Questions from the Community: Investigators Discuss Available Research Guiding the Care of Patients with Relapsed/Refractory Multiple Myeloma

> Monday, June 2, 2025 6:00 PM – 7:00 PM CT (7:00 PM – 8:00 PM ET)

> > Faculty Ajay K Nooka, MD, MPH Paul G Richardson, MD

> > > Moderator Neil Love, MD



## Faculty



Ajay K Nooka, MD, MPH Professor, Department of Hematology and Medical Oncology Director, Myeloma Program Associate Director of Clinical Research Winship Cancer Institute Emory University School of Medicine Atlanta, Georgia



MODERATOR Neil Love, MD Research To Practice Miami, Florida

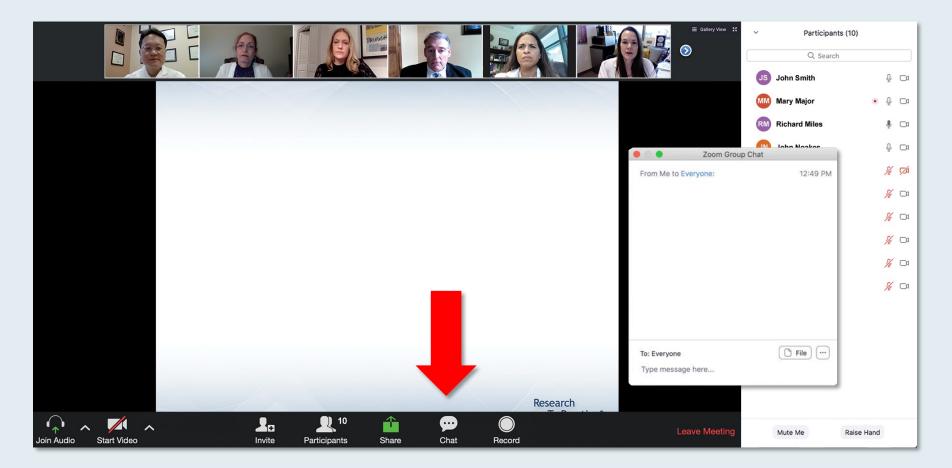


Paul G Richardson, MD

Clinical Program Leader and Director of Clinical Research Jerome Lipper Multiple Myeloma Center Dana-Farber Cancer Institute RJ Corman Professor of Medicine Harvard Medical School Boston, Massachusetts



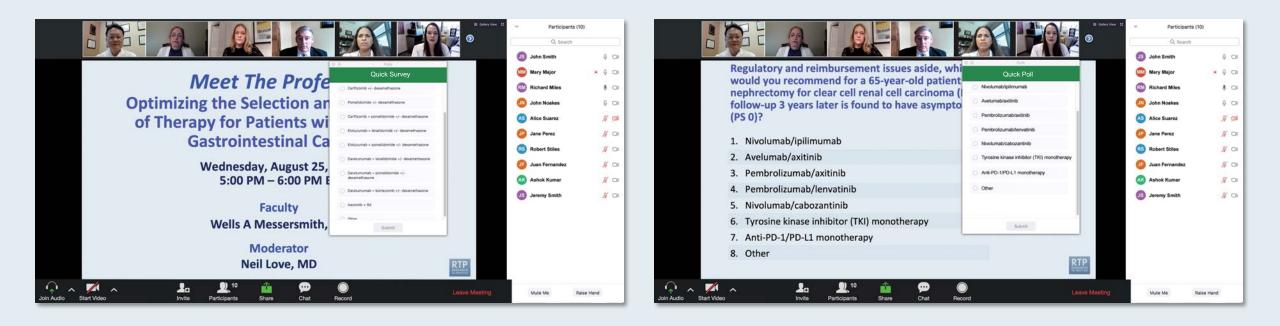
#### We Encourage Clinicians in Practice to Submit Questions



Feel free to submit questions now before the program begins and throughout the program.



# Clinicians in the Audience, Please Complete the Pre- and Postmeeting Surveys





	Immunotherapy and Antibody-Drug	
Friday May 30	Conjugates in Lung Cancer 11:15 AM - 12:45 PM CT (12:15 PM - 1:45 PM ET)	
	Colorectal Cancer 6:30 PM - 8:30 PM CT (7:30 PM - 9:30 PM ET)	
	EGFR Mutation-Positive Non-Small Cell Lung Cancer 6:30 PM - 8:30 PM CT (7:30 PM - 9:30 PM ET)	
Saturday May 31	Urothelial Bladder Cancer 6:45 AM - 7:45 AM CT (7:45 AM - 8:45 AM ET)	
	Non-Hodgkin Lymphoma 7:00 PM - 9:00 PM CT (8:00 PM - 10:00 PM ET)	
	<b>Prostate Cancer</b> 7:00 PM - 9:00 PM CT (8:00 PM - 10:00 PM ET)	
Sunday June 1	Chronic Lymphocytic Leukemia (Webinar) 7:00 AM - 8:00 AM CT (8:00 AM - 9:00 AM ET)	
	HER2-Positive Gastrointestinal Cancers 7:00 PM - 8:30 PM CT (8:00 PM - 9:30 PM ET)	
	Ovarian and Endometrial Cancer 7:00 PM - 9:00 PM CT (8:00 PM - 10:00 PM ET)	
Monday June 2	Renal Cell Carcinoma (Webinar) 7:00 AM - 8:00 AM CT (8:00 AM - 9:00 AM ET)	
	Multiple Myeloma (Webinar) 6:00 PM - 7:00 PM CT (7:00 PM - 8:00 PM ET)	
	Metastatic Breast Cancer 7:00 PM - 9:00 PM CT (8:00 PM - 10:00 PM ET)	
Tuesday June 3	Soft Tissue Sarcoma and Other Connective Tissue Neoplasms (Webinar) 7:00 AM - 8:00 AM CT (8:00 AM - 9:00 AM ET)	



# Consensus or Controversy? Clinical Investigators Provide Perspectives on the Current and Future Clinical Care of Patients with Metastatic Breast Cancer

Monday, June 2, 2025 7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)

#### Faculty

Harold J Burstein, MD, PhD Javier Cortés, MD, PhD Rebecca A Dent, MD, MSc Kevin Kalinsky, MD, MS Joyce O'Shaughnessy, MD

Moderator Hope S Rugo, MD



RTP Live from Chicago: Investigator Perspectives on Available Research Findings and Challenging Questions in the Management of Soft Tissue Sarcoma and Other Connective Tissue Disorders

> **Tuesday, June 3, 2025** 7:00 AM - 8:00 AM CT (8:00 AM - 9:00 AM ET) **Faculty Rashmi Chugh, MD Mrinal Gounder, MD Moderator** Neil Love, MD



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# Dr Nooka — Disclosures Faculty

Advisory Boards and Consulting Agreements (Honoraria)	Adaptive Biotechnologies Corporation, AstraZeneca Pharmaceuticals LP, Cellectar Biosciences Inc, GSK, Janssen Biotech Inc, K36 Therapeutics, Kite, A Gilead Company, ONK Therapeutics, Opna Bio, Pfizer Inc, Sanofi, Sebia	
Data and Safety Monitoring Boards/Committees	Janssen Biotech Inc	
Grant/Research Support (for Investigator-Initiated Studies)	Amgen Inc, GSK, Janssen Biotech Inc, Merck, Takeda Pharmaceuticals USA Inc	
Grant/Research Support (to University)		



# Dr Richardson — Disclosures Faculty

Consulting Agreements	Bristol Myers Squibb, Celgene Corporation, GSK, Karyopharm Therapeutics, Oncopeptides, Regeneron Pharmaceuticals Inc, Sanofi
Contracted Research	Oncopeptides



#### **Dr Love — Disclosures**

**Dr Love** is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following companies: Aadi Bioscience, AbbVie Inc, ADC Therapeutics, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Arvinas, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, Black Diamond Therapeutics Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Clovis Oncology, Coherus BioSciences, CTI BioPharma, a Sobi Company, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, Exact Sciences Corporation, Exelixis Inc, Genentech, a member of the Roche Group, Genmab US Inc, Geron Corporation, Gilead Sciences Inc, GSK, Hologic Inc, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Jazz Pharmaceuticals Inc, Johnson & Johnson, Karyopharm Therapeutics, Kite, A Gilead Company, Kura Oncology, Legend Biotech, Lilly, MEI Pharma Inc, Merck, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Mural Oncology Inc, Natera Inc, Novartis, Novartis Pharmaceuticals Corporation on behalf of Advanced Accelerator Applications, Novocure Inc, Nuvalent, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Rigel Pharmaceuticals Inc, R-Pharm US, Sanofi, Seagen Inc, Servier Pharmaceuticals LLC, SpringWorks Therapeutics Inc, Stemline Therapeutics Inc, Syndax Pharmaceuticals, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, TerSera Therapeutics LLC, and Tesaro, A GSK Company.



#### **Commercial Support**

This activity is supported by an educational grant from GSK.

#### Research To Practice CME Planning Committee Members, Staff and Reviewers

Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.



This educational activity contains discussion of non-FDA-approved uses of agents and regimens. Please refer to official prescribing information for each product for approved indications.



