 (3.8)	40 (21.5)	17 (9.1)

- Neutropenia is an on-target reversible AE; only 1 patient discontinued treatment due to neutropenia with MeziKd (none with Kd)
- A reduction in grade 3/4 hypertension was observed with MeziKd, potentially associated with the lower K dose
- Grade 3/4 VTE[e] occurred in 2.8% (MeziKd) and 0.5% (Kd) of patients
- Grade 5 TEAEs were observed in 7.3% (MeziKd) and 4.3% (Kd) of patients
  - The majority were in the context of myeloma progression

Neutropenia was the most common grade 3/4 AE and was managed effectively with dose interruptions/modifications and/or G-CSF

Richardson PG, et al. J Clin Oncol 2026;44(16_suppl):LBA7506.

CELMoD triplets for RRMM: mezigdomide–PI regimen
Phase 3 SUCCESSOR-2 trial of mezigdomide + Kd vs Kd
Confirmatory analysis group for safety (n= 474)

Summary of infections

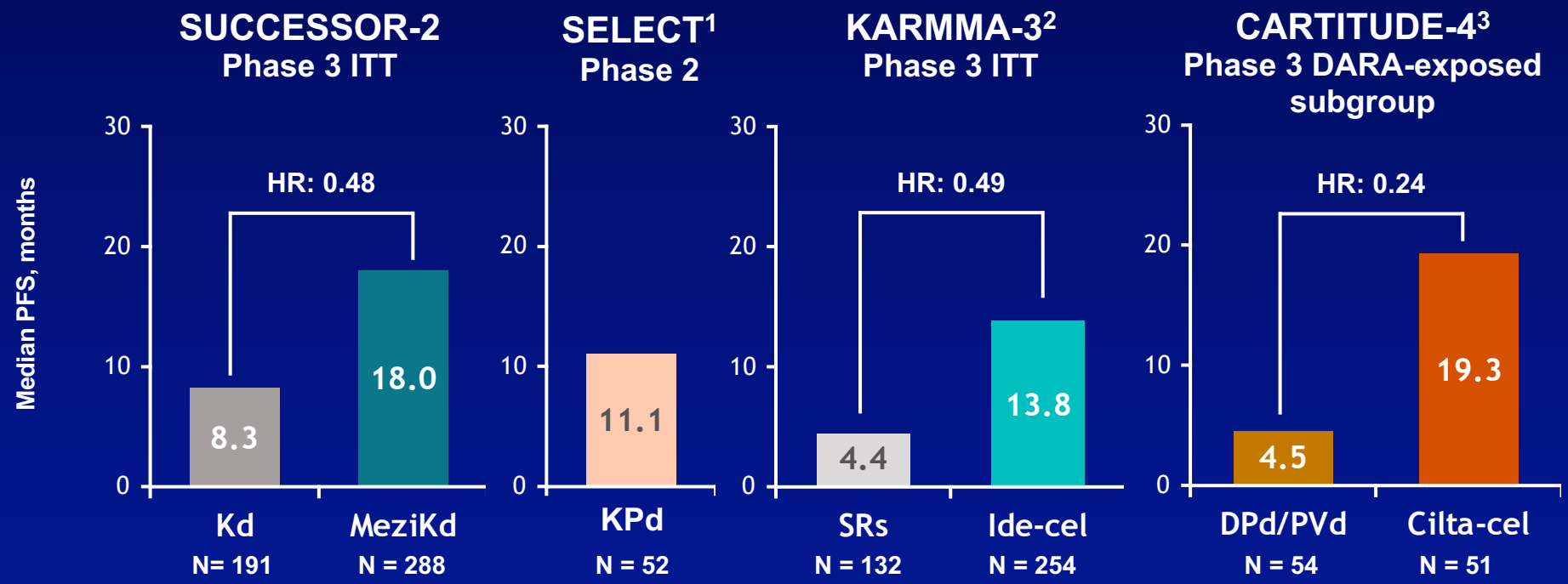
TEAE,[a] n (%)	MeziKd (N = 288)			Kd (N = 186)[b]		
	Any grade	Grade 3	Grade 4	Any grade	Grade 3	Grade 4
Any infection	210 (72.9)	82 (28.5)	16 (5.6)	100 (53.8)	28 (15.1)	1 (0.5)
URTI	79 (27.4)	13 (4.5)	0	31 (16.7)	3 (1.6)	0
Pneumonia	58 (20.1)	39 (13.5)	6 (2.1)	21 (11.3)	10 (5.4)	1 (0.5)
Influenza	30 (10.4)	9 (3.1)	0	18 (9.7)	2 (1.1)	0
COVID-19	29 (10.1)	5 (1.7)	0	11 (5.9)	0	0
RTI	29 (10.1)	7 (2.4)	0	8 (4.3)	0	0
UTI	26 (9.0)	8 (2.8)	0	9 (4.8)	1 (0.5)	0
Nasopharyngitis	17 (5.9)	0	0	18 (9.7)	0	0
Bronchitis	17 (5.9)	6 (2.1)	0	7 (3.8)	0	0

- Most infections (68.6% MeziKd; 98.0% Kd) were not associated with grade 3/4 neutropenia
- Incidence of hypogammaglobulinemia was low
  - 10.1% (MeziKd) versus 6.5% (Kd)
  - 31.6% (MeziKd) versus 21.0% (Kd) of patients received ≥1 dose of IGRT
- Incidence of fatal infections was low (2.4% MeziKd; 1.1% Kd)

Infections were mostly well managed following standard clinical practice and supportive care, with low incidence of grade 4 events.

Richardson PG, et al. J Clin Oncol 2026;44(16_suppl):LBA7506.

Contextualization of Clinical Benefit seen in SUCCESSOR 2 for Anti-CD38 mAb- and LEN-exposed RRMM Patients across multiple settings



Median prior LOT, n (range)	2 (1–9)	2 (1–9)	2 (1–2)	3 (2-4)	3 (2-4)	NR	NR
LEN-ref., %	76.9	74.4	100	73	79	100	100
Anti CD38 mAb-exposed, %	100	100	77	100	100	100	100
Anti CD38 mAb-refractory, %	85.3	86.1	75	95	94	83.3	90.5

Trials are not intended for direct comparison. Side-by-side data are presented solely to summarize information.

All patient were exposed to LEN. DPd, daratumumab, pomalidomide, and dexamethasone; IIT, intention-to-treat; NR, not reported; PVd, pomalidomide, bortezomib, and dexamethasone; SR, standard of care regimen.

1. Perrot A, et al. *Leuk Lymphoma* 2024;65(6):833-842; 2. Ailawadhi S, et al. *Blood* 2024;144(23):2389-2401; 3. Einsele H, et al. *Lancet Oncol* 2026;27(2):254-268.

CELMoD triplets for RRMM: mezigdomide–mAb regimens

Mezigdomide + Dara-dex or Elo-dex

CC-92480-MM-002 Phase 1/2 Study: Mezigdomide + Dara-dex / Elo-dex[1]

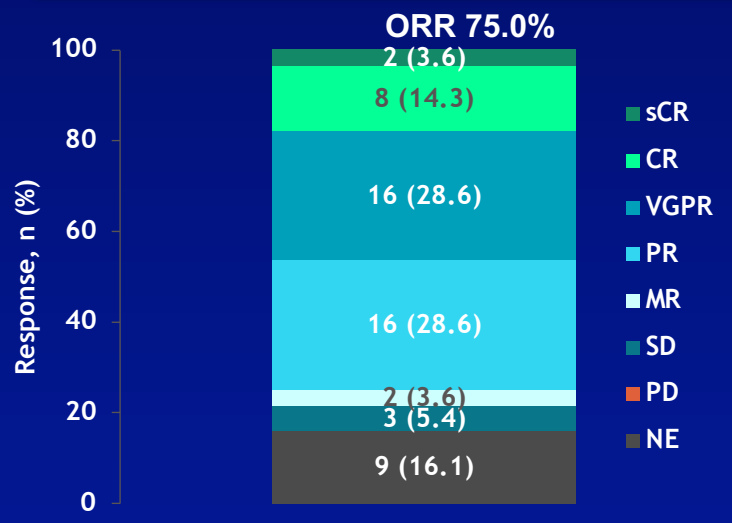
Mezigdomide + Dara-dex (N=56)

- Median age 67 years
- Median time since diagnosis 8.2 years
- Median 2 prior therapies
- 82.5% IMiD-refractory
- 61.4% PI-refractory
- 15.8% prior ASCT
- 8.8% prior CD38 mAb

Mezigdomide + Elo-dex (N=20)

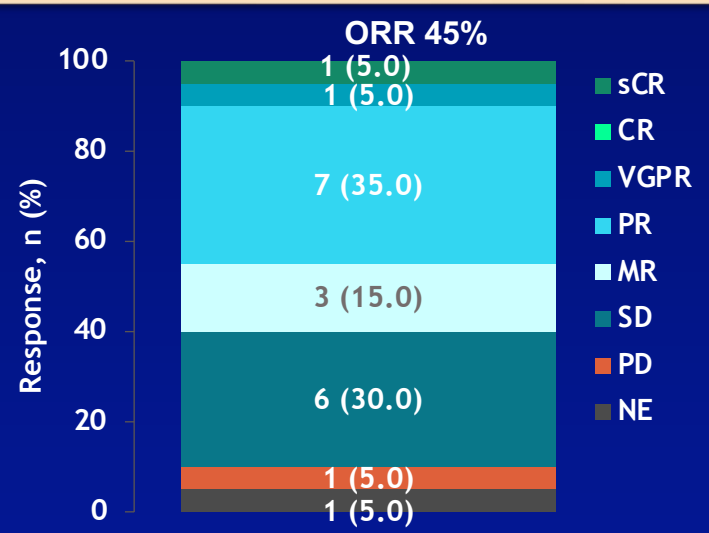
- Median 3 prior therapies
- 85% prior CD38 mAb

Mezigdomide + Dara-dex (N=56)



- DOR / PFS not mature
- Grade 3/4 neutropenia 53.6%
- Grade 3/4 thrombocytopenia 7.1%
- Grade 3/4 anemia 10.7%
- Grade 3/4 infections 19.6%

Mezigdomide + Elo-dex (N=20)



- DOR / PFS not mature
- Grade 3/4 neutropenia 40%
- Grade 3/4 thrombocytopenia 10%
- Grade 3/4 anemia 20%
- Grade 3/4 infections 35%

1. Richardson PG, et al. Blood 2023;142(supplement 1):1013.

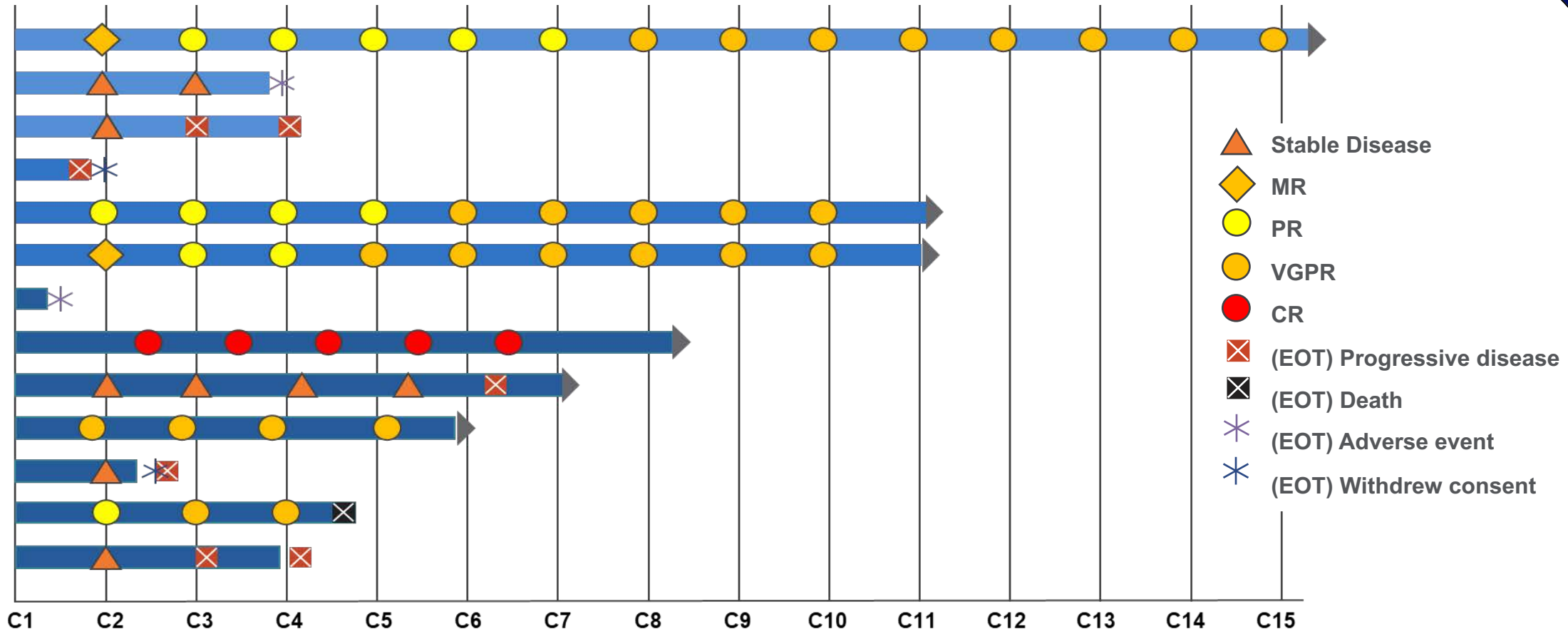
CELMoD triplets for later-relapse RRMM: combination with targeted agents

STOMP Arm 12: Mezigdomide + Selinexor-dex

Cohort 1
40 mg Seli
0.6 mg Mezi
40 mg Dex

Cohort 2
60 mg Seli
0.6 mg Mezi
40 mg Dex

Cohort 3
60 mg Seli
1.0 mg Mezi
40 mg Dex



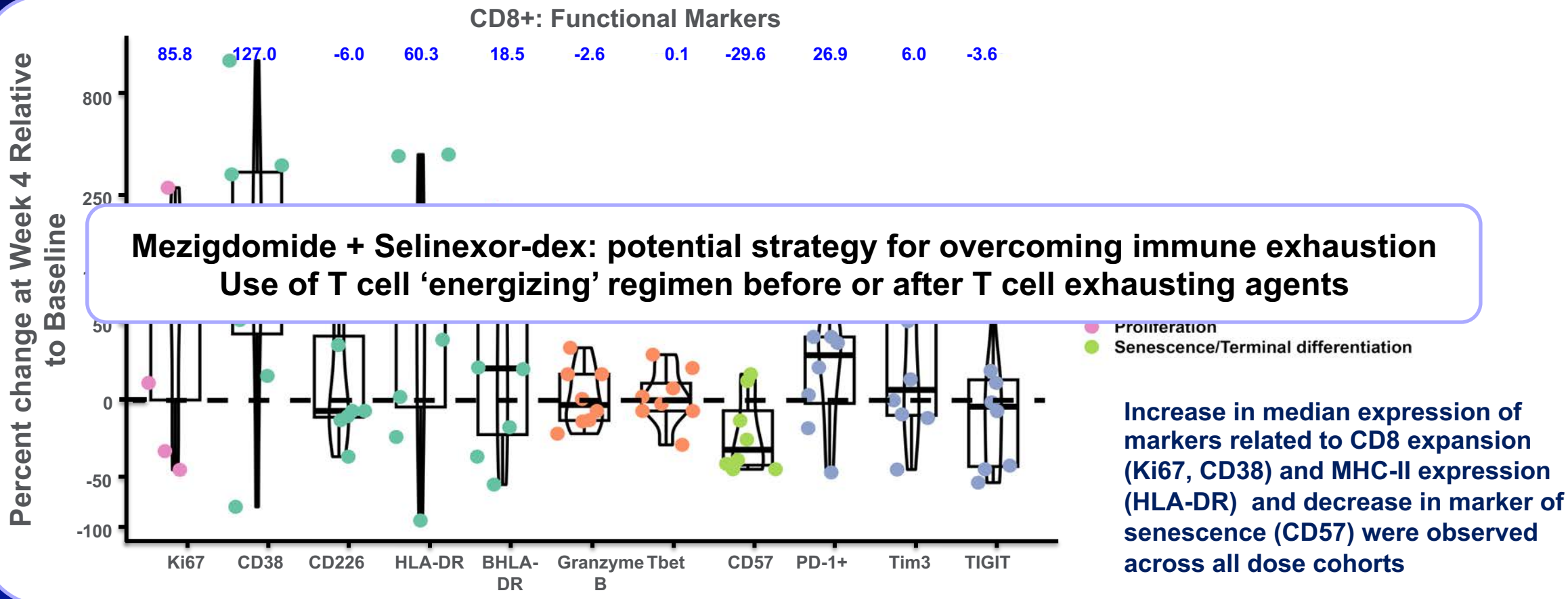
ORR: 50% (6/12) – all VGPR or better

Mo CC, et al. Blood 2025;146(Supplement 1):4010. Mo C, et al. 7th European Myeloma Network Meeting, April 16–18, 2026, Prague, Czechia, poster #P43.

