Data + Perspectives: Investigators Discuss the Optimal Management of Relapsed/Refractory Multiple Myeloma

A CME-Accredited Satellite Symposium During the Society of Hematologic Oncology 2026 Annual Meeting

Wednesday, September 9, 2026
11:56 AM – 12:56 PM

Faculty

Meletios-Athanasios (Thanos) C Dimopoulos, MD
Noopur Raje, MD

Moderator

Robert Z Orlowski, MD, PhD

RTP RESEARCH TO PRACTICE

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Prof Dimopoulos — Disclosures
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Advisory Committees and Consulting Agreements	Amgen Inc, AstraZeneca Pharmaceuticals LP, BeOne, Bristol Myers Squibb, GSK, Janssen Biotech Inc, Menarini Group, Regeneron Pharmaceuticals Inc, Sanofi, Swixx Biopharma, Takeda Pharmaceutical Company Limited

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Dr Raje — Disclosures
Faculty

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Contracted Research	Pfizer Inc
Data and Safety MonitoringBoards/ Committees	Bristol Myers Squibb

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Dr Orlowski — Disclosures
Moderator

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Contracted Research	Asylia Therapeutics Inc, Biotheryx, Heidelberg Pharma, Regeneron Pharmaceuticals Inc
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The program moderator will address as many cases or questions as possible with the faculty panel during the program.

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Download Program Slides Here

https://asset.researchtopractice.com/2026/Webinar/SOHO/RR_MM_Sep9.pdf

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- The live meeting is being video and audio recorded.
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RTP RESEARCH TO PRACTICE

Data + Perspectives: Investigators Discuss the Optimal Management of Relapsed/Refractory Multiple Myeloma

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RTP RESEARCH TO PRACTICE

Agenda

Module 1 – New and Emerging Strategies with Bispecific Antibodies in Multiple Myeloma (MM) – Dr Raje

Module 2 – Utility of Antibody-Drug Conjugates for Relapsed/Refractory (R/R) MM – Dr Orlowski

Module 3 – Potential Role of Cereblon E3 Ligase Modulators and Other Promising Novel Agents and Strategies for R/R MM – Prof Dimopoulos

Agenda

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New and Emerging Strategies with Bispecific Antibodies in Multiple Myeloma

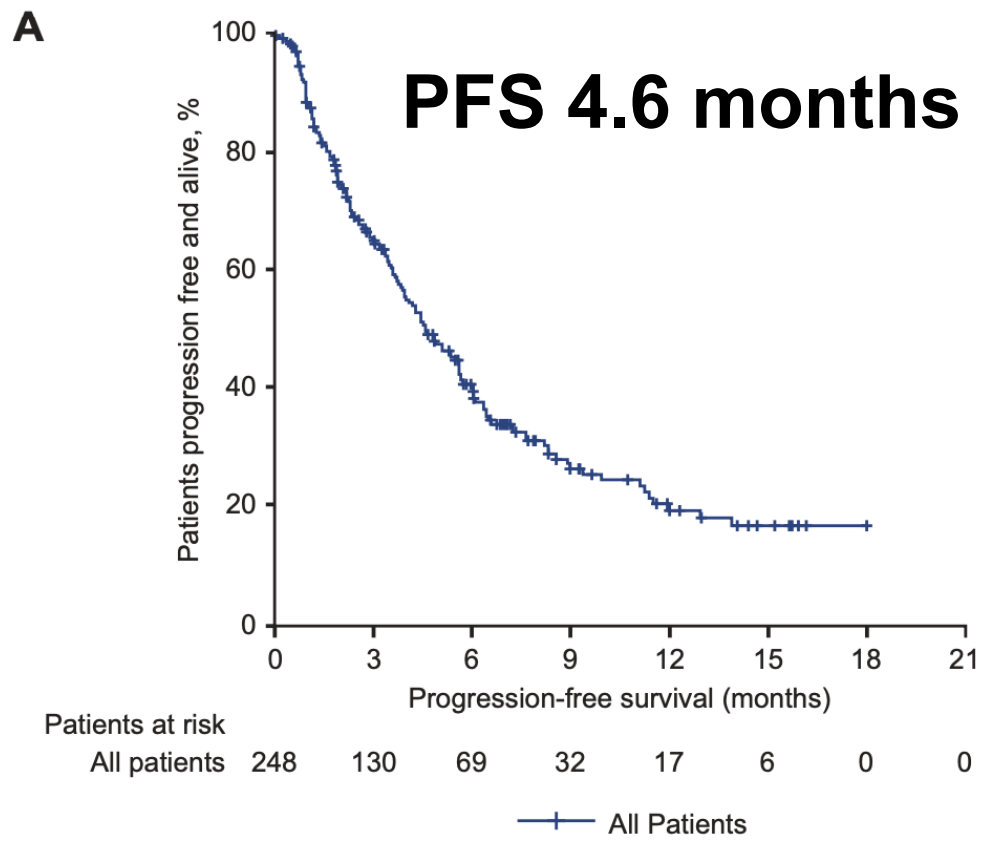
Noopur Raje, MD
Center for Multiple Myeloma
MGH Cancer Center
Professor of Medicine
Harvard Medical School

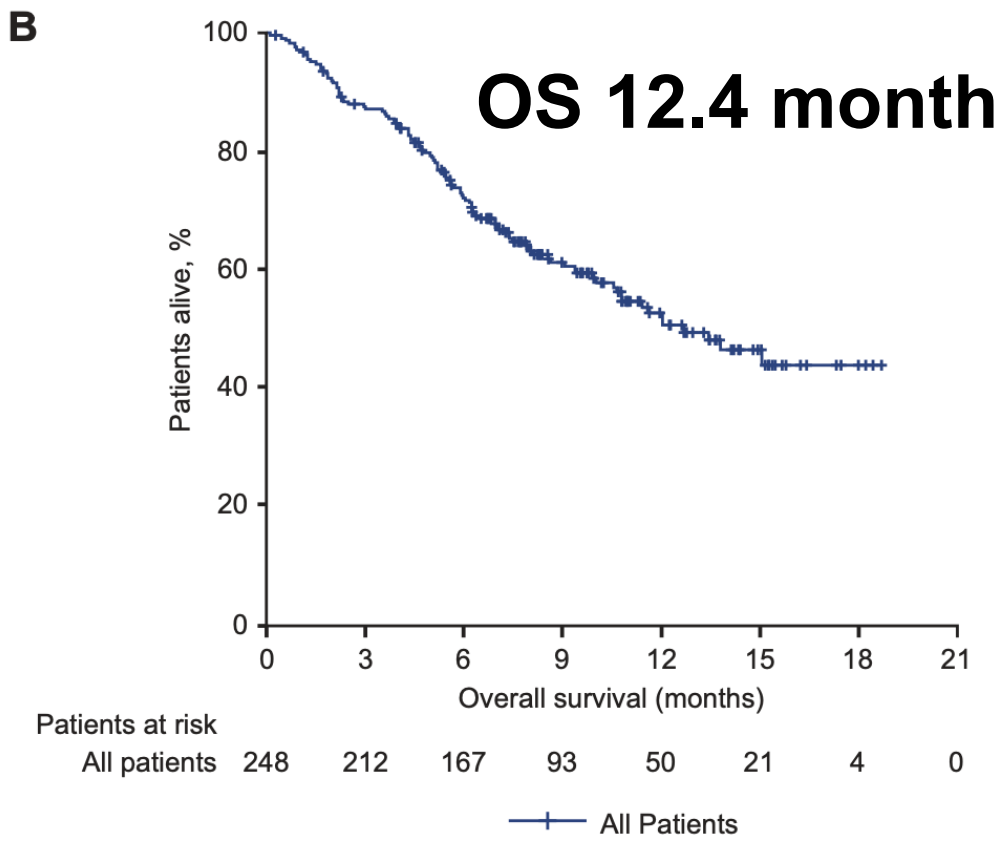
MASSACHUSETTS GENERAL HOSPITAL

Mass General Brigham
Cancer Institute

Triple-class-exposed disease has *historically* had poor outcomes

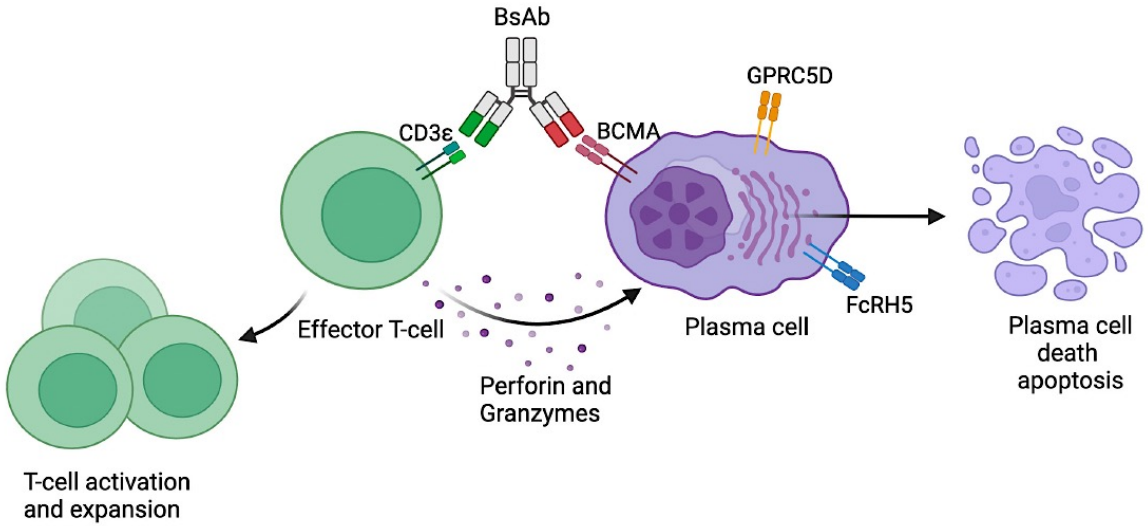
LocoMMotion: prospective study of real life standard of care of triple-class exposed RRMM patients
Proteasome inhibitor, immunomodulatory drug, anti-CD38 monoclonal antibody
Data cut off: May 2021





Mateos MV et al, *Leukemia* 2022

Bispecific Antibody Targets and Mechanism of Action

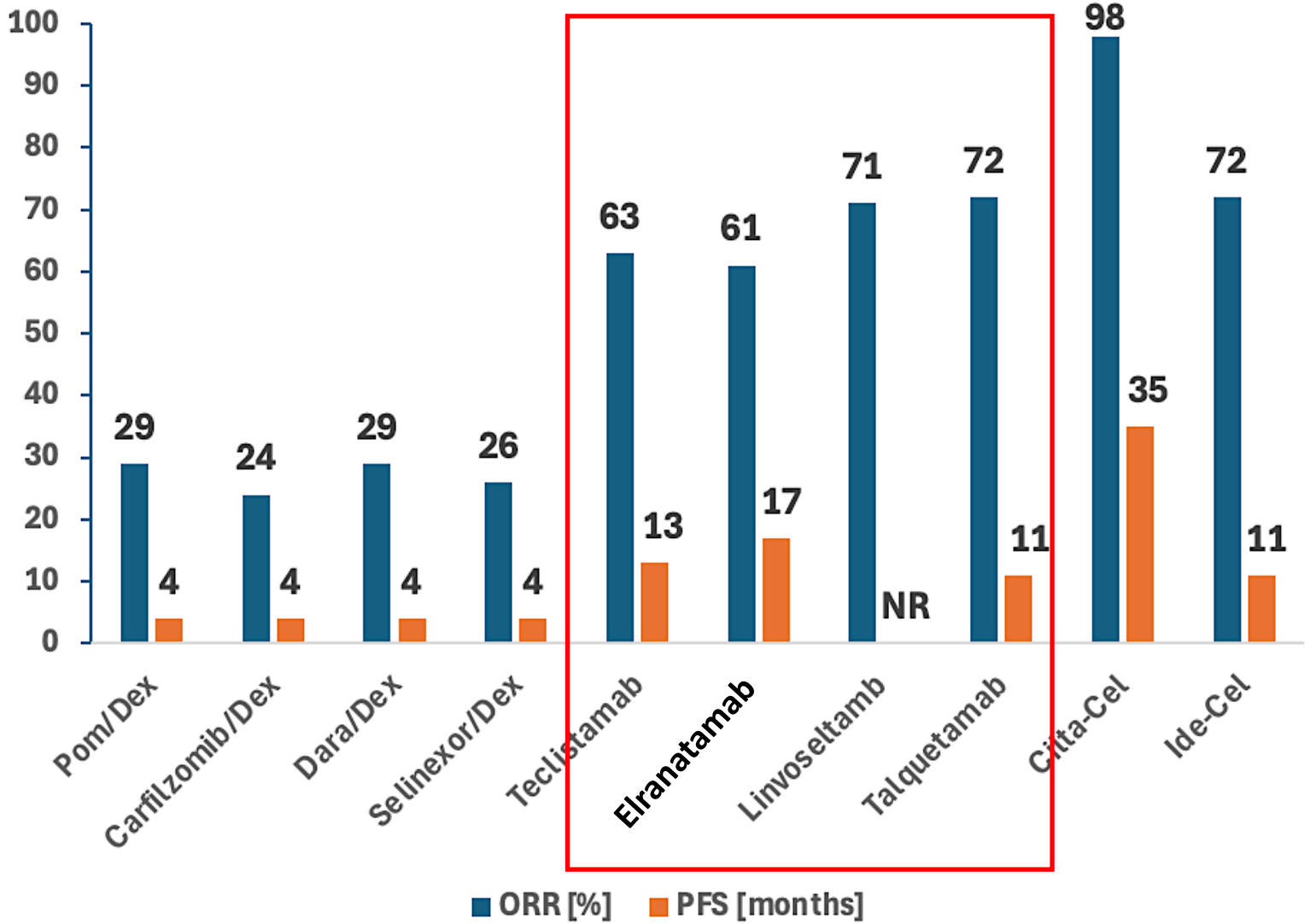


	BCMA	GPRC5D	FcRH5
Expression	Plasma cells, Plasmablasts	Plasma cells, hair follicle, eccrine glands, filiform papillae of tongue	B-cell lineage cells including plasma cells
Biologic Significance	Survival/growth of plasma cells	Unclear	Unclear
Location	16p13	12p13	1q21
Extracellular Shedding?	Yes	No	Yes

Reese et al, *Frontiers in Immunology*, 2024; Yu et al, *Journal of Hematology & Oncology*; Rodriguez-Otero et al, *Blood Cancer Journal*, 2024; Li et al, *Cancer Cell*, 2017; Ise et al, *Leukemia* 2007

Lymphoma · Leukemia & Myeloma Congress
Celebrating 25 Years of Excellence

PFS and ORR of Recently Approved Myeloma Drugs in RRMM

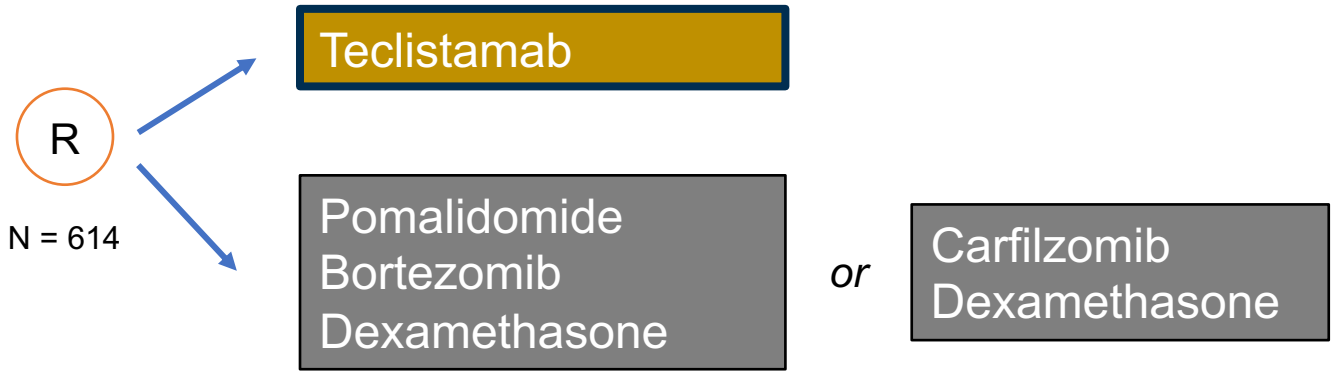


San Miguel et al, *Lancet Oncology*, 2013; Siegel et al, *Blood*, 2012; Lonial et al, *Lancet,* 2016; Chari et al, *NEJM* 2019; Moreau et al, *NEJM*, 2022; Lesokhin et al, *Nature Medicine*, 2023; Bumma et al, *JCO,* 2024; Chari et al, *NEJM*, 2022; Berdeja et al, *Lancet*, 2021; Munshi et al, *NEJM*, 2021

Moving anti-BCMA bispecific antibody monotherapy to earlier lines of therapy

MajesTEC-9 Study Design

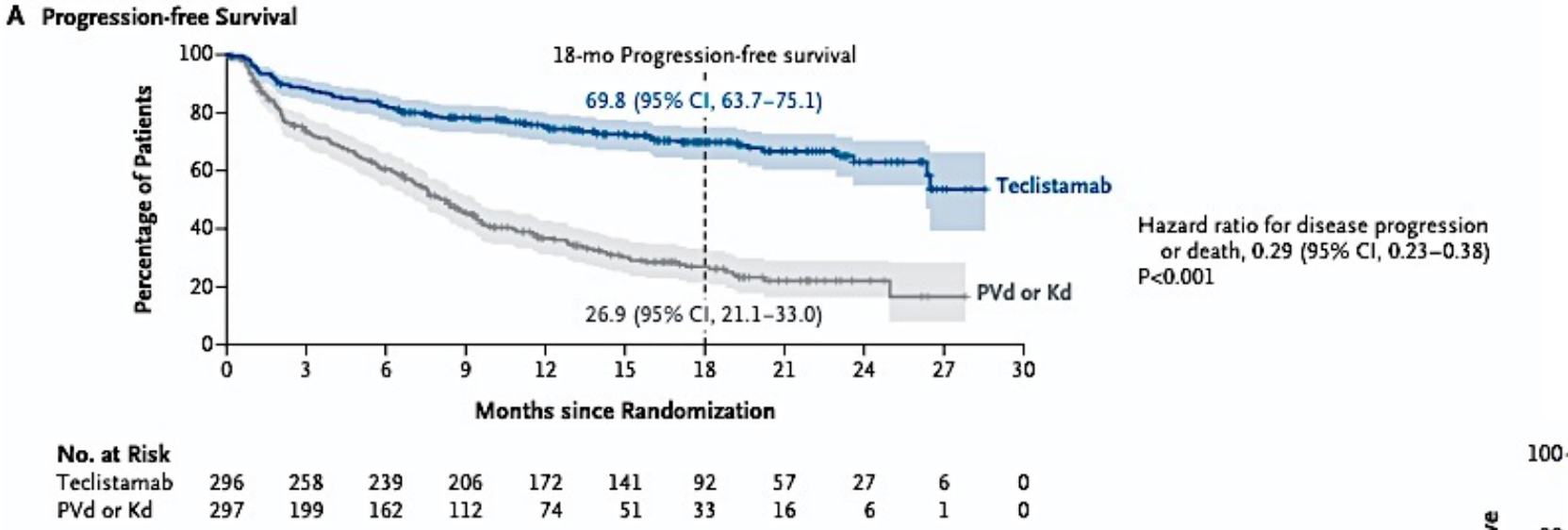
1-3 prior lines of therapy, *including lenalidomide and anti-CD38 antibody therapy*

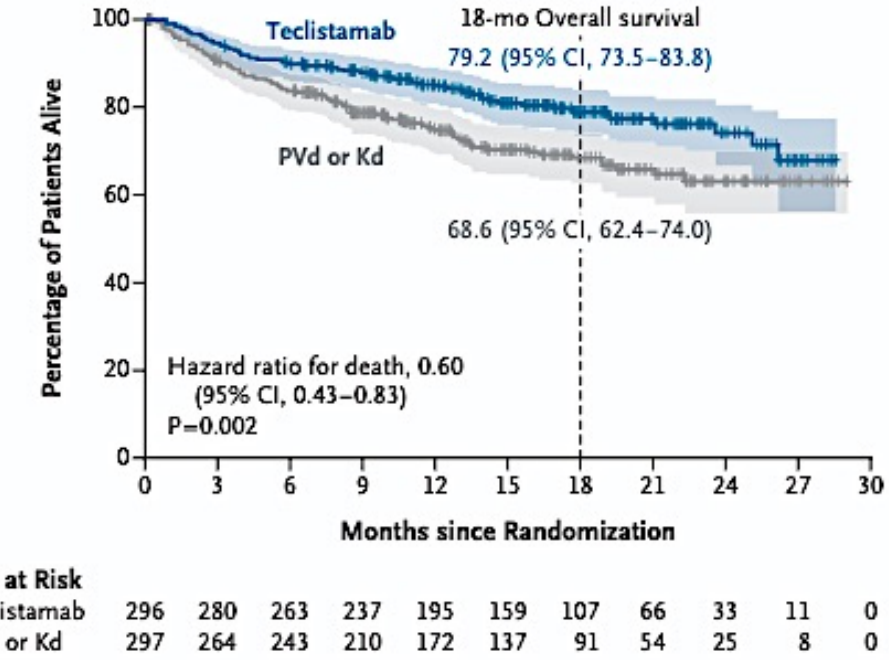


Primary endpoint: PFS

Touzeau C et al. *N Engl J Med* 2026;395:440-53.

MajesTEC-9: Teclistamab in Multiple Myeloma with One to Three Previous Lines of Therapy

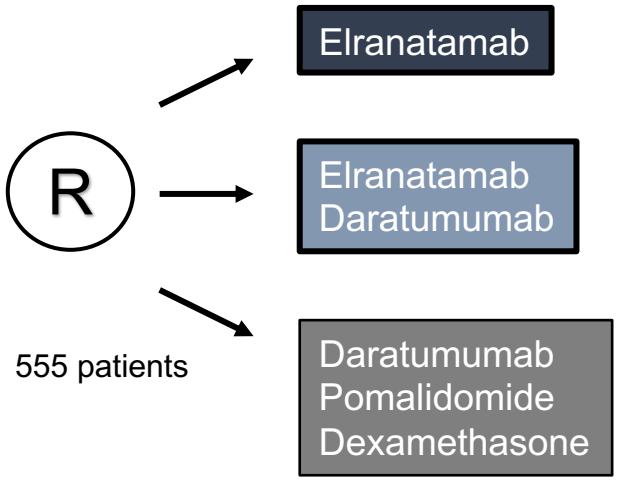




Touzeau C et al. *N Engl J Med* 2026;395:440-53.