#### Agenda

#### **Introduction: ASCO 2025 Showstoppers**

Module 1: Up-Front Treatment of Multiple Myeloma (MM) – Survey Questions

Module 2: Emerging Novel Therapies for Relapsed/Refractory (R/R) MM – Faculty Presentation

**Module 3:** Emerging Novel Therapies for R/R MM – Survey Questions

**Module 4:** Current Management of R/R MM – Faculty Presentation

**Module 5:** Current Management of R/R MM – Survey Questions

Module 6: ASCO and EHA 2025



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Module 6: ASCO and EHA 2025



Randomized Trial of Standard Chemotherapy Alone or Combined with Atezolizumab as Adjuvant Therapy for Patients with Stage III Deficient DNA Mismatch Repair (dMMR) Colon Cancer (Alliance A021502; ATOMIC)

Sinicrope F et al. ASCO 2025;Abstract LBA1.

Three-year DFS was 86.4 % in the atezolizumab/mFOLFOX6 arm and 76.6 % in the mFOLFOX6 arm (HR, 0.50; 95% CI, 0.35–0.72).



Camizestrant + CDK4/6 Inhibitor (CDK4/6i) for the Treatment of Emergent ESR1 Mutations During First-Line (1L) Endocrine-Based Therapy (ET) and Ahead of Disease Progression in Patients (pts) with HR+/HER2– Advanced Breast Cancer (ABC): Phase 3, Double-Blind ctDNA-Guided SERENA-6 Trial

Turner N et al. ASCO 2025;Abstract LBA4.

Hazard ratio for PFS was 0.44 (95% CI 0.31–0.60, p<0.00001; median PFS 16.0 vs 9.2 months).

PFS rate at 24 months was 29.7% vs 5.4%.



Trastuzumab Deruxtecan (T-DXd) + Pertuzumab (P) vs Taxane + Trastuzumab + Pertuzumab (THP) for First-Line (1L) Treatment of Patients (pts) with Human Epidermal Growth Factor Receptor 2-Positive (HER2+) Advanced/Metastatic Breast Cancer (a/mBC): Interim Results from DESTINY-Breast09

Tolaney S et al. ASCO 2025;Abstract LBA1008.

T-DXd + P significantly improved PFS by BICR (hazard ratio 0.56; 95% CI 0.44, 0.71; *P* < 0.00001).

ILD occurred in 12.1% of 383 patients (predominantly Grade 1/2) who received T-DXd + P. Grade 5 ILD occurred in 2 patients.



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Module 6: ASCO and EHA 2025



Survey of 50 Community-Based General Medical Oncologists May 14-24, 2025



# Questions from General Medical Oncologists — First-Line Treatment of MM

• Myeloma is so complicated now.



# Questions from General Medical Oncologists — First-Line Treatment of MM; Smoldering Myeloma

- The juice has to be worth the squeeze there are so many options already, for MM to stand out there has to be a definite advantage in PFS, OS, or tox
- Should all patients get an anti-CD38 and which one?
- I basically never use isatuximab. Much less chair time with subcutaneous dara
- In what situations (reimbursement aside) would you recommend daratumumab for smoldering myeloma — what dose and for how long?



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#### May 30 – June 3, 2025

McCormick Place | Chicago, IL & Online am.asco.org #ASCO25

#### **Research To Practice\***

AN INTEGRATED APPROACH TO ONCOLOGY EDUCATION

# Emerging Novel Therapies for Relapsed/Refractory (R/R) MM, With A Focus On Belantamab Mafodotin and the CELMoDs

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



DANA-FARBER CANCER INSTITUTE

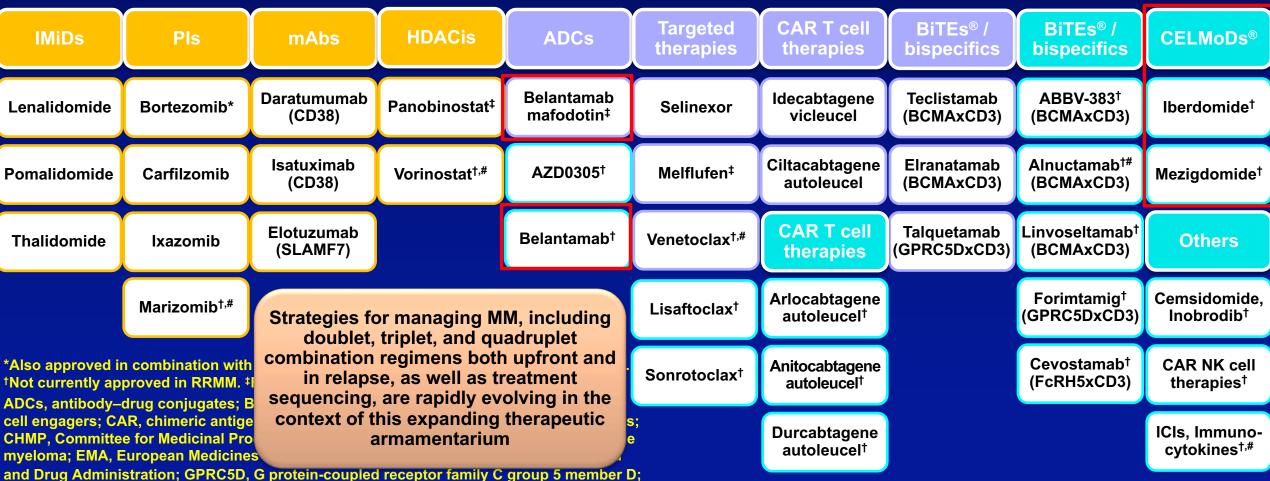


# Treatment of MM in 2025: multiple therapies approved or under investigation

Backbone/standard-of-care agents

Recent approvals / later relapse

**Emerging therapies for MM\*\*** 



ICIs, immune checkpoint inhibitors; IMiDs®, immunomodulatory drugs; mAbs, monoclonal antibodies; PIs, proteasome inhibitors; RRMM, relapsed/refractory multiple myeloma.

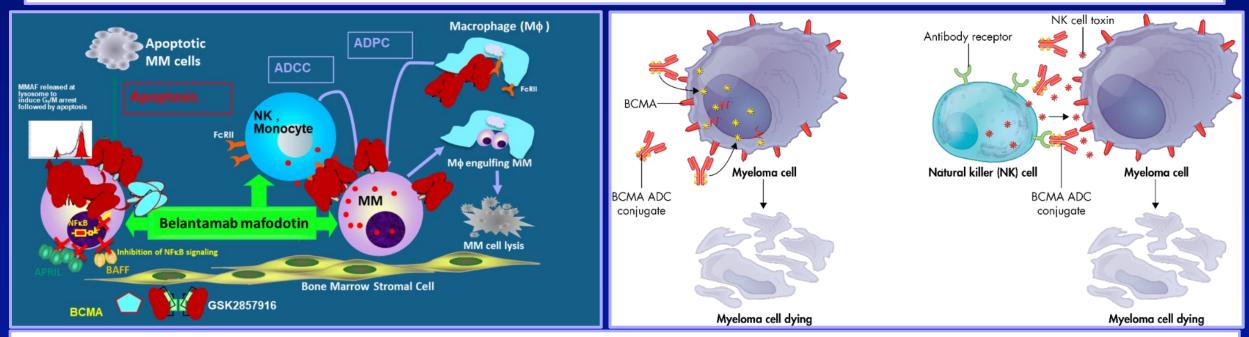
Adapted from Richardson PG. 5th Oxford Myeloma Workshop, January 30–31, 2025, Oxford, UK.

# BCMA-targeted antibody–drug conjugate (ADC) therapy for RRMM Ongoing development of belantamab mafodotin<sup>1,2</sup>

#### First ADC approved in RRMM (2020)

#### US and EU marketing authorisation withdrawn following DREAMM-3 not meeting its primary endpoint<sup>3,4</sup>

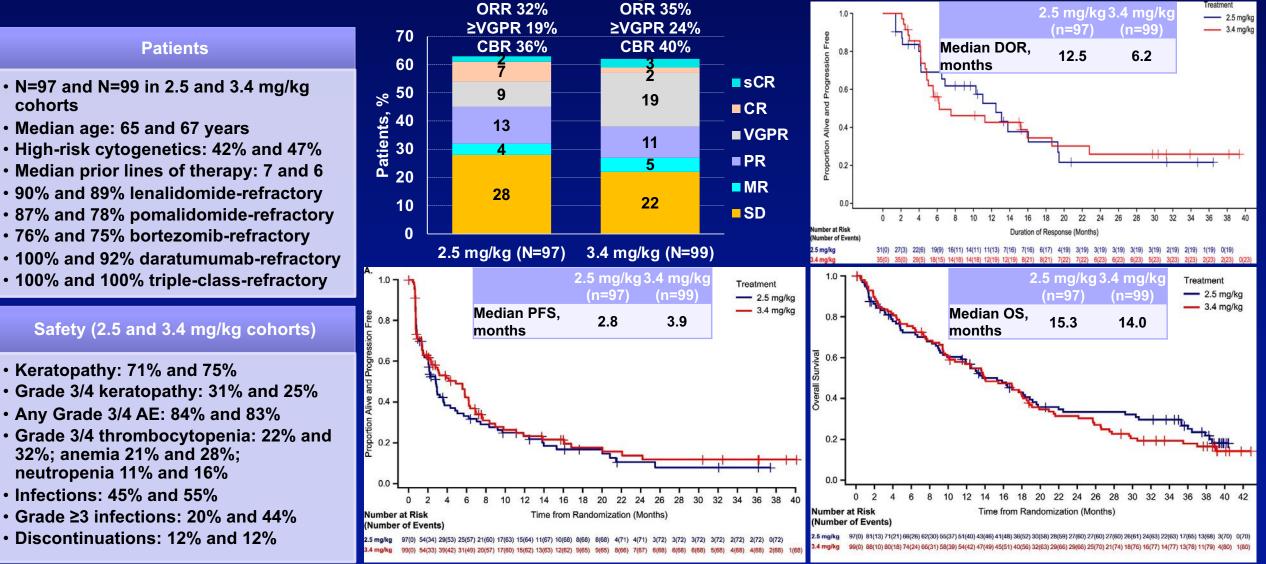
Remains under investigation in combination regimens in multiple studies, with positive results from the DREAMM-7<sup>5</sup> and DREAMM-8<sup>6</sup> phase 3 trials in RRMM