CELMoD triplets for later-relapse RRMM: combination with targeted agents

STOMP Arm 12: Mezigdomide + Selinexor-dex

Mezi-Seli-dex results in CD8+ T cell proliferation and activation



Mezigdomide + Selinexor-dex: potential strategy for overcoming immune exhaustion
Use of T cell 'energizing' regimen before or after T cell exhausting agents

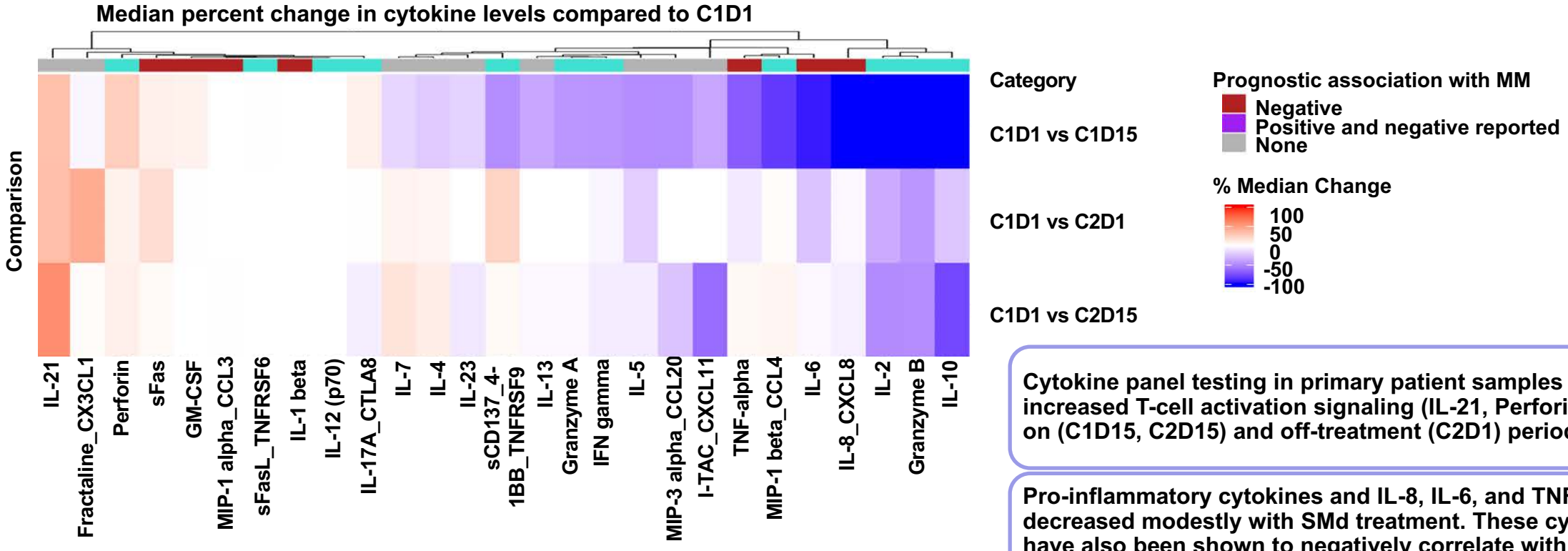
Increase in median expression of markers related to CD8 expansion (Ki67, CD38) and MHC-II expression (HLA-DR) and decrease in marker of senescence (CD57) were observed across all dose cohorts

Mo CC, et al. Blood 2025;146(Supplement 1):4010. Mo C, et al. 7th European Myeloma Network Meeting, April 16–18, 2026, Prague, Czechia, poster #P43.

CELMoD triplets for later-relapse RRMM: combination with targeted agents

STOMP Arm 12: Mezigdomide + Selinexor-dex

Mezi-Seli-dex upregulates T-cell activation-related cytokines and suppresses pro-inflammatory cytokines inversely associated with poor MM prognosis



Cytokine panel testing in primary patient samples indicated increased T-cell activation signaling (IL-21, Perforin) during on (C1D15, C2D15) and off-treatment (C2D1) periods

Pro-inflammatory cytokines and IL-8, IL-6, and TNF-alpha decreased modestly with SMd treatment. These cytokines have also been shown to negatively correlate with MM prognosis.[1-3]

Mo CC, et al. Blood 2025;146(Supplement 1):4010. Mo C, et al. 7th European Myeloma Network Meeting, April 16–18, 2026, Prague, Czechia, poster #P43.
1. Zhang XG, et al. Blood 1989;74:11–13. 2. Herrero AB, et al. Am J Path 2016;186:2171–82. 3. Jourdan M, et al. Eur Cytokine Netw 1999;10:65–70.

CELMoD triplets for later-relapse RRMM: combination with novel targeted agents

Mezigdomide-dex + tazemetostat (EZH2 inhibitor) / BMS-986158 (BET inhibitor) / trametinib (MEK inhibitor)

CA057-003 (NCT05372354) Phase 1/2 trial in patients with RRMM

Mezi-dex + Taz (N=16)

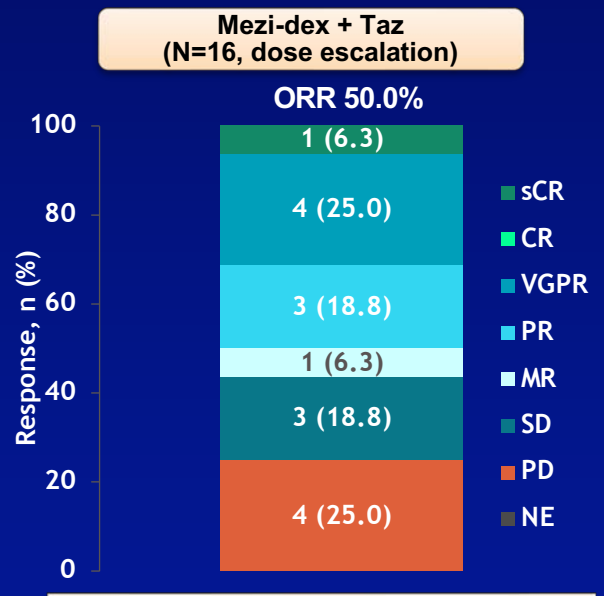
- 31.3% high-risk cytogenetics
- Median 5 prior lines
- 68.8% prior T-cell redirecting therapy
- 87.5% CD38 mAb-refractory
- 81.3% triple-class refractory

Mezi-dex + BMS-986158 (N=20)

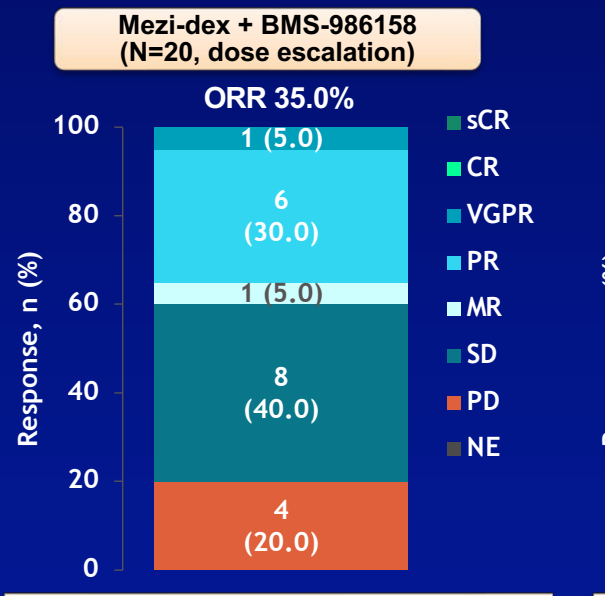
- 30.0% high-risk cytogenetics
- Median 5 prior lines
- 60.0% prior T-cell redirecting therapy
- 85.0% CD38 mAb-refractory
- 75.0% triple-class refractory

Mezi-dex + Tram (N=20)

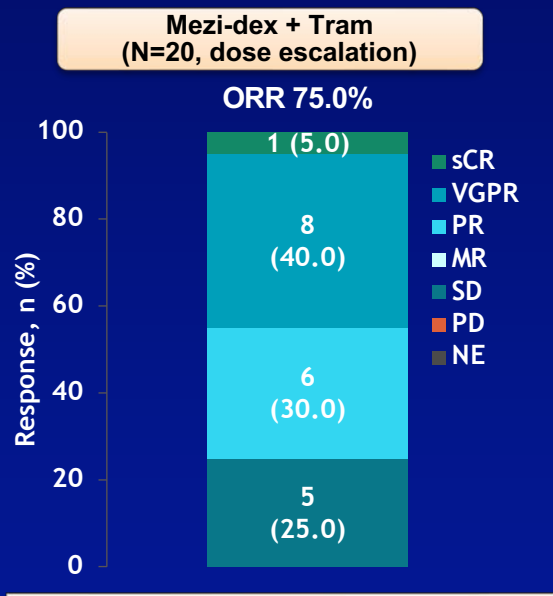
- 15.0% high-risk cytogenetics
- Median 4 prior lines
- 45.0% prior T-cell redirecting therapy
- 90.0% CD38 mAb-refractory
- 90.0% triple-class refractory



- Median DOR not reached
- Median PFS 6.7 months
- Grade 3/4 neutropenia 50.0%
- Grade 3/4 thrombocytopenia 6.1%
- Grade 3 anemia 12.5%
- Infections 68.8% (Grade 3/4 25.0%)
- Grade 3/4 pneumonia 12.5%



- Median DOR not reached
- Median PFS 4.6 months
- Grade 3/4 neutropenia 65.0%
- Grade 3/4 thrombocytopenia 40.0%
- Grade 3 anemia 35.0%
- Infections 50.0% (Grade 3/4 15.0%)
- Grade 3/4 pneumonia 5.0%



- Median DOR 6.5 months
- Median PFS 8.7 months
- Grade 3/4 neutropenia 80.0%
- Grade 3/4 thrombocytopenia 15.0%
- Grade 3/4 anemia 15.0%
- Infections 85.0% (Grade 3/4 25.0%)
- Grade 3/4 pneumonia 5.0%

Costa LJ, et al. Blood 2024;144(supplement 1):677.

Phase 3 studies of CELMoD triplets in RRMM: combination with SOC mAbs or PIs

Study	Treatment					
SUCCESSOR-1 (NCT05519085)[1]	~810 patients 1–3 prior lines	Stage 1: Mezi + Vd Determine recommended Mezi dose	Stage 2	Mezi + Vd Pom-Vd	Primary endpoint: PFS	Primary completion: Jan 2027
SUCCESSOR (NCT0555297					t:	Primary completion: Mar 2026
EXCALIBER-RRMM (NCT04975997)[3]					Primary endpoint: PFS	Primary completion: Nov 2027

Iberdomide: updates in RRMM

Feb 2026: US FDA accepts NDA for iberdomide in RRMM

- NDA for iberdomide plus Dara-dex in RRMM
  - Also granted Breakthrough Therapy designation
- Based on planned analysis of MRD-neg rates in EXCALIBER-RRMM
- PDUFA date: August 17, 2026

BMS Press Release. See https://www.myeloma.org/news-events/multiple-myeloma-news/fda-accepts-new-drug-application-iberdomide-rrmm

1. Richardson PG, et al. Clin Lymphoma Myeloma Leuk 2023;23(Supplement 1):S495–6, abstract MM-372.
2. Richardson PG, et al. J Clin Oncol 2023;41(16_suppl):abstract TPS8070.
3. Lonial S, et al. Future Oncol 2025;21(14):1761–9.

CELMoD triplets and quadruplets for RRMM: combination with mAbs or PIs

Iberdomide + Isa-dex or Dara-Kd

Iberdomide + Isa-dex for functional high-risk RRMM IBIS AMaRC 20-01 study[1]

29/50 functional high-risk RRMM patients
sing ≤18 months after first-line therapy

ALLG MM25 (Viber-M): Iberdomide + venetoclax + dex in t(11;14) RRMM (N=44)

- Analysis in first 20 patients
- Median age 65 yrs
- 75% 1 prior line, 25% 2 prior lines; 75% R exposed (65% R-refractory), 20% CD38 mAb-refractory
- ORR 80%; 25% ≥VGPR
- Grade ≥3 AEs 55%, including neutropenia 45%, thrombocytopenia 10%, infections 20%

Sim S, et al. Blood 2025;146(Supplement 1):249.

Safety

- Grade 3/4 neutropenia 52%, insomnia 8%, infusion-related reaction 2%, upper respiratory tract infection 4%
- 2 grade 5 AEs: lung infection, sepsis

Iberdomide + Dara-Kd in RRMM (Phase 2 ReKInDLE study)[2]

30 RRMM patients after 1–3 prior lines

dian age 63 years (range 44–77); 33% high-risk (IMWG

Iber maintenance post salvage ASCT

- 15 patients with RRMM undergoing salvage ASCT
- Median age 61 yrs; 66% high-risk cytogenetics
- Median 2 prior lines; 73% triple-class refractory
- Post salvage ASCT: 7% CR/MRD-neg, 33% CR/MRD-pos, 13% VGPR, 33% PR, 14% SD
- Median follow-up 15.4 months
- Best response to iberdomide: 25% CR/MRD-neg, 25% VGPR, 25% PR, 25% SD
- Median PFS from start of iberdomide 9.3 months
- Grade 3 AEs: 1 neutropenia, 2 maculopapular rash, 3 infections

Tijaro Ovalle N, et al. Blood 2025;146(Supplement 1):4048.

thrombocytopenia, 3% anemia

- 6 (20%) SAEs, including 3 (10%) lung infections

1. Lim S-L, et al. Blood 2025;146(Supplement 1):5841. 2. Landgren O, et al. Blood 2025;146(Supplement 1):251.

Overcoming T-cell exhaustion

Improving CAR T-cell function with CELMoDs

2024

Preclinical benefit of CELMoD-dex on TCE outcome

- Immunocompetent CRBN+ mouse model
- Dex alone shown to moderate T-cell proliferation in response to TCE and to give moderate sustained cytokine production
- Incremental TCE step-up dosing combined with iberdomide or mezigdomide plus dex was feasible and tolerable
- Pretreatment with iber-dex before TCE gave 100% response rate, highest over

Meyeier EW

EHA2025 Congress

Immune system reactivation with mezigdomide regimens

- Analysis of immune profiles in 56 patients with RRMM receiving mezigdomide-dexamethasone-based regimens
- 28 patients had T cell redirecting therapy (TCRT) in last regimen
- TCRT-treated patients had increases in immune cell subsets related to persistent activation and lower Treg counts

oliferation levels, tivation, and a shift prior TCRT

CELMoDs and CAR Ts/BsAbs in RRMM

Enhancing CAR T cells with iberdomide

- Analysis of functional effect of iberdomide-dex on CAR T cells in 7 patients and on immune activation in 17 patients with RRMM previously treated with CAR T-cell therapy
- Increases in CD4+ T cells, central memory and effector memory T cells, and T-cell-expressing activation markers in iberdomide-treated samples obtained for CAR T-cell therapy production
- Manufactured CAR T cells had higher proliferation rates and decreased proportions of exhausted cells
- Ex vivo treatment with iberdomide enhanced CAR T cell expansion and functionality
- In patients with prior CAR T-cell therapy, iberdomide increased T/NK cell proliferation and promoted shift to an activated effector memory phenotype

Aleman A, et al. HemaSphere 2025;9(S1):PF685.

2026 ASCO ANNUAL MEETING

Expansion of highly activated CAR T cell population after mezigdomide exposure post–ide-cel

- Phase 1 study (NCT06048250) of mezigdomide started 60–120 days post-ide-cel; 6 RRMM patients (median age 81 years, median 5 prior lines) with peripheral blood immunoprofiling data
- Trend towards increased BCMA CAR T cells by C1D8 – % of BCMA CAR T cells associated with achieving CR
- Early increases in HLA-DR+/CD38+ T cells/CAR T cells – associated with inflammation and disease activity in other settings
- Early increases in CD8+ effector memory cells, CTLA-4+ T cells
- Early decreases in suppressive cells (e.g. CD8+ TEMRA)
- Shift from exhausted to activated T-cell phenotype

Liu LW, et al. J Clin Oncol 2026;44(16_suppl):7540.