Randomized phase III studies of anti-BCMA bispecific antibody in progress in relapsed myeloma

MagnetisMM-5

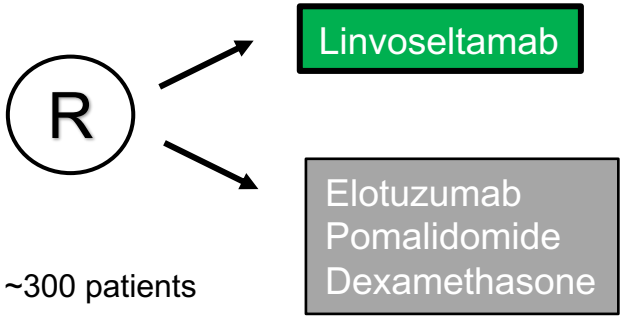


Primary endpoint: PFS

1-4 prior lines of therapy, including lenalidomide and PI

Prior anti-CD38 allowed if > 6 months

LINKER-MM3



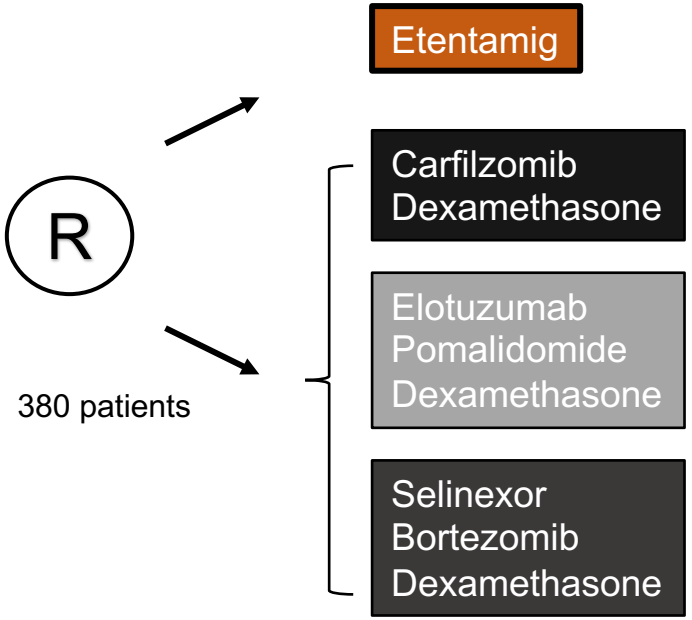
Primary endpoint: PFS

1-4 prior lines of therapy, including lenalidomide and PI

Prior anti-CD38 antibody allowed

Patients in the EU and the UK must have had 2-4 prior lines of therapy, including an anti-CD38 antibody

CERVINO



Primary endpoints: PFS and ORR

≥ 2 prior lines of therapy, including lenalidomide, PI, **and anti-CD38 antibody**

Grosicki S et al., ASCO 2022; Weisel K et al., IMS 2023; Costa LJ et al., IMS 2024

Elranatamab Significantly Improves Progression-Free Survival for Double-Class Exposed Patients with Relapsed or Refractory MM

Press Release: April 29, 2026

"[The manufacturer] announced positive topline results from the Phase 3 MagnetisMM-5 study evaluating elranatamab as monotherapy in adults with relapsed or refractory multiple myeloma (RRMM) who received at least one prior line of treatment.

The study demonstrated a statistically significant and clinically meaningful improvement in the primary endpoint of progression-free survival (PFS), as assessed by blinded independent central review (BICR), versus standard-of-care daratumumab plus pomalidomide and dexamethasone (DPd). The safety and tolerability of elranatamab was consistent with its known safety profile.

The PFS results exceeded the pre-specified interim analysis target hazard ratio for efficacy, with most elranatamab-treated patients remaining progression-free. The trial remains ongoing to assess overall survival, a key secondary endpoint, which was not yet mature at the time of this interim analysis. These data will be discussed with global health authorities, and detailed results from MagnetisMM-5 will be submitted for presentation at a future medical congress."

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

Positive Topline Results from the Phase III CERVINO Trial of Etentamig versus Standard Available Therapies (SAT) for Triple-Class Exposed Relapsed/Refractory Multiple Myeloma

Press Release: September 3, 2026

"The study met its dual primary endpoints of objective response rate (ORR) and progression-free survival (PFS). Full results will be presented in a plenary session at the 23rd International Myeloma Society Annual Meeting, taking place September 23-26, 2026, in Glasgow, Scotland. At the data cutoff, the Phase 3 CERVINO trial included 393 patients who had received a median of three prior lines of therapy. At the median follow-up of 11.4 months, etentamig demonstrated statistically significant and clinically meaningful efficacy with a manageable safety profile:

- Significantly higher ORR with etentamig vs. SAT (74.0% [95% CI, 67.25–79.97] vs. 45.7% [95% CI, 38.59–52.91]; P<0.0001).
- Significantly improved PFS with etentamig vs. SAT (HR, 0.40; 95% CI, 0.29–0.54; P<0.0001). The PFS benefit was observed across all pre-specified subgroups evaluated.
- 12-month overall survival (OS) was 87.9% for etentamig vs. 72.0% for SAT (HR, 0.48; 95% CI: 0.29–0.77; nominal P=0.0012); prespecified efficacy boundary for OS was not crossed at data cutoff.

This was the first planned efficacy interim analysis of the CERVINO study and, based on the significant benefit, the Independent Data Monitoring Committee (IDMC) recommended unblinding the study."

https://news.abbvie.com/2026-09-03-AbbVie-Announces-Positive-Topline-Results-from-the-Phase-3-CERVINO-Trial-Showing-Etentamig-Significantly-Improved-Response-Rate-and-Progression-Free-Survival-in-Patients-with-Relapsed-Refractory-Multiple-Myeloma

Combining bispecific antibodies with other systemic therapies

Phase 3 Randomized Study of Teclistamab Plus Daratumumab Versus Investigator's Choice of Daratumumab and Dexamethasone With Either Pomalidomide or Bortezomib (DPd/DVd) in Patients With Relapsed Refractory Multiple Myeloma (RRMM): Results of MajesTEC-3

Maria-Victoria Mateos,[1] Nizar J. Bahlis,[2] Aurore Perrot,[3] Ajay K. Nooka,[4] Jin Lu,[5] Charlotte Pawlyn,[6,7] Roberto Mina,[8] Gaston Caeiro,[9] Alain Kentos,[10] Vania Hungria,[11] Donna Reece,[12] Ting Niu,[13] Anne K. Mylin,[14] Charlotte Toftmann Hansen,[15] Raphael Teipel,[16] Britta Besemer,[17] Meletios A. Dimopoulos,[18,19] Elena Zamagni,[20,21] Satoshi Yoshihara,[22] Kihyun Kim,[23] Chang Ki Min,[24] Paul Geerts,[25] Elena Van Leeuwen-Segarceanu,[26] Agata Tyczynska,[27] Juan Luis Reguera Ortega,[28] Magnus Johansson,[29] Markus Hansson,[30] Mehmet Turgut,[31] Mark Grey,[32] Surbhi Sidana,[33] Paula Rodriguez-Otero,[34] Joaquin Martinez-Lopez,[35] Hamza Hashmi,[36] Robin Carson,[37] Rachel Kobos,[38] Weili Sun,[39] Kristen Lantz,[37] Anne Seifert,[40] Deborah Briseno-Toomey,[41] Lisa O'Rourke,[37] Maria Rubin,[38] Diego Vieyra,[37] Lijuan Kang,[39] Luciano J. Costa[42]

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Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

ORIGINAL ARTICLE

Teclistamab plus Daratumumab in Relapsed or Refractory Multiple Myeloma

L.J. Costa,[1] N.J. Bahlis,[2] A. Perrot,[3] A.K. Nooka,[4] J. Lu,[5] C. Pawlyn,[6,7] R. Mina,[8] G. Caeiro,[9] A. Kentos,[10] V. Hungria,[11] D. Reece,[12] T. Niu,[13] A.K. Mylin,[14] C.T. Hansen,[15] R. Teipel,[16] B. Besemer,[17] M.A. Dimopoulos,[18,19] E. Zamagni,[20,21] S. Yoshihara,[22] K. Kim,[23] C.K. Min,[24] P. Geerts,[25] E. Van Leeuwen-Segarceanu,[26] A. Tyczynska,[27] J.L. Reguera,[28] M. Johansson,[29] M. Hansson,[30] M. Turgut,[31] M. Grey,[32] S. Sidana,[33] P. Rodriguez-Otero,[34] J. Martinez-Lopez,[35] H. Hashmi,[36] R. Carson,[37] R. Kobos,[38] W. Sun,[39] K. Lantz,[37] A. Seifert,[40] D. Briseno-Toomey,[41] L. O'Rourke,[37] M. Rubin,[38] D. Vieyra,[37] L. Kang,[39] and M.V. Mateos,[42] for the MajesTEC-3 Trial Investigators*

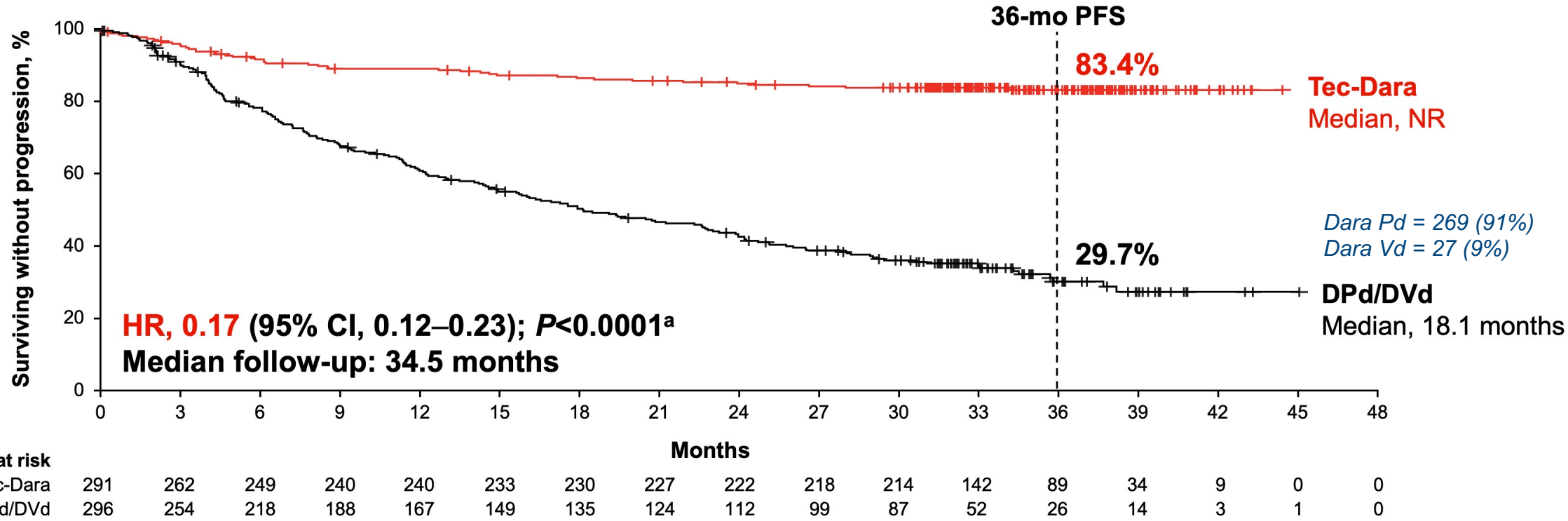
2025

Mateos M-V et al., ASH 2025, LBA-6

Rationale for combining daratumumab with teclistamab

Direct anti-myeloma effect of daratumumab
Daratumumab depletes immunosuppressive T-cells
Daratumumab enhances CD8+ T-cell cytotoxicity
Above creates a synergy between the two drugs

MajesTEC-3: Teclistamab and daratumumab v. SOC



1-3 prior lines of therapy, including PI and lenalidomide
Sensitive to anti-CD38 antibody (i.e., naïve or not refractory)
Daratumumab exposure: 5.3% overall
Higher dose of teclistamab, 3 mg/kg (starting with cycle 3)
No dexamethasone after C1D8

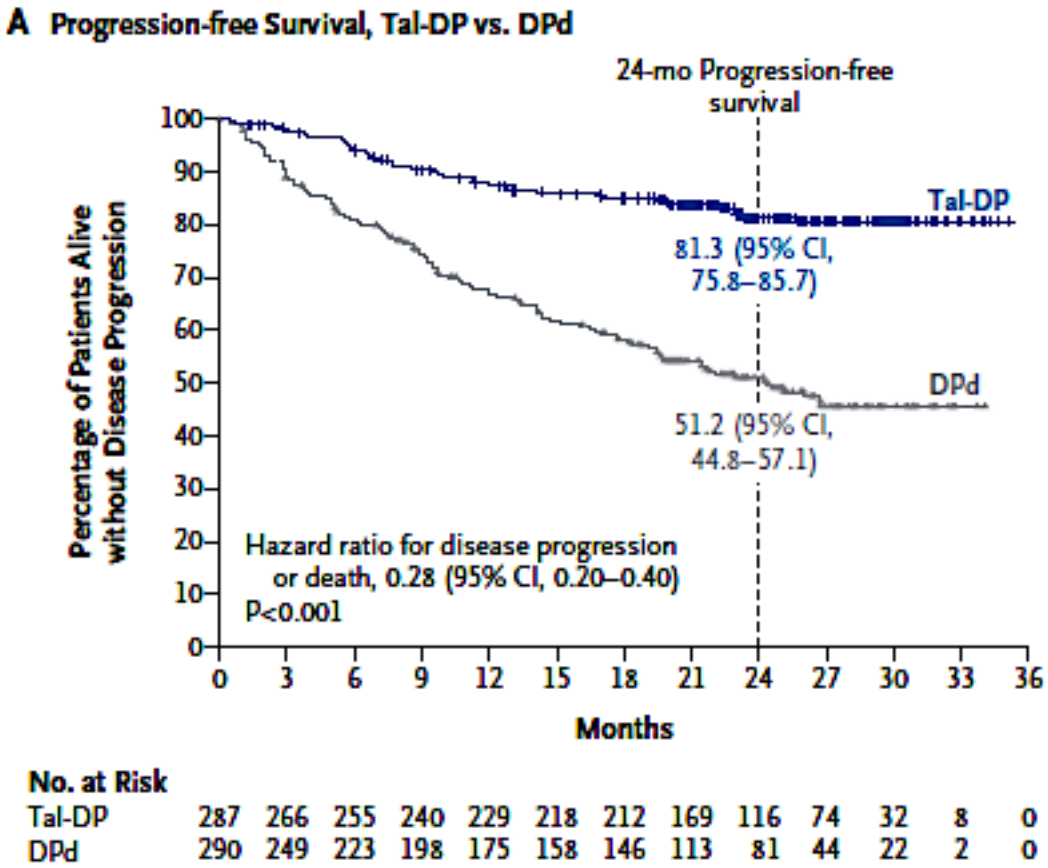
Dramatic improvement in PFS with HR 0.17 with potential plateau in PFS

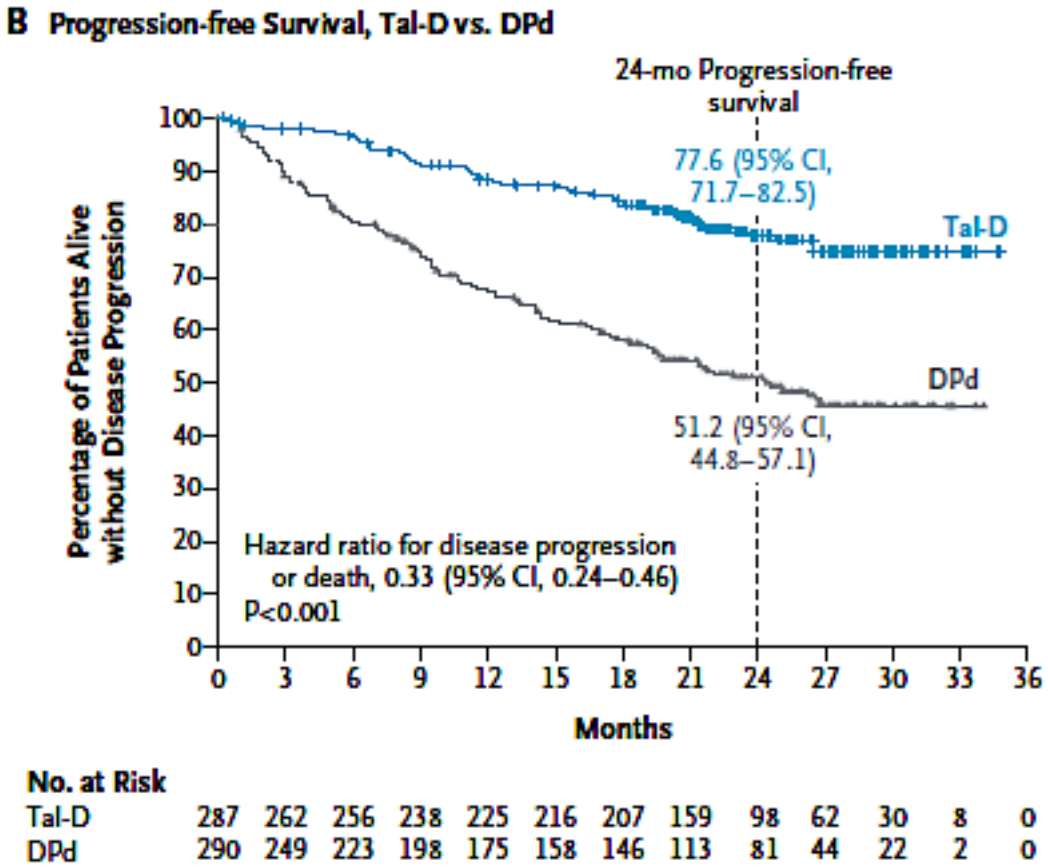
APOLLO dara Pd median PFS 12.4 months
CASTOR dara Vd median PFS 16.7 months

Approved by FDA in March 2026 for relapse after 1 prior line of therapy including a proteasome inhibitor and an immunomodulatory drug

Mateos MV et al., ASH 2025; Dimopoulos MA et al., *Lancet Oncol* 2021; Spencer A et al., *Haematologica* 2018

MonumenTAL-3: Phase III Trial of Talquetamab with Daratumumab in Relapsed or Refractory Myeloma





24-month OS (HR 0.47):
Tal-DP 89.2%
DPd 79.1%

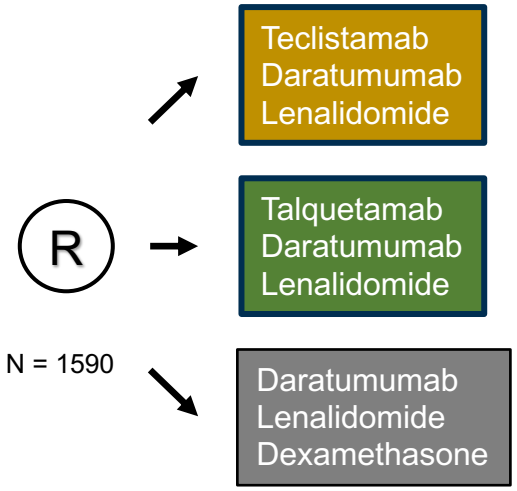
24-month OS (HR 0.51):
Tal-D 87.9%
DPd 79.1%

Mina R et al. *N Engl J Med* 2026;395:671-83.

Randomized phase III anti-BCMA bispecific antibody trials in progress

Newly diagnosed, transplant not eligible or not intended

MajesTEC-7

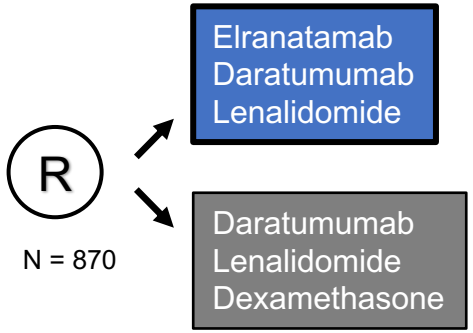


Tec and talq arms, dex given cycles 2-4

Transplant ineligible **or transplant not intended**

Dual primary endpoint: PFS and sustained MRD negative (10^{-5}) CR duration ≥ 12 months

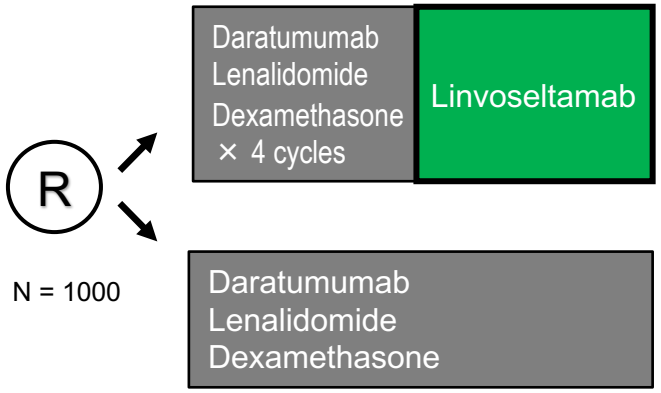
MagnetisMM-6



Transplant ineligible

Dual primary endpoint: PFS and sustained MRD-negative (10^{-5}) duration ≥ 12 months

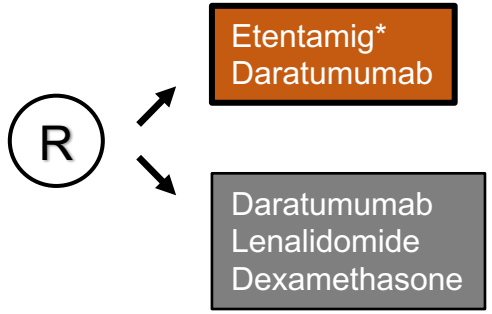
LINKER-MM6/EMN39



Transplant ineligible

Dual primary endpoint: PFS and MRD-negative (10^{-5})

ENTRUST (IFM/PETHEMA)



**Dose will be based on ongoing phase 2*

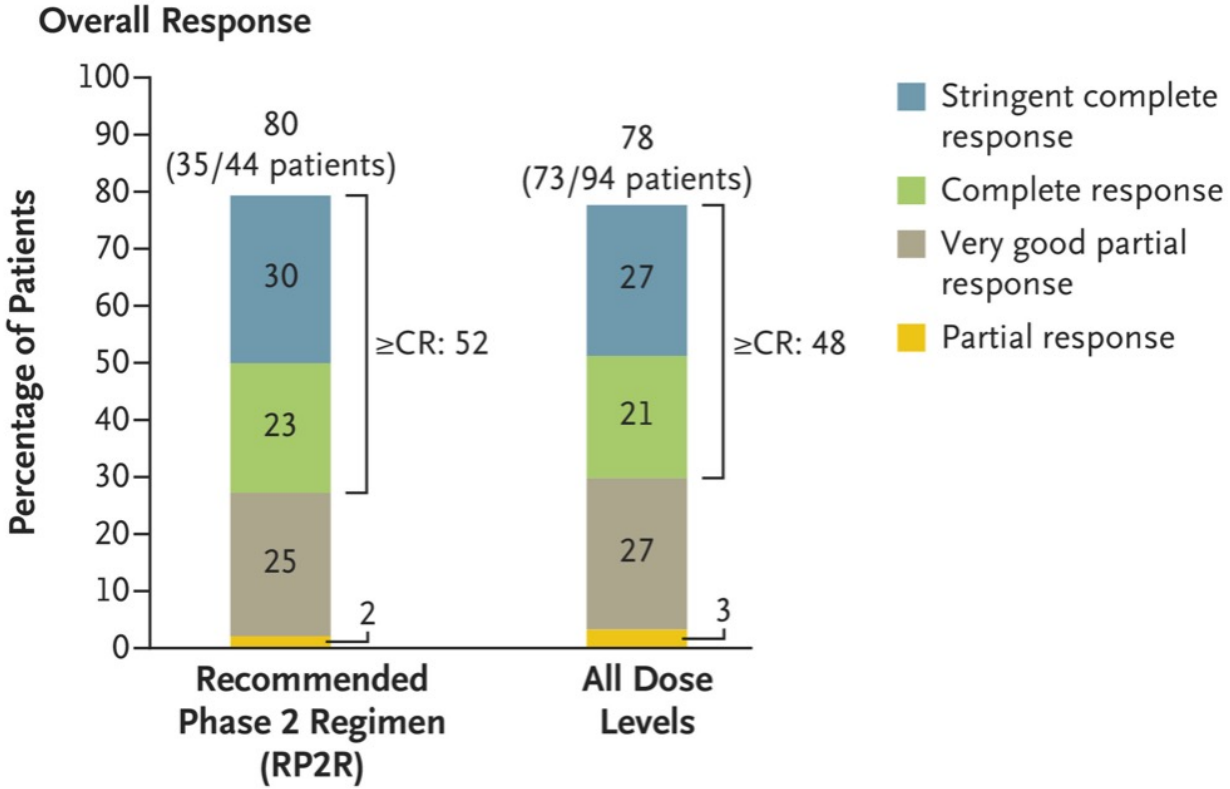
Transplant ineligible
IMWG Frailty Index ≥1