Humanized IgG1 Fc-engineered ADC comprising a BCMA-targeted antibody covalently linked via a cysteine linker to the microtubule inhibitor monomethyl auristatin F (MMAF)

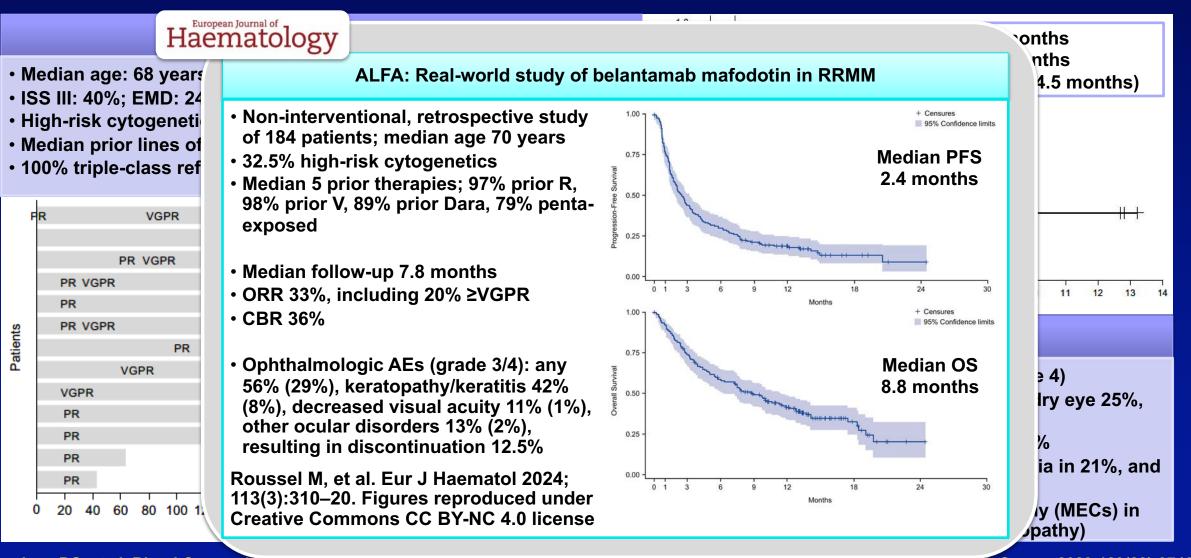
1. Trudel S, et al. Lancet Oncol 2018;19(12):1641–53. 2. Richardson PG, et al. Blood Cancer J 2020;10(10):106. 3. Dimopoulos MA, et al. Lancet Haematol 2023;10(10):e801–12. 4. Mukhopadhyay P, et al. Blood Cancer J 2025;15(1):15. 5. Hungria V, et al. N Engl J Med 2024;391(5):393–407. 6. Dimopoulos MA, et al. N Engl J Med 2024;391(5):408–21. Left-hand figure adapted from Tai YT, Anderson KC. Immunotherapy 2015;7(11):1187–99. Right-hand figure adapted from Cho S-F, et al. Front Immunol 2018;9:1821.

# Belantamab mafodotin: initial approval based on DREAMM-2 in heavily pretreated RRMM



Lonial S, et al. Lancet Oncol 2020;21(2):207–21. Lonial S, et al. Cancer 2021;127(22):4198–212. Nooka A, et al. Cancer 2023;129(23):3746–60. Figures reproduced under Creative Commons CC BY-NC 4.0 license.

# DREAMM-2: belantamab mafodotin lyophilised presentation cohort

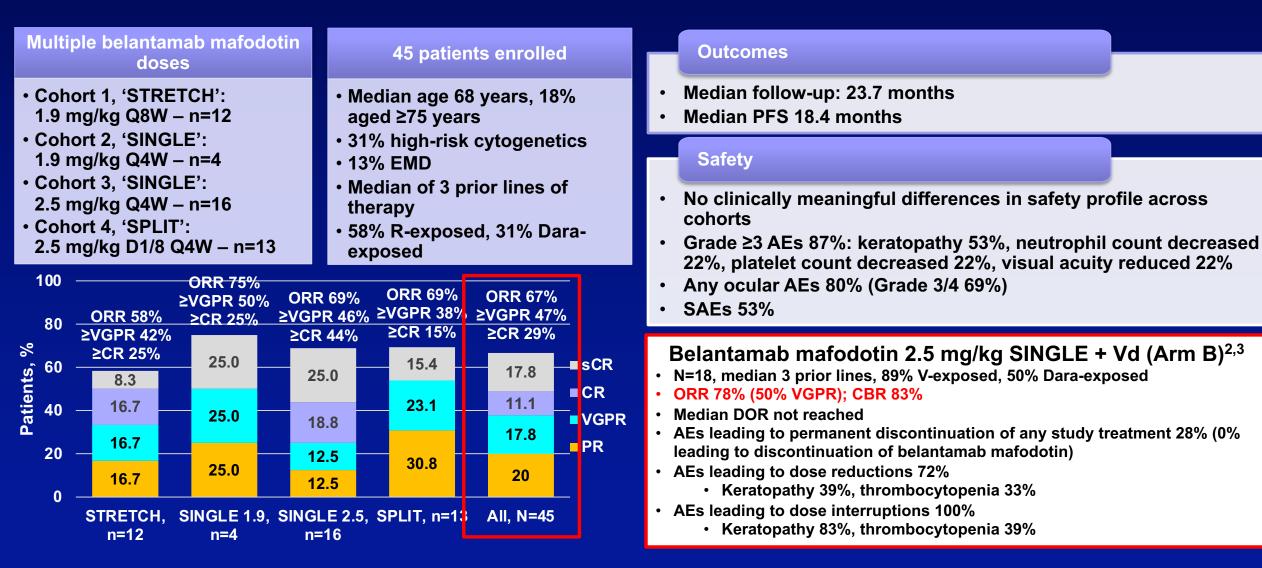


# **DREAMM-3: Belantamab mafodotin vs Pom-dex** as 3<sup>rd</sup>-line therapy<sup>1</sup>

Patients (N=325)	Exposure	Outcomes	
<ul> <li>218 received belamaf 2.5 mg/kg Q3W vs 107 Pom-dex</li> <li>Median age 68 years</li> <li>54% vs 62% male</li> <li>24% vs 26% ISS stage III</li> <li>Median 4 vs 3 prior lines</li> <li>Median 4 vs 3 prior</li> </ul>		<ul> <li>Median follow-up: 11.5 vs 10.8 months</li> <li>Median PFS: 11.2 vs 7.0 months (HR 1.03, stratified Cox model, not significant)</li> <li>MRD-neg ≥VGPR 7% vs 0</li> <li>1-year DOR 77% vs 48%</li> <li>Median PFS2 18.7 vs 12.7 months</li> <li>Median OS 21.2 vs 21.1 months</li> </ul>	
• 40% vs 38% prior dara			
Pom-dex 28	8 ORR 36%	Safety <ul> <li>AEs 97% vs 93%</li> <li>Grade 3/4 AEs 76% vs 70%</li> </ul>	
Belamaf	25 ORR 41%	<ul> <li>Grade 5 AEs 7% vs 11%</li> <li>SAEs 43% vs 39%</li> </ul>	
0 10 20 • PR	30 40 50 60 ■CR/VGPR	<ul> <li>AEs leading to discontinuation 15% vs 17%</li> <li>Consistent safety profile in 50 patients receiving belamaf for ≥52 weeks<sup>2</sup></li> </ul>	

1. Dimopoulos MA, et al. Lancet Haematol 2023;10(10):e801–12. 2. Hungria VTM, et al. Blood 2023;142(suppl 1):abstract 3357.