ASH 2025: Novel combination studies in RRMM with CELMoDs and CAR Ts/BsAbs

MagnetisMM-30: Elranatamab + iberdomide[1]

- 22 patients with RRMM following 2–4 prior lines
- Median age 68 yrs, 41% high-risk cytogenetics, 18% EMD
- Median 2.5 prior lines; 50% triple-class refractory
- Median follow-up 6.1 months
  - Unconfirmed ORR 91%; 68% ≥VGPR, 46% ≥CR
- Grade 3/4 AEs 68%, including neutropenia 59%, anemia 14%, thrombocytopenia 14%
- CRS 68% (all Grade 1/2), 9% ICANS
- Infections 41% (5% Grade 3/4)

CADMIUM (Alliance A062102): Ide-cel + iberdomide[2]

- Randomized Phase 2 study (NCT06179888) of iberdomide maintenance post ide-cel
- Patients with RRMM, ≥4 prior lines of therapy
- 6–12 patients in part 1 (safety run-in)
  - 60 patients in part 2, randomized to iberdomide or observation post ide-cel
- Primary endpoint: PFS
  - Secondary endpoints: OS, best response, deepening of response, including MRD-neg CR conversion

CA088-1005: Arlo-cel + mezigdomide[3] or iberdomide

- Phase 1 study (NCT06121843) of arlo-cel plus novel therapies including mezigdomide and iberdomide
  - Dose-finding and dose-expansion study, with up to 30 patients in the latter part
  - Patients with RRMM following ≥3 (dose-finding, n=10 in dose-expansion) and 1–3 (n=20 in dose-expansion) prior lines of therapy
- Primary endpoint: AEs and RP2D
  - Secondary endpoints: preliminary efficacy (ORR, CR rate, VGPR rate) and pharmacokinetics

CA057-1040: Elranatamab + mezigdomide[4]

- Phase 1b/2a study (NCT06988488) of elranatamab plus mezigdomide
  - Phase 1 dose-escalation and phase 2 dose-expansion study, 22 patients in 2 phase 2 arms
  - Patients with RRMM following 2–4 prior lines of therapy, including an IMiD, a PI, and a CD38 mAb
- Primary endpoint: AEs and DLTs
  - Secondary endpoints: ORR, CR rate, VGPR rate, TTR, DOR, PFS and OS

MELT-MM: Elranatamab + mezigdomide[5]

- Phase 1/2 study (NCT06645678) of elranatamab plus mezigdomide
  - 75 patients receiving one of 3 dose levels of mezigdomide
  - Patients with RRMM ≥2 prior lines of therapy, including R and a PI
- 11 patients enrolled to date: 8 at mezi 0.3 mg/kg, 3 at mezi 0.6 mg/kg
  - Median 4 prior lines
  - ORR (n=10) 90% (50% CR/sCR)
  - CRS 55% (all grade 1)

1. Suvannasankha A, et al. Blood 2025;146(Supplement 1):100. 2. Tuchman S, et al. Blood 2025;146(Supplement 1):2289 . 3. Bal S, et al. Blood 2025;146(Supplement 1):5807. 4. Bar N, et al. Blood 2025;146(Supplement 1):8246. 5. Byun JM, et al. Blood 2025;146(Supplement 1):5835.

CELMoD doublets/triplets for NDMM

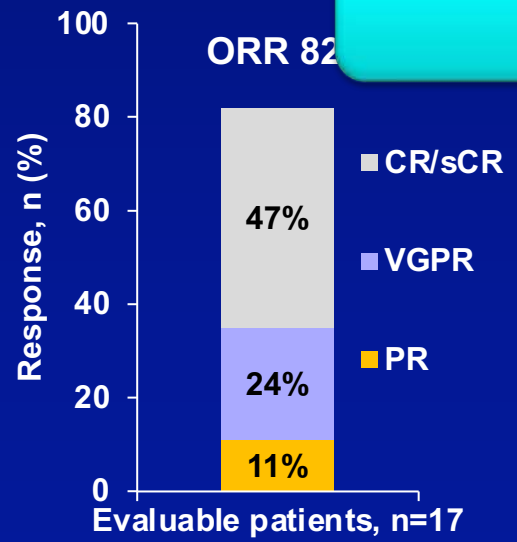
Iberdomide-dex ± Dara

EHA2025 Congress

International Myeloma Society 22nd Annual MEETING & EXPOSITION September 17–20, 2025 Toronto, Canada

Iber-dex in 18 elderly/frail transplant-ineligible NDMM patients[1]

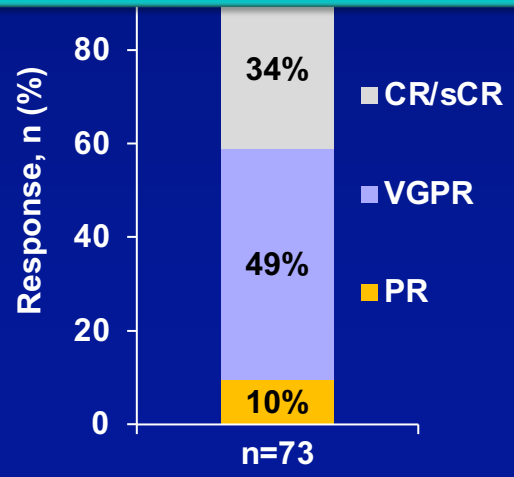
- Iberdomide 1.6 mg (Days 1–21, 28-day cycles) + weekly dex 40 mg (20 mg if ≥ 75 years)
- Median age 79 years, 12 (67%) were frail per modified IMWG criteria
- High-risk cytogenetic abnormalities in 5 (28%) patients, EMD in 6 (33%)
- ISS stage III in 9 (50%); R-ISS stage III in 5 (28%)



- Median treatment exposure: 20 cycles
- Common AEs: neutropenia 78%, infections 72%
- Grade 3/4 neutropenia in 12 patients (67%) and infections in 7 patients (39%)
- Anemia 33%
- Thrombocytopenia 28%
- Rash 44% (grade 3/4 in 6%)
- Diarrhea 33% (all grade 1/2)

Iber-Dara-dex in 77 elderly/frail transplant-ineligible NDMM patients

- Iberdomide 1.6/1.0 mg (Days 1–21, 28-day cycles) + Dara 1800 mg (standard schedule) + weekly dex 40 mg (20 mg if ≥ 75 years)
- Median age 77 years, 51 (69%) were frail per modified IMWG criteria, with 30 being ultra-frail
- ISS stage III in 29%
- Analyses after first 6 cycles; median follow-up 11.1 months



- 12-month OS 81.1%

Safety

- Grade 3/4 AEs: neutropenia 68%, thrombocytopenia 7%, anemia 5%, febrile neutropenia 5%
- Infections 48% (17% Grade ≥3), including 39% (9%) respiratory infections
- Rash 23% (3% Grade ≥3)
- Diarrhea 17% (1% Grade ≥3)

Iberdomide: updates in NDMM
Future impact on CELMoDs in RRMM

1. Puig N, et al. HemaSphere 2025;9(S1):PS1784. 2. González-Calle V, et al. Clin Lymphoma Myeloma Leuk 2025;25(Supplement 2):S363–4, OA-63.

CELMoD triplets for NDMM

Iberdomide + Dara-dex

75 transplant-ineligible NDMM patients

- Iberdomide 1.0, 1.3, 1.6 mg
- 25 patient[illegible]se level
- NDMM wi[illegible]
- Biomarker de[illegible]

2026 ASCO ANNUAL MEETING

IDEAL: Efficacy and safety of iberdomide + Dara-Vd in NDMM

- 44 transplant-eligible/-ineligible NDMM pts receiving Iber-Dara-Vd at RP2D for 12 cycles followed by Iber maintenance for 24 cycles
- Median age 65 years; 52.3% high-risk disease
- ORR 100%
- ≥CR 36.4% after induction, 52.3% overall
- MRD-negative (10^{-5}) response 29.5% after induction, 47.7% overall
- Median follow-up 18.3 months
- 12-month PFS 91%, 18-month PFS 88%
- 12-month OS 97%, 18-month OS 94%
- Common toxicities: neutropenia, rash, PN, diarrhea, infections

Kapoor P, et al. J Clin Oncol 2026;44(16_suppl):7514.

Activity

- >90% sFLC reductions across all dose levels
- ORR 100%
- 6 patients proceeded to ASCT
- At 3 months post-ASCT, ORR 100% (3 CRs, 2 VGPRs, 1 PR)
- 1 patient with documented sCR and MRD-neg at data cutoff
- Median PFS not reached

AMERICAN SOCIETY OF HEMATOLOGY 2025

[illegible]dian follow-up 22.3 months[2]

[illegible] MRD-neg CR at any time
[illegible] these patients, 64% were
[illegible]RD-neg at 12 months
[illegible] MRD-neg VGPR at any time
[illegible] these patients, 72% were
[illegible]RD-neg at 12 months

- Strong reductions in sFLCs across iberdomide dose levels, sustained through cycle 6

1. Amatangelo M, et al. Blood 2024;144(Supplement 1):1973. 2. Jeyaraju D, et al. Blood 2025;146(Supplement 1):2255.

Iberdomide in NDMM

EMN26: Iberdomide as post-ASCT maintenance

120 NDMM patients[1]

- ≥PR after PI-IMiD-containing induction, 1/2 ASCT, ± consolidation
- Median age 59 years, 54% male
- 31% / 57% / 12% R-ISS stage I / II / III
- 21% high-risk cytogenetics
- [illegible] patients per dose cohort (0.75, 1.0, 1.3 mg)

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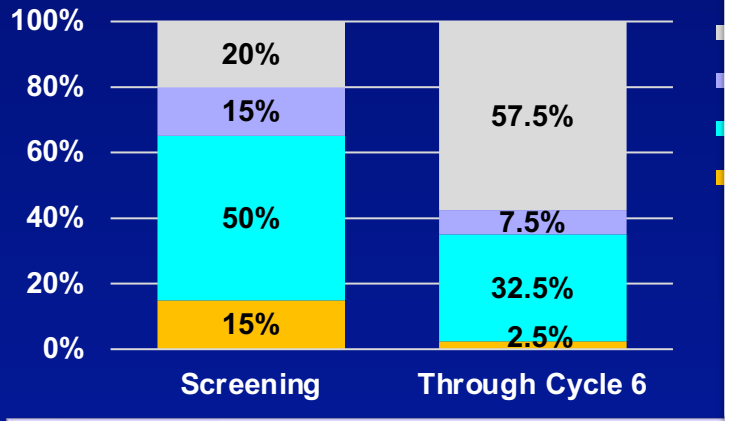
Iberdomide maintenance after upfront ASCT in MM

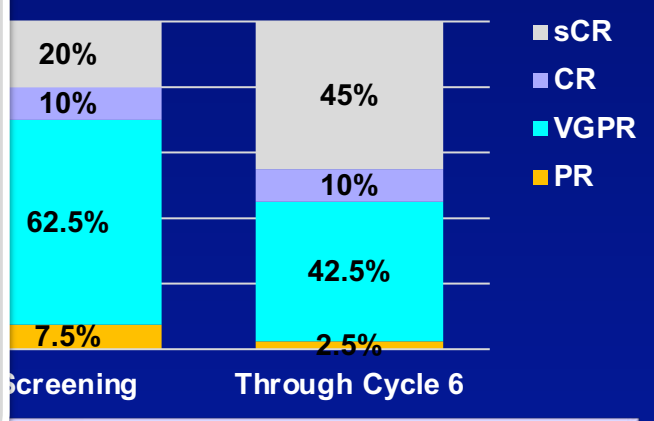
- 38 patients with ≥VGPR after triplet/quadruplet induction and ASCT
- Median age 61 years; 34% high-risk disease
- At day 80–100 post-ASCT: 100% ≥VGPR, 58% ≥CR, 87% MRD-neg
- Median 18 cycles of iberdomide received to date
- 19 patients deepened response to sCR
- 3 patients converted from MRD-pos to MRD-neg
- MRD-neg rate 85% post cycle 12, 100% post cycle 24
- Grade 3/4 neutropenia in 19/5 patients
- 11/6 patients discontinued within/after 1 year, including 5/4 due to neutropenia

Wildes T, et al. J Clin Oncol 2026;44(16_suppl):7528.

0.75 mg, n=40



1.3 mg, n=40



0.75 mg cohort[2]

- 59% improved response depth through cycle 6
- Best response ≥CR 78%
- 50% MRD-pos to MRD-neg
- 2-year PFS 92%
- Grade ≥3 neutropenia 48%, infections 8%

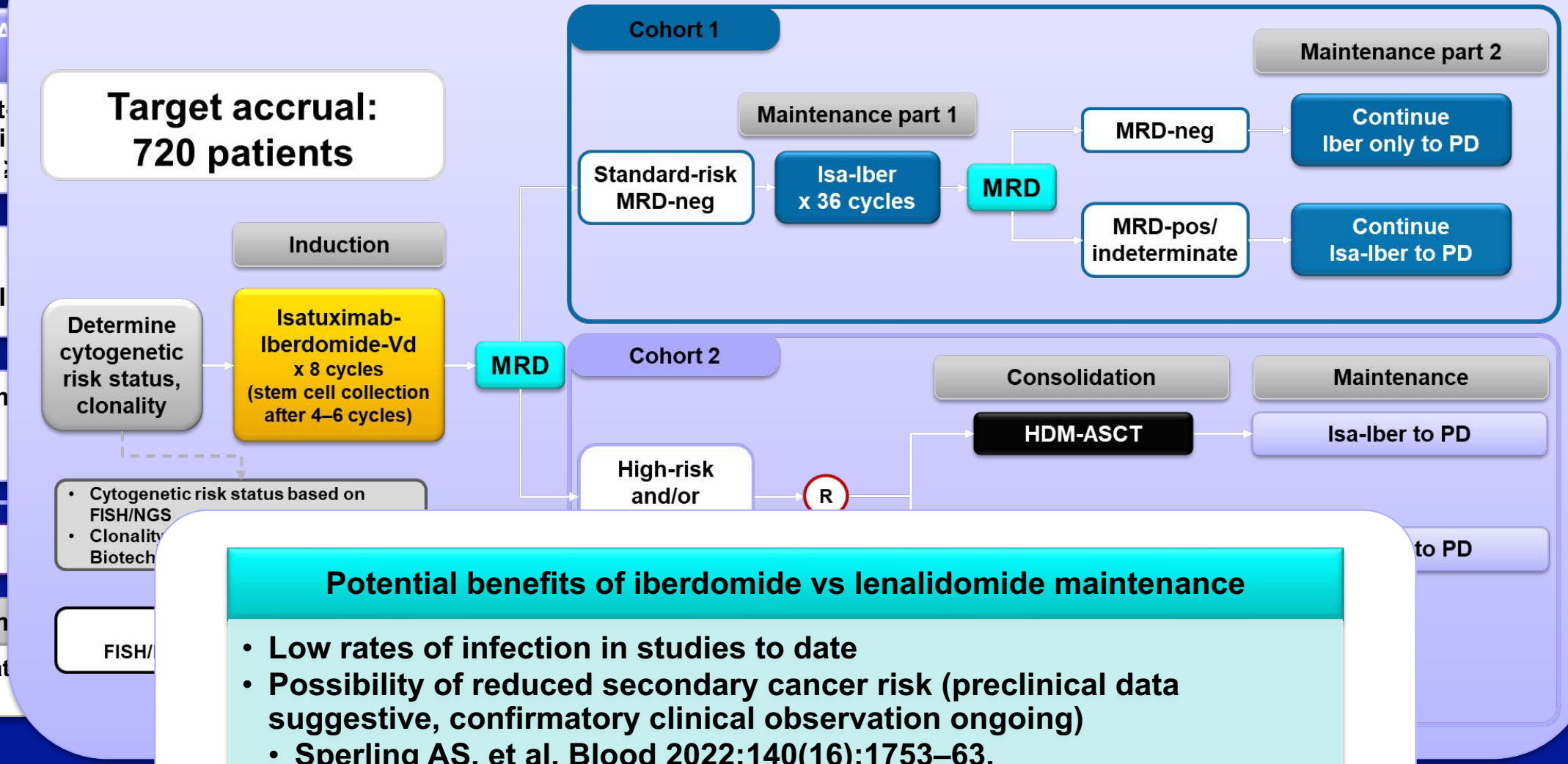
1.3 mg cohort[2]

- 38% improved response depth through cycle 6
- Best response ≥CR 70%
- 53% MRD-pos to MRD-neg
- 2-year PFS 84%
- Grade ≥3 neutropenia 60%, infections 18%

1. Gay F, et al. Hemasphere 2024;8(S1):1703–4. 2. van de Donk NWCJ, et al. Blood 2025;146(Supplement 1):101.

Iberdomide in NDMM: a replacement for lenalidomide?

DETERMINATION 2 study design



Potential benefits of iberdomide vs lenalidomide maintenance

- Low rates of infection in studies to date
- Possibility of reduced secondary cancer risk (preclinical data suggestive, confirmatory clinical observation ongoing)
  - Sperling AS, et al. Blood 2022;140(16):1753–63.