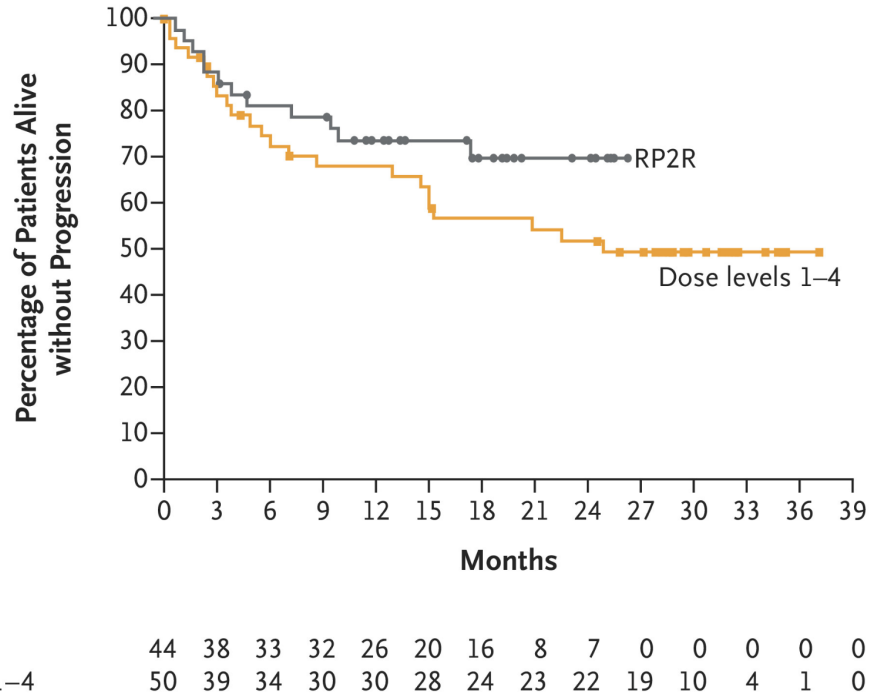
Dual primary endpoint: PFS and MRD-negative (10^{-5})

Touzeau C, et al., ASCO 2024. Grosicki S, et al., ASCO 2023. Manier S et al., ASH 2025

Combining bispecific antibodies with other bispecific antibodies

RedirecTT-1: Talquetamab + Teclistamab in R/R MM





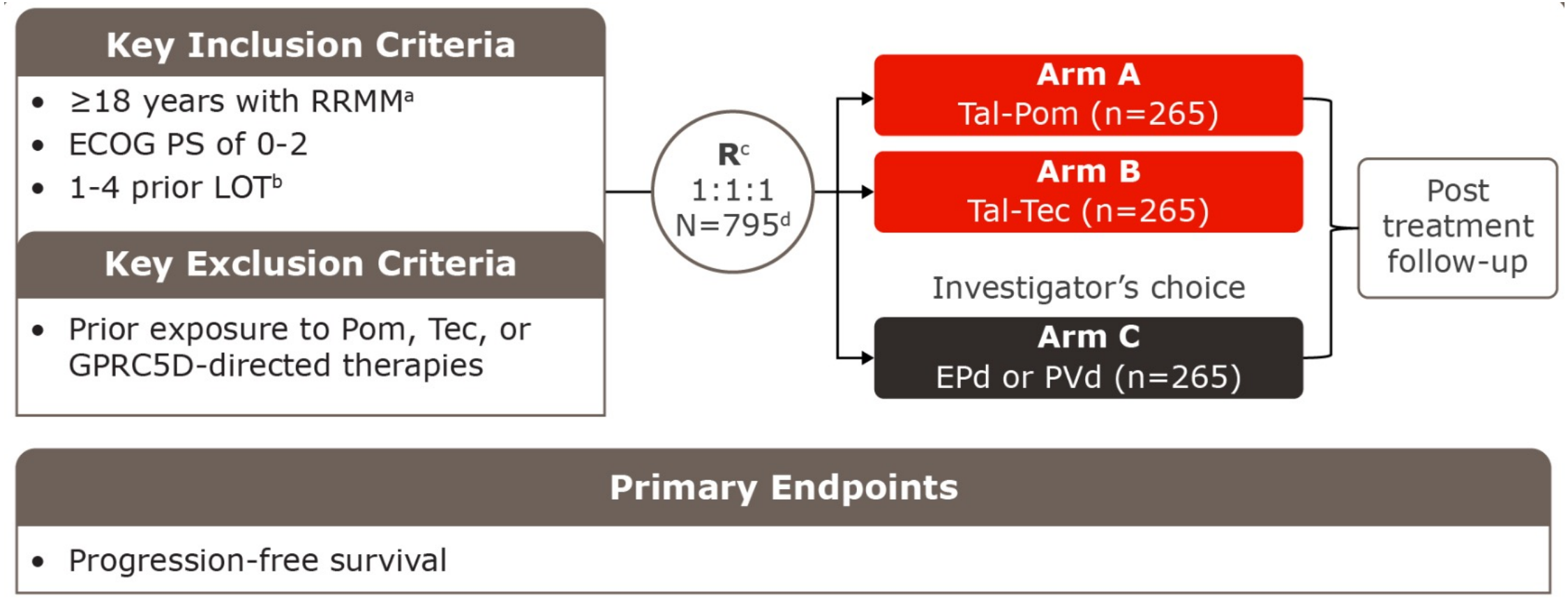
No. at Risk

RP2R	44	38	33	32	26	20	16	8	7	0	0	0	0	0
Dose levels 1–4	50	39	34	30	30	28	24	23	22	19	10	4	1	0

With the recommended phase 2 regimen:
12-month PFS: 74%
18-month PFS: 70%

Cohen YC et al. *N Engl J Med* 2025;392(2):138-149.

MonumenTAL-6: Phase III Trial of Talquetamab-Based Combinations in Early Relapsed R/R MM



Nooka AK et al. ASH 2024;Abstract 4757.

Positive Topline Results from the MonumenTAL-6 Phase III Trial of Teclistamab with Talquetamab for Relapsed/Refractory Multiple Myeloma in Earlier Lines of Therapy

Press Release: July 23, 2026

"[The manufacturer] announced positive topline results from the three-arm investigational Phase III MonumenTAL-6 study evaluating teclistamab-cqyv + talquetamab-tgvs, a BCMA and GPRC5D dual antigen targeting regimen, and talquetamab-tgvs + pomalidomide in adult patients with relapsed or refractory multiple myeloma (RRMM) who received 1 to 4 prior lines of therapy, including an anti-CD38 antibody and lenalidomide.

The study demonstrated statistically significant and clinically meaningful improvements in progression-free survival and overall survival for both investigational arms compared with investigator's choice standard of care. Teclistamab-cqyv + talquetamab-tgvs delivered the greatest benefit, reducing the risk of disease progression or death by 89% (HR, 0.11) and the risk of death by 62% (HR, 0.38).

Based on the strength of the data, the Independent Data Monitoring Committee recommended unblinding the study at the first interim analysis. The full results of the Phase 3 MonumenTAL-6 study will be presented at a future major medical meeting and shared with global health authorities."

https://www.jnj.com/media-center/press-releases/tecvayli-talvey-reduced-the-risk-of-disease-progression-or-death-by-89-and-the-risk-of-death-by-62-in-earlier-line-relapsed-refractory-multiple-myeloma.

Novel bispecific antibody targets in MM

CAMMA 1: Randomized dose-expansion of FcRH5 x CD3 bispecific antibody cevostamab with pomalidomide, and dexamethasone

Patients

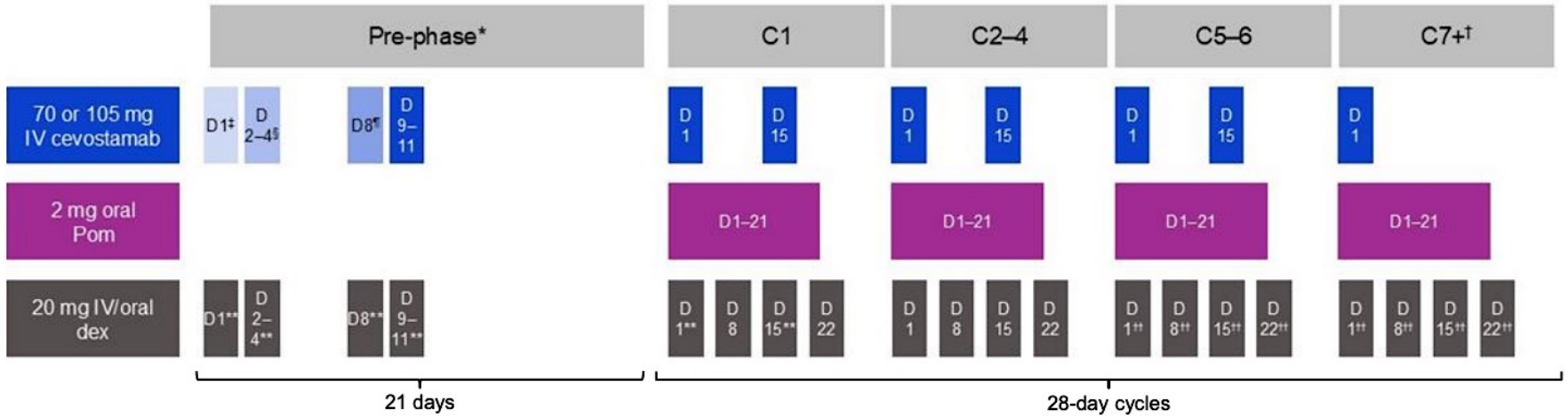
- RRMM with ≥1 prior line including an IMiD and a PI
- Pom-refractory patients excluded

Objectives

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

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

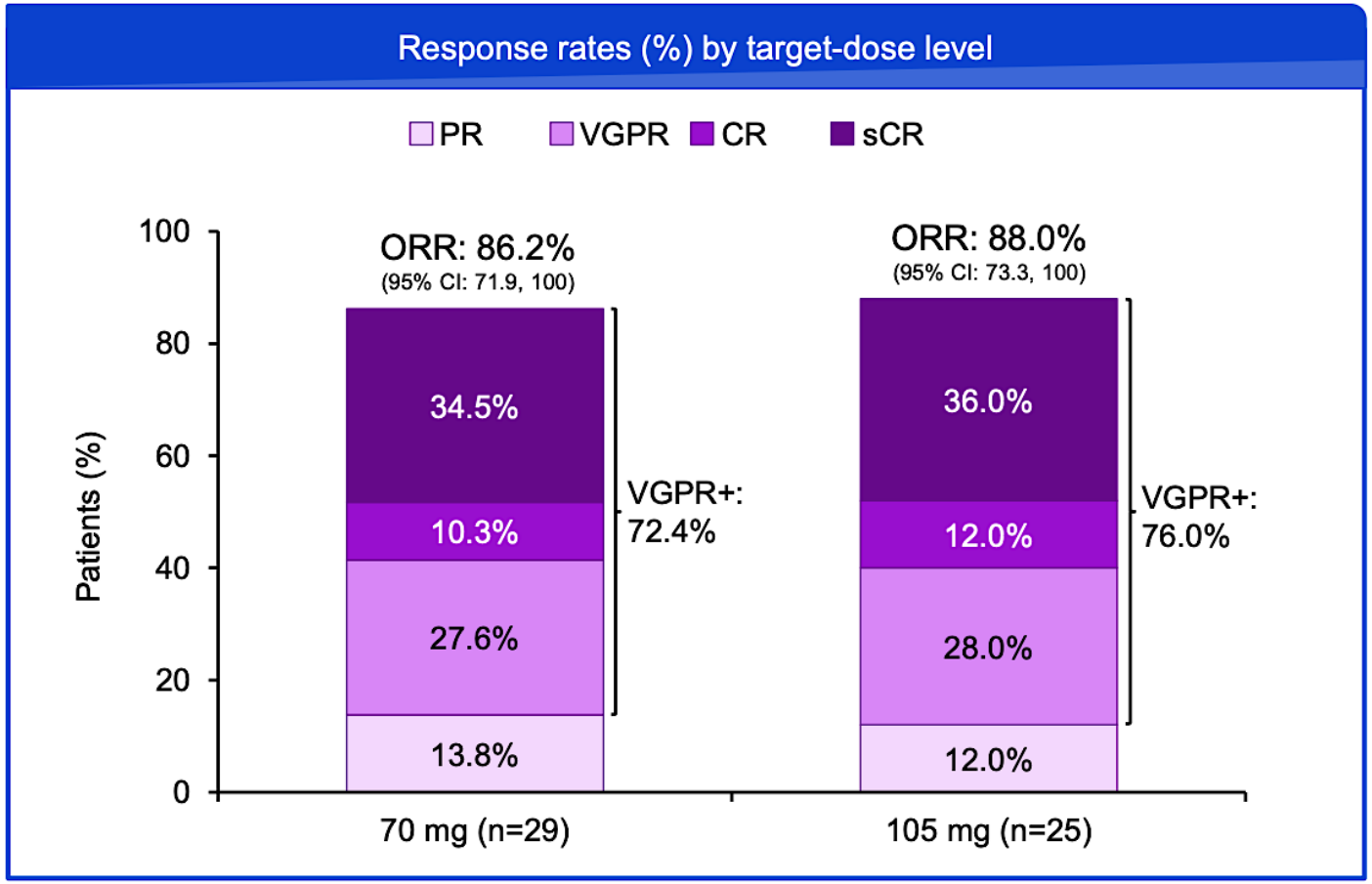
- Subsequent expansion cohort with limited follow-up
- Patients randomised 1:1 to 70 mg or 105 mg cevostamab target dose
- Cevostamab initiated with **triple step-up dosing** (0.3/1.2/3.6 mg)



Courtesy of Hans Lee, MD

Mian et al, *IMS* 2025

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

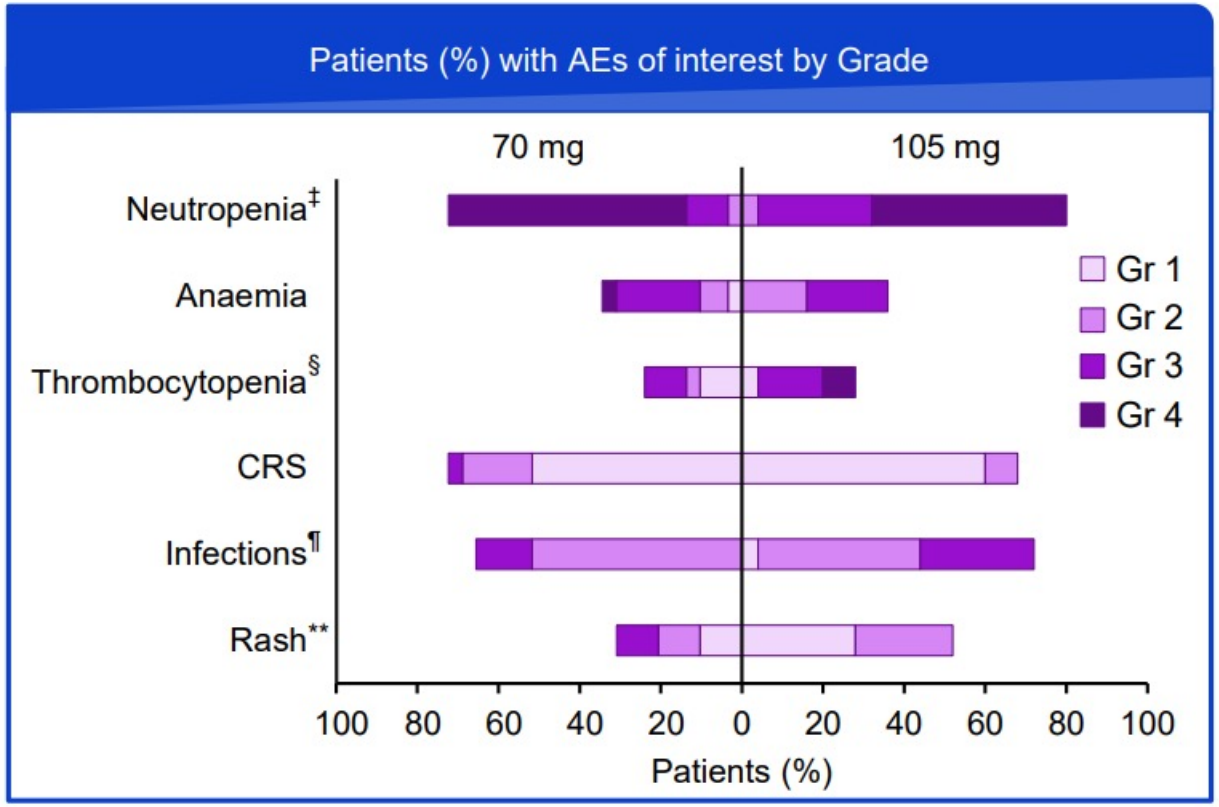


Courtesy of Hans Lee, MD

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.

Courtesy of Hans Lee, MD

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)

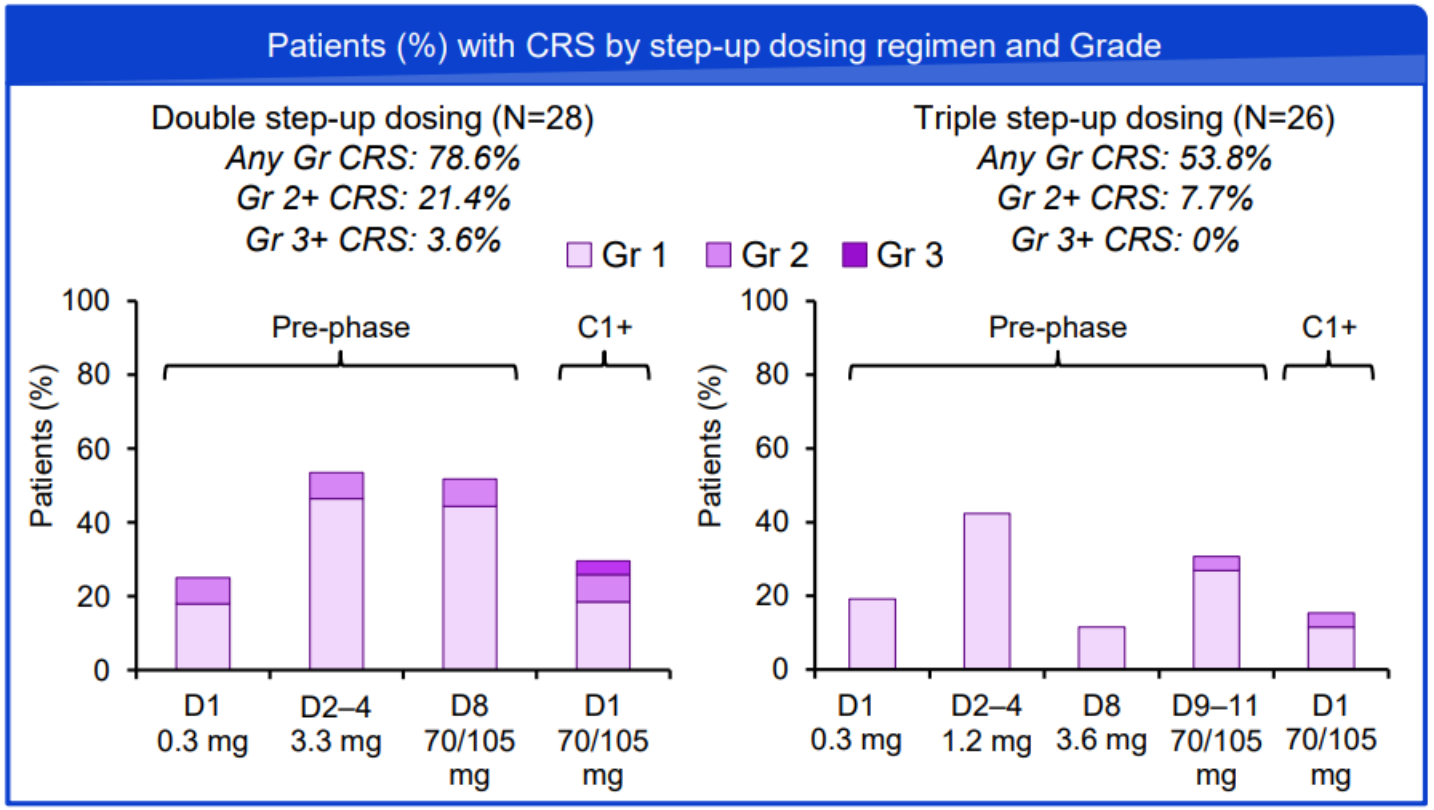
No Gr 4+ AEs of infection occurred and no AE of infection led to discontinuation of cevostamab, pom or dex

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.

Courtesy of Hans Lee, MD

Mian et al, *IMS* 2025

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.

Courtesy of Hans Lee, MD

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

Courtesy of Hans Lee, MD

Mian et al, *IMS* 2025

Faculty Case Presentations

RTP
RESEARCH
TO PRACTICE

Prof Dimopoulos: Case Presentation

Diagnosis	67y, male, IgG-κ MM, diagnosed 6 years ago R-ISS II, 1q21 addition, no other high-risk cytogenetics Anemia and multiple lytic bone lesions; no extramedullary disease
1L	Dara-VRd → ASCT → lenalidomide maintenance
First relapse	Biochemical progression while receiving lenalidomide
2L	KPd (carfilzomib/pomalidomide/dexamethasone) → VGPR; progression after ~2 years
Current relapse	Rising M-protein, anemia; ECOG PS 1

Prof Dimopoulos: Case Presentation (cont'd) Lab Values at Relapse

Hb	**9.8 g/dL**
Platelets	142 ×10^9/L
Creatinine	1.1 mg/dL
Calcium	9.5 mg/dL
IgG M-protein	**2.1 g/dL**
κ FLC	**325 mg/L**
λ FLC	7 mg/L
Bone marrow plasma cells	~35%

Imaging: PET/CT shows several FDG-avid skeletal lesions but **no extramedullary disease**.