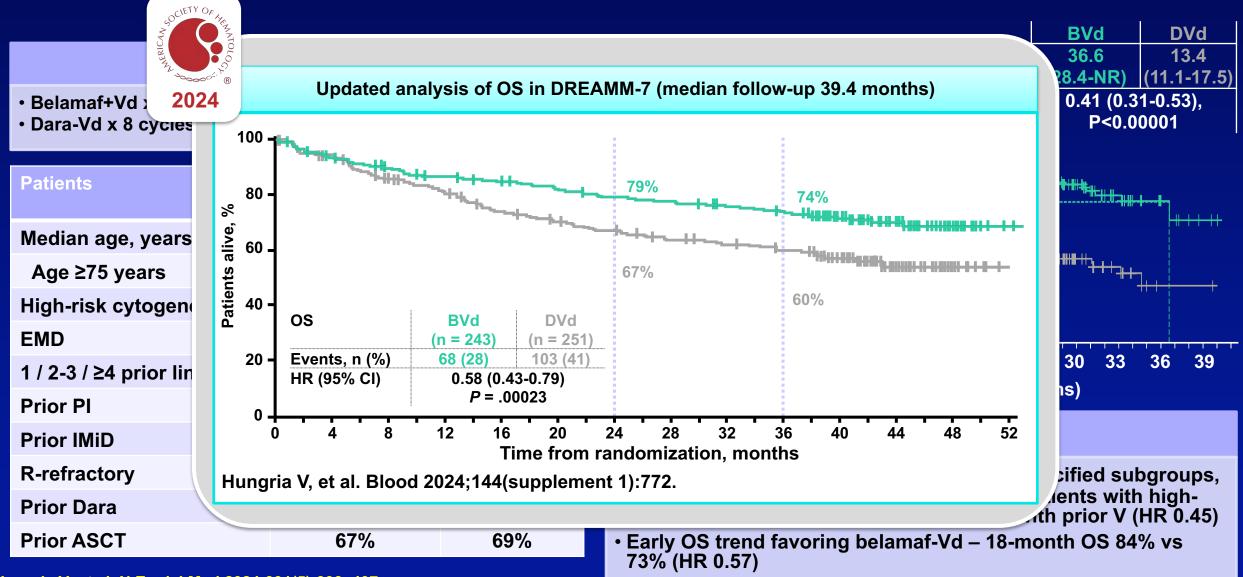
# DREAMM-6: Belantamab mafodotin + Rd (Arm A)<sup>1</sup>



#### 1. Popat R, et al. Blood Cancer J 2024;14(1):184.

2. Nooka A, et al. J Clin Oncol 2020;38(15\_suppl):abstract 8502. 3. Popat R, et al. Blood 2020;136(suppl 1):abstract 1419.

#### BCMA-targeted ADC for early-relapse RRMM ■ DREAMM-7: Belantamab mafodotin + Vd vs Dara-Vd as ≥2<sup>nd</sup>-line therapy



Hungria V, et al. N Engl J Med 2024;391(5):393-407.



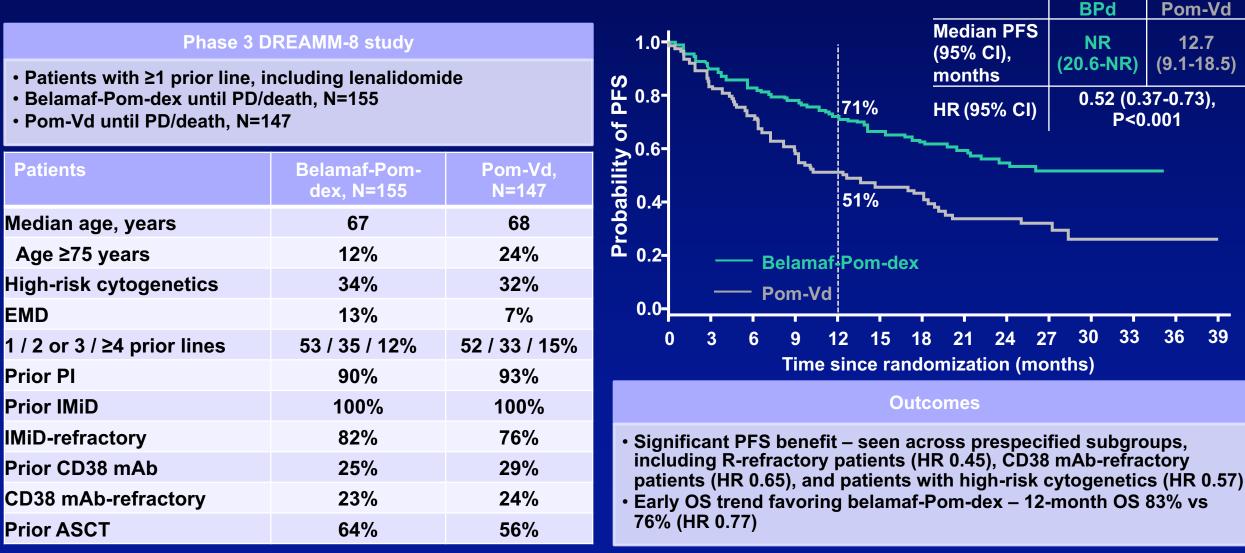
#### **BCMA-targeted ADC for early-relapse RRMM DREAMM-7: Belantamab mafodotin + Vd vs** Dara-Vd as ≥2<sup>nd</sup>-line therapy 2024 2025 **ASCO** ANNUAL MEETING Outcomes in patients with high-risk cytogenetics (HRC) PFS in patients by MRD status 2024 • 50% vs 46% had HRC • Patients achieving CR MRD-neg status 17% vs 17% t(4;14); 3% vs 2% t(14;16) Median PFS and OS not reached in either arm • 12% vs 14% del17p 10% and 21% of patients in the Belamaf-Vd and Dara-Vd • 39% vs 31% amp1q arms, respectively, had PFS events • With belantamab mafodotin + Vd vs Dara-Vd in patients with 5% and 4% had OS events Patients, % ≥1 HRC Patients not achieving heg status Median PFS 33.2 vs 11.1 months Median PFS 25.0 nthe 38% 18-month OS rat 39% vs 17%) Phase 1 study of Bela-RVd in RRMM with 1–3 prior lines Hungria V, et al. Blood 1 2024 I 2025;43(16 supplement):7546. 19 patients; median age 63 years 33% 20% 20 53% high-risk cytogenetics 4% 12% 42% R-refractory, 11% V-refractory, 26% Dara-refractory 25.1 10 79% (34%) 29% (3%) Median follow-up 16.1 months 16.9 • ORR 100%, including 74% ≥VGPR and 53% ≥CR 68% (24%) 11% (<1%) 0 MRD-neg 53% (10<sup>-5</sup>) / 37% (10<sup>-6</sup>) 51% (7%) 7% (0) BVd (n=243) DVd (n=251) Common AEs (grade ≥3): eye disorders 95% (32%), blurred 47% (2%) 2% (0) vision 90% (37%), fatigue 58% (0%), hypokalemia 53% (11%) Median DOR 40.8 vs 17.8 months 43% (5%) 5% (0) Atrash S, et al. Blood 2024;144(supplement 1):4751.

Hungria V, et al. N Engl J Med 2024;391(5):



#### BCMA-targeted ADC for early-relapse RRMM

#### DREAMM-8: Belantamab mafodotin + Pom-dex vs Pom-Vd as ≥2<sup>nd</sup>-line therapy

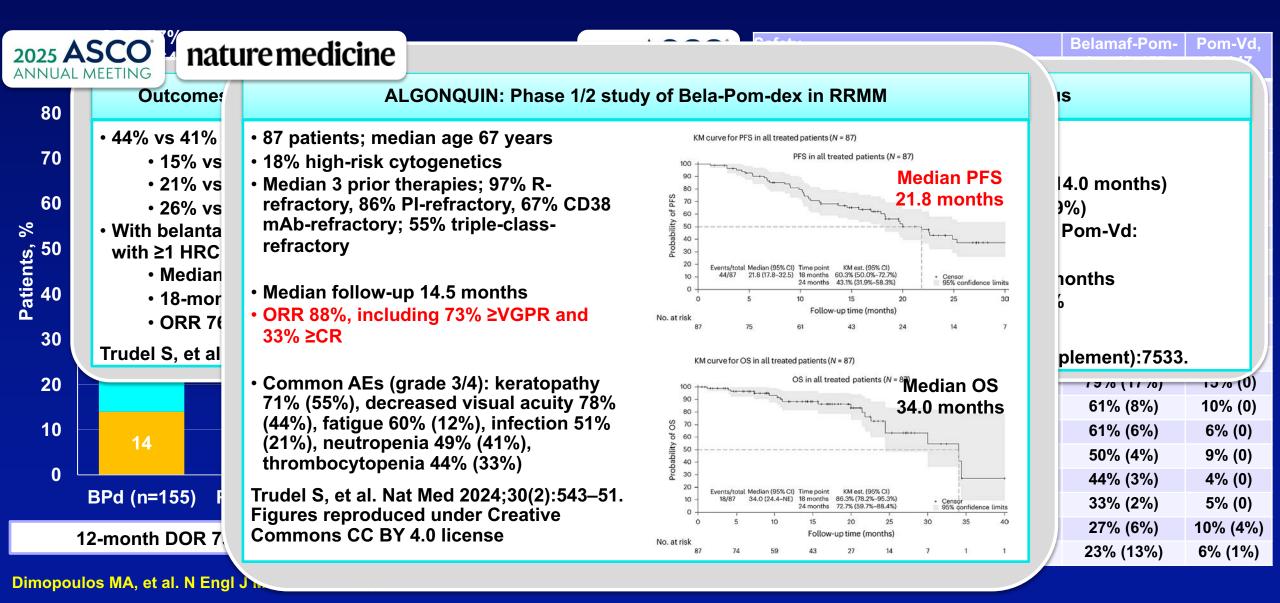


Dimopoulos MA, et al. N Engl J Med 2024;391(5):408-421.