ClinicalTrials.gov, Fe
Perrot A, et al. Blood 2

Conclusions and next steps/future directions in the evolution of treatment with CELMoDs for RRMM

CELMoDs: targeted protein degradation, with improved activity vs IMiDs

- More potent binding of cereblon and degradation of Ikaros / Aiolos
- Greater anti-MM activity, including in IMiD-resistant models
- Enhanced immunomodulatory effects, including immune-stimulating properties

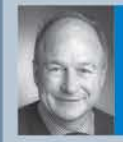
Integration of CELMoDs into RRMM treatment

- Oral agents with ease of real-world application
- Integration with standard-of-care partner drugs/drug classes in early-relapse RRMM
  - Positive findings from SUCCESSOR-2 and EXCALIBER-RRMM Phase 3 trials potentially leading to approvals
  - SUCCESSOR-1 Phase 3 trial and Phase 2 studies ongoing in RRMM
- Encouraging activity in heavily pretreated RRMM – addressing an urgent unmet medical need
  - Novel combination strategies under investigation in later-relapse RRMM, e.g. with selinexor, tazemetostat, based on synergistic mechanisms of action

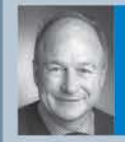
Integration of CELMoDs with CAR T-cell therapies and bispecific antibodies in RRMM

- Immune-‘energizing’/‘reactivating’ agents, potentially enhancing activity of CAR Ts and bispecifics
- Utility in combination and in sequence, e.g. as maintenance post CAR T-cell therapy, under ongoing investigation

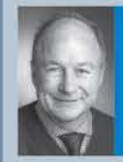
How would you indirectly compare the global efficacy and tolerability of the CELMoDs iberdomide and mezigdomide to that of standard immunomodulatory drugs (IMiDs), such as lenalidomide and pomalidomide, for patients with MM?

	Efficacy	Tolerability
 Dr Alsina	CELMoDs are more efficacious	CELMoDs are more tolerable
 Dr Lee	CELMoDs are more efficacious	Iberdomide is more tolerable; mezigdomide is less tolerable
 Dr Lonial	CELMoDs are more efficacious	CELMoDs are more tolerable
 Dr Richardson	CELMoDs are more efficacious	CELMoDs are more tolerable
 Dr Fonseca	CELMoDs are more efficacious	CELMoDs are more tolerable
 Dr Mikhael	CELMoDs are more efficacious	CELMoDs are more tolerable

Based on emerging data from the Phase III EXCALIBER-RRMM trial, do you believe iberdomide is likely to obtain regulatory approval in the near future?
Would you like to have access to iberdomide for your patients with R/R MM at the current time?

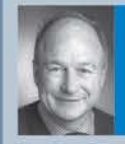
	Regulatory approval?	Current access?
 Dr Alsina	Yes	Yes
 Dr Lee	Yes	Yes
 Dr Lonial	Yes	Yes
 Dr Richardson	Yes	Yes
 Dr Fonseca	Yes	Yes
 Dr Mikhael	Yes	Yes

If iberdomide were available today, where in the therapeutic sequence and for which types of patients would you most likely employ it?

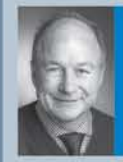
 Dr Alsina	Substitute lenalidomide with iberdomide in newly diagnosed, maintenance and relapsed settings
 Dr Lee	Third line after second-line BCMA-targeted therapy for older, frail patients
 Dr Lonial	Early, in first line or maintenance
 Dr Richardson	First relapse
 Dr Fonseca	Ultimately replace IMiDs as approved
 Dr Mikhael	Frail patients who are not candidates for CAR T-cell therapy or bispecific antibodies

RTP RESEARCH TO PRACTICE

Based on emerging data from the Phase III SUCCESSOR-2 trial, do you believe mezigdomide is likely to obtain regulatory approval in the near future?
Would you like to have access to mezigdomide for your patients with R/R MM at the current time?

	Regulatory approval?	Current access?
 Dr Alsina	Yes	Yes
 Dr Lee	Yes	Yes
 Dr Lonial	Yes	Yes
 Dr Richardson	Yes	Yes
 Dr Fonseca	Yes	Yes
 Dr Mikhael	Yes	Yes

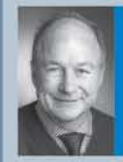
If mezigdomide were available today, where in the therapeutic sequence and for which types of patients would you most likely employ it?

 Dr Alsina	Third or fourth relapse
 Dr Lee	Third line after second-line BCMA-targeted therapy, particularly for those with more advanced disease such as EMD
 Dr Lonial	Second or later relapse
 Dr Richardson	First relapse
 Dr Fonseca	Replace IMiDs as early as possible
 Dr Mikhael	Partner to carfilzomib in relapse peri-CAR T-cell therapy or bispecific antibody

EMD = extramedullary disease

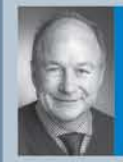
RTP RESEARCH TO PRACTICE

If both iberdomide and mezigdomide become available, which one would you be more likely to employ first?

 Dr Alsina	Iberdomide
 Dr Lee	Mezigdomide
 Dr Lonial	Iberdomide
 Dr Richardson	Mezigdomide
 Dr Fonseca	Mezigdomide
 Dr Mikhael	Mezigdomide

RTP RESEARCH TO PRACTICE

If both agents become available, would you use mezigdomide after a patient experiences disease progression on iberdomide? What about the converse?

 Dr Alsina	Yes, either sequence
 Dr Lee	Yes, mezigdomide after disease progression on iberdomide
 Dr Lonial	Yes, mezigdomide after disease progression on iberdomide
 Dr Richardson	Yes, either sequence
 Dr Fonseca	Yes, either sequence
 Dr Mikhael	Yes, mezigdomide after disease progression on iberdomide

RTP RESEARCH TO PRACTICE

Agenda

Module 1: Integrating Bispecific Antibodies into the Management of Relapsed/Refractory (R/R) Multiple Myeloma (MM) — Dr Lee

Module 2: Current Utility of Antibody-Drug Conjugates for MM — Dr Lonial

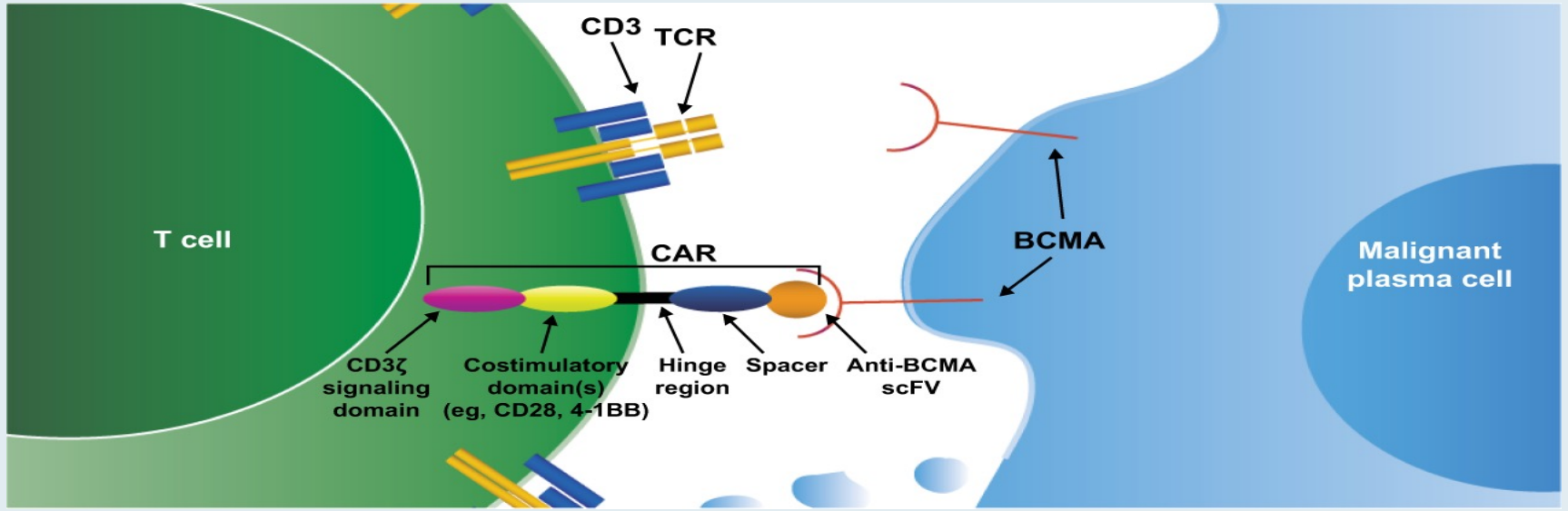
Module 3: Potential Role of Cereblon E3 Ligase Modulators in Therapy for MM — Dr Richardson

Module 4: Chimeric Antigen Receptor T-Cell Therapy for R/R MM — Dr Alsina

Chimeric Antigen Receptor (CAR) T-Cell Therapy for Relapsed/Refractory (R/R) Multiple Myeloma (MM)

Melissa Alsina, M.D.
Head, Myeloma Section, BMT-CI
H. Lee Moffitt Cance Center
Tampa, Fl

FDA-Approved Autologous CAR T Therapy for R/R MM



Initial approvals: patients with **R/R MM after ≥4 prior LOT, including an IMiD, PI, and an anti-CD38 mAb.**

Expanded indications granted (April 2024):

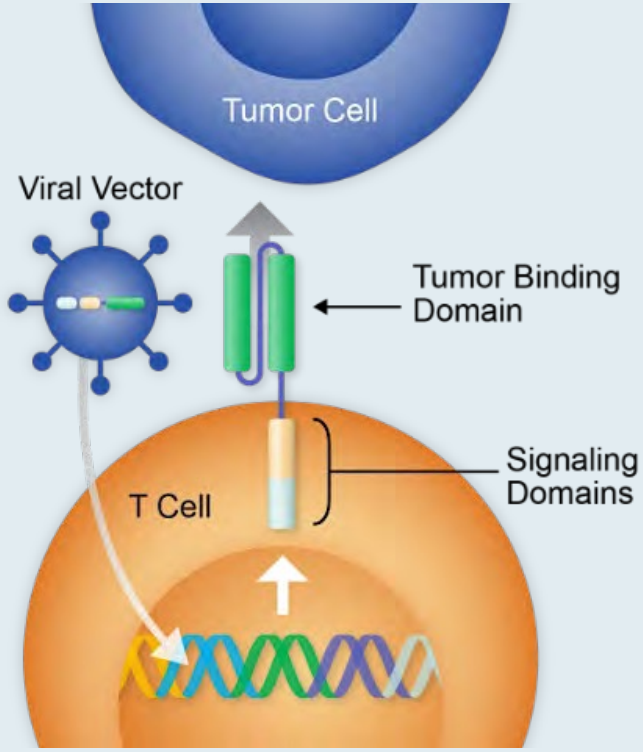
ide-cel after ≥2 prior LOT including an IMiD, PI, and an anti-CD38 mAb (KarMMa-3) and **cilta-cel after ≥1 prior LOT** including a PI and an IMiD and refractory to len (CARTITUDE-4).

Berdeja. Lancet. 2021;398:314. Ciltacabtagene autoleucel PI. Idecabtagene vicleucel PI.

RTP RESEARCH TO PRACTICE

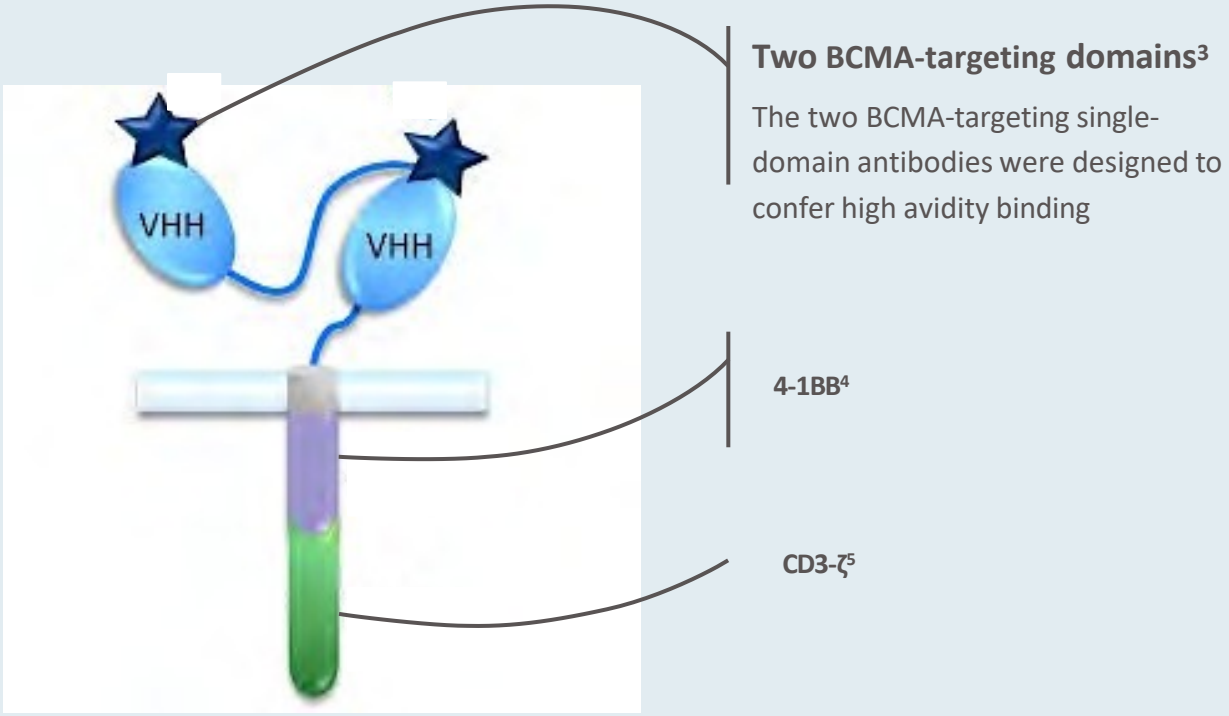
Ide-cel and Cilta-cel Constructs

Idecabtagene Vicleucel (ide-cel) CAR T



Second-generation CAR construct[1]

Ciltacabtagene Autoleucel (cilta-cel) CAR T



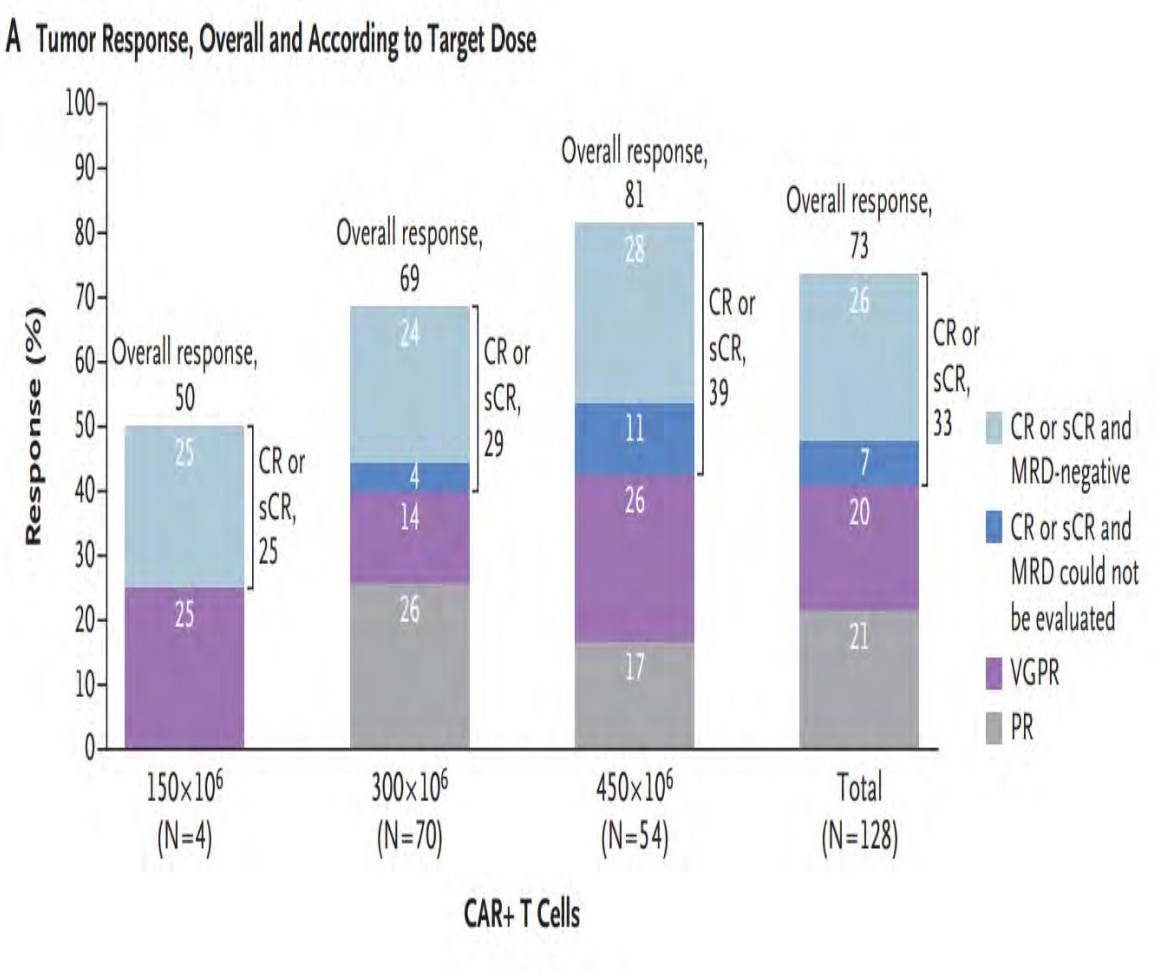
Dual epitope-binding CAR construct[1,2]