Prof Dimopoulos: Case Presentation (cont'd) Treatment Selection and Course

Current therapy	**Teclistamab + daratumumab + IVIG regardless IgG levels**
Early toxicity	Grade 1 CRS during step-up dosing; no ICANS; subsequently managed as outpatient
Response	Rapid decline in M-protein → **VGPR by cycle 2 → CR/MRD-negative response**
Current status	Remains on therapy with ongoing response; receives IVIG and antiviral/PJP prophylaxis; no infection

QUESTIONS FOR THE FACULTY

For which patients are you prioritizing teclistamab/daratumumab, and for which do you still prefer bispecific antibody monotherapy? How are you generally sequencing each of these relative to other options?

How comfortable are you employing teclistamab/daratumumab for a patient like this who has previously received daratumumab?

QUESTIONS FOR THE FACULTY

How are you currently sequencing talquetamab relative to BCMA-targeted bispecific antibodies for patients with and without prior exposure to BCMA-targeted therapy?

Where do you see emerging talquetamab-containing combinations, such as talquetamab/daratumumab with or without pomalidomide and talquetamab/pomalidomide, fitting in? What about the dual antigen-targeting regimen of teclistamab/talquetamab?

Dr Orlowski: Patient Case

- A now 82 yo F who presented with SMM diagnosed in 2015 and followed w/ watchful waiting until developing anemia and a rising paraprotein in 2019
  - BM showed 70% PCs & t(11;14), -13, biallelic del 17p
- Started on Dara-Rd producing a VGPR by cycle 6 but declined ASCT and had progression after 18 months
- Switched to Dara-CyBorD with a PR by cycle 6 but then progressed by cycle 9
- Collected T cells for ide-cel and received talquetamab bridging but PD noted on talq

Dr Orlowski: Patient Case (Continued)

- Received hyper-fractionated Cyclo-dex with response and then had ide-cel which produced a CR
- Relapse noted after 18 months, which was treated with Ven-dex after confirming persistence of t(11;14), which also showed no BCMA expression
- After an initial PR that lasted 6 months, disease progression as noted with hyperviscosity symptoms
- ? Cevostamab

QUESTIONS FOR THE FACULTY

How often do your patients lose BCMA expression after exposure to BCMA-targeted therapy?

What would you recommend next for this patient outside of a clinical trial?

How would you indirectly compare the efficacy of cevostamab to that of BCMA-targeted bispecific antibodies? What about to that of talquetamab? How would you indirectly compare the tolerability of cevostamab to that of BCMA-targeted bispecific antibodies and of talquetamab?

QUESTIONS FOR THE FACULTY

If cevostamab/pomalidomide/dexamethasone were available, how would you most likely sequence it relative to available and emerging BCMA- and/or GPRC5D-targeted bispecific antibody-containing regimens? Which patients might represent ideal candidates for cevostamab?

With 3 BCMA-targeted bispecific antibodies already available, what role do you foresee for etentamig in R/R MM?

Agenda

Module 1 – New and Emerging Strategies with Bispecific Antibodies in MM – Dr Raje

Module 2 – Utility of Antibody-Drug Conjugates for R/R MM – Dr Orlowski

Module 3 – Potential Role of Cereblon E3 Ligase Modulators and Other Promising Novel Agents and Strategies for R/R MM – Prof Dimopoulos

Utility of Antibody Drug Conjugates for Relapsed/ Refractory Multiple Myeloma

Robert Z. Orlowski, M.D., Ph.D.

Deputy Chair, Department of Lymphoma/Myeloma

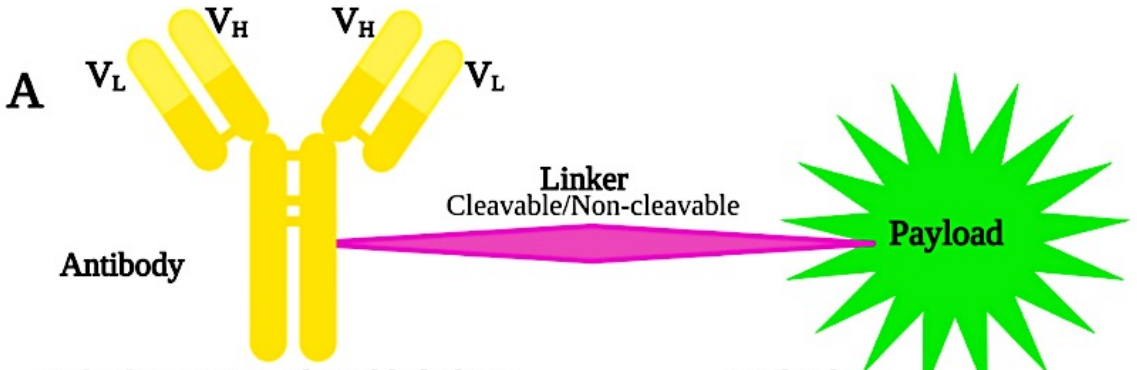
Florence Maude Thomas Cancer Research Professor

Director, Myeloma Translational Research

Cancer®

UT MD Anderson

ADC Design



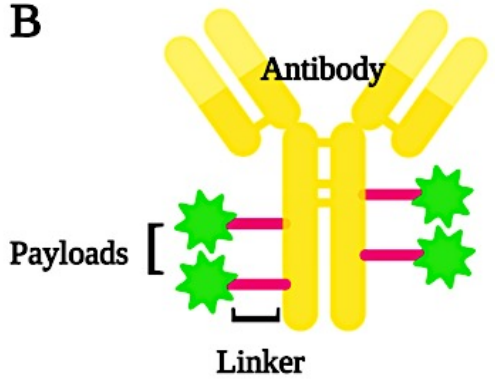
Antibody isotype:
IgG1 and IgG4

Cleavable linkers:
pH-sensitive: hydrazone linker
glutathione-sensitive disulfide linkers: N-succinimidyl-4-(2-pyridyldithio) butyrate (SPDB)
lysosomal protease-sensitive peptide linkers: valine-citruline linker (vc),valine–alanine (va), alanine–alanine; maleimidocaproyl-valine-citrulline-p-aminobenzoyloxycarbonyl (mc-VC-PABC), triazole-containing *para*-aminobenzyloxycarbonyl (PABC)–peptide linker (CL2A)
β-glucuronidase-sensitive linker

Non-cleavable linkers:
thioether or maleimidocaproyl group (mc), succinimidyl-4-(N-maleimidomethyl) cyclohexane-1-carboxylate (SMCC)

Payload:

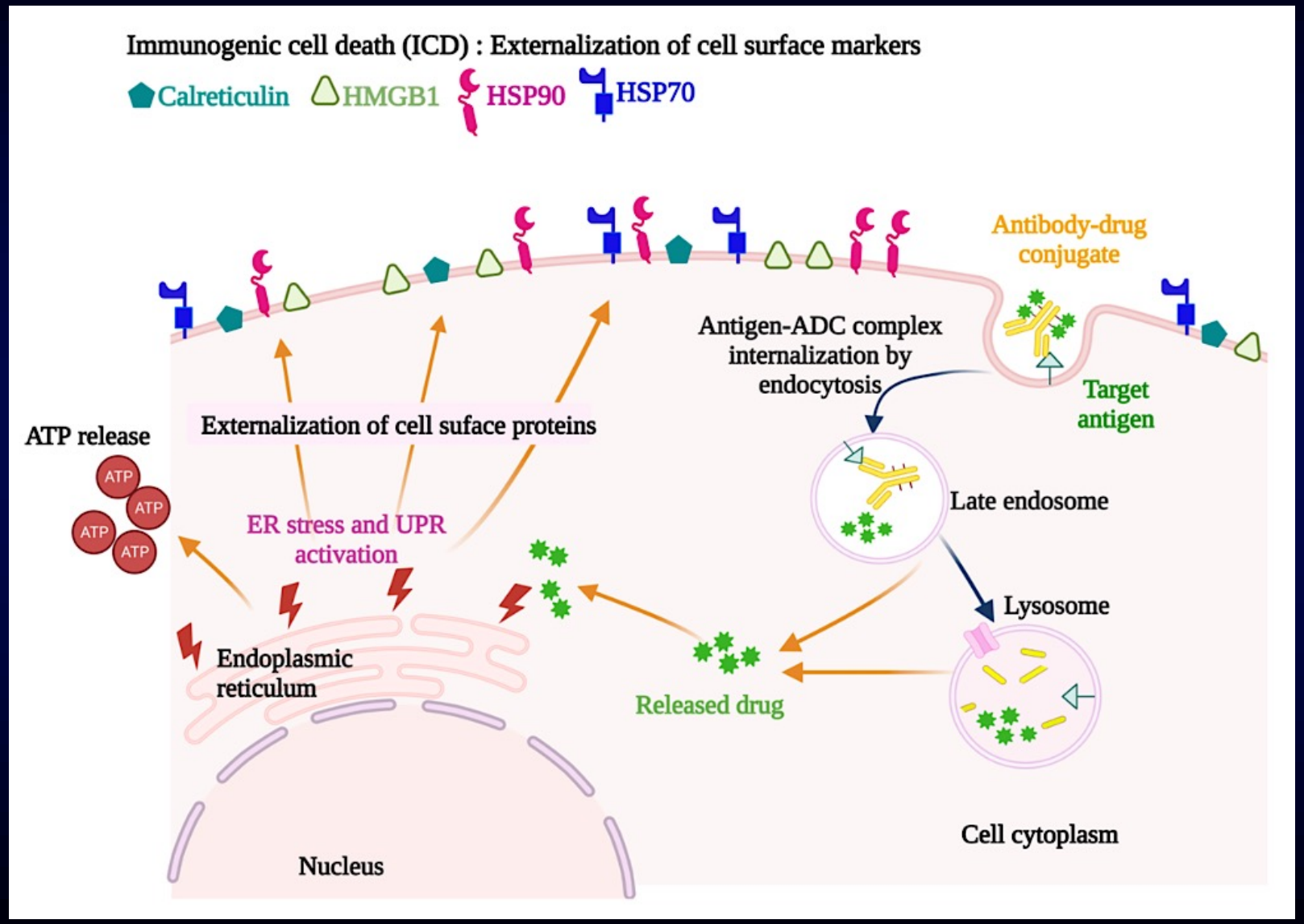
1. **Tubulin inhibitors**
   auristatins:
   MMAE monomethyl auristatin E
   MMAF monomethyl auristatin-F
   maytansinoids:
   thiol-containing maytansinoids DM1 and DM4
   tubulysins: tubulysin A
2. **DNA damaging agents**
   calicheamicins, duocarmycins, exatecans, pyrrolobenzodiazepine (PBD) dimers
3. **Topoisomerase I inhibitor**
   SN38 active metabolite of irinotecan
4. **RNA polymerase II inhibitor**
   α-Amanitin.



Antibody-drug conjugate drug to antibody ratio (DAR) 4

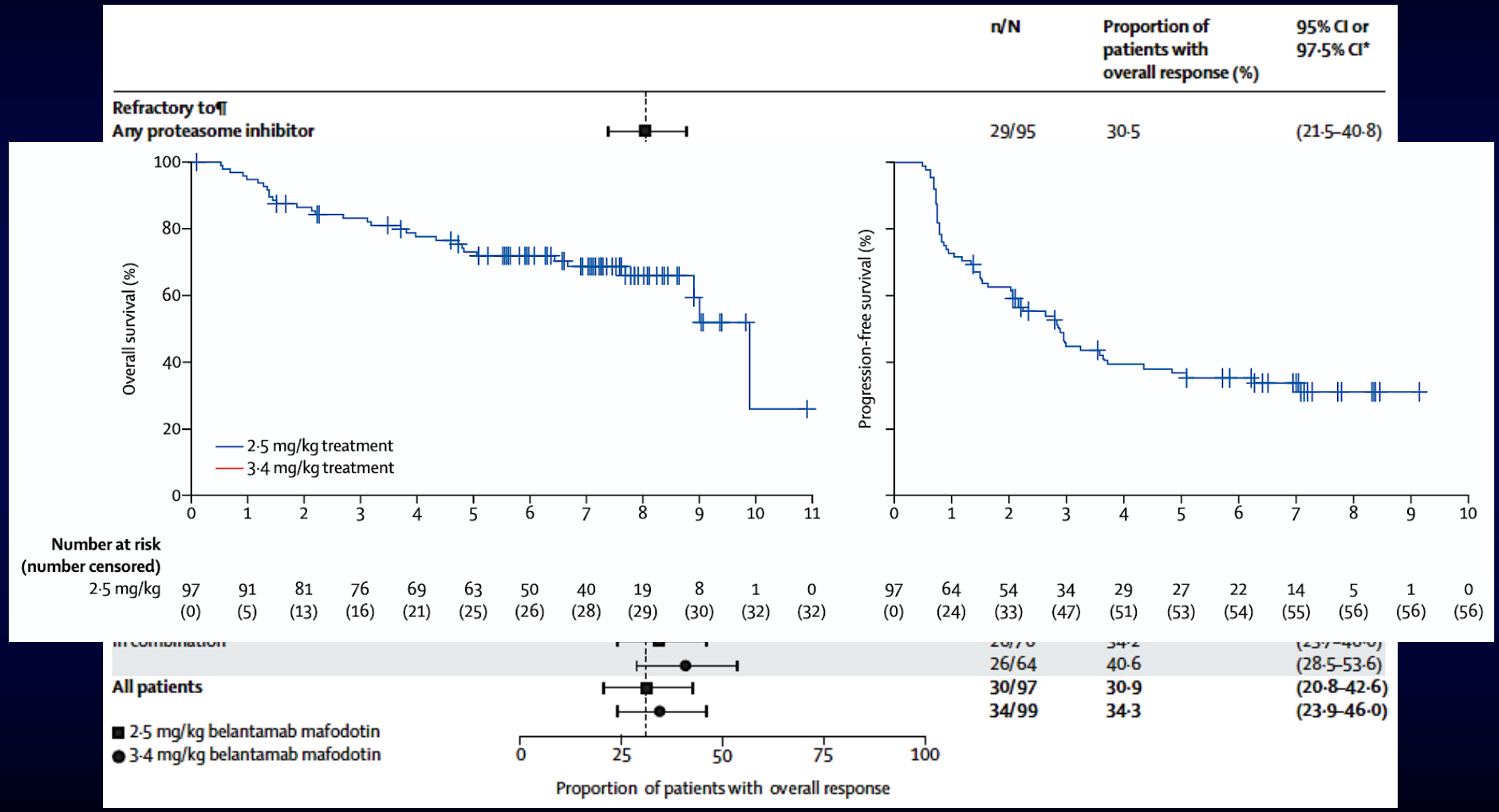
Ray, U & Orlowski, RZ. https://pubmed.ncbi.nlm.nih.gov/37111346/

MOA: Direct Cytotoxicity & ICD



Ray, U & Orlowski, RZ. https://pubmed.ncbi.nlm.nih.gov/37111346/

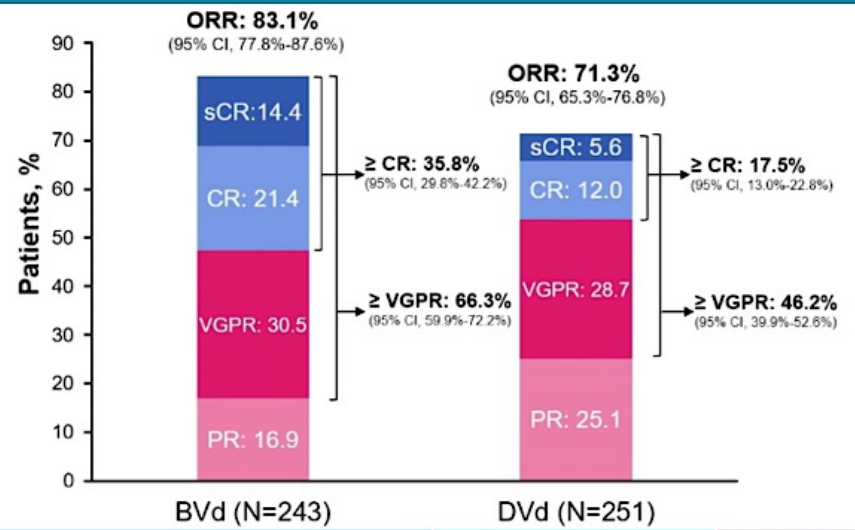
BelaMaf Single-agent: DREAMM-2



Lonial, S et al. https://pubmed.ncbi.nlm.nih.gov/31859245/

Bela-Vd: DREAMM-7

ORR

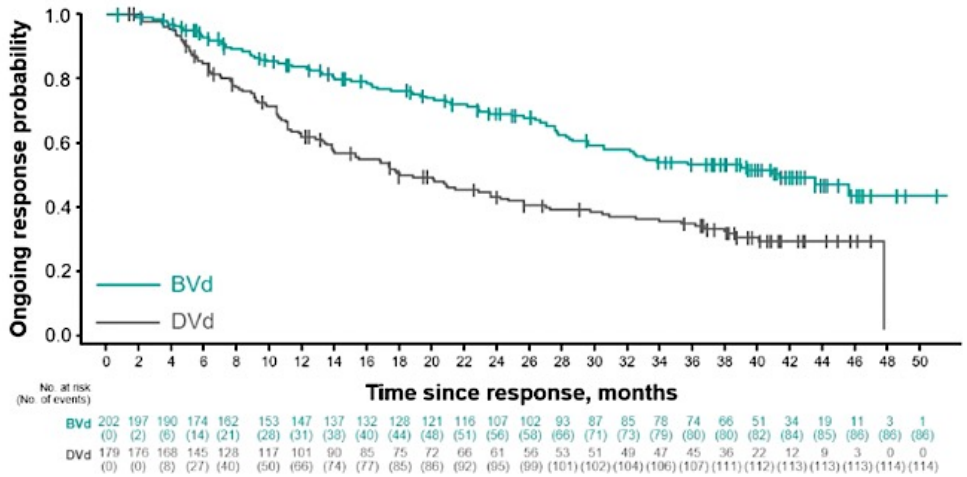


Responses, % (95% CI)	BVd (n=243)	DVd (n=251)
≥CR and MRD neg (10^{-5})	25.1 (19.8-31.0)	10.4 (6.9-14.8)
≥VGPR and MRD neg (10^{-5})	38.7 (32.5-45.1)	17.9 (13.4-23.2)

MRD neg. from the primary analysis

- ≥CR and MRD neg: 24.7% vs 9.6% (*P*<0.00001)
- ≥VGPR and MRD neg: 38.7% vs 17.1% (*P*<0.00001)

DOR



DOR	BVd (n=243)	DVd (n=251)
Responders, n	202	179
Events, n (%)	86 (43)	114 (64)
Ongoing response, n (%)	79 (39)	39 (22)
Median DOR, months (95% CI)	40.8 (30.5-NR)	17.8 (13.8-23.6)

Hungria, V et al. https://pubmed.ncbi.nlm.nih.gov/40680754/

Safety

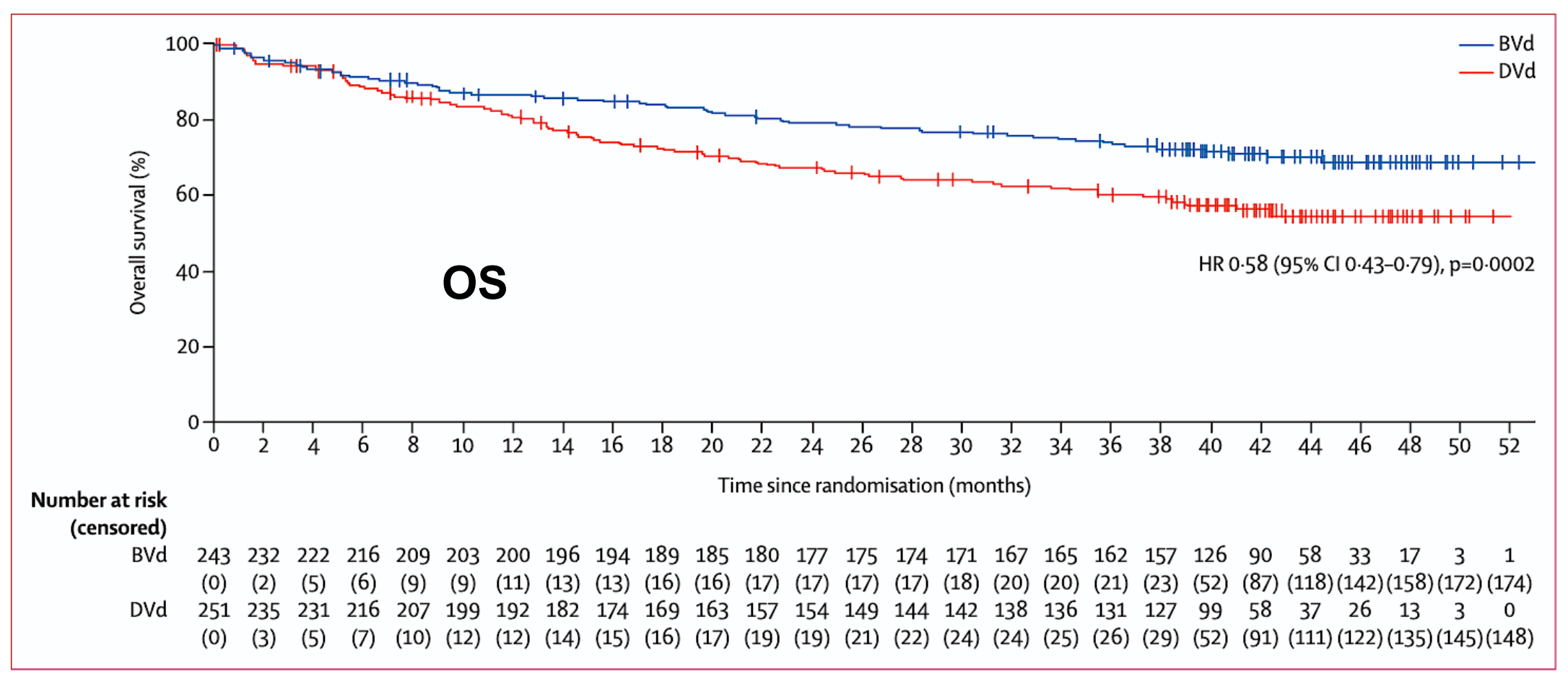
AEs, n (%)	BVd (n=242)	DVd (n=246)
Any AE	242 (100)	246 (100)
Related to study treatment	242 (100)	234 (95)
Grade 3/4	230 (95)	191 (78)
Related to study treatment	222 (92)	166 (67)
Leading to treatment discontinuation	77 (32)	47 (19)
Related to study treatment	67 (28)	36 (15)
Leading to dose reduction	181 (75)	146 (59)
Leading to dose delay	229 (95)	186 (76)
Any SAE	129 (53)	94 (38)
Related to study treatment	50 (21)	32 (13)
Fatal SAEs	26 (11)	20 (8)
Related to study treatment	7 (3)	2 (<1)

Exposure-Adjusted Rate (per 100 P-Y)	BVd (n=242)	DVd (n=246)
Grade 3/4	57.17	55.71
Leading to treatment discontinuation	19.14	13.71
Leading to dose reduction	44.99	42.58
Leading to dose delay	56.92	54.25
Any SAE	32.07	27.42

Deaths, n (%)		BVd (n=242)	DVd (n=246)
Deaths		69 (29)	101 (41)
Primary cause of death	Cancer	23 (10)	53 (22)
	Due to MM	3 (1)	7 (3)
	Not due to MM	19 (8)	44 (18)
	Other	1 (<1)	2 (<1)
	CV condition	8 (3)	4 (2)
	Sepsis	8 (3)	4 (2)
	Stroke	0	1 (<1)
	Trauma	0	1 (<1)
	Other non-CV condition	24 (10)	25 (10)