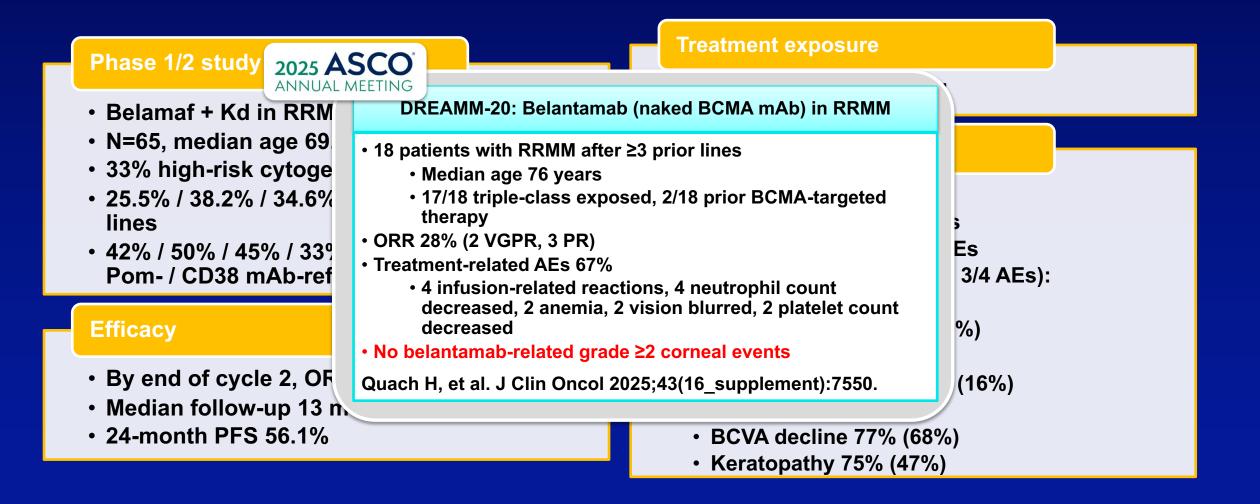
#### **BCMA-targeted ADC for early-relapse RRMM**

#### DREAMM-8: Belantamab mafodotin + Pom-dex vs Pom-Vd as ≥2<sup>nd</sup>-line therapy



# AMaRC 19-02 BelaCarD study: Belantamab mafodotin + Kd in RRMM

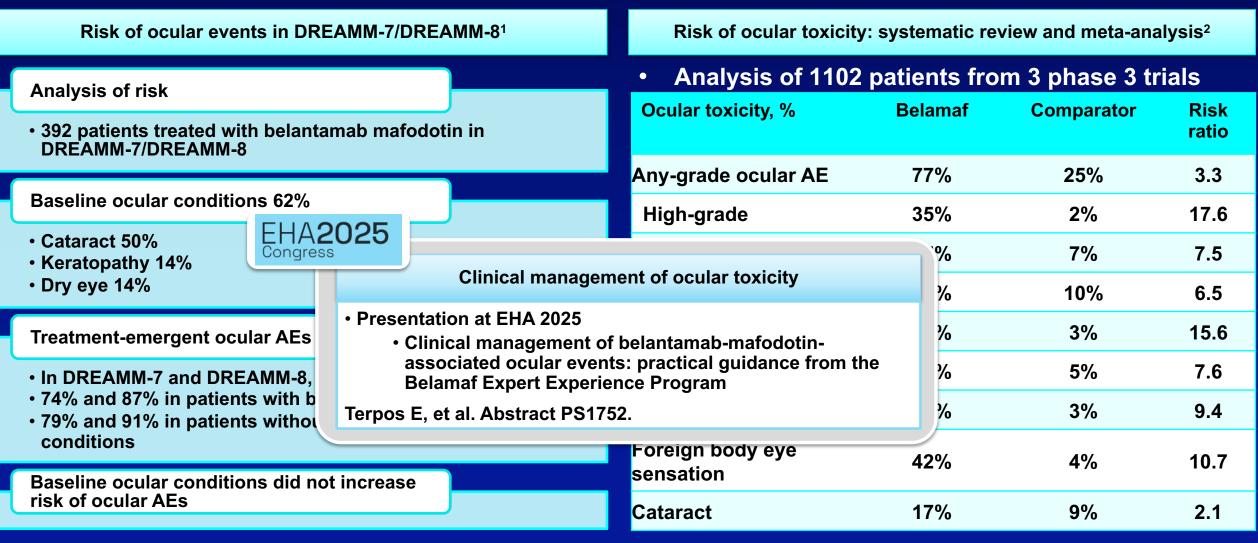
2023



# Risk of ocular toxicity with belantamab mafodotin in RRMM

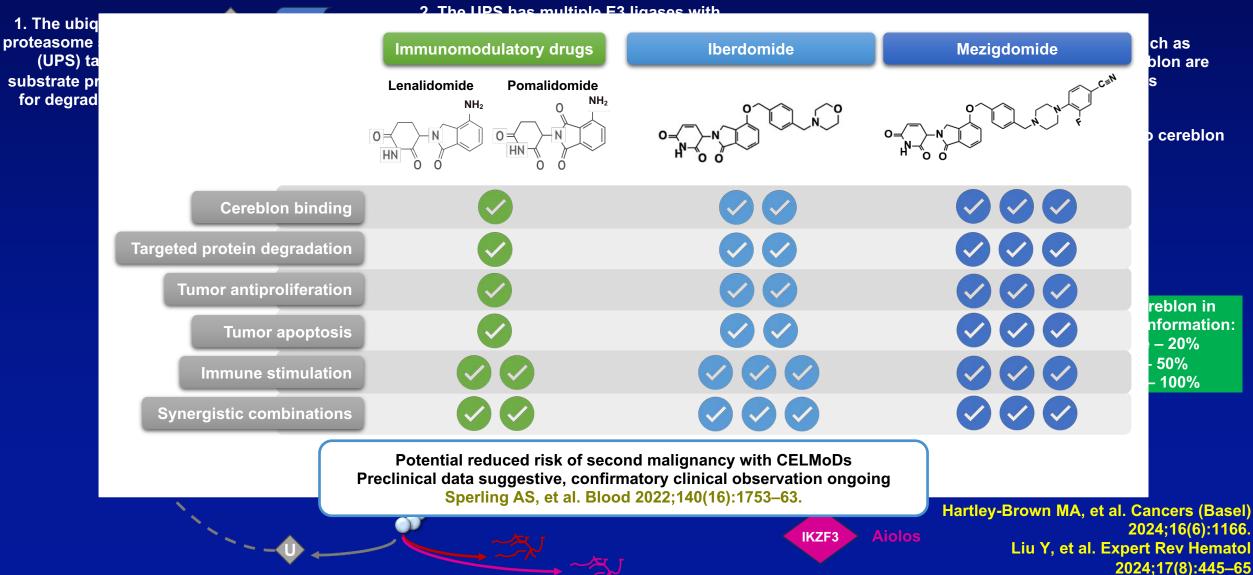
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ANNUAL MEETING

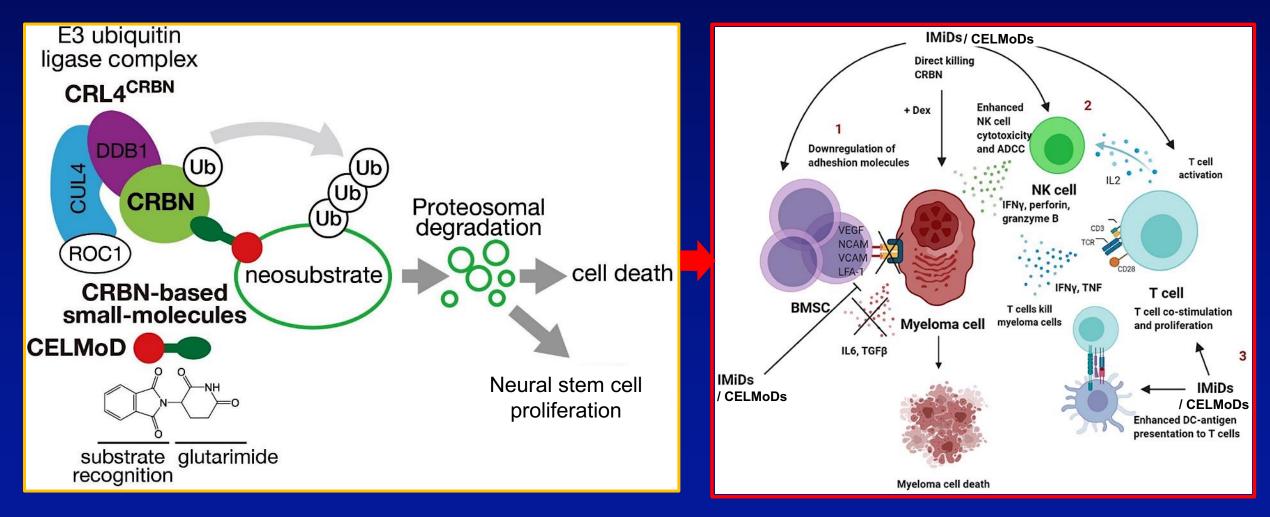


1. Quach H, et al. J Clin Oncol 2025;43(16\_supplement):7544. 2. Hattin R, et al. J Clin Oncol 2025;43(16\_supplement):12040.