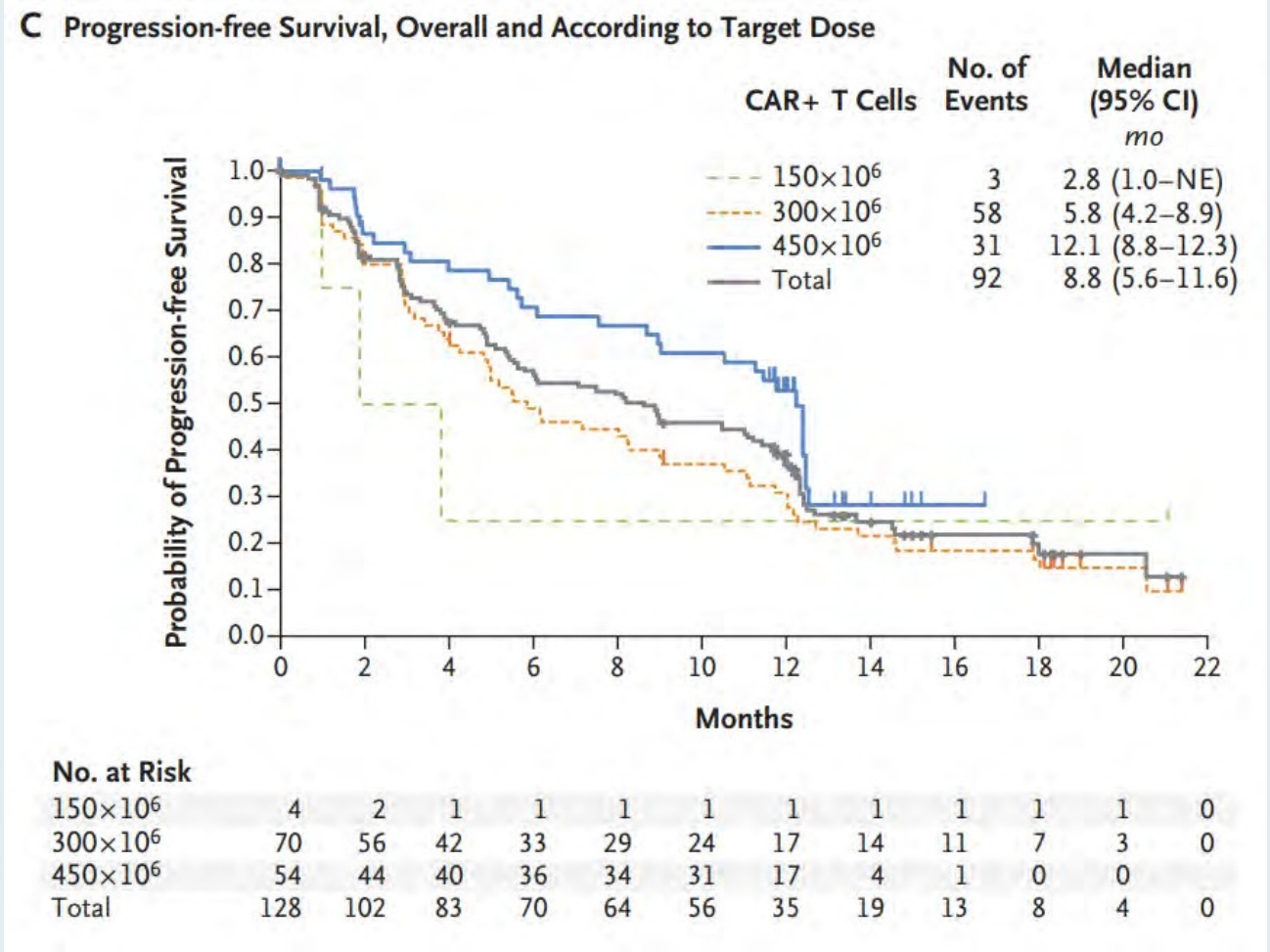
- BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; CD, cluster of differentiation; ide-cel, idecabtagene vicleucel; MM, multiple myeloma; MND, murine leukemia-derived promoter; scFv, single-chain variable fragment.
- 1. Raje N et al. *N Engl J Med*. 2019;380(18):1726-1737. 2. Friedman KM et al. *Hum Gene Ther*. 2018;29(5):585-601. 3. Song DG et al. *Cancer Res*. 2011;71(13):4617-4627. 4. Zhao WH et al. *J Hematol Oncol*. 2018;11(1):141. 5. Berdeja JG et al. ASCO 2020. Abstract 8505.

RTP RESEARCH TO PRACTICE

Phase II KarMMa Study

Ide-cel in RR Myeloma



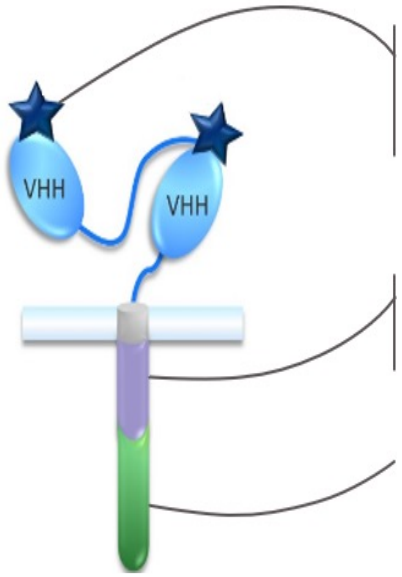


Munshi NC et al. NEJM 2021

RTP RESEARCH TO PRACTICE

CARTITUDE-1 update: 30% of heavily pretreated patients with relapsed myeloma alive and disease 5 years post-cilta-cel!!

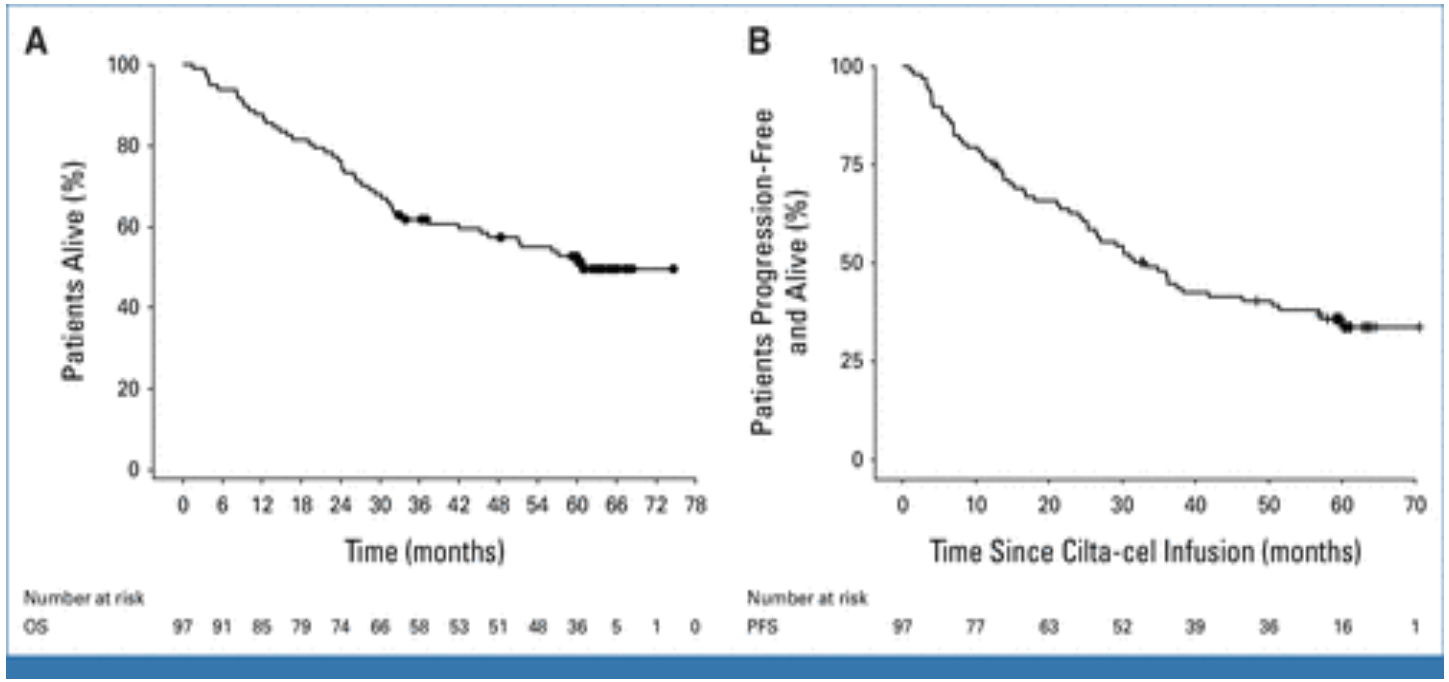
Overall population (N=97)
Median follow-up: 61.3 months



Two BCMA-targeting domains
The 2 BCMA-targeting single-domain antibodies were designed to confer high avidity binding

4-1BB

CD3-ζ



Jagannath S, et al. *J Clin Oncol*. 2025; 43(25):2766-2771; Friedman KM, et al. *Hum Gene Ther*. 2018;29:585–601; Song D-G, et al. *Cancer Res* 2011;71:4617–4627; Zhao WH, et al. *J Hematol Oncol*. 2018;11:141; Berdeja JG, et al. *Lancet*. 2021;398(10297):314-324

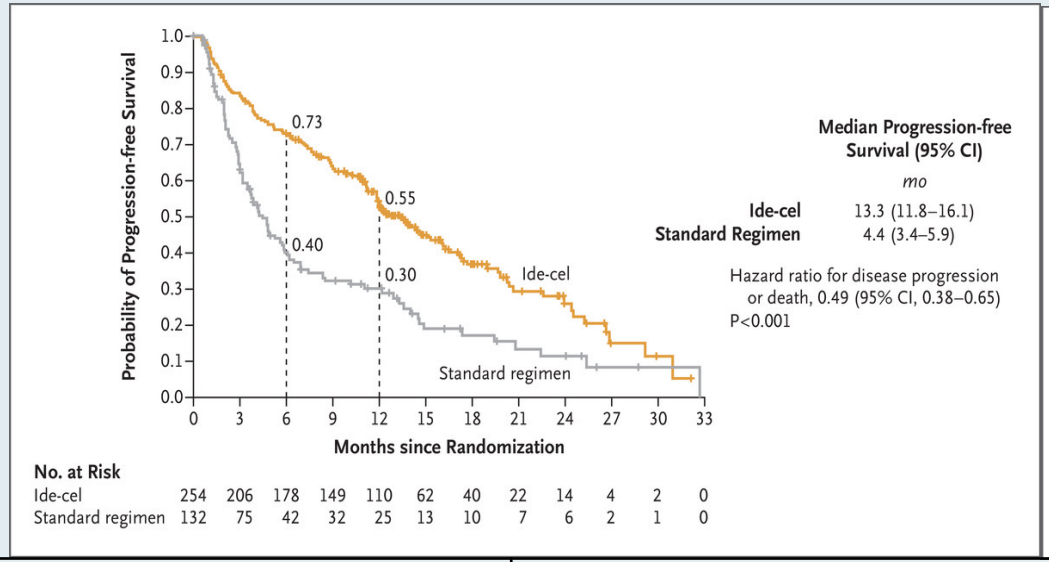
CARTITUDE-1: Long-term Safety and Future Directions

- **Safety profile consistent for patients in long-term remission (no progression ≥5 yrs + ~28 mo follow-up)**
  - **No new cases of CNP or parkinsonism**
  - **2 new cases of secondary primary malignancies – solid tumors**
  - **Some new cases of neurological events and grade 3 infections not related to cilta-cel**
- **Phase III studies for <u>newly diagnosed MM</u>**
  - **CARTITUDE-5: VRd + Cilta-cel vs VRd + Rd maintenance (NCT04923893)**
  - **CARTITUDE-6: DVrd + Cilta-cel vs DVRd + ASCT + DVRd (NCT05257083)**

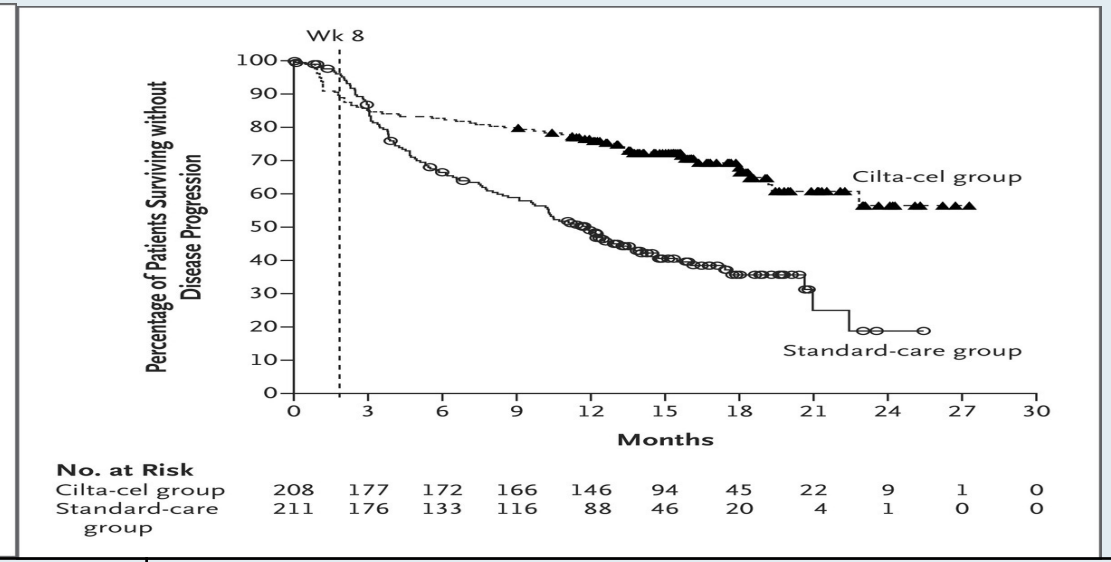
Voorhees. ASCO 2025. Abstr 7507.

KARMMA-3 and CARTITUDE-4, CAR-T outperforms SOC

P Rodriguez-Otero et al. N Engl J Med 2023;388:1002-1014.