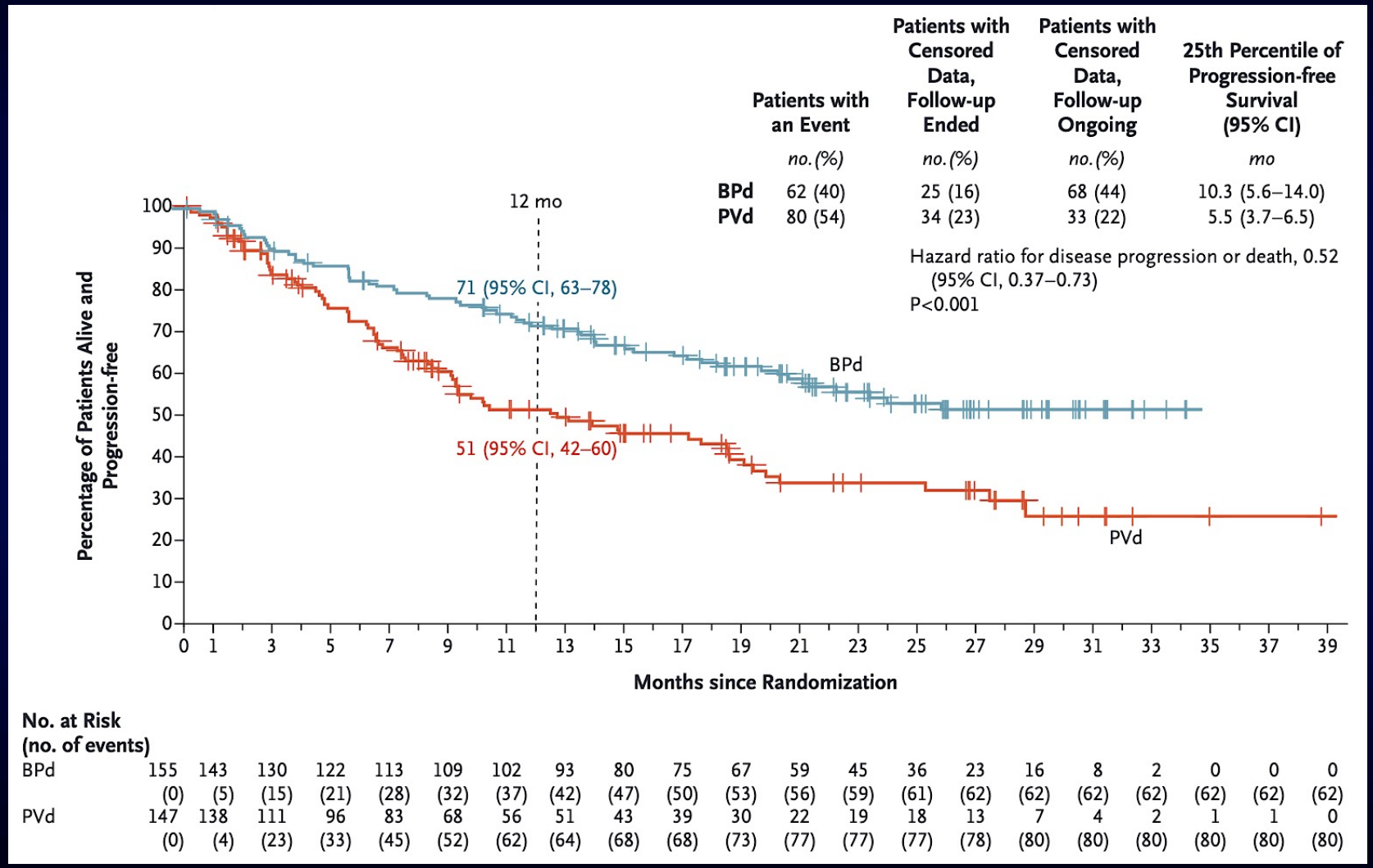
Hungria, V et al. https://pubmed.ncbi.nlm.nih.gov/38828933/

Latest DREAMM-7 Updates



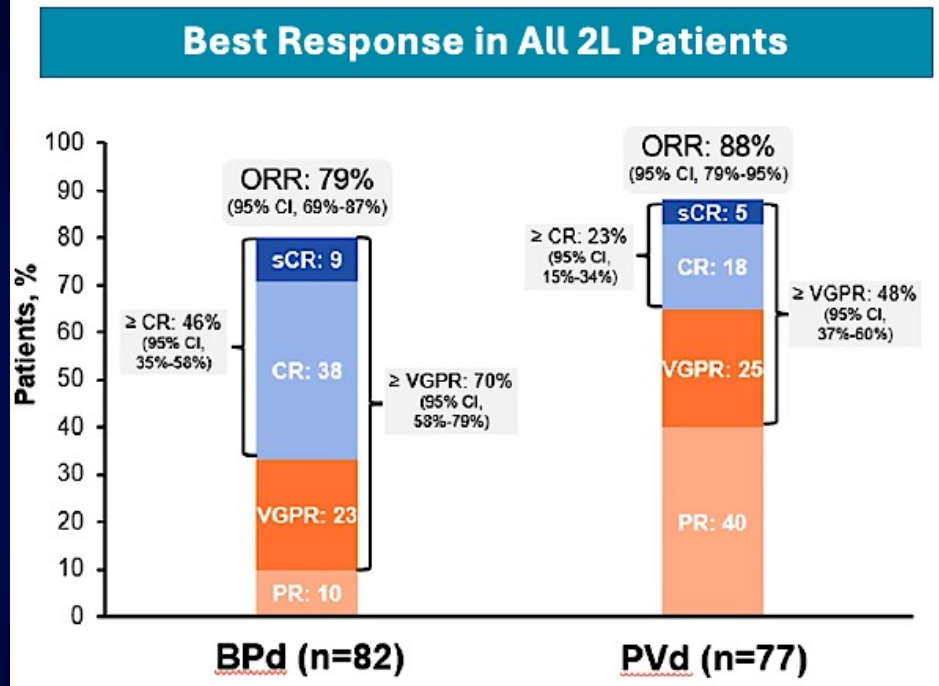
Hungria, V et al. https://pubmed.ncbi.nlm.nih.gov/38828933/

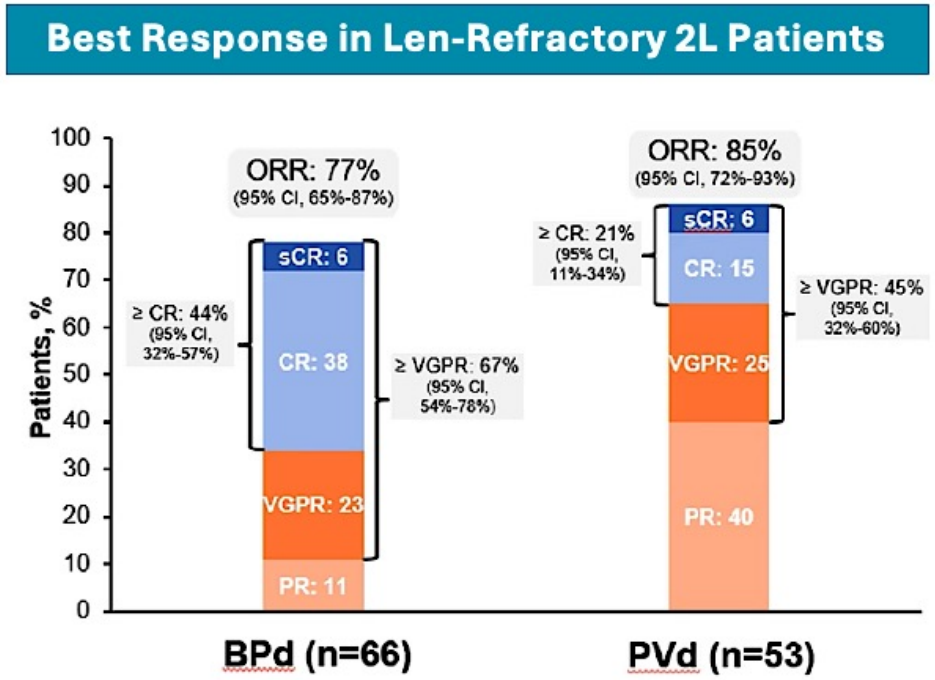
BelaMaf-Pd: DREAMM-8



Dimopoulos, MA et al. https://pubmed.ncbi.nlm.nih.gov/38828951/

Focus on 2nd Line & MRD

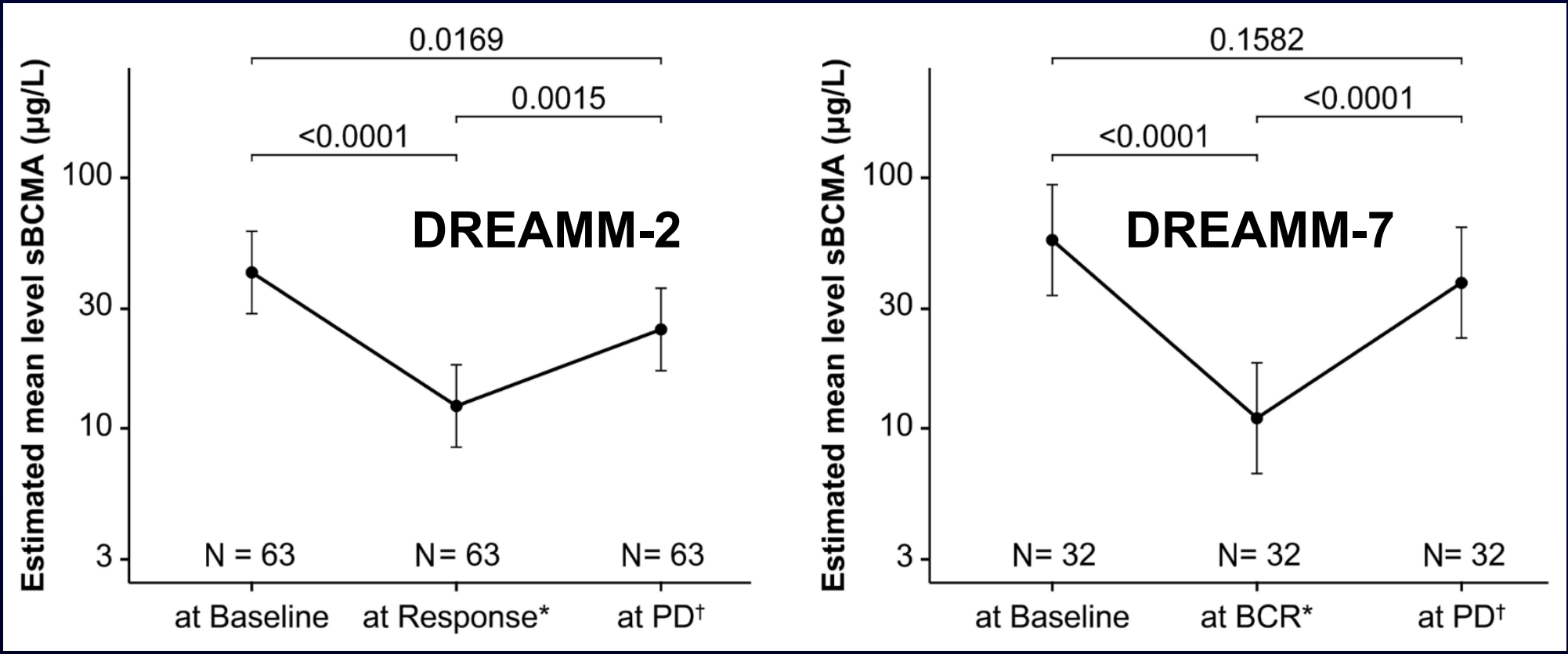




MRD-Negativity Rate (≥CR)	All 2L		Len-Refractory 2L	
	BPd (n=82)	PVd (n=77)	BPd (n=66)	PVd (n=53)
MRD-negativity rate, % (95% CI)	33 (23-44)	5 (1-13)	33 (22-46)	6 (1-16)

Beksac, M et al. ASH 2024. Abstract 4731.

BelaMaf Doesn't Impact sBCMA



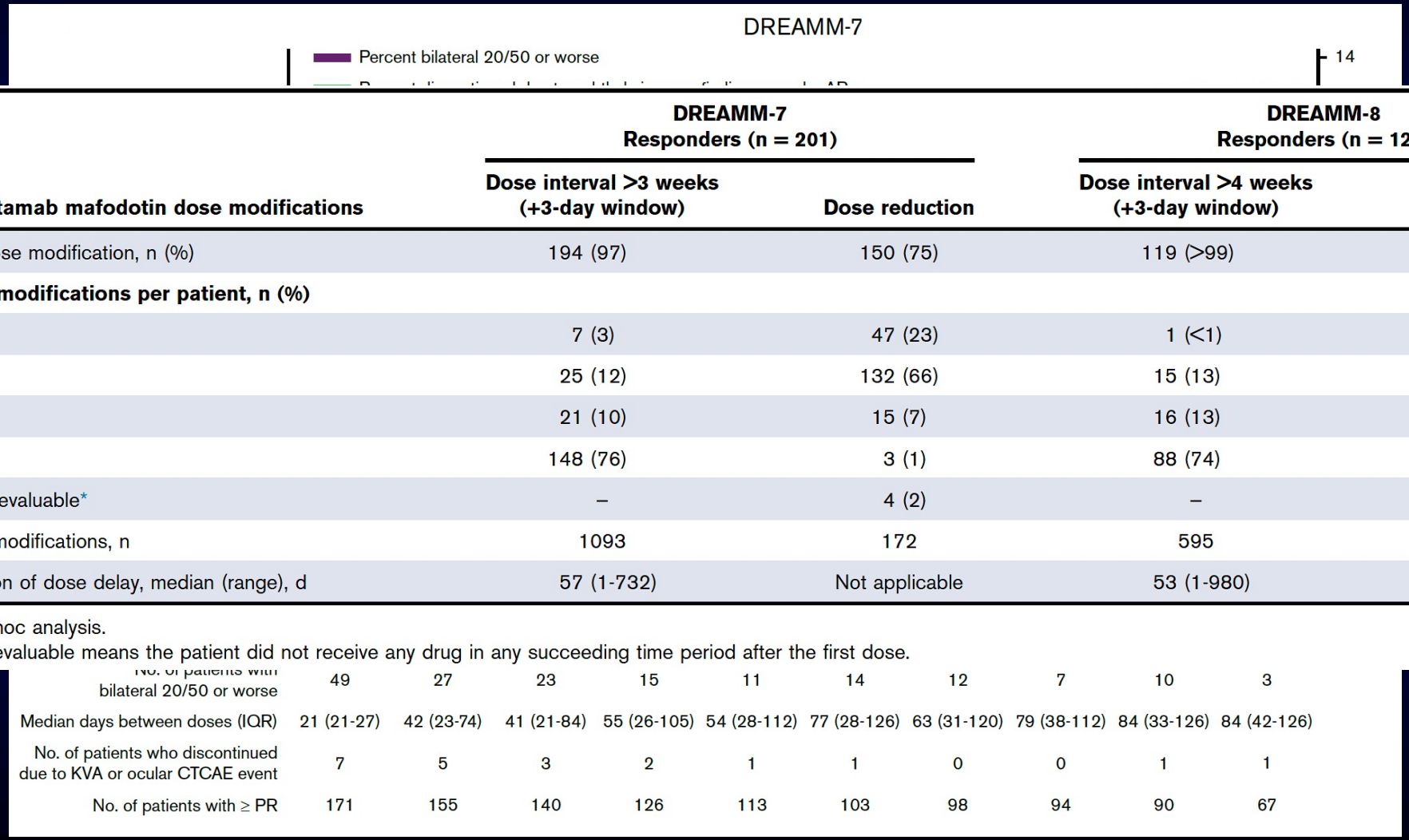
Musa, H et al. https://pubmed.ncbi.nlm.nih.gov/40874339/

Ocular Toxicity & Dosing Changes

Regimen	Severity of ophthalmic exam finding	DREAMM-7 BVd (Cycle length = 3 weeks)	DREAMM-8 BPd (Cycle length = 4 weeks)
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 of *either* component (ocular exam finding or BCVA) 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

Mateos, M-V. et al. https://pubmed.ncbi.nlm.nih.gov/40763276/

Dosing Interval & Ocular Events



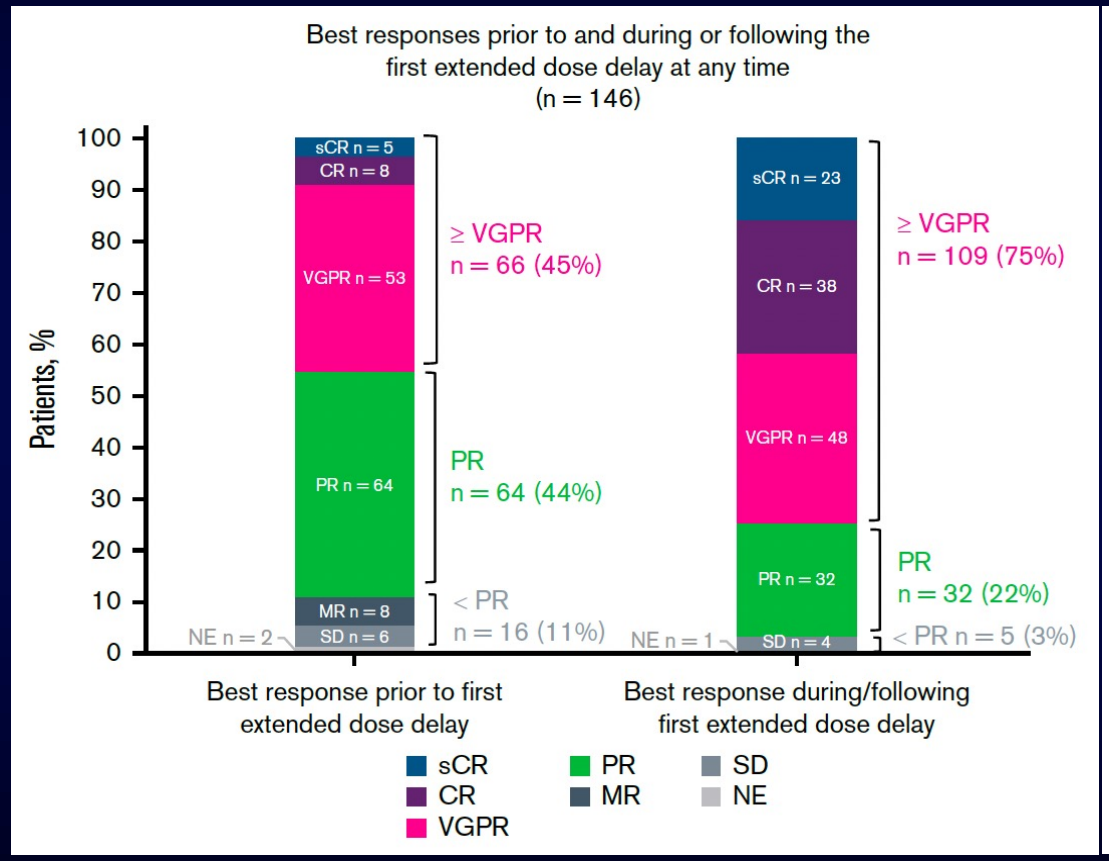
Belantamab mafodotin dose modifications	DREAMM-7 Responders (n = 201)		DREAMM-8 Responders (n = 120)	
	Dose interval >3 weeks (+3-day window)	Dose reduction	Dose interval >4 weeks (+3-day window)	Dose reduction
Any dose modification, n (%)	194 (97)	150 (75)	119 (>99)	83 (69)
Dose modifications per patient, n (%)				
0	7 (3)	47 (23)	1 (<1)	35 (29)
1	25 (12)	132 (66)	15 (13)	80 (67)
2	21 (10)	15 (7)	16 (13)	3 (3)
≥3	148 (76)	3 (1)	88 (74)	0
Not evaluable*	–	4 (2)	–	2 (2)
Dose modifications, n	1093	172	595	86
Duration of dose delay, median (range), d	57 (1-732)	Not applicable	53 (1-980)	Not applicable

Post hoc analysis.
*Not evaluable means the patient did not receive any drug in any succeeding time period after the first dose.