## CELMoDs ~ targeting cereblon: novel immunomodulators and protein degraders for RRMM



## Novel immunomodulators for RRMM CELMoDs<sup>®</sup>: iberdomide<sup>1</sup> and mezigdomide<sup>2</sup>

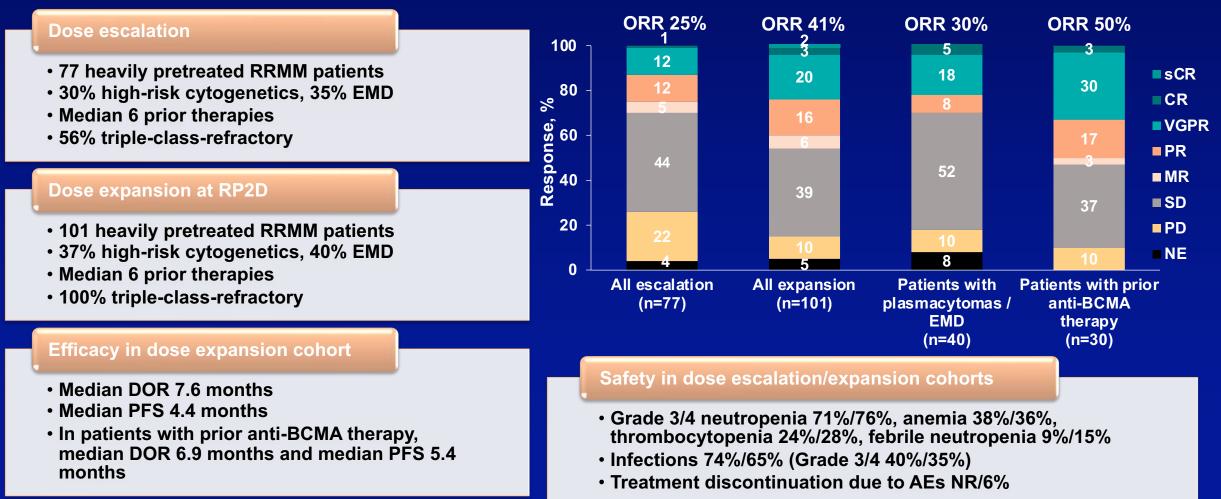


1. Lonial S, et al. Lancet Haematol 2022;9(11):e822–32. 2. Richardson PG, et al. N Engl J Med 2023;389(11):1009–22. Figures adapted from: (left) Sato T, et al. Front Cell Dev Biol 2021;9:629326; (right) D'Souza C, et al. Front Immunol 2021;12:632399.

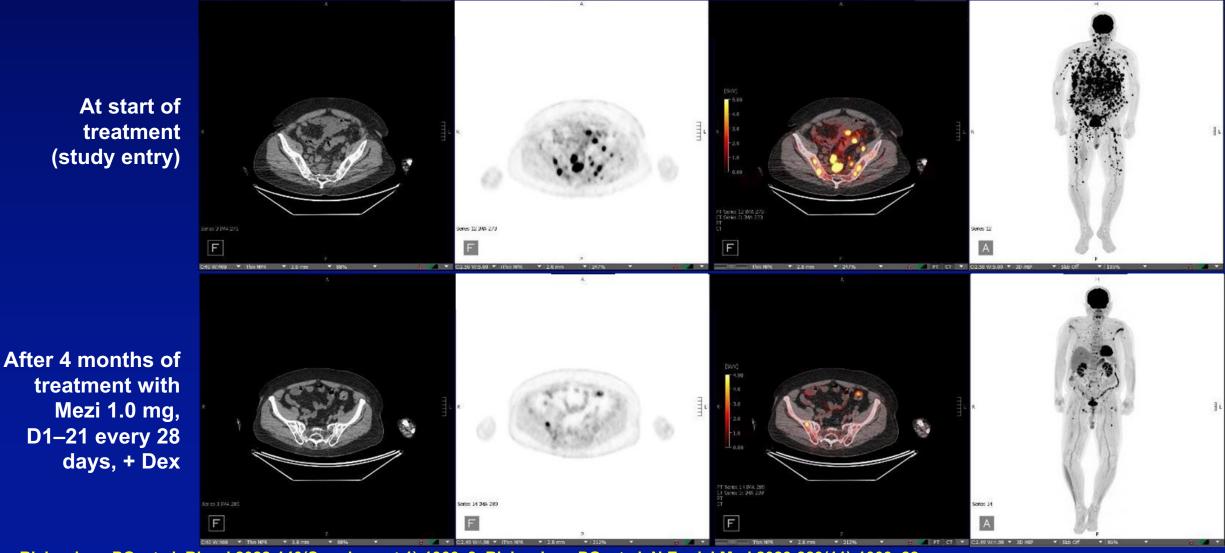


## CELMoD doublets for RRMM Mezigdomide + dex: Phase 1/2 study, N=178

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



## CELMoD doublets for RRMM Mezigdomide + dex induces responses in patients with EMD



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 + Vd or Kd



#### CC-92480-MM-002 Phase 1/2 Study: Mezigdomide + Vd / Kd<sup>1,2</sup>

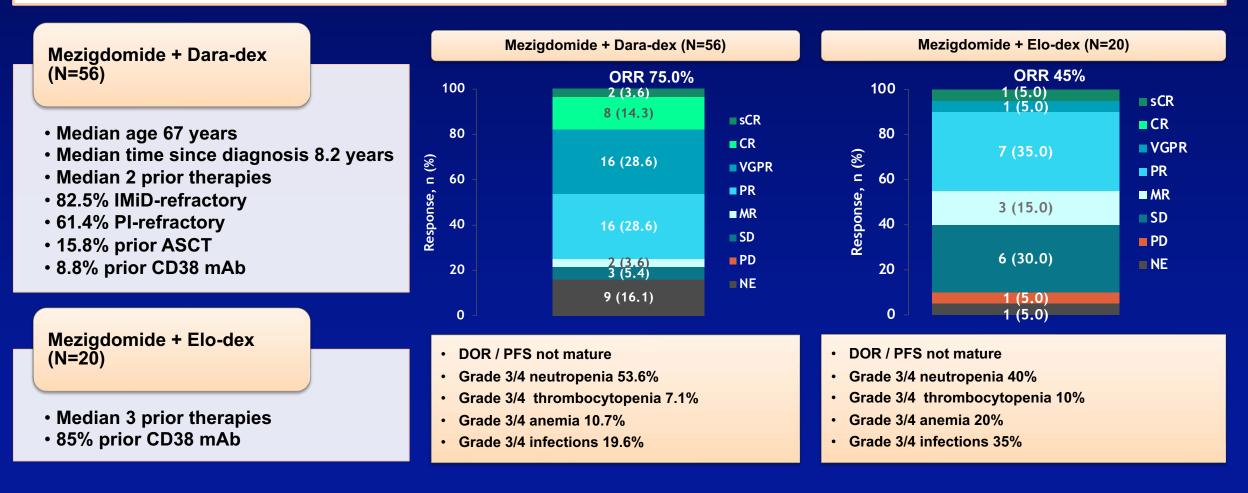
	Mezigdomide + Vd (N=28)		Mezigdomide + Vd (N=28, dose escalation)		(1.0	Mezigdom mg, N=38 /	ide + Vd 0.6 mg, N=	11)	Mezigo	domide + Kd (N=27)	
	<ul> <li>•42.9% high-risk cytogenetics</li> <li>•Median 3 prior therapies</li> <li>•82.1% R-refractory</li> <li>•50.0% PI-refractory</li> </ul>	100	ORR 75.0% 4 (14.3)	sCR	100 -	ORR 84.2% 3 (7.9) 4 (10.5)	3	<sup>%</sup> ■ sCR ■ CR	100		sCR VGPR
L	<ul> <li>•50.0% CD38 mAb-refractory</li> <li>•Median duration of treatment: 12.5 cycles</li> </ul>	80 - ⊗ ⊑ 60 -	1 (3.6) 6 (21.4)	CR VGPR	80 - (%) 1 60 -	17	(27.3)	■ VGPR ■ PR	80 - (%) ⊂ 60 -	8	■ PR ■ MR ■ SD
	Mezigdomide + Vd 1.0mg (N=38) / 0.6 mg (N=11) •53.1% high-risk cytogenetics •Median 1 prior therapy	Gesponse, 40	10 (35.7)	PR MR	u <sup>6</sup> 0 - 40 - 40 -	(44.7)	6 (54.5)	■ MR ■ SD ■ PD	L <sup>6</sup> esbourse <sup>,</sup>		PD NE
	•63.3% R-refractory •16.3% PI-refractory •34.7% CD38 mAb-refractory	<u>ළ</u> 20 -	1 (3.6) 5 (17.9)	SD PD NE	ළ 20 -	8 (21.1) 1 (2.6)	1 (9.1)	■ NE	ີ <u>ຂ</u> 20 -	(40.7) 2 (7.4)	
	•Median duration of treatment: 15 cycles	0	1 (3.6)		0 -	3 (7.9) 1 (2.6) 1 (2.6)	1 (9.1)		0	1 (3:7)	
	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	• M • G • G • G	ledian DOR 10.9 months ledian PFS 11.2–13.4 months irade 3/4 neutropenia 35.7% irade 3/4 thrombocytopenia irade 3 anemia 14.3% ifections 71.4% (Grade 3/4 1 irade 3/4 pneumonia 10.7%	<ul> <li>Median DOR 19.4 months</li> <li>Median PFS 16.6 / 20.8 months</li> <li>Grade 3/4 neutropenia 63.3%</li> <li>Grade 3/4 thrombocytopenia 26.5%</li> <li>Grade 3 anemia 6.1%</li> <li>Infections 79.6% (Grade 3/4 32.7%)</li> <li>Grade 3/4 pneumonia 22.4%</li> </ul>			<ul> <li>Median PF</li> <li>Grade 3/4</li> <li>Grade 3/4</li> <li>Grade 3/4</li> <li>Infections</li> </ul>	DR 11.9 months S 11.7–13.8 months neutropenia 44.4% thrombocytopenia anemia 14.8% 70.4% (Grade 3/4 3 pneumonia 3.7%	14.8%		

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.