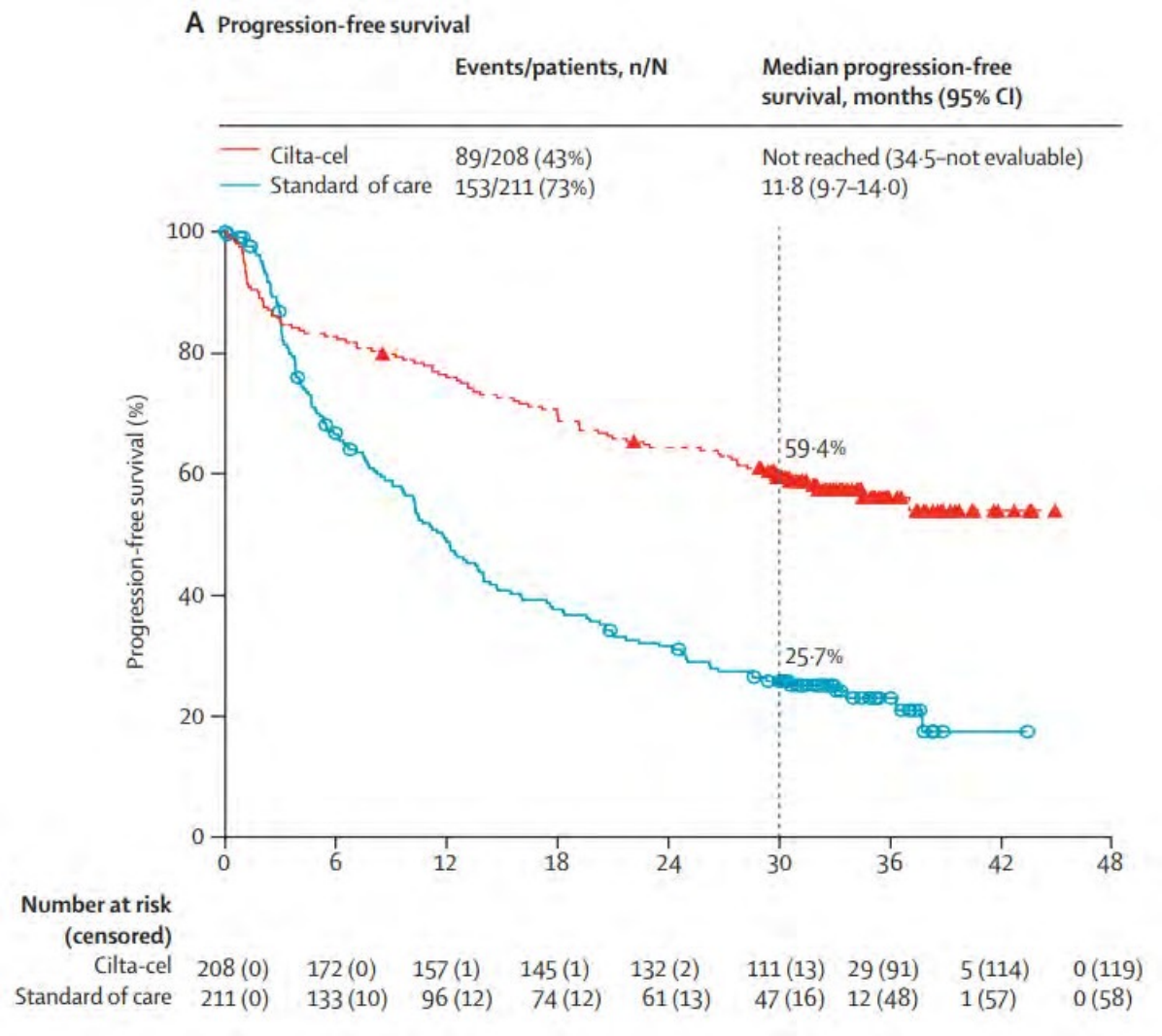


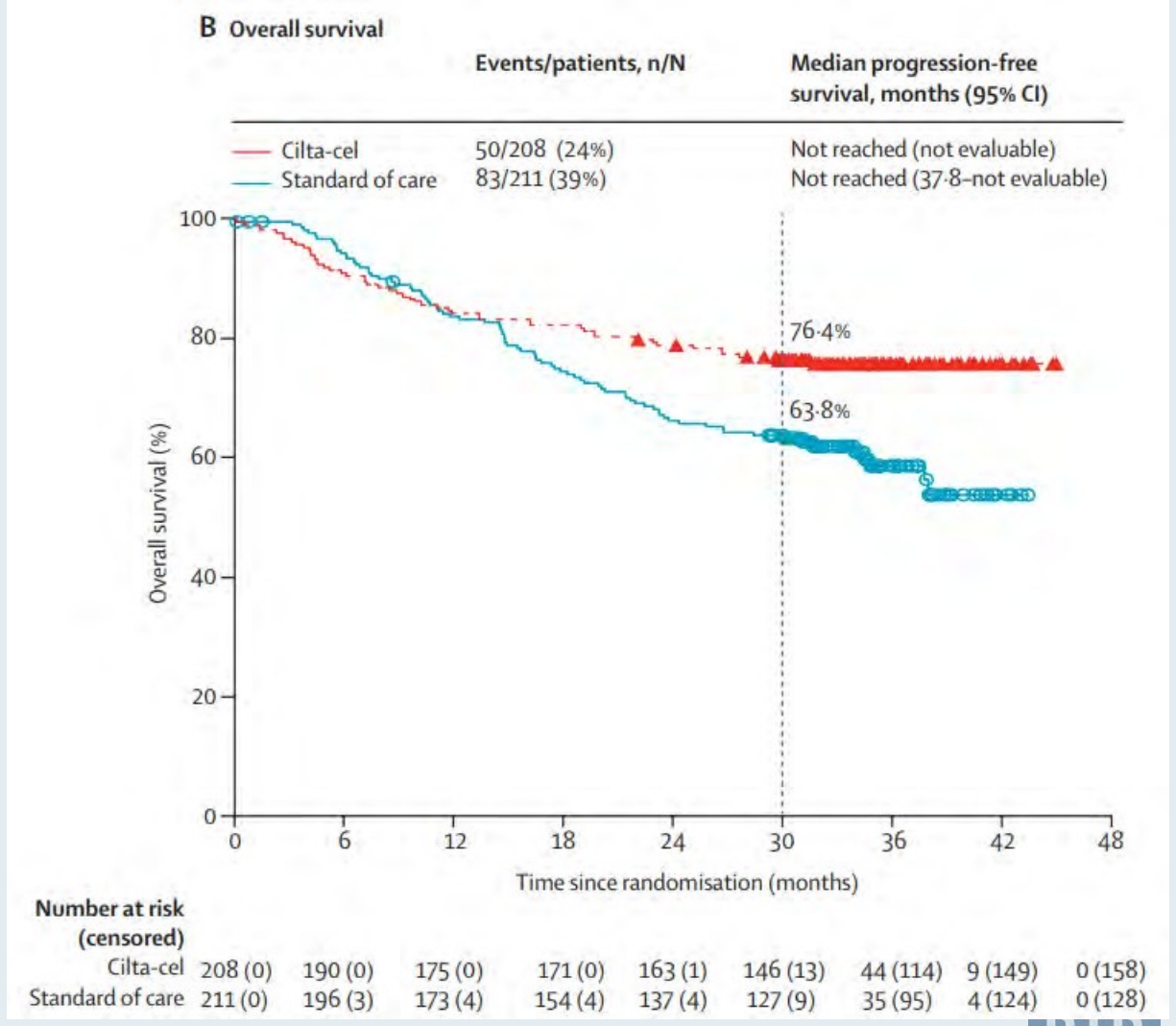
J San-Miguel et al. N Engl J Med 2023;389:335-347.



Parameter	KarMMa-3		CARTITUDE-4	
	Ide-Cel	SOC	Cilta-Cel	SOC
Inclusion criteria	2-4 prior lines including PI + IMiD + Dara		1-3 prior lines, Len-refractory	
Prior lines of therapy, n, median (range)	3 (2-4)	3 (2-4)	2 (1-3)	2 (1-3)
Refractory to anti-CD38 antibodies, n (%)	242 (95)	123 (93)	50 (24)	46 (22)
Triple-class refractory, n (%)	164 (65)	89 (67)	30 (14)	33 (16)
ORR, n (%)	181 (71)	55 (42)	176 (85)	142 (67)
::: CR, n (%)	98 (39)	7 (5)	152 (73)	46 (22)
::: VGPR, n (%)	153 (60)	20 (16)	169 (81)	96 (46)
MRD-negative 10^{-5}, n (%)	51/254 (20)	1 (1)	126/144 (88)	33/101 (33)
DOR, mo, median	14.8	9.7	Not reached; 85% at 12 mo	Not reached; 63% at 12 mo
PFS, mo, median	13.3	4.4	Not reached; 76% at 12 mo	11.8 49% at 12 mo

CARTITUDE-4: PFS and OS

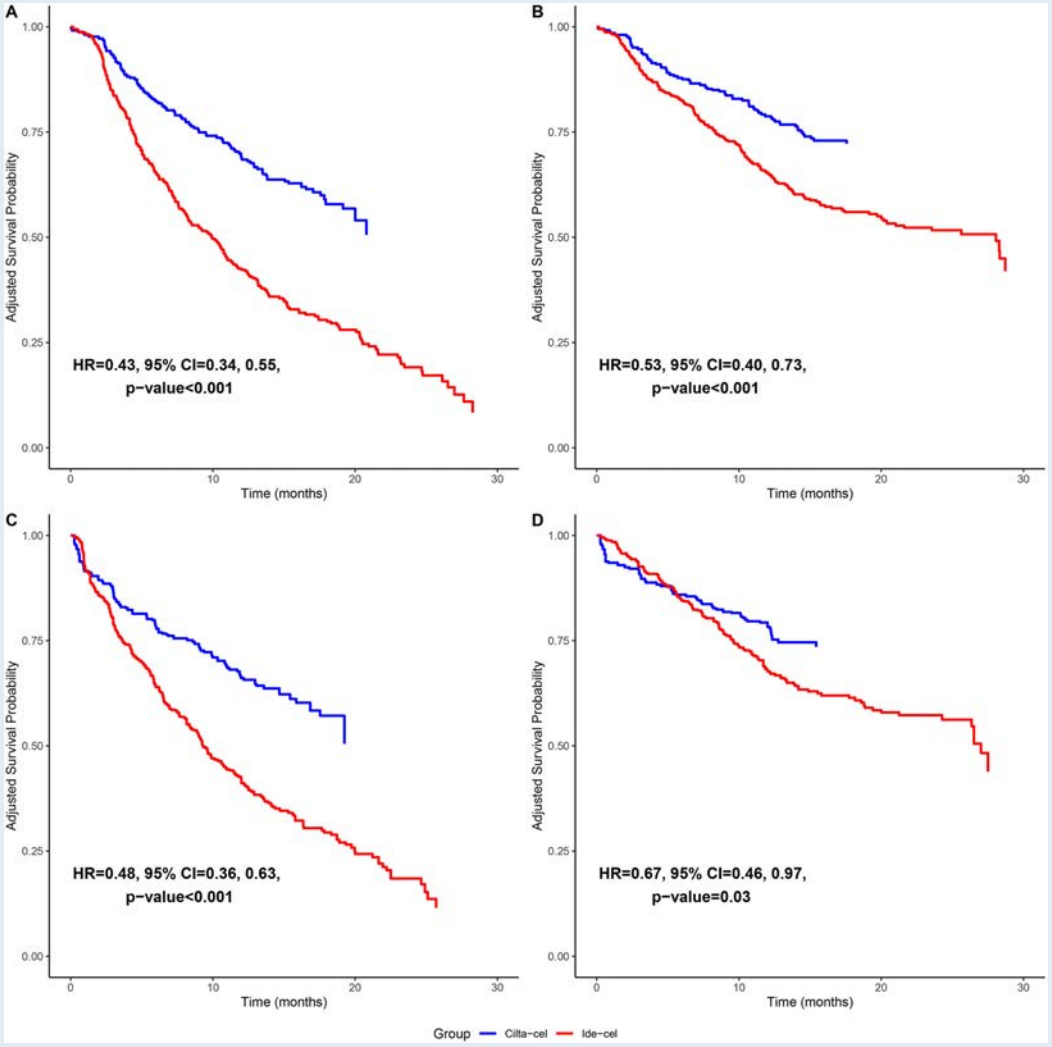




Einsele H et al. Lancet Oncol. 2025

A Comparison of Standard of Care Idecabtagene Vicleucel and Ciltacabtagene Autoleucel in Relapsed/Refractory Multiple Myeloma

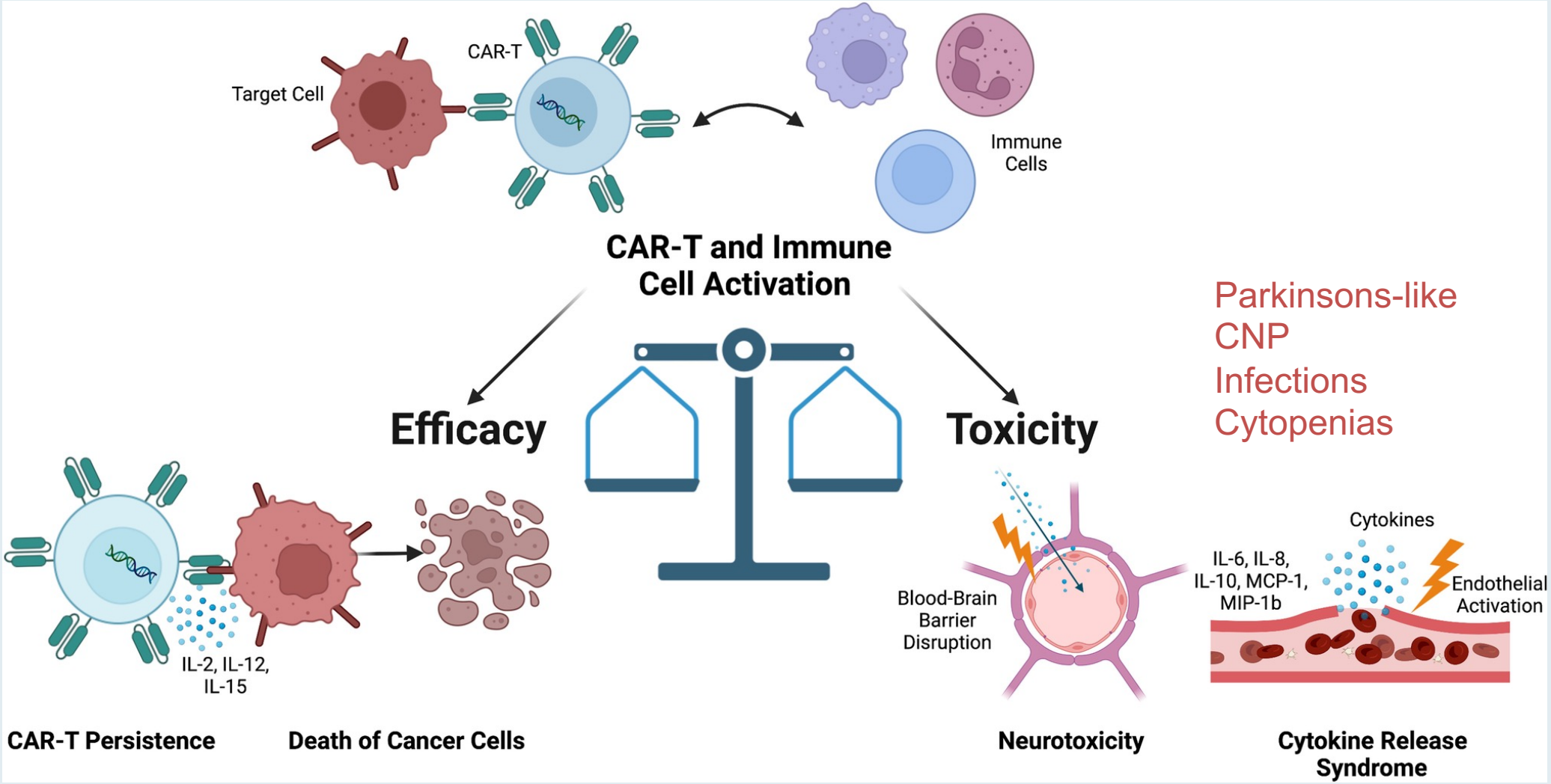
Ide-cel N=350
Cilta-cel N=236



Hansen et al, US Immunotherapy Consortium, JCO 2025

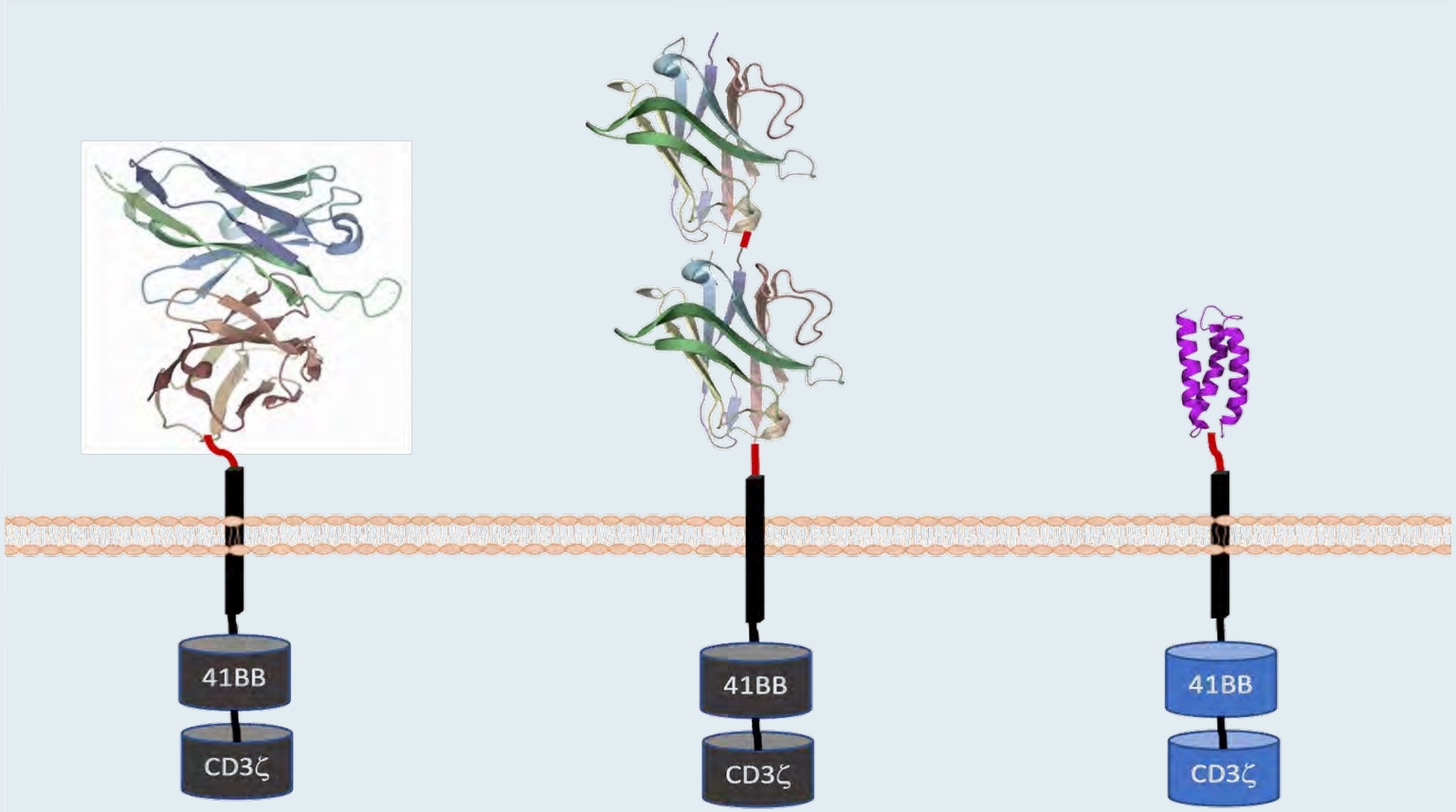
RTP RESEARCH TO PRACTICE

Balance between efficacy and toxicity



Anitocabtagene autoleucel (anito-cel/CART-ddBCMA)