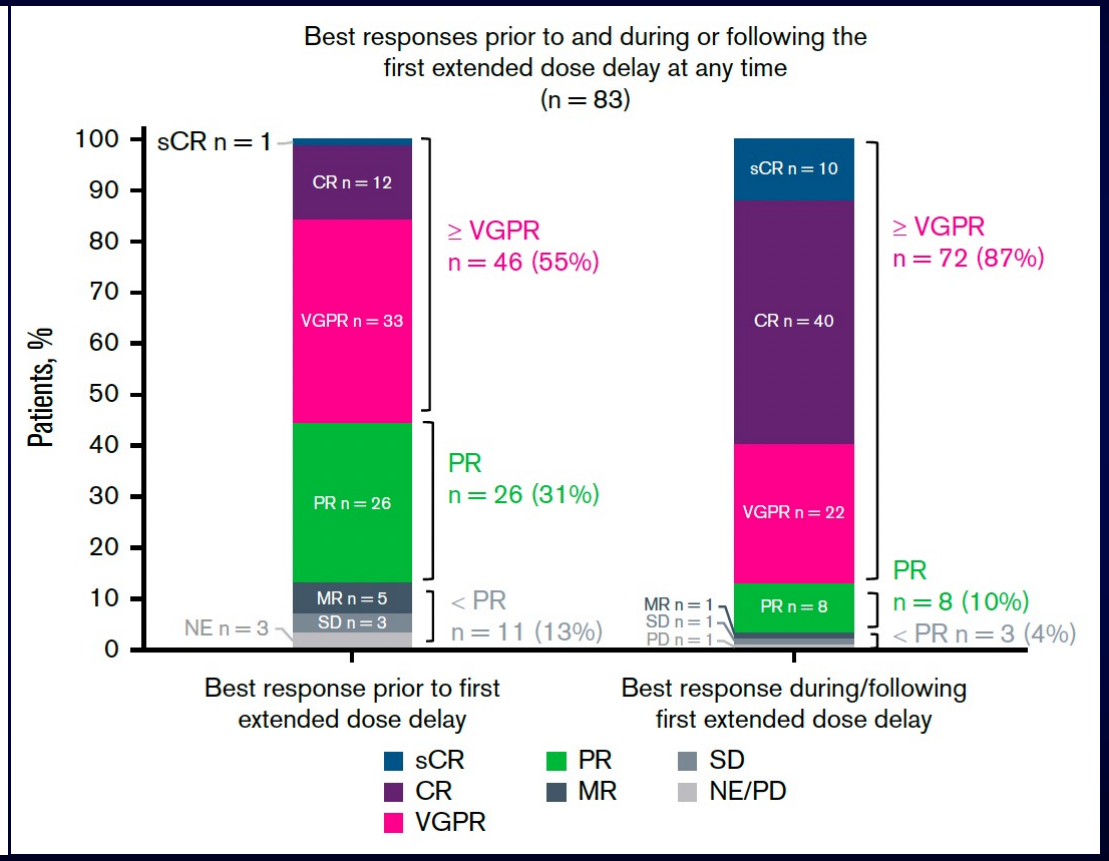
No. of patients with bilateral 20/50 or worse	49	27	23	15	11	14	12	7	10	3
Median days between doses (IQR)	21 (21-27)	42 (23-74)	41 (21-84)	55 (26-105)	54 (28-112)	77 (28-126)	63 (31-120)	79 (38-112)	84 (33-126)	84 (42-126)
No. of patients who discontinued due to KVA or ocular CTCAE event	7	5	3	2	1	1	0	0	1	1
No. of patients with ≥ PR	171	155	140	126	113	103	98	94	90	67

Mateos, M-V. et al. https://pubmed.ncbi.nlm.nih.gov/40763276/

Responses Improve Despite Delays



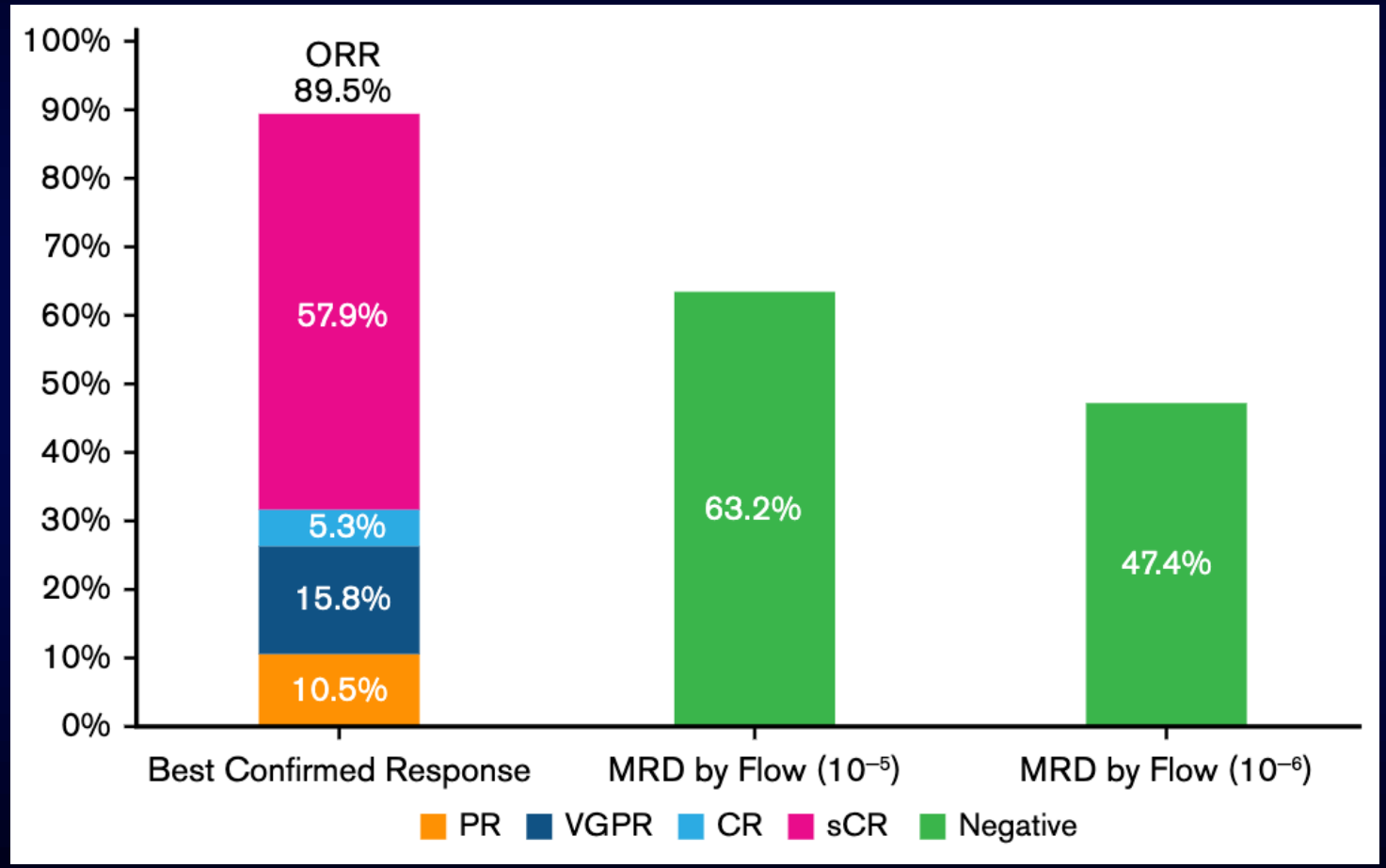
DREAMM-7



DREAMM-8

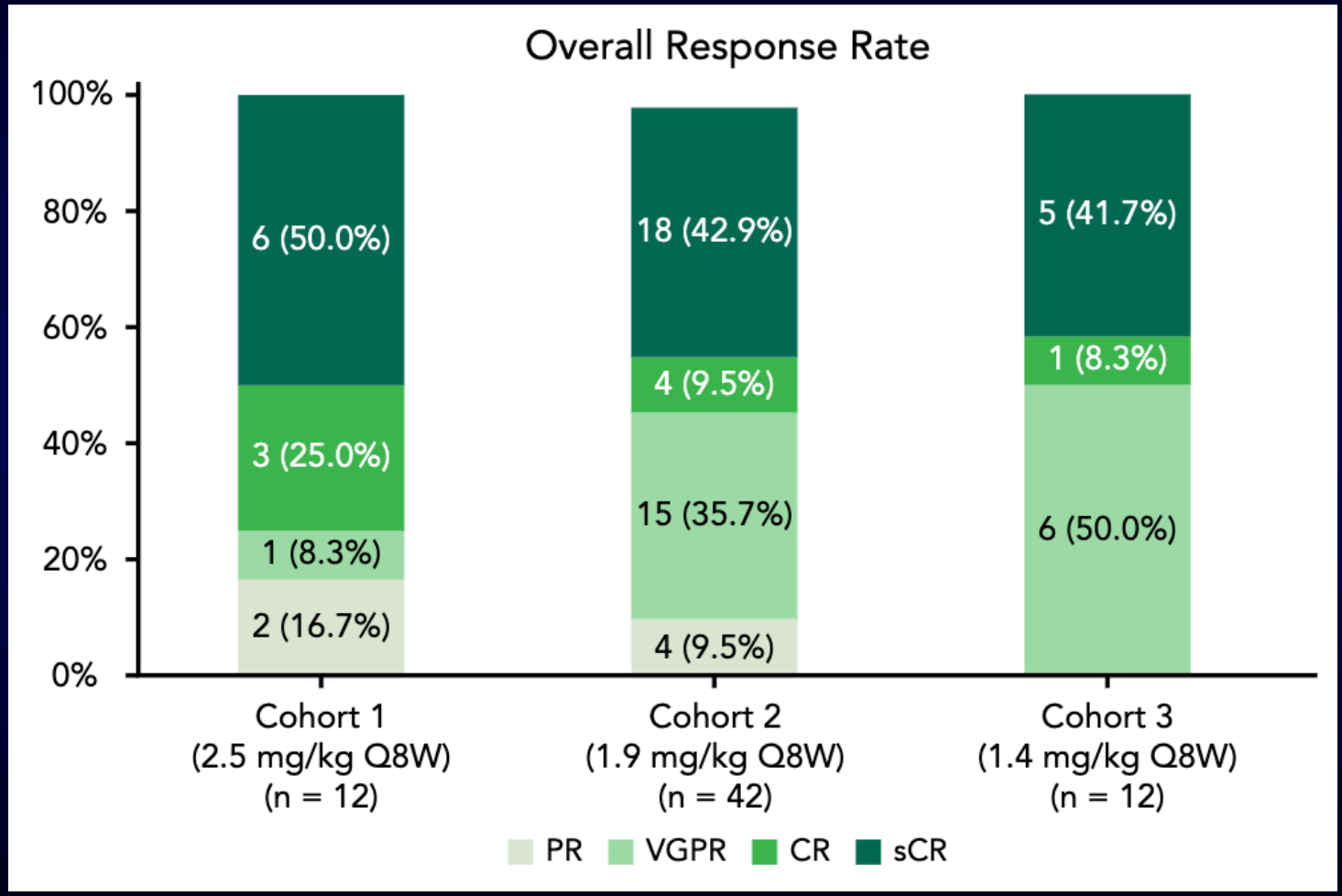
Mateos, M-V. et al. https://pubmed.ncbi.nlm.nih.gov/40763276/

Selected Other Trials: Bela-KRd in RRMM



Atrash, S et al. https://pubmed.ncbi.nlm.nih.gov/41719502/

Bela-Rd in IF/F NDMM



Terpos, E et al. https://pubmed.ncbi.nlm.nih.gov/41346230/

Selected Ongoing Studies

- [ ] **NCT04892264**

Belantamab Mafodotin, Lenalidomide, and Daratumumab for the Treatment of Relapsed, Refractory, or Previously Untreated **Multiple Myeloma**

- [ ] **NCT04680468**

Study of **Belantamab** Mafodotin as Pre- and Post-autologous Stem **Cell** Transplant and Maintenance for **Multiple Myeloma**

- [ ] **NCT05055063**

A Phase 1 With Extension Cohort, Single Arm, Single Center, Open Label Trial of **Belantamab** Mafodotin for the Treatment of High-Risk Smoldering **Multiple Myeloma**

https://clinicaltrials.gov/

Conclusions

- BelaMaf-based combos provide effective options in the early RRMM setting
- Multiple mechanisms of action, including direct cytotoxic and ICD-based effects
- Toxicities are predictable & manageable by adjustments that do not impact benefit
- ? Minimal impact on antigen expression and immune TME to enable repeat targeting of BCMA
- Other ADCs are in development, including agents targeting BCMA, GPRC5D, and other cell surface proteins

Faculty Case Presentations

RTP
RESEARCH
TO PRACTICE

Dr Raje: A patient with R/R MM

- 67-year-old female diagnosed with lambda light chain multiple myeloma, normal FISH
- Presented 13 years back with cord compression requiring decompression surgery
- Received RVd, refused transplant and placed on Len maintenance
- Received KPd at first relapse, 5 years into her diagnosis
- Received investigational BCMA CAR T cells—had short lived response on 4 months
- Relapsed and then received Belamaf in combination with isatuximab and Pom on a clinical trial—is in remission now for 18 months and is on ongoing therapy

QUESTIONS FOR THE FACULTY

For which patients are you prioritizing belantamab mafodotin/bortezomib/dexamethasone (Bela-Vd)? What is the earliest point that you would administer it? When do you opt for Bela-Vd rather than CAR T-cell therapy or a bispecific antibody?

Are you comfortable recommending Bela-Vd for patients who have previously received BCMA-directed CAR T-cell therapy, a BCMA-directed bispecific antibody or both?

Would you consider combining belantamab mafodotin with agents other than bortezomib/dexamethasone? If so, under what circumstances and which ones?

Prof Dimopoulos: Case Presentation

Diagnosis	72y, woman IgA-λ MM, diagnosed 4 years ago R-ISS II; no high-risk cytogenetics, anemia and vertebral compression fracture
1L	Dara-VRd x 4 → ASCT → DaraVRD x 2 → Dara-Len maintenance 2y (sustained MRD negative) → Lenalidomide maintenance
Relapse	Biochemical followed by symptomatic progression on lenalidomide; new focal bone lesion
Status at relapse	Lenalidomide refractory; prior PI and anti-CD38 exposed; ECOG PS 1

Prof Dimopoulos: Case Presentation (cont'd) Lab Values at Relapse

Hb	**10.2 g/dL**
Platelets	178 ×10^9/L
Creatinine	0.9 mg/dL
Calcium	9.8 mg/dL
IgA	**2,850 mg/dL**
M-protein	**1.8 g/dL**
λ FLC	**280 mg/L**
Bone marrow plasma cells	~25%

PET/CT: new FDG-avid lesion involving the left iliac bone; no soft-tissue EMD.

Prof Dimopoulos: Case Presentation (cont'd) Treatment Selection and Course

Current therapy	**Belantamab mafodotin + bortezomib + dexamethasone (BVd)**
Response	M-protein falls rapidly → **VGPR**, at C3D1 subsequently deepening
At cycle 4, the patient reports:	"My vision is blurry when I read."
Ophthalmologic examination:	Punctuate keratopathy/corneal epithelial changes with reduction in visual acuity, grade 2, belamaf-related

Prof Dimopoulos: Case Presentation (cont'd) Management of Ophthalmic Toxicity

Management	Belantamab dose held; intensified artificial tear administration; ophthalmologic monitoring; bortezomib/dexamethasone continued
Outcome	Vision improved; belantamab restarted with modified interval from Q8W to Q12W
Current status	Ongoing disease control without new skeletal lesions, now patient in CR, MRD negative

QUESTIONS FOR THE FACULTY

In terms of safety and tolerability, how would you rate your experience with belantamab mafodotin? In your experience, how often do ocular events affect visual acuity versus presenting subclinically on routine screening?

How do you approach screening for and management of belantamab mafodotin-associated ocular toxicity? What dosing interval of belantamab mafodotin do you typically employ?

Agenda

Module 1 – New and Emerging Strategies with Bispecific Antibodies in MM – Dr Raje

Module 2 – Utility of Antibody-Drug Conjugates for R/R MM – Dr Orlowski

Module 3 – Potential Role of Cereblon E3 Ligase Modulators and Other Promising Novel Agents and Strategies for R/R MM – Prof Dimopoulos

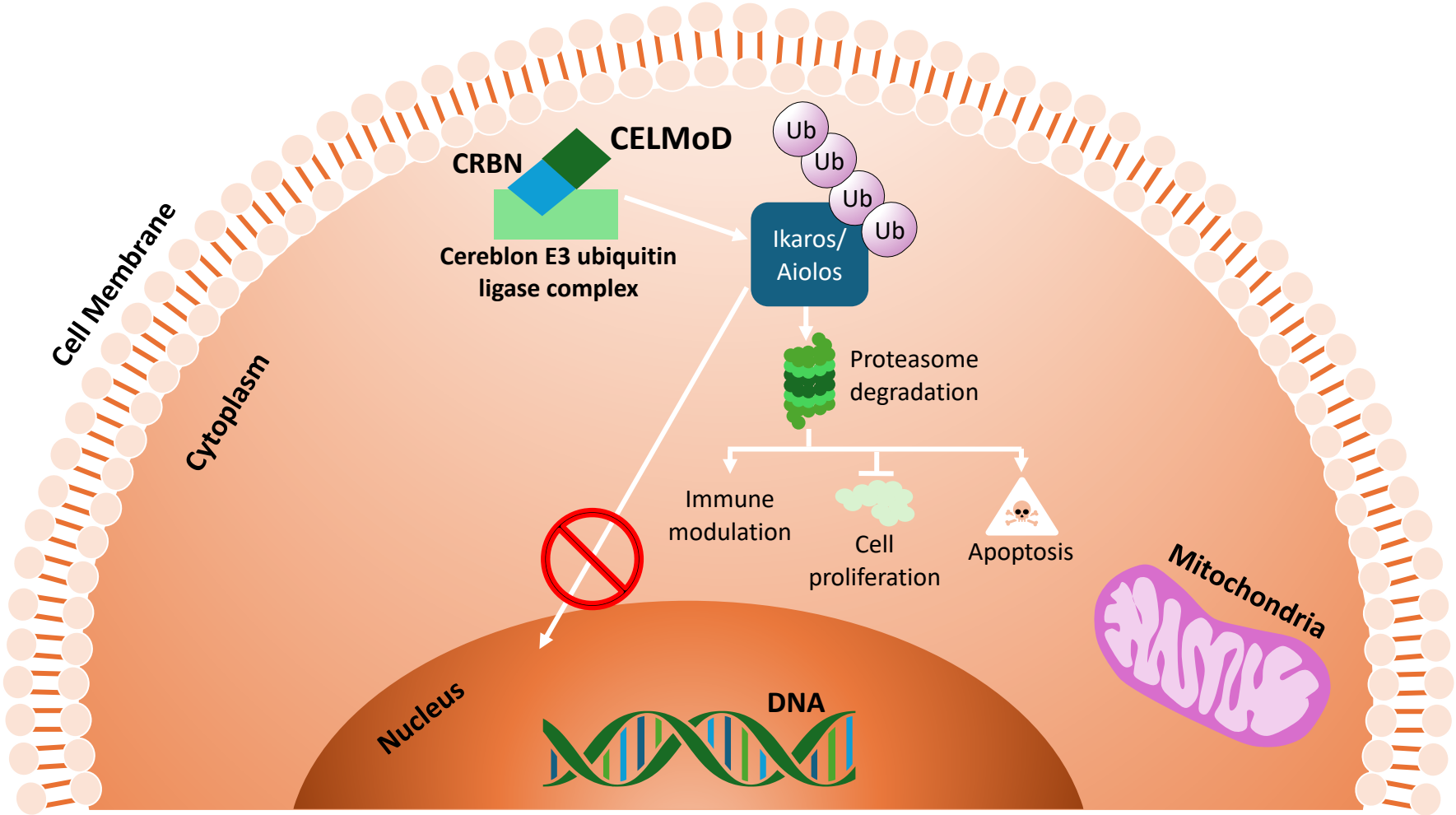
SOHO 2026 Symposium on the
Management of Relapsed/Refractory Multiple Myeloma

Potential Role of Cereblon E3 Ligase Modulators (CELMoDs) and Other Promising Novel Agents and Strategies for R/R MM

Meletios (Thanos) Dimopoulos, MD
Professor of Hematology/Oncology, Director
Plasma Cell Dyscrasias Unit, Department of Clinical Therapeutics,
National and Kapodistrian University of Athens
School of Medicine, Athens, Greece

Protein Degradation in MM

- The ubiquitin-proteasome system forms a primary means for cellular protein degradation
- The ubiquitin ligase enzyme complex is a component of this system and tags proteins for proteasomal degradation with ubiquitin
- CELMoDs bring ligase and target proteins into proximity to start protein degradation by the ubiquitin-proteasome system
- CELMoDs are derived from the TPD (targeted protein degradation) platform and represent a novel class of targeted protein degraders with a unique mechanism of action

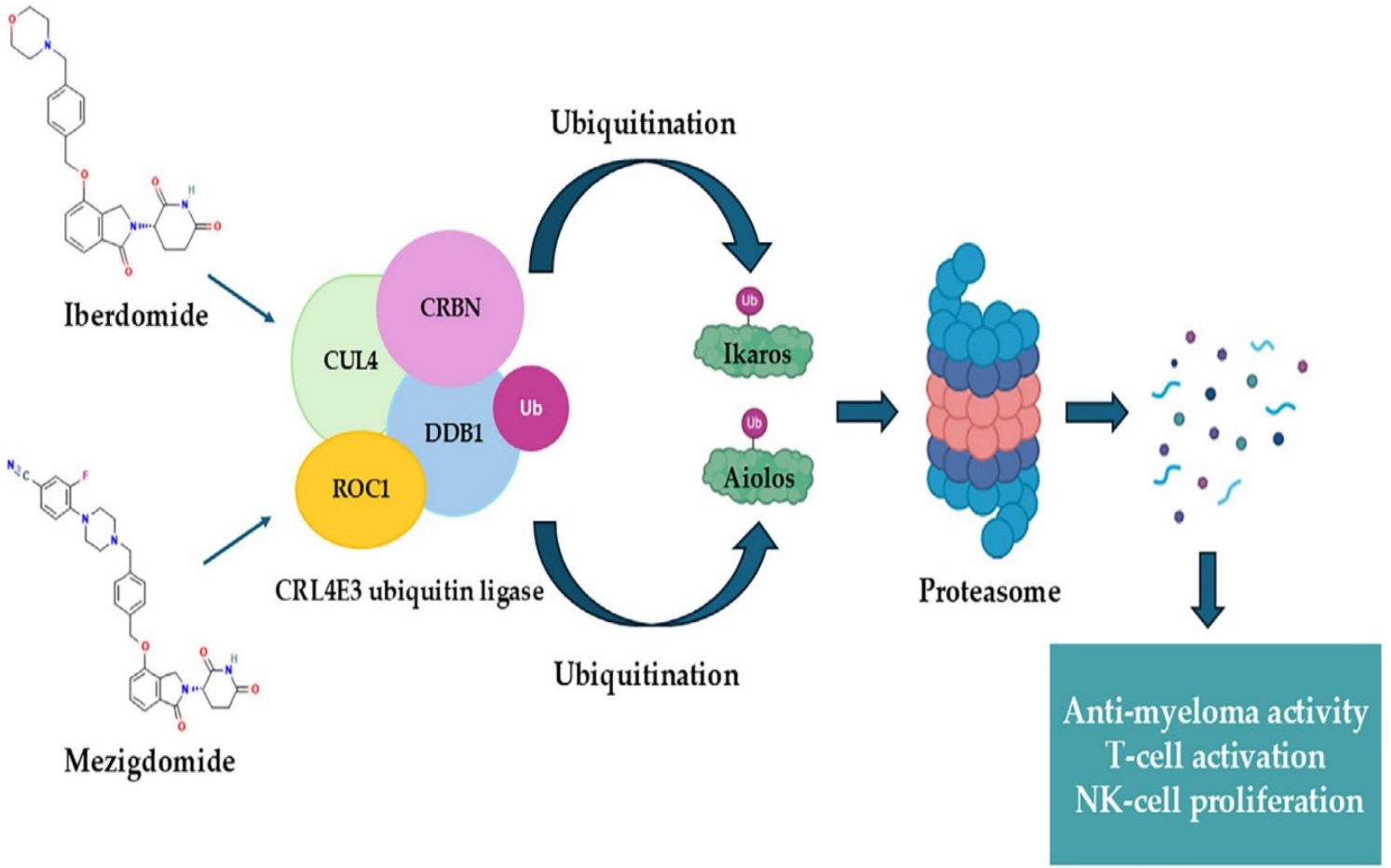


CELMoDs in development with clinical data
Iberdomide (CC-220)
Mezigdomide (CC-92480)

Charlinski et al. Cancers 2021;13:4666; Ito et al. Int J Hematol 2016;104:293.