## CELMoD triplets for RRMM Mezigdomide + Dara-dex or Elo-dex



#### CC-92480-MM-002 Phase 1/2 Study: Mezigdomide + Dara-dex / Elo-dex<sup>1</sup>



## CELMoD triplets for RRMM 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)	_	Mezi-dex + Taz (N=16, dose escalation)			ezi-dex + BMS-98615 =20, dose escalation			Mezi-dex + Tram (N=20, dose escalation)
<ul> <li>•31.3% high-risk cytogenetics</li> <li>•Median 5 prior lines</li> <li>•68.8% prior T-cell redirecting thera</li> </ul>	100	ORR 50.0% 1 (6.3)		100	ORR 35.0% 1 (5.0)	sCR	100 -	ORR 75.0% 1 (5.0)
•87.5% CD38 mAb-refractory •81.3% triple-class refractory	80 -	4 (25.0)	sCR CR	80 - %	6 (30.0)	■ VGPR ■ PR	80 - %	■ VGPR 8 ■ PR (40.0) ■ MR
Mezi-dex + BMS-986158 (N=20)	<u> </u>	3 (18.8)	■ VGPR ■ PR	c 60 -	1 (5.0)	■ MR ■ SD	⊂ 60 -	SD D NE
•30.0% high-risk cytogenetics •Median 5 prior lines •60.0% prior T-cell redirecting thera	- 04 Response,	1 (6.3) 3 (18.8)	■ MR ■ SD	- 40 -	8 (40.0)	PD NE	Response	6 (30,0)
•85.0% CD38 mAb-refractory •75.0% triple-class refractory	20 - 0 -	4 (25.0)	PD NE	20 -	4 (20.0)		20 - 0 -	5 (25.0)
Mezi-dex + Tram (N=20)		edian DOR not reached			DOR not reached			an DOR 6.5 months
<ul> <li>•15.0% high-risk cytogenetics</li> <li>•Median 4 prior lines</li> <li>•45.0% prior T-cell redirecting therapy</li> <li>•90.0% CD38 mAb-refractory</li> <li>•90.0% triple-class refractory</li> </ul>	• Gi • Gi • Gi • In	edian PFS 6.7 months rade 3/4 neutropenia 50.0% rade 3/4 thrombocytopenia rade 3 anemia 12.5% fections 68.8% (Grade 3/4 2 rade 3/4 pneumonia 12.5%	6.1%	<ul> <li>Grade</li> <li>Grade</li> <li>Grade</li> <li>Grade</li> <li>Infection</li> </ul>	PFS 4.6 months 3/4 neutropenia 65.0 3/4 thrombocytoper 3 anemia 35.0% ons 50.0% (Grade 3/4 3/4 pneumonia 5.0%	iia 40.0% 15.0%)	<ul> <li>Grad</li> <li>Grad</li> <li>Grad</li> <li>Grad</li> <li>Infec</li> </ul>	an PFS 8.7 months le 3/4 neutropenia 80.0% le 3/4 thrombocytopenia 15.0% le 3/4 anemia 15.0% ctions 85.0% (Grade 3/4 25.0%) le 3/4 pneumonia 5.0%



## CELMoD doublets for RRMM + NDMM Iberdomide + dex

#### CC-220-MM-001: Iberdomide-dex expansion cohorts<sup>1–4</sup>

#### Cohort D (N=107)<sup>1,2</sup>

- •29.9% high-risk cytogenetics
- Median 6 prior therapies
- 100% IMiD-refractory
- •97.2% PI-refractory
- •100% CD38 mAb-refractory
- •97.2% triple-class refractory
- Median duration of treatment: 4 cycles

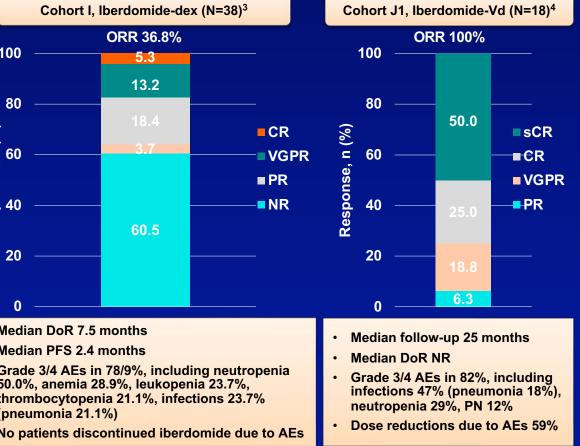
#### Cohort I (N=38, BCMAexposed)<sup>3</sup>

- •31.6% high-risk cytogenetics
- •Median 7 prior therapies
- •100% triple-class exposed
- •100% exposed to BCMA-targeted therapy: 36.8% prior CAR T cell therapy, 34.2% prior ADC, 23.7% prior T-cell engager
- •Median duration of treatment: 3.5 cycles

#### Cohort J1 (N=18, NDMM)

•Median age 77.5 years•61% high-risk cytogenetics

C C	Cohort D, Iberdomide (N=107) <sup>1,2</sup>	e-dex	Coh	ort I, Ibe
100	ORR 26.2% 0.9 7.5		100 —	0
80 ——	17.8	sCR	80 ——	
(%)	10.3		(%	
(%) 60 40 20 0	43.0 14.0 6.5	VGPR PR MR SD NE	(%) u <sup>(</sup> əsuodsə u (%) u	
<ul> <li>Median P</li> <li>Median C</li> <li>Grade 3/4 28.0/0%, 1</li> </ul>	oR 7.0 months FS 3.0 months S 10.4 months neutropenia 25.2/19 hrombocytopenia 6 s 24.3/2.8% (COVID-	.5/15.0%,	<ul> <li>Median Dol</li> <li>Median PFS</li> <li>Grade 3/4 A 50.0%, aner thrombocyt (pneumonia</li> <li>No patients</li> </ul>	5 2.4 mo Es in 78 mia 28.99 topenia 2 a 21.1%)



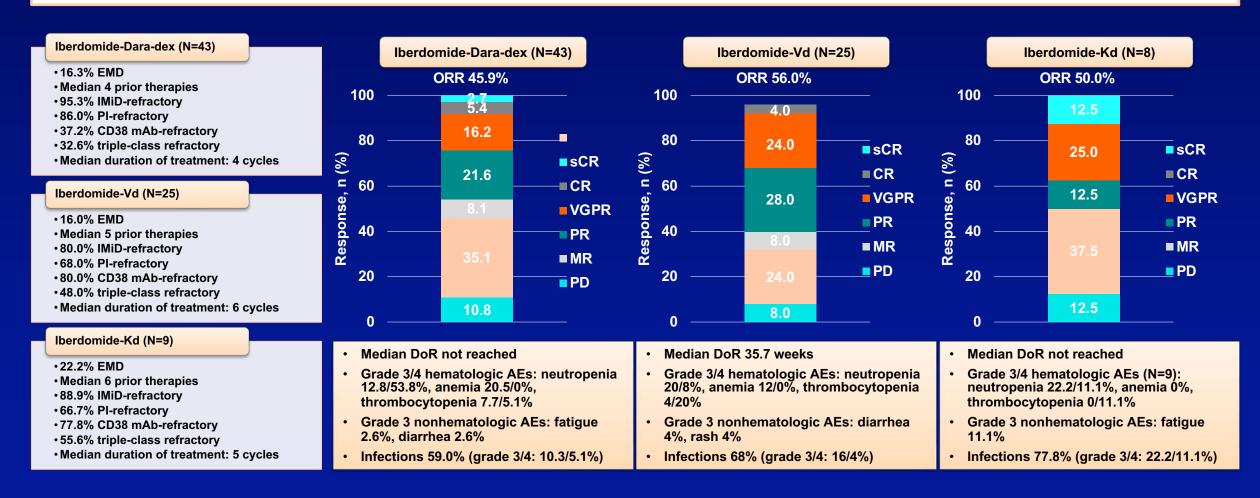
2025 AS

ANNUAL MEETING

1. Lonial S, et al. Blood 2021;138(suppl 1):abstract 162. 2. Lonial S, et al. Lancet Haematol 2022;9(11):e822–32. 3. Lonial S, et al. Blood 2022;140(suppl 1):abstract 1918. 4. White D, et al. J Clin Oncol 2025;43(16\_supplement):7532.