Autologous BCMA-directed CAR T-cell therapy using a novel, D-Domain binder[1]



scFv
(~25 kDa)

Bivalent camelid VHh
(~25 kDa)

D-Domain
(~8 kDa)

D-Domain Attributes:
Non-Antibody Derived Synthetic Protein[1,2]

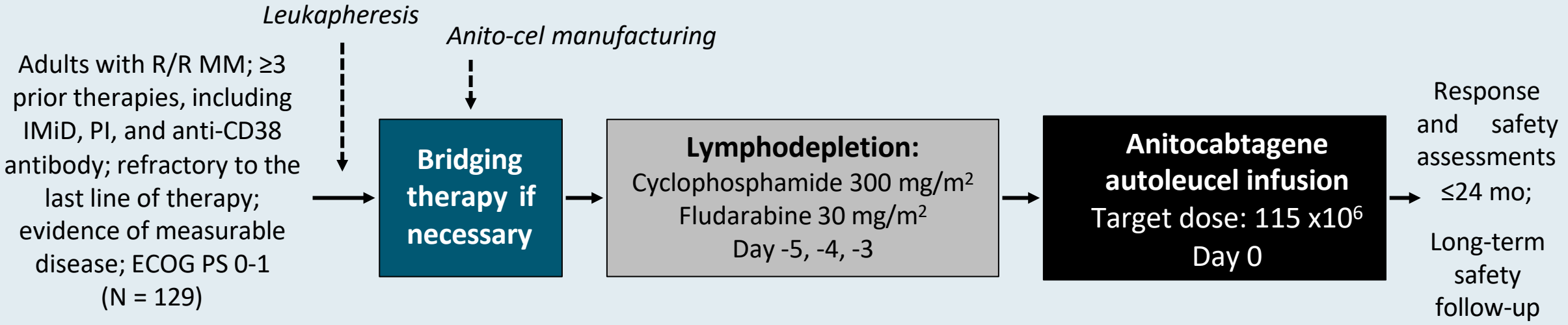
Size	**Small D-Domain construct facilitates high transduction efficiency, CAR positivity, and CAR density on the T-cell surface[2-4]**
Stability	**Rapid D-Domain folding, lack of disulfide bonds, and a hydrophobic core enables stability at and beyond physiologic conditions[5,6]**
Structure	**Due to small size and compact structure, D-Domain CARs have a low risk of tonic signaling[6]**

[1]Rotte, et al. *Immuno-Oncology Insights* 2022; 3(1), 13–24; [2]Frigault, et al. *Blood Adv.* 2023; 7(5):768-777; [3]Cante-Barrett, et al. *BMC Res. Notes* 2016; 9:13; [4]Buonato, et al. *Mol. Cancer Ther.* 2022; 21(7):1171-1183; [5]Zhu, et al. *Proc. Nat. Acad. Sci.* 2003; 100(26): 15486-15491; [6]Qin, et al. *Mol. Ther.* 2019; 27(7): 1262-1274.

RTP RESEARCH TO PRACTICE

iMMagine-1: A Phase II Study of Anitocabtagene Autoleucel for R/R MM

- **Multicenter, open-label, Phase II study**

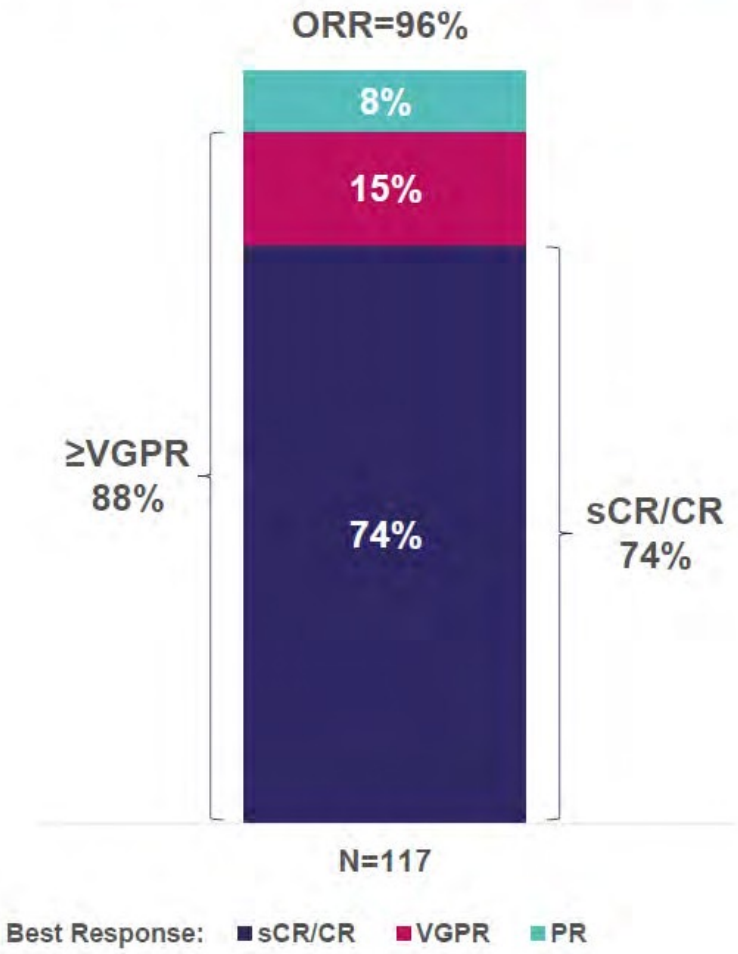


- **Primary objectives**: Overall response rate per 2016 IMWG criteria
- **Secondary objectives**: sCR/CR rate, ORR for pts with 3 prior LOT, PFS, OS, DoR, VGPR and PR rate, MRD, HRQoL, safety

Freeman. ASH 2024. Abstr 1031.

iMMagine-1: ORR and Depth of Response

Efficacy Evaluable Patients, N=117



- Responses continue to deepen over time
- At a median follow-up of 15.9 months, IRC-assessed ORR was 96% and sCR/CR rate was 74%

	Median (months)	Interquartile Range	Min, Max
Time to first response	1.0	1.0, 1.9	0.9, 13.8
Time to best response	4.8	2.1, 9.0	0.9, 23.8
Time to sCR/CR	3.2	2.0, 9.2	0.9, 23.8

Patel et al. ASH 2025; Abstract 256

RTP RESEARCH TO PRACTICE

GPRC5D AS A NOVEL TARGET FOR MULTIPLE MYELOMA

GPRC5D

Orphan receptor highly expressed on MM cells

Restricted expression profile in normal tissues

Preserves BCMA-targeting therapies for later lines

5 GPRC5D therapies currently in clinical development

Bispecifics
Talquetamab
Forimtamig

CAR-T
MCARH109
OriCAR-017
BMS-986393

> 70% Overall response rate
including in heavily pre-treated and high-risk patients in **almost all therapies***

*ORR for [illegible]

Safety profile and adverse event management

AEs unique to GPRC5D-targeting therapies

Dysgeusia/Dysphagia
Supportive care and dose adjustments

Skin/Rash
Emollient, topical/oral steroids

Nail
Often resolve without intervention

Most were **low grade, manageable**, and led to **low treatment discontinuation**

AEs related to T-cell engaging therapies

CRS
Steroids, antihistamine, paracetamol for pre-treatment, and tocilizumab/steroids at onset

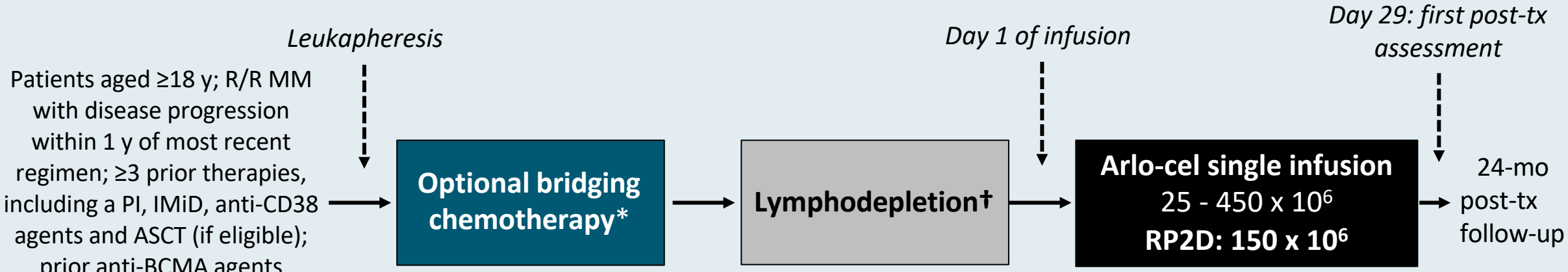
ICANS
Tocilizumab and corticosteroids

Infections

Rodriguez-Otero P et al. Blood Cancer J 2024

Arlocabtagene Autoleucel for R/R MM: Study Design

- **Multicenter, multicohort, open-label, first-in-human Phase I study**

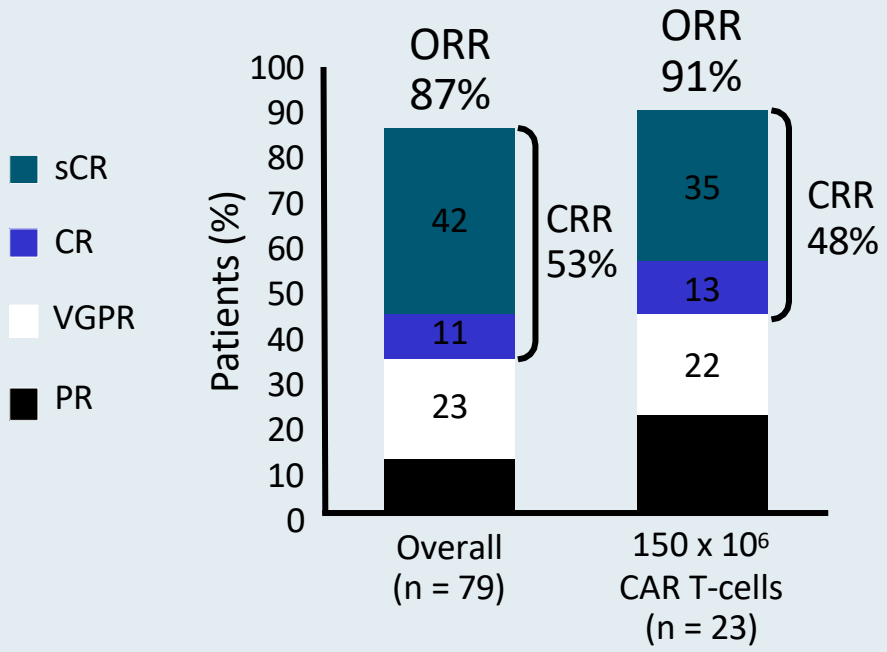


*If needed for disease control; limited to ≤28 days and stopped ≥19 days before infusion.
†Patients in 2 cohorts who had received ≥3 prior therapies (a PI, IMiD, anti-CD38 therapy and ASCT, if eligible) received either fludarabine + cyclophosphamide or bendamustine. Patients in 1 cohort who had received 1-3 prior therapies (a PI, IMiD and ASCT, if eligible) received fludarabine + cyclophosphamide.

- **Primary objectives**: safety and tolerability (MTD/RP2D)
- **Secondary objectives**: ORR, CRR, DoR, TTR by IMWG criteria, PFS, OS

Bal. ASH 2024. Abstr 922.

Arlo-cel for R/R MM: Extended Follow-up



Response	Evaluable Patients (n = 79)
Median DoR, mo (95% CI)	18.0 (13.3-23.0)
Median TTR, mo (range)	1 .0 (0.9-6.0)
Median follow-up, mo (range)	16.1 (2.8-25.2)

Median PFS	mo (95% CI)
All evaluable patients (n = 79)	18.3 (11.8 -21.9)
Prior anti-BCMA therapy (n = 38)	19.0 (8.9-NA)
No prior anti-BCMA therapy (n = 41)	18.3 (11.8-23.9)

OS	All Patients (n = 84)
Median OS, mo	NR
12-mo OS rate, % (95% CI)	90 (81-95)
18-mo OS rate, % (95% CI)	87 (76-93)
21-mo OS rate, % (95% CI)	84 (72-91)

Bal. ASH 2024. Abstr 922.

RTP RESEARCH TO PRACTICE

Arlo-cel for R/R MM: TEAEs (≥30% of Treated Patients)

TEAE, n (%)	All Patients (n = 84)		Treated at RP2D (n = 26)	
	Any Grade	Grade 3/4	Grade 3/4	Grade 3/4
Any	84 (100)	72 (86)	26 (100)	22 (85)
Hematologic TEAEs (occurring in ≥30%)				
▪ Neutropenia	62 (74)	59 (70)	20 (77)	18 (69)
▪ Anemia	42 (50)	27 (32)	13 (50)	11 (42)
▪ Thrombocytopenia	39 (46)	24 (29)	10 (38)	5 (19)
Nonhematologic TEAEs (occurring in ≥30%)				
▪ Infections	46 (55)	16 (19)	13 (50)	3 (12)
▪ Hypokalemia	38 (45)	4 (5)	12 (46)	2 (8)
▪ Hypocalcemia	29 (35)	2 (2)	7 (27)	0
▪ Headache	31 (37)	1 (1)	9 (35)	0
▪ Hypophosphatemia	28 (33)	2 (2)	11 (42)	1 (4)
▪ Nausea	26 (31)	1 (1)	8 (31)	1 (4)
▪ Fatigue	28 (33)	2 (2)	12 (46)	1 (4)
▪ Dysgeusia	26 (31)	0	9 (35)	0
▪ Diarrhea	25 (30)	1 (1)	10 (38)	1 (4)

- **Hematologic TEAEs were the most frequent; low occurrence of grade 3/4 infections**

Bal. ASH 2024. Abstr 922.

Arlo-cel for R/R MM: Select TRAEs

TRAE, n (%)	All Patients (n = 84)	
	Any Grade	Grade 3/4
CRS	69 (82)	3 (4)
ICANS	8 (10)	2 (2)
Other neurotoxicity events	10 (12)	6 (7)
MAS/HLH	0	3 (4)

- CRS primarily grade 1/2; grade 5 CRS (n = 1, at 450 x 10^6 DL)
- Select grade ≤4 neurotoxicity events occurred at the 150-450 x 10^6 DL: dizziness, ataxia, neurotoxicity, dysarthria, and/or nystagmus
  - Median time to onset: 30.5 days
- Weight loss (n = 5) palsy, or Guillain-Barré syndrome
- No reports of parkinsonism, cranial nerve

Bal. ASH 2024. Abstr 922.

On-Target/Off-Tumor Event	All Patients (N=84)
Skin*	
▪ Patients with an event, n (%)	25 (30)
▪ Patients with event resolution, n (%)	22 (88)
▪ Median time to resolution, days	26
Nail*	
▪ Patients with an event, n (%)	16 (19)
▪ Patients with event resolution, n (%)	12 (75)
▪ Median time to resolution, days	98
Oral*†	
▪ Patients with an event, n (%)	27 (32)
▪ Patients with event resolution, n (%)	19 (70)
▪ Median time to resolution, days	66

*No grade 3/4; intervention was not required for 79% of patients.
†Including dysgeusia and dysphagia.