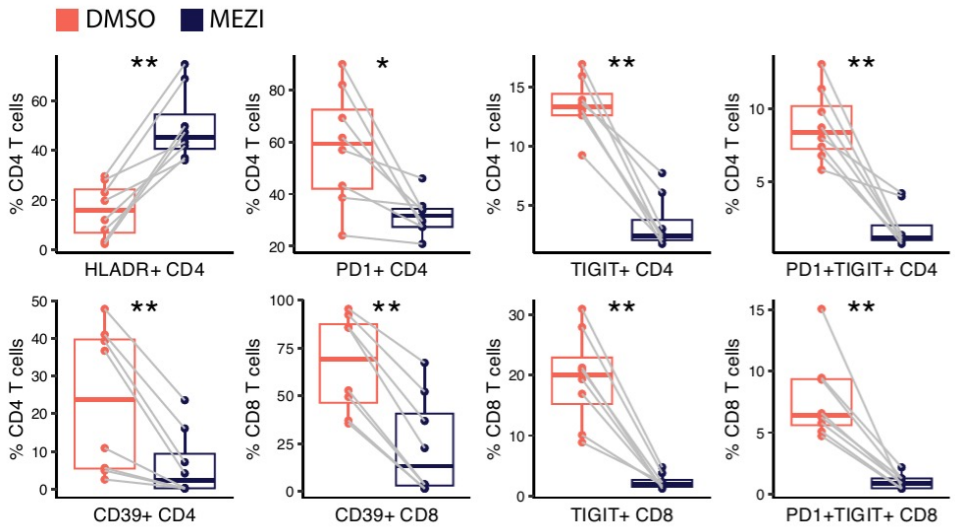
Mechanism of action mezigdomide - iberdomide

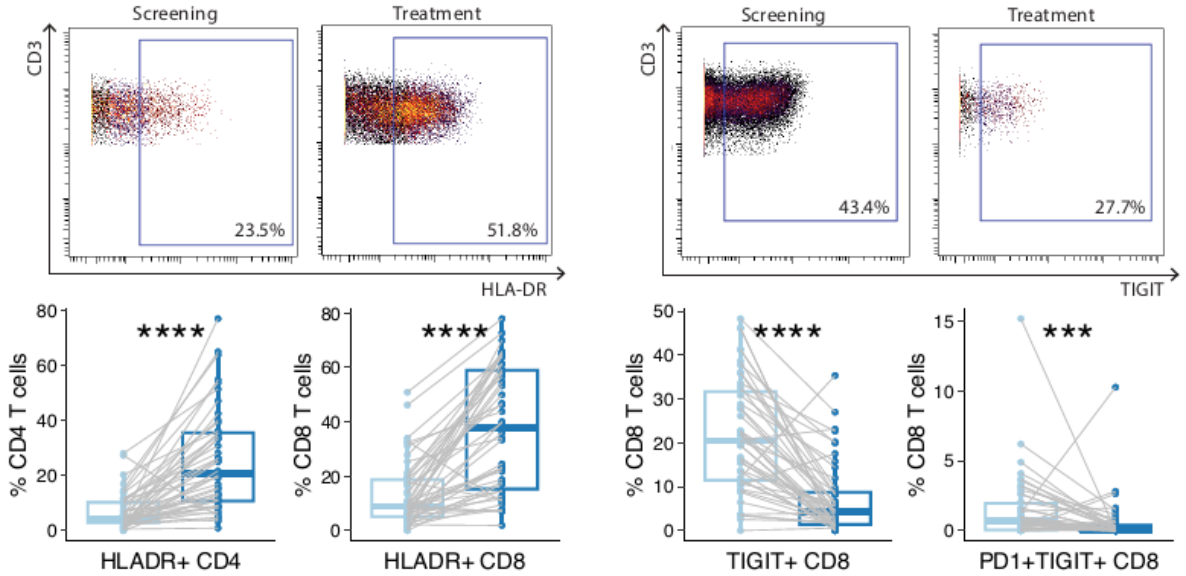
- **Iberdomide and mezigdomide bind to cereblon within the CRL4 E3 ubiquitin ligase complex,**
- **They enhance recruitment and ubiquitination of the transcription factors Ikaros (IKZF1) and Aiolos (IKZF3).**
- **Polyubiquitinated substrates are subsequently degraded by the proteasome, resulting in**
- ✓ **suppression of IRF4/MYC-dependent survival pathways and**
- ✓ **promoting down-stream immunomodulatory effects, including augmented T-cell activation, NK-cell expansion, and anti-myeloma activity.**



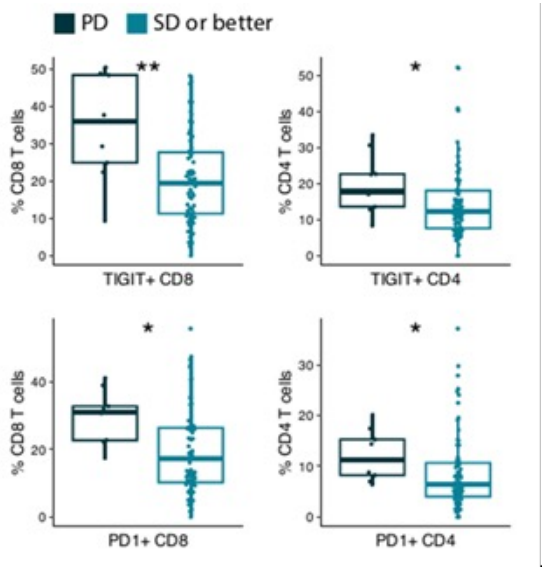
Alvaro ME et al. Eur J Haematol. 2026; 116:697–708

Mezigdomide stimulates T-cell activation and reduces T-cell exhaustion markers both pre-clinically and clinically

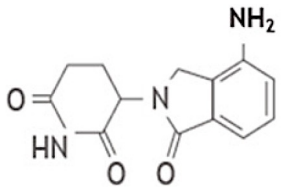
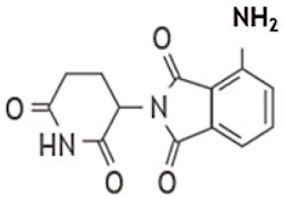
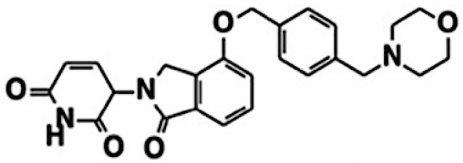
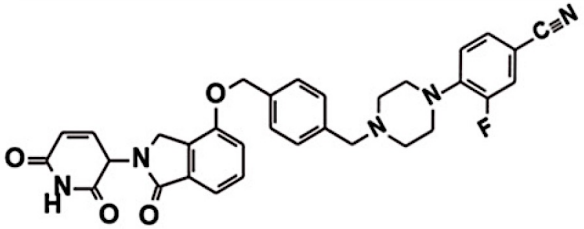




- Core question: Can CELMoDs rescue dysfunctional immune responses in late-line disease?
  - **Clinical response correlated with reduced exhaustion features**

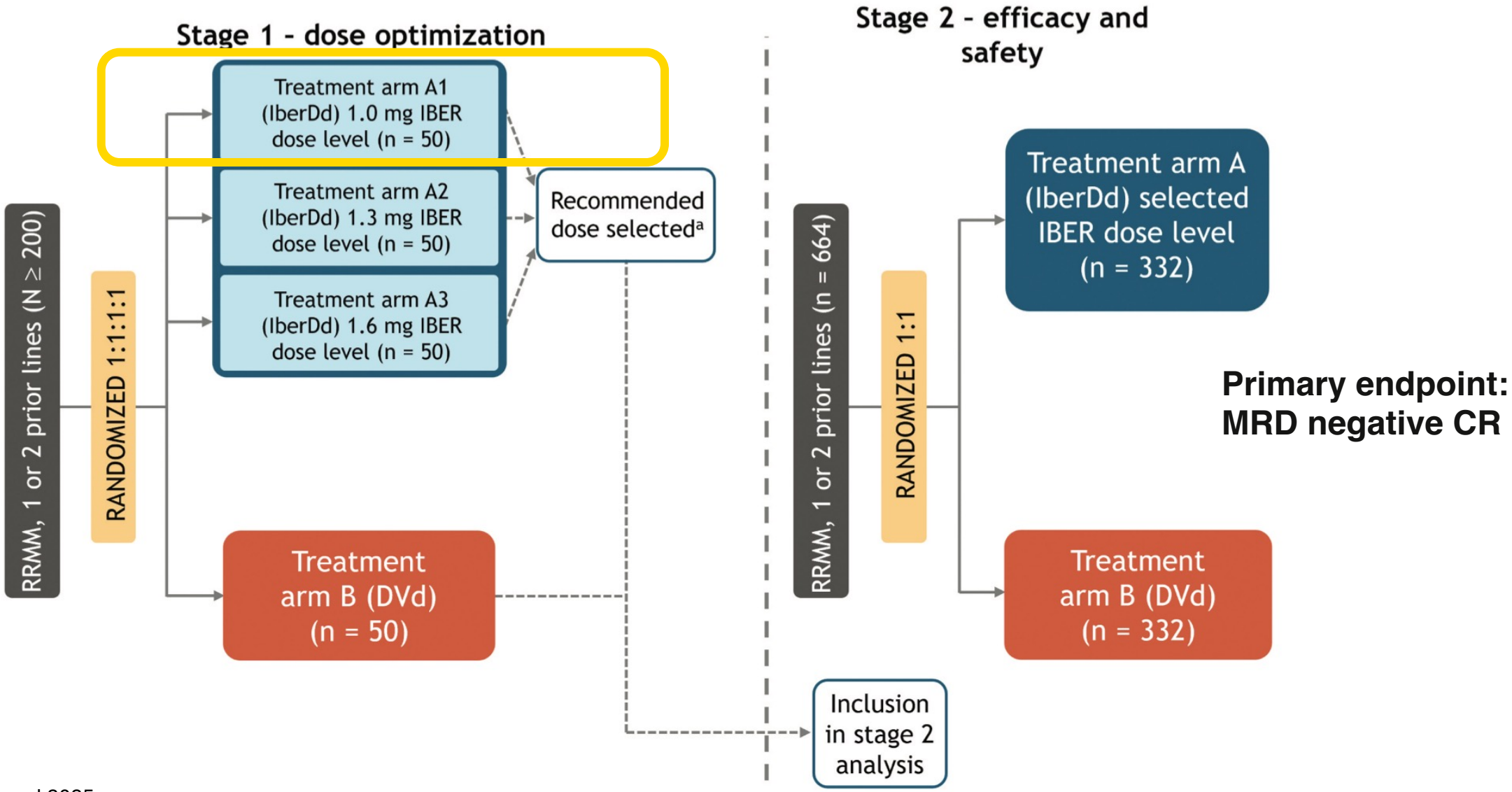


Chen LY et al., Blood 2026

	Immunomodulatory drugs		Iberdomide	Mezigdomide
	Lenalidomide	Pomalidomide		
				
Cereblon binding	✓		✓✓	✓✓✓
Targeted protein degradation	✓		✓✓	✓✓✓
Tumor antiproliferation	✓		✓✓	✓✓✓
Tumor apoptosis	✓		✓✓	✓✓✓
Immune stimulation	✓✓		✓✓✓	✓✓✓
Synergistic combinations	✓✓		✓✓✓	✓✓✓

Hartley-Brown MA, et al. *Cancers (Basel)*. 2024;16(6):1166.

EXCALIBER-RRMM phase III study - design



Primary endpoint: MRD negative CR

Lonial S et al. Future Oncol 2025

Table 4: Efficacy Results in EXCALIBER-RRMM in the Primary Efficacy Population for MRD Negativity

Endpoint	Iberdomide + Daratumumab and Hyaluronidase-fihj + Dexamethasone (IberDd) (N=207)	Daratumumab and Hyaluronidase-fihj + Bortezomib + Dexamethasone (DVd) (N=213)
Minimal Residual Disease (MRD) negative complete response (≥CR) at any time, n(%)*	85 (41)	44 (21)
(95% CI)	(34, 48)	(15, 27)
p-value†	<0.0001	

Response was based on Independent Review Committee (IRC) assessment per International Myeloma Working Group (IMWG) 2016 criteria.

* Based on a threshold of 10^{-5} using a Hematogenix Next Generation Flow Cytometry assay.

† The 2-stage combined one-sided p-value based on Miettinen-Nurminen with CMH weights, stratified by number of prior lines (1 vs 2), Age (≤70 vs >70) and ISS staging (I and II vs III).

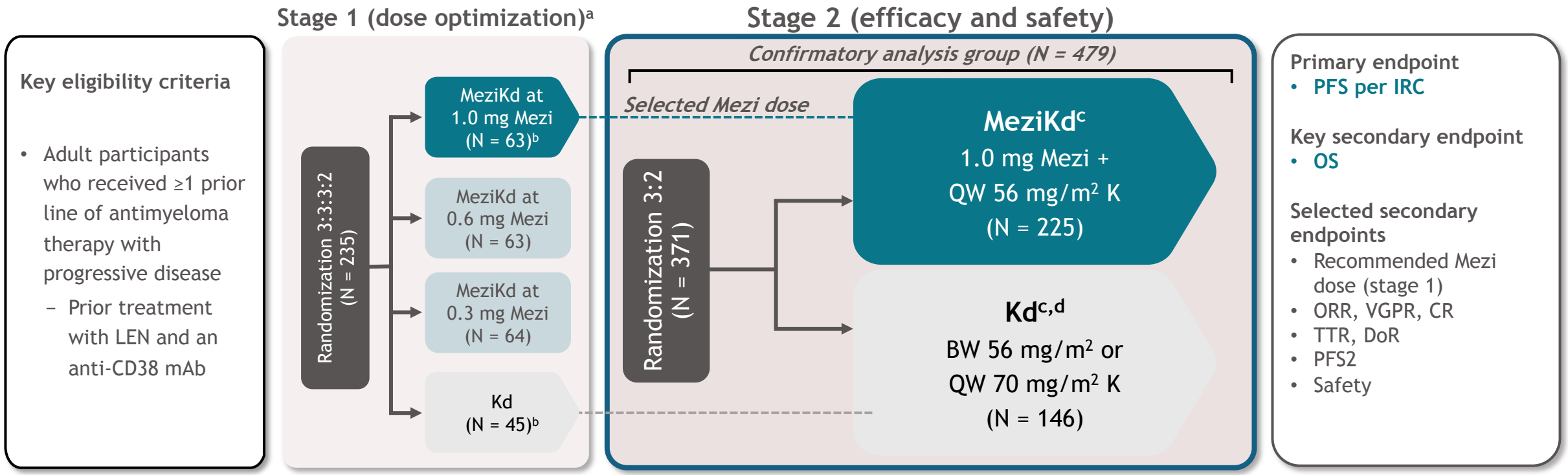
Iberdomide. Package Insert. 2026

FDA grants accelerated approval to iberdomide with daratumumab and hyaluronidase-fihj and dexamethasone for multiple myeloma

On August 13, 2026, the Food and Drug Administration granted accelerated approval to iberdomide in combination with daratumumab and hyaluronidase-fihj and dexamethasone for adults with multiple myeloma who have received at least one prior line of therapy including a proteasome inhibitor and an immunomodulatory agent.

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-iberdomide-daratumumab-and-hyaluronidase-fihj-and-dexamethasone

SUCCESSOR-2: Study Design



In the MeziKd arm, patients received:
- **Mezi 1.0 mg orally once daily on D1-21 of each 28-day cycle**
- **K[e] 56 mg/m² IV on D1, 8, and 15 in C1-12 and on D1 and 15 in C ≥ 13**
- **DEX[c] 40 mg orally/IV on D1, 8, 15, and 22**

NCT05552976. [a]Patients enrolled in stage 1 on a dose of Mezi not chosen for stage 2 had the option to move to the selected dose if some criteria were met; [b]Patients from these stage 1 arms were included in the confirmatory analysis groups; [c]DEX dosing – MeziKd arm: 40 mg, option of 20 mg if > 75 years of age, BMI < 18.5 kg/m², poorly controlled diabetes, or prior intolerance to steroid therapy; Kd arm: 20 mg, 10 mg option for stated criteria (BW regimen) or 40 mg, 20 mg option for stated criteria (QW regimen); [d]QW regimen made available July 2023; [e]K dose on C1D1 was 20 mg/m². BMI, body mass index; BW, twice weekly; C, cycle; D, day; DEX, dexamethasone; DoR, duration of response; IRC, independent review committee; IV, intravenous; K, carfilzomib; OS, overall survival; PFS2, second progression-free survival; QW, weekly; TTR, time to response.

SUCCESSOR-2: Prior Therapy

	MeziKd (N = 288)	Kd (N = 191)
Prior LOTs, median (range)	2.0 (1–9)	2.0 (1–8)
No. of prior LOTs, n (%)		
1 prior LOT	43 (14.9)	33 (17.3)
2 prior LOTs	109 (37.8)	68 (35.6)
3 prior LOTs	64 (22.2)	35 (18.3)
4+ prior LOTs	72 (25.0)	55 (28.8)

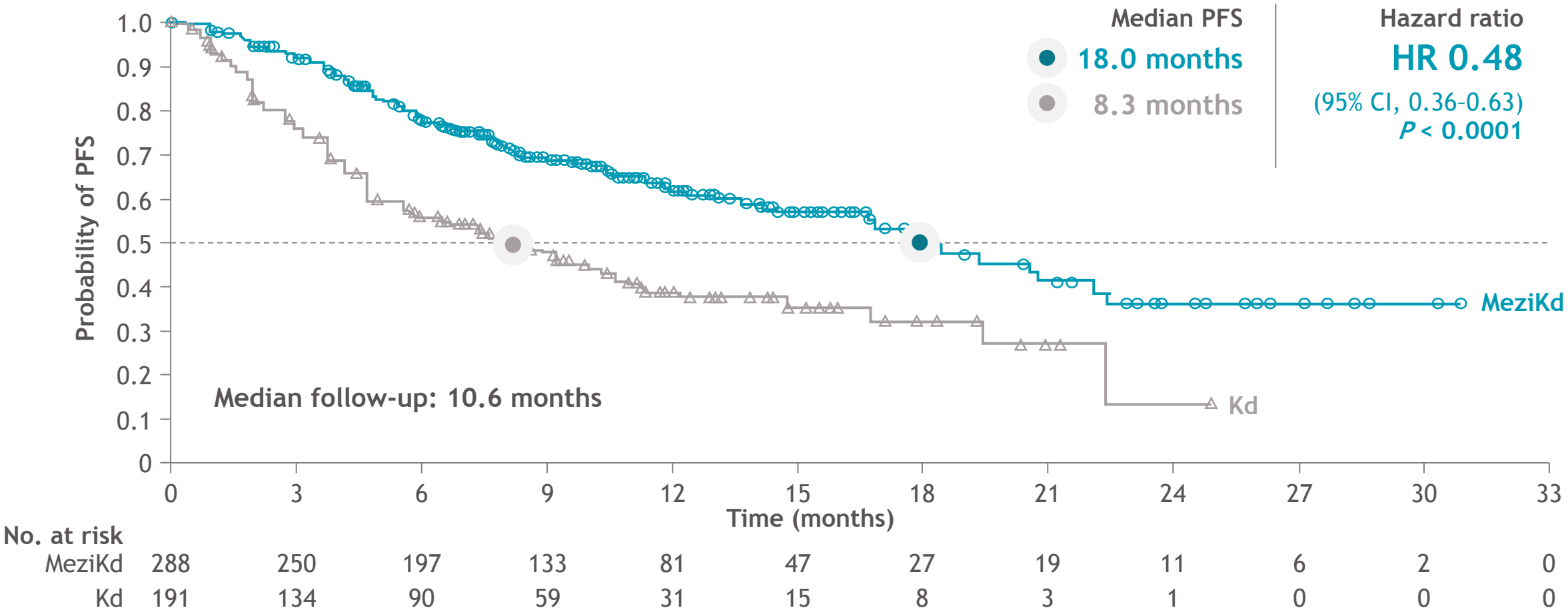
With a median of 2 prior LOTs, 86% of patients were refractory to anti-CD38 mAbs and 93% to their last LOT

	MeziKd (N = 288)	Kd (N = 191)
Prior therapy exposure, n (%)		
Anti-CD38 mAb	288 (100)	191 (100)
LEN	288 (100)	191 (100)
Triple-class exposed	265 (92.0)	176 (92.1)
POM	114 (39.6)	64 (33.5)
BCMA-targeted therapy	23 (8.0)	12 (6.3)
T cell-redirecting therapy	28 (9.7)	12 (6.3)
Refractory status, n (%)[a]		
To last prior LOT	264 (91.7)	181 (94.8)
Anti-CD38 mAb	248 (86.1)	163 (85.3)
LEN	220 (76.4)	143 (74.9)
POM	99 (34.4)	56 (29.3)
PI	138 (47.9)	102 (53.4)
Anti-CD38 mAb and LEN	199 (69.1)	127 (66.5)
Triple-class refractory[b]	111 (38.5)	75 (39.3)

Data cutoff: January 15, 2026. In the confirmatory analysis group, defined as all patients from stages 1 and 2 randomized to 1.0 mg Mezi plus Kd or Kd. Percentages may not total 100 due to rounding. [a]Refractory is defined as disease that is nonresponsive on therapy (failure to achieve minimal response or development of progressive disease while on therapy) or progresses within 60 days of last dose; [b]Triple-class refractory is defined as refractory to an IMiD, PI, and anti-CD38 mAb. BCMA, B-cell maturation antigen; PI, proteasome inhibitor.

Dimopoulos MA et al. EHA 2026;Abstract LB5004

SUCCESSOR-2: PFS (Primary Endpoint)

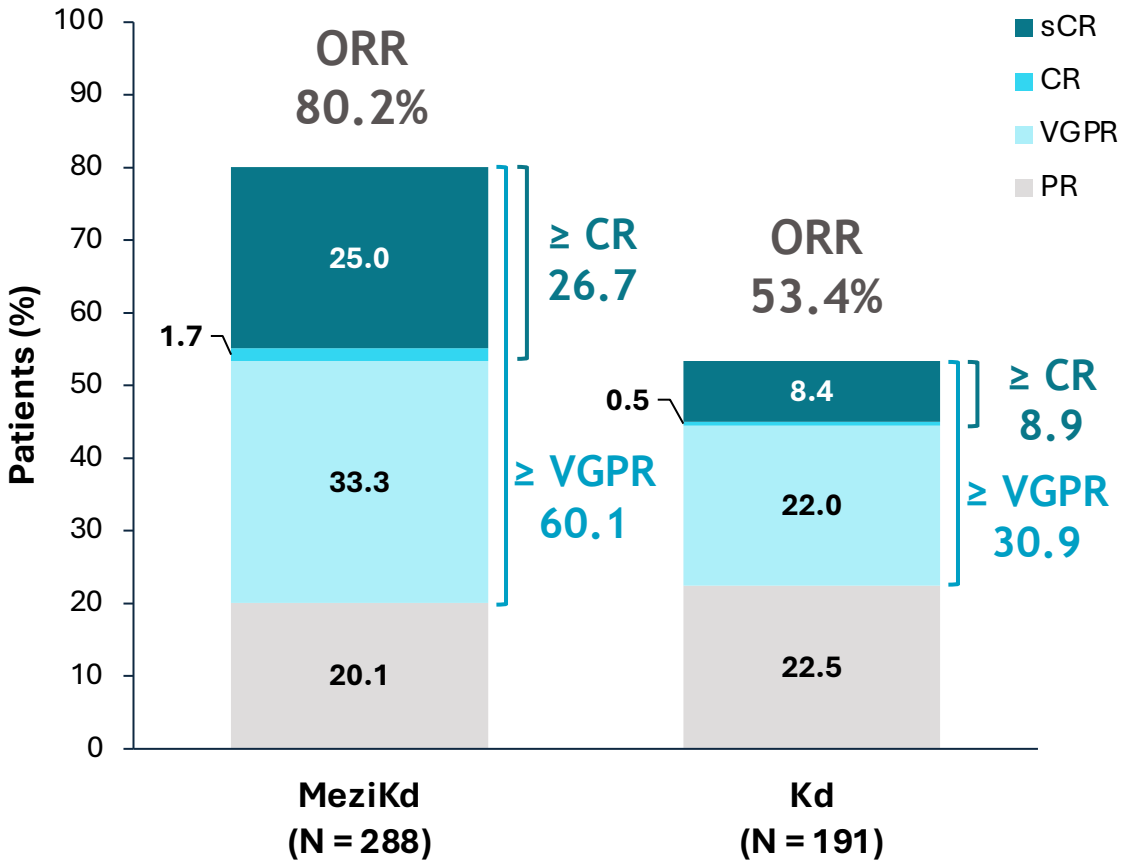


In anti-CD38 mAb- and LEN-exposed patients who had received ≥ 1 prior LOT (range 1-9), MeziKd significantly reduced the risk of progression or death by 52%

Data cutoff: January 15, 2026. In the confirmatory analysis group, defined as all patients from stages 1 and 2 randomized to 1.0 mg Mezi plus Kd or Kd. CI, confidence interval; HR, hazard ratio.