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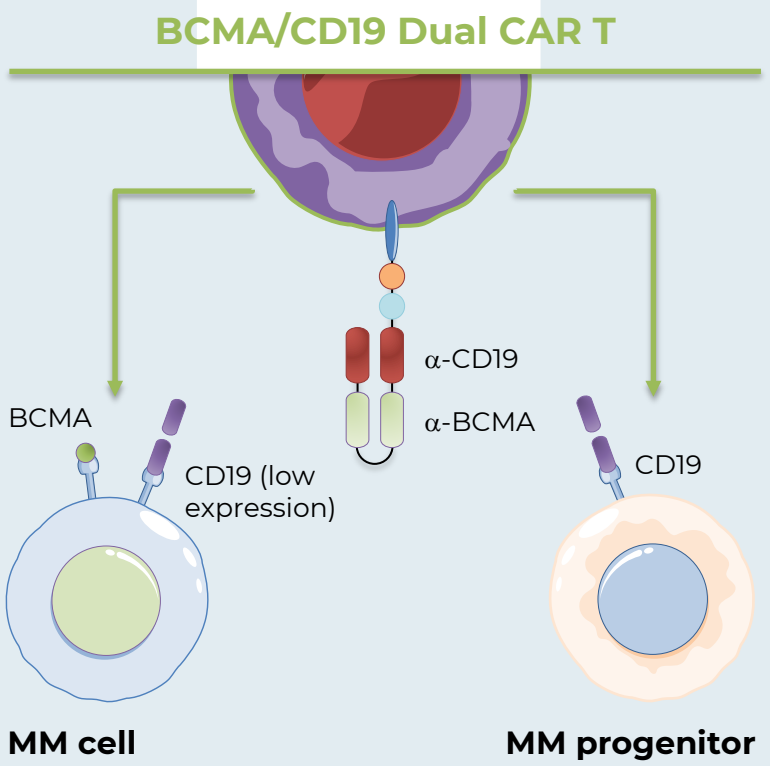
AZD0120: A Novel BCMA/CD19 Dual CAR T With Next-Generation Manufacturing

Dual Target



Next-Generation Manufacturing

Faster to Patients

Manufactured in <3 days

Better T Cells

Younger, fitter naive T cells

Safety profile enabling outpatient administration and monitoring

Making cell therapy available to more patients

AZD0120 was formerly named GC012F, and next-generation manufacturing refers to the FasTCAR platform.
BCMA, B-cell maturation antigen; CAR T, chimeric antigen receptor T-cell therapy; MM, multiple myeloma.

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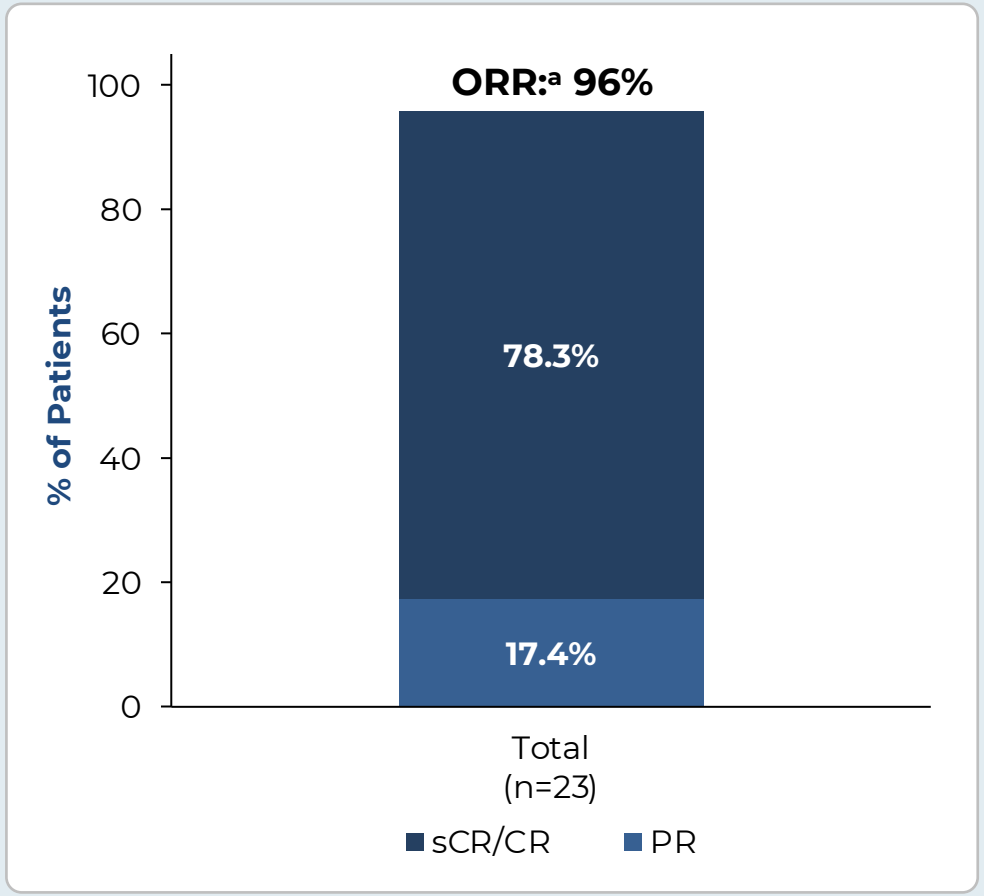
Efficacy: 96% ORR, 78% CR

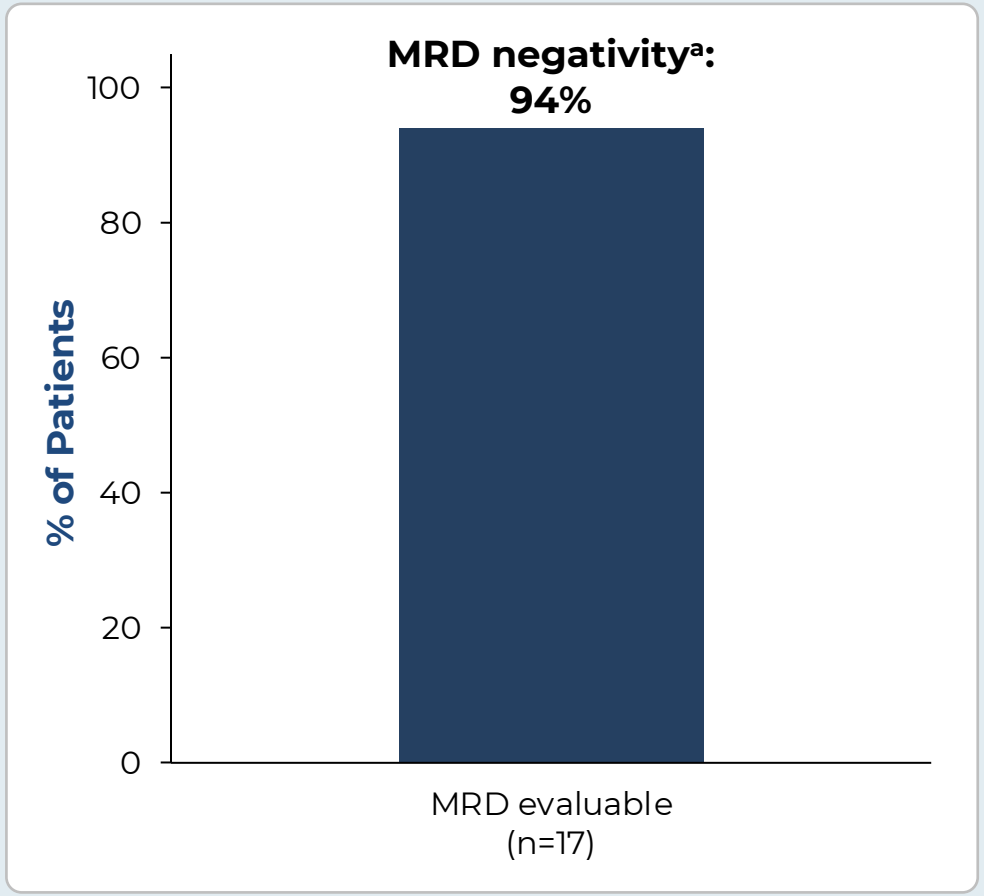


- **Median time to first response = 28 days**

	Total (n=23)	BCMA CAR T Exposed (n=5)
ORR	96%	100%
sCR/CR	78%	80%
Follow-up, median (range), mo	3.9 (0.9–19.7)	3.9 (3.0–4.0)

Efficacy-evaluable population defined as all patients who received conformed AZD0120 infusion at the targeted DL with measurable disease at baseline and at least one post-baseline efficacy assessment.
[a]Response as assessed by study investigator using IMWG criteria.
BCMA, B-cell maturation antigen; CAR T, chimeric antigen receptor T-cell therapy; CR, complete response; DL, dose level; IMWG, International Myeloma Working Group; ORR, overall response rate; PR, partial response; sCR, stringent complete response.

MRD Status in Evaluable Patients



- 17 patients evaluable for MRD by NGS ($<10^{-5}$)
- 94% achieved MRD negativity
- All MRD-negative patients achieved MRD negativity by month 1

[a]MRD negativity was defined based on IMWG criteria as the absence of clonal plasma cells in bone marrow aspirate with a minimum test sensitivity to detect 1 in 10^5 nucleated cells (10^{-5} threshold) by NGS.
IMWG, International Myeloma Working Group; MRD, minimal residual disease; NGS, next-generation sequencing.

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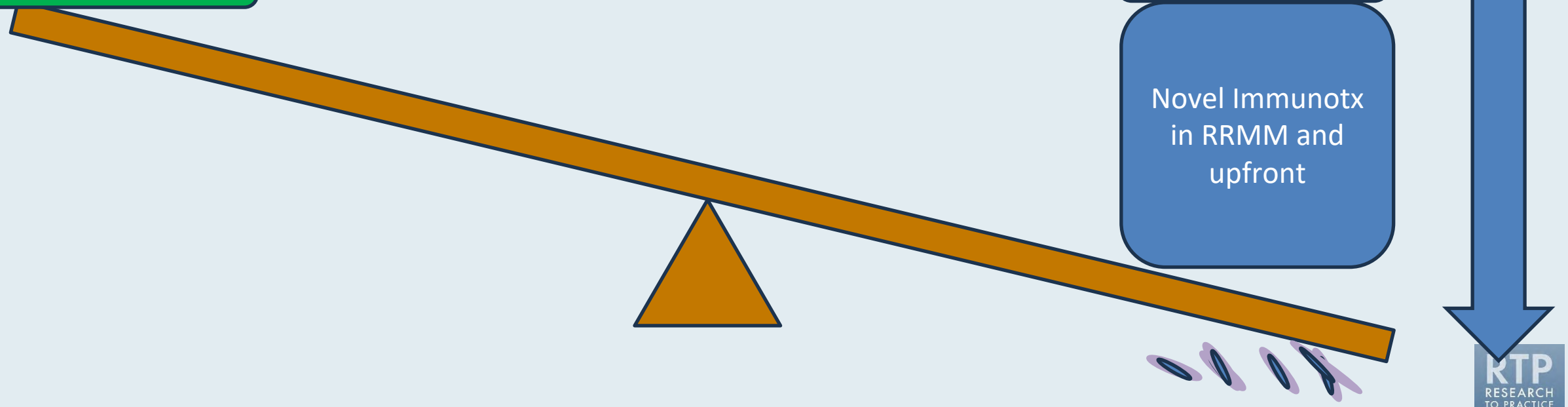
… a look at the future

Challenges

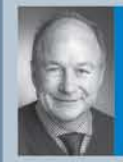
- Sequencing
- High risk Disease
- Toxicity/Frailty
- BMT?
- Access

Opportunities

- Quadruplet therapy
- MRD negativity
- Novel Maintenance
- Novel Immunotx in RRMM and upfront



Regulatory and reimbursement issues aside, which next line of therapy would you most likely recommend for a 65-year-old patient with standard-risk MM who receives initial treatment with RVd/daratumumab followed by autologous stem cell transplant (ASCT) and experiences disease progression after 8 years of maintenance*?

 Dr Alsina	Ciltacabtagene autoleucel
 Dr Lee	Teclistamab/daratumumab
 Dr Lonial	Ciltacabtagene autoleucel
 Dr Richardson	Belantamab mafotodin/bortezomib/dexamethasone
 Dr Fonseca	Ciltacabtagene autoleucel
 Dr Mikhael	Ciltacabtagene autoleucel

* 3 years of daratumumab/lenalidomide followed by an additional 5 years of lenalidomide alone

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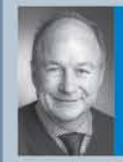
Regulatory and reimbursement issues aside, which next line of therapy would you most likely recommend for a 65-year-old patient with high-risk (del[17p]) MM who receives initial treatment with RVd/daratumumab followed by ASCT and experiences disease progression after 4 years of maintenance daratumumab/lenalidomide?

 Dr Alsina	Ciltacabtagene autoleucel
 Dr Lee	Ciltacabtagene autoleucel
 Dr Lonial	Ciltacabtagene autoleucel
 Dr Richardson	Ciltacabtagene autoleucel
 Dr Fonseca	Ciltacabtagene autoleucel
 Dr Mikhael	Ciltacabtagene autoleucel

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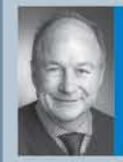
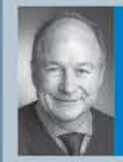
In which circumstances, if any, would you favor idecabtagene vicleucel over ciltacabtagene autoleucel?

 Dr Alsina	Elderly patients (>75 years of age) with a high frailty score
 Dr Lee	Elderly (>80 years of age), frail patient who wanted single-infusion, time off therapy approach
 Dr Lonial	CAR T-cell therapy candidate who is worried about neurologic toxicity
 Dr Richardson	Frailty
 Dr Fonseca	None
 Dr Mikhael	Rarely, perhaps if a patient with a history of neurologic disease

Approximately what proportion of patients with R/R MM who are being cared for in community-based clinics and are good candidates for CAR T-cell therapy would you estimate are being referred for this form of treatment?

 Dr Alsina	25%
 Dr Lee	20%-25%
 Dr Lonial	20%
 Dr Richardson	20%
 Dr Fonseca	75%
 Dr Mikhael	10%

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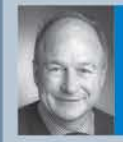
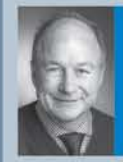
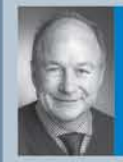
How would you indirectly compare the global efficacy and tolerability of GPRC5D-targeted CAR T-cell therapy, such as arlocabtagene autoleucel, to that of BCMA-targeted CAR T-cell therapy for R/R MM?

	Efficacy	Tolerability
 Dr Alsina	Not enough data are available to tell	Tolerability is about the same
 Dr Lee	BCMA-targeted CAR T-cell therapy is more efficacious	Tolerability is about the same
 Dr Lonial	Not enough data are available to tell	GPRC5D-targeted CAR T-cell therapy is more tolerable
 Dr Richardson	Efficacy is about the same	Tolerability is about the same
 Dr Fonseca	Not enough data are available to tell	Not enough data are available to tell
 Dr Mikhael	BCMA-targeted CAR T-cell therapy is more efficacious	Not enough data are available to tell

If arlocabtagene autoleucel were to become available for patients with R/R MM, in which clinical situations would you prioritize its use?

 Dr Alsina	After BCMA-targeted therapy failure
 Dr Lee	After BCMA-targeted therapy failure
 Dr Lonial	Would prefer GRPC5D-targeted therapy over talquetemab due to better tolerability
 Dr Richardson	After BCMA-targeted therapy failure
 Dr Fonseca	Later-line relapse
 Dr Mikhael	After prior BCMA-targeted therapy

If GPRC5D-targeted CAR T-cell therapy were to become available for patients with R/R MM, would you be comfortable administering BCMA- and GPRC5D-targeted CAR T-cell therapy in sequence?

 Dr Alsina	Yes
 Dr Lee	Yes
 Dr Lonial	Yes
 Dr Richardson	Yes
 Dr Fonseca	Yes
 Dr Mikhael	Yes

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Consensus or Controversy? Documenting and Discussing Investigators' Approaches to the Management of Myelofibrosis

A CME/MOC-Accredited Virtual Event Held
Adjunct with the 2026 ASCO® Annual Meeting

Tuesday, June 2, 2026
4:00 PM – 5:00 PM CT (5:00 PM – 6:00 PM ET)

Faculty

Professor Claire Harrison
Raajit K Rampal, MD, PhD

Moderator

Neil Love, MD

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Thank you for joining us!
Your feedback is very important to us.

Please complete the survey currently up on the iPads for attendees in the room and on Zoom for those attending virtually. The survey will remain open up to 5 minutes after the meeting ends.

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