Dimopoulos MA et al. EHA 2026;Abstract LB5004

SUCCESSOR-2: Treatment Response



	MeziKd (N = 288)	Kd (N = 191)
Time to response, median (range), months[a]	1.1 (0.7–7.4)	1.1 (0.9–7.9)
12-month DoR, % (95% CI)	72 (65–78)	54 (41–66)

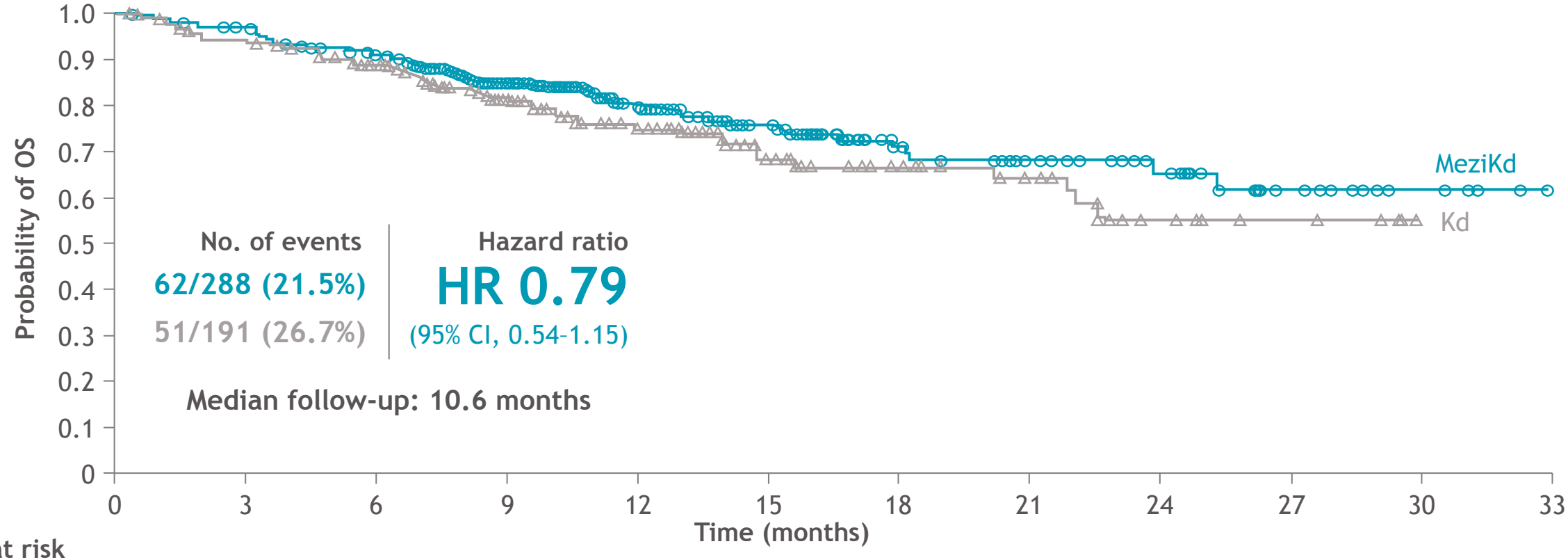
- Minimal residual disease analysis is ongoing, and results will be reported in future presentations

With a median follow up of 10.6 months, the addition of Mezi to Kd deepened response, doubling the rate of VGPR or better and tripling the rate of CR or better

Data cutoff: January 15, 2026. In the confirmatory analysis group, defined as all patients from stages 1 and 2 randomized to 1.0 mg Mezi plus Kd or Kd. Best overall response was evaluated by an independent review committee. Percentages may not total 100 due to rounding. [a]Time to response is defined as the time from randomization to the first documentation of response (PR or better).

Dimopoulos MA et al. EHA 2026;Abstract LB5004

SUCCESSOR-2: Overall Survival



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

Data cutoff: January 15, 2026. In the confirmatory analysis group, defined as all patients from stages 1 and 2 randomized to 1.0 mg Mezi plus Kd or Kd. Deaths occurred in 21.5% (MeziKd) and 26.7% (Kd) of patients.

Dimopoulos MA et al. EHA 2026;Abstract LB5004

SUCCESSOR-2: 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

Data cutoff: January 15, 2026. [a]Includes TEAEs of any grade that occurred in ≥ 20% of patients and grade 3/4 TEAEs that occurred in ≥ 10% of patients in either treatment arm in the confirmatory analysis group of the safety population, defined as all patients from stages 1 and 2 randomized to 1.0 mg Mezi plus Kd or Kd who received ≥ 1 dose of study treatment. TEAEs were graded per the National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0; [b]Excludes 5 patients who were randomized but not treated; [c]Includes preferred terms of neutropenia and neutrophil count decrease; [d]Includes preferred terms of thrombocytopenia and platelet count decrease; [e]Standardized MedDRA Query for embolism and thrombosis – various terms. G-CSF, granulocyte colony-stimulating factor; MedDRA, Medical Dictionary for Regulatory Activities; SAE, serious adverse event; TEAE, treatment-emergent adverse event; URTI, upper respiratory tract infection; VTE, venous thromboembolism.

Dimopoulos MA et al. EHA 2026;Abstract LB5004

SUCCESSOR-2: Summary of Infections

TEAE,[a] n (%)	MeziKd (N = 288)			Kd (N = 186)[b]		
	Any grade	Grade3	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

Data cutoff: January 15, 2026. As of December 2024, *Pneumocystis jirovecii* pneumonia prophylaxis was required in both arms. [a]TEAEs that occurred in ≥ 5% of patients in either treatment arm in the confirmatory analysis group of the safety population, defined as all patients from stages 1 and 2 randomized to 1.0 mg Mezi plus Kd or Kd who received ≥ 1 dose of study treatment; [b]Excludes 5 patients who were randomized but not treated.
IGRT, immunoglobulin replacement therapy; RTI, respiratory tract infection; UTI, urinary tract infection.

Dimopoulos MA et al. EHA 2026;Abstract LB5004

Expanding Clinical Development of CELMoD-Based Therapy

Study	Phase	Setting / population	CELMoD-containing regimen	Comparator / design
EMN26	II	NDMM, post-ASCT maintenance	Iberdomide maintenance at different dose levels	Single-arm/dose-finding maintenance strategy
IBEX — NCT06107738	II	NDMM, post-ASCT maintenance	Iberdomide + daratumumab	Single-arm
CADMIUM / Alliance A062102 — NCT06179888	II	R/R MM after ide-cel	Iberdomide maintenance after ide-cel	Iberdomide vs usual monitoring
Post–CAR-T mezigdomide study — NCT06048250	I	R/R MM after BCMA CAR-T	Mezigdomide maintenance	Early-phase feasibility/safety study
SUCCESSOR-1 — NCT05519085	III	R/R MM	Mezigdomide + bortezomib + dexamethasone (MeziVd)	Pomalidomide + bortezomib + dexamethasone (PVd)
ICON	I/II	R/R MM	Iberdomide + low-dose cyclophosphamide + dexamethasone	Single-arm
Iberdomide + ixazomib + dexamethasone	II	R/R MM	Iberdomide + ixazomib + dexamethasone	Single-arm
Iberdomide + belantamab mafodotin ± dexamethasone	II	R/R MM	Belantamab mafodotin + iberdomide ± dexamethasone	Combination study

Next-generation CAR-T platforms to overcome antigen escape, improve T-cell fitness and persistence, and eliminate the logistical vulnerabilities

Current challenges	*Rationale for next-generation platform*
BCMA loss/downregulation	Novel targets: GPRC5D, FcRH5, etc.
Antigen heterogeneity	Dual/multitarget CAR-T
T-cell exhaustion	Improved CAR design / fitter T-cell phenotype
Limited persistence	Optimized constructs/manufacturing
Manufacturing failure	Allogeneic/off-the-shelf platforms
Progression while awaiting CAR-T	Shorter manufacturing time
Relapse after BCMA CAR-T	Non-BCMA CAR-T / target switching

Arlocabtagene autoleucel-a GPRC5D-targeted CAR T-cell therapy

- Phase 1, dose-escalation/expansion study (NCT04674813)
- RRMM ≥3 prior antimyeloma treatment regimens (IMiD, PI, antiCD38)
- Arlo-cel was administered as a one-time intravenous infusion
- Primary endpoints: safety and maximum tolerated dose (MTD)

- N=84, median of 5 prior regimens
- **49% prior BCMA-targeted therapy, of whom 38% received CAR T-cell therapy.**

Bal S et al. *Blood*. 2026. doi:10.1182/blood.2025030750

Arlocabtagene autoleucel-a GPRC5D-targeted CAR T-cell therapy

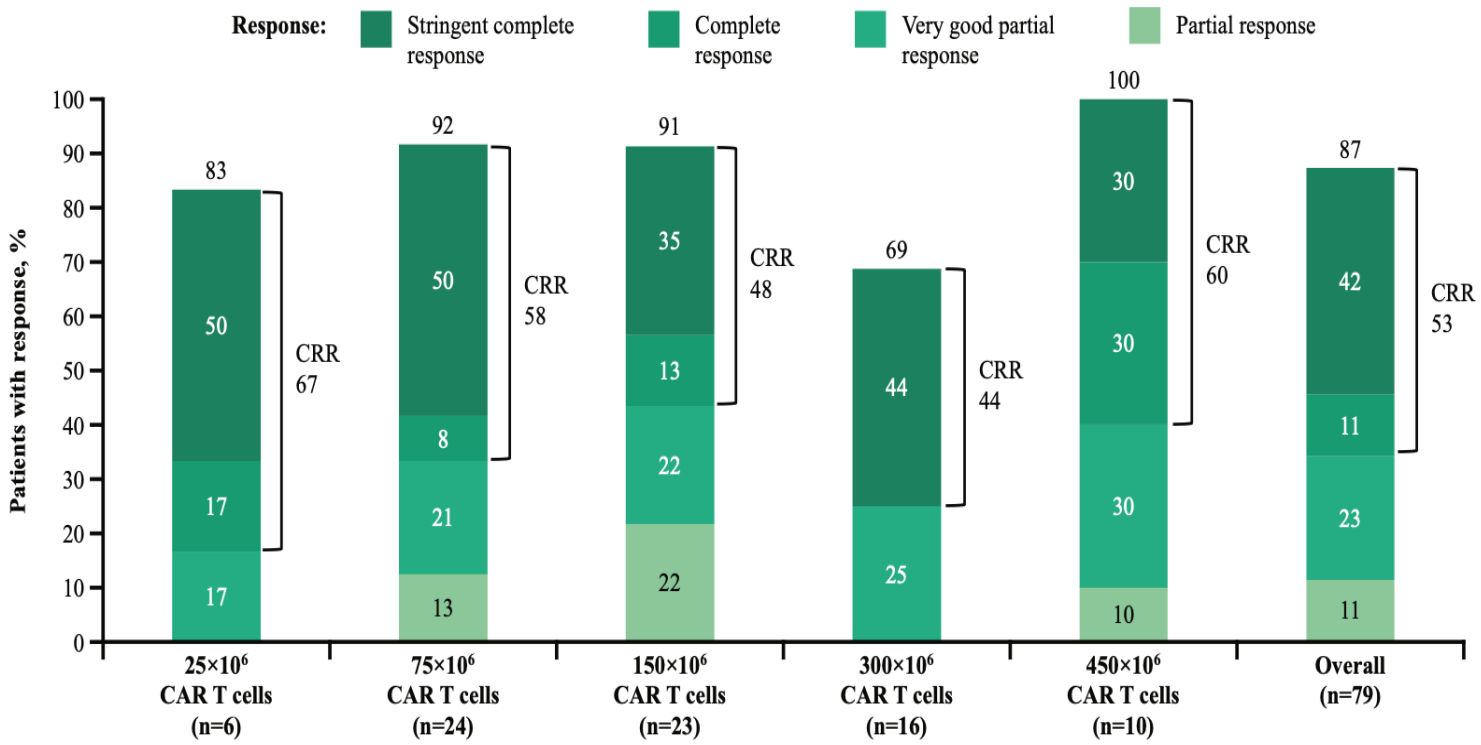
- CRS: 82%; one death at highest dose level
- ICANS: 10%
- Other neurotoxicities:12%

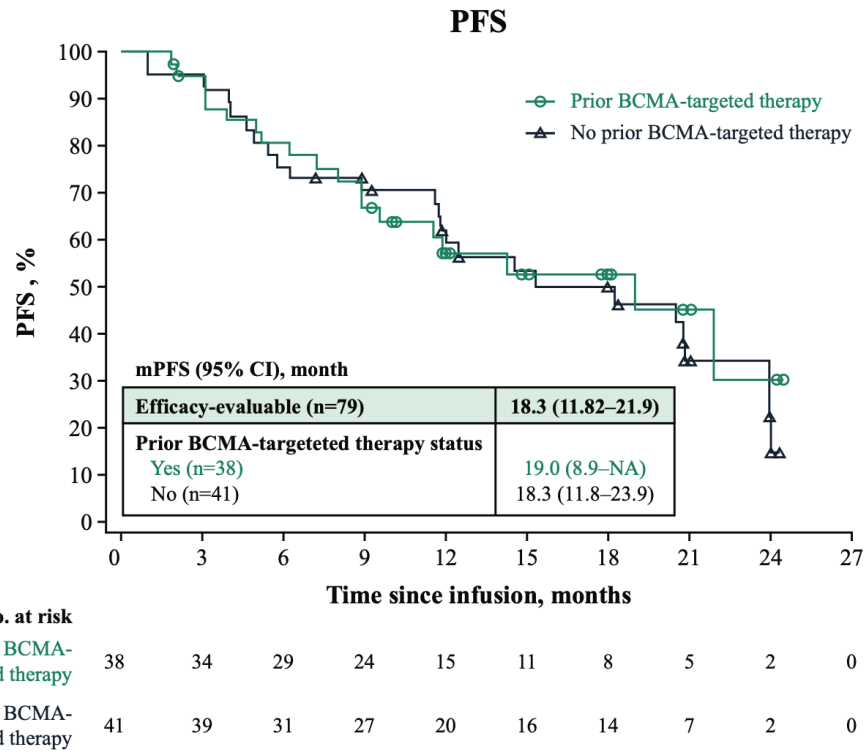
Most grade 1/2 and frequency appeared dose-dependent.

- On-target/off-tumor skin (30%), nail (19%), and oral (32%) adverse events were transient, grade 1/2; most resolved without intervention.
- MTD was not reached.

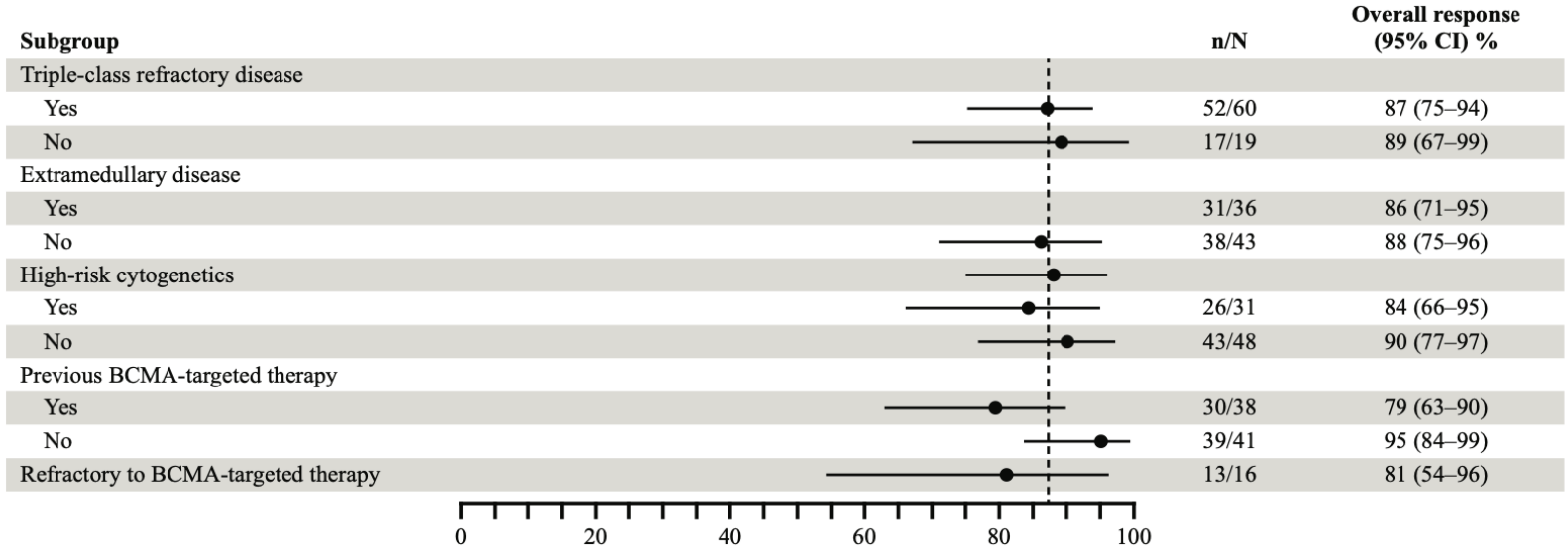
Bal S et al. *Blood*. 2026. doi:10.1182/blood.2025030750

Arlocabtagene autoleucel-a GPRC5D-targeted CAR T-cell therapy





- ✓ Median follow-up: 16.1 months
- ✓ ORR: 87% (CR 53%)
- ✓ Median DoR: 18.0 months
- ✓ Median PFS: 18.3 months (95% CI, 11.8-21.9)
- ✓ 1-year OS rate: 90%



Bal S et al. *Blood*. 2026. doi:10.1182/blood.2025030750

Ongoing Arlo-cel trials

Study	Phase	Population	Treatment arms / regimen
QUINTESSENTIAL NCT06297226	Phase II	Adults with heavily pretreated R/R MM	Arlocabtagene autoleucel (arlo-cel; BMS-986393)
QUINTESSENTIAL-2 NCT06615479	Phase III, randomized, open-label	Adults with R/R MM	Arlo-cel vs investigator-selected standard-of-care regimen

Positive Topline Results Announced from the Registrational Phase II QUINTESSENTIAL Trial of Arlocabtagene Autoleucel

Press Release: September 8, 2026

"[The manufacturer] announced positive Phase 2 results from the registrational QUINTESSENTIAL trial (NCT06297226) of arlocabtagene autoleucel (arlo-cel; BMS-986393) in adult patients with quadruple-class exposed relapsed and refractory multiple myeloma (RRMM).

Results show the study met its primary endpoint with arlo-cel demonstrating a statistically significant and clinically meaningful overall response rate (ORR) in patients with quadruple-class exposed RRMM who had received four or more prior lines of therapy. Quadruple-class exposed consists of those who had been treated with an immunomodulatory inhibitor (IMiD), a proteasome inhibitor (PI), an anti-CD38 therapy and a BCMA-targeted therapy.

The study also met the key secondary endpoint of complete response rate (CRR) in patients with RRMM who had been quadruple-class exposed after four or more prior lines of therapy, and the key secondary endpoints of ORR and CRR after three or more prior lines of therapy. The safety profile of arlo-cel was consistent with that of other CAR T cell therapies and other GPRC5D-targeting therapies in multiple myeloma."

https://news.bms.com/news/corporate-financial/2026/Bristol-Myers-Squibb-Announces-Positive-Topline-Results-from-Registrational-Phase-2-QUINTESSENTIAL-Trial-of-the-Potential-First-in-Class-GPRC5D-Directed-CAR-T-Cell-Therapy-Arlocabtagene-Autoleucel----/default.aspx

Faculty Case Presentations

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Dr Orlowski: Patient Case

- A now 59 yo M who presented with leg pain due to lytic lesions leading to a diagnosis of myeloma
  - BM had 95% PCs with t(4;14) and +1q
- Initial therapy with Dara-VRd produced a CR. Collected stem cells but declined ASCT due to his work schedule and was maintained on VR
- Progressed after 2.5 years and received Elo-Pd followed by ASCT and Elo-P maintenance
- Relapsed after 2 years: Collected T cells followed by talquetamab bridging, which produced cytoreduction

Dr Orlowski: Patient Case (Continued)

- Received cilta-cel complicated by transient cranial nerve palsy
- Relapse noted after 9 months with persistent lymphopenia and $CD4^+/CD8^+$ counts
- ? Iberdomide/dara-dex

QUESTIONS FOR THE FACULTY – CELMoDs

What are your thoughts on iberdomide/daratumumab/dexamethasone (IberDd) as the next line of therapy for this patient? Given its recent FDA approval, how do you foresee using IberDd relative to other options in the R/R setting?

Do you have any qualms about the use of MRD negativity as an endpoint in the pivotal study of IberDd?

How comfortable would you be employing IberDd for a patient like this who had previously received daratumumab? What about for a patient whose disease was refractory to one or more standard IMiDs?

QUESTIONS FOR THE FACULTY – CELMoDs

Would you currently consider combining iberdomide with agents other than daratumumab/dexamethasone? If so, under what circumstances and which ones? Can CELMoDs be substituted for standard IMiDs in any IMiD-containing regimen?

If iberdomide- and mezigdomide-containing triplets were to be approved, how would you select between them? Are there specific types of patients for whom you would prefer IberDd over mezigdomide/carfilzomib/dexamethasone or vice versa? Would you use these regimens in sequence?

QUESTIONS FOR THE FACULTY – CELMoDs

How should CBC monitoring and growth factor support be approached for patients receiving iberdomide? What about mezigdomide? How do CELMoDs compare to standard IMiDs in terms of gastrointestinal toxicities and rates of second cancer?

Dr Raje: A patient with R/R MM

- 64-year-old male who was initially treated with RVd transplant and Len maintenance
- Received Dara-Pd at relapse
- Received Cilta-cel and remission lasted 24 months
- Liked the idea of a treatment-free interval and wanted to explore CAR T-cell therapy options
- Was consented and treated with Arlo-cel—continues in remission 12 months into Arlo-cel

QUESTIONS FOR THE FACULTY – GPRC5D-Targeted CAR T-Cell Therapy

How would you indirectly compare the global efficacy of arlocabtagene autoleucel (arlo-cel) to that of BCMA-targeted CAR T-cell therapy? How would you indirectly compare their tolerability?

If arlo-cel were to reach the clinic, how do you see it fitting in? Would you prioritize arlo-cel over currently available BCMA-targeted CAR T-cell therapies in any circumstances? Would you be comfortable administering BCMA- and GPRC5D-targeted CAR T-cell therapy to the same patient in sequence?

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QUESTIONS FOR THE FACULTY – GPRC5D-Targeted CAR T-Cell Therapy

Would you administer arlo-cel to a patient who had already received talquetamab? Can GPRC5D expression be lost?

How do nail, skin and oral toxicities with arlo-cel compare to those with GPRC5D-targeting bispecific antibodies? Is there any difference in severity/persistence given the one-time versus continuous administration of arlo-cel?

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

For those attending virtually please complete the survey currently on Zoom. The survey will remain open up to 5 minutes after the meeting ends.

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Virtual/Zoom attendees:
The CME credit link is posted in the chat room.

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