## CELMoD triplets for RRMM Iberdomide + Dara-dex, Vd, or Kd

#### CC-220-MM-001: Iberdomide + Dara-dex, Vd, or Kd<sup>1</sup>

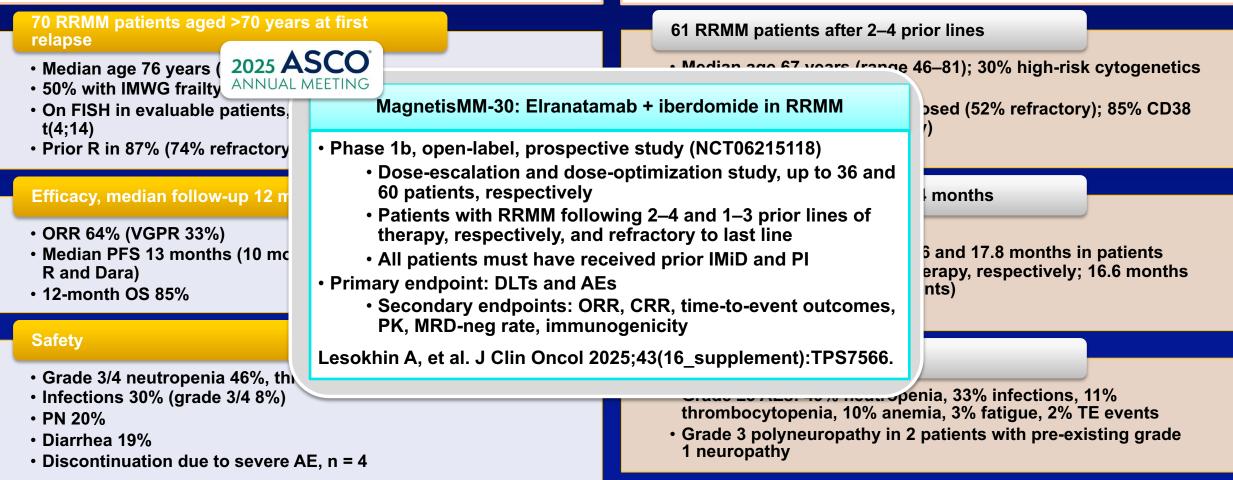


#### 1. Lonial S, et al. HemaSphere 2021;5(S2):49–50, abstract S187.

## CELMoD triplets for RRMM Iberdomide + Ixa-dex or Cy-dex

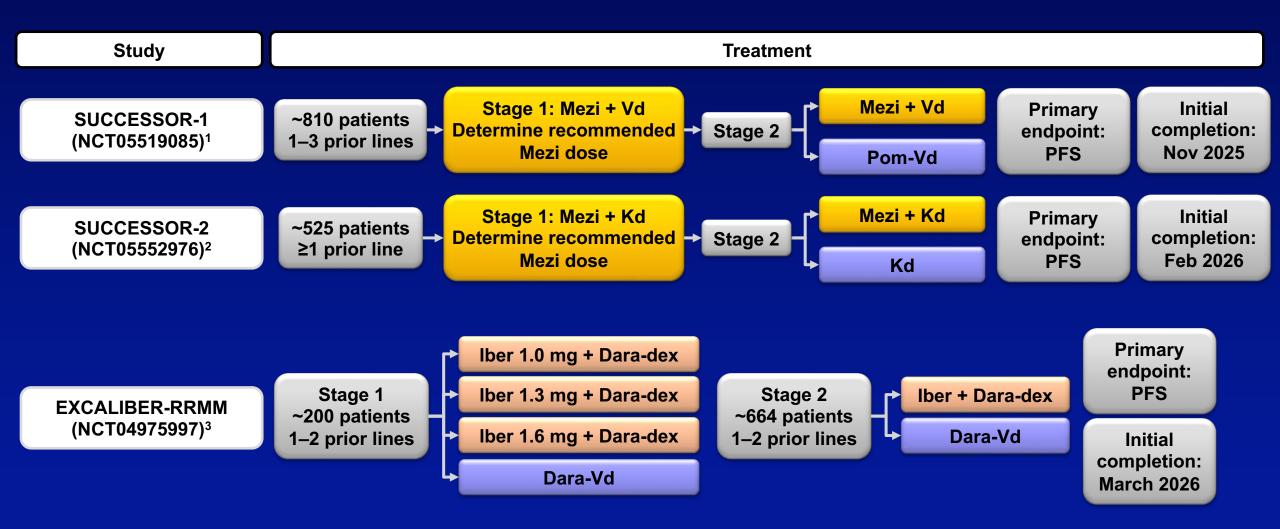
#### Iberdomide + Ixa-dex as all-oral 2nd line therapy for RRMM (IFM Phase 2 I2D study)<sup>1</sup>

#### Iberdomide + Cy-dex in RRMM (Phase 2 ICON study)<sup>2</sup>



1. Touzeau C, et al. HemaSphere 2024;8(S1):1621–2. 2. Korst CLBM, et al. HemaSphere 2024;8(S1):1589–90.

## Phase 3 studies of CELMoD triplets in 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; doi: 10.1080/14796694.2025.2501920.

## **Conclusions and Future Directions**

#### Belantamab mafodotin re-emerging as potential treatment option for RRMM

- Positive findings from two phase 3 trials of belantamab mafodotin in RRMM<sup>1,2</sup> suggesting new possible opportunities for belantamab mafodotin-based regimens in this setting
- Under review for re-approval at the US FDA, EU EMA, and elsewhere
- Novel triplet and quadruplet combinations demonstrating substantial efficacy in RRMM
- Challenges include management of ocular toxicity and integration with other BCMA-targeted T-cell engaging therapies in the RRMM treatment algorithm<sup>3</sup>
- Building on belantamab mafodotin: next-generation ADCs with novel targets also emerging

Phase 2 studies and ongoing Phase 3 trials of CELMoDs – Mezigdomide and Iberdomide – in RRMM

- Encouraging activity of Mezigdomide<sup>4</sup> and Iberdomide<sup>5</sup> in heavily pretreated RRMM with numerous partner drugs/drug classes addressing an
  urgent unmet medical need
- Multiple CELMoD combination strategies currently under investigation in RRMM e.g. SUCCESSOR-1, SUCCESSOR-2, EXCALIBER
- Oral agents with potential to enhance activity of immune-based therapy and ease of real-world application<sup>6</sup>
- Importance of optimizing use and treatment sequencing of CELMoDs in the context of immune therapies, with studies ongoing

#### Increasingly busy novel therapeutic landscape

- Large number of novel therapies and potential targets resulting in an increasingly busy landscape
- Development of novel therapies within the context of huge progress with immunotherapies (CAR Ts, BsAbs)<sup>7,8</sup>
- Challenging fiscal environment
- Importance of optimizing the use of all available and emerging treatment options and novel targets to improve patient outcome critical importance of patient subgroups, and immune exhaustion making small molecular approaches additionally important

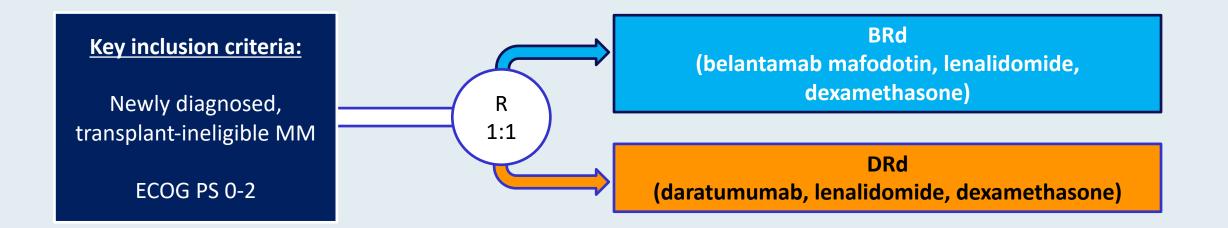
1. Hungria V, et al. N Engl J Med 2024;391(5):393–407. 2. Dimopoulos MA, et al. N Engl J Med 2024;391(5):408–21. 3. Rees MJ, Kumar S. Leuk Lymphoma 2024;65(3):287–300. 4. Richardson PG, et al. N Engl J Med 2023;389(11):1009–22. 5. Lonial S, et al. Lancet Haematol 2022;9(11):e822–32. 6. Liu Y, et al. Exp Rev Hematol 2024;17(8):445–65. 7. Rodriguez-Otero P, et al. Lancet Oncol 2024;25(5):e205–16. 8. Martino M, et al. Expert Rev Hematol 2024;17(7):375–90.

## Appendix



DREAMM-10 Trial: Phase III Study of Belantamab Mafodotin with Lenalidomide and Dexamethasone (BRd) versus Daratumumab with Lenalidomide and Dexamethasone (DRd) in Transplant-Ineligible Newly Diagnosed MM

Trial identifier: NCT06679101 Estimated enrollment: 520





Lonial S et al. ASCO 2025; Abstract TPS7567; www.clinicaltrials.gov. NCT06679101. Accessed May 2025.

## Agenda

## **Introduction: ASCO 2025 Showstoppers**

Module 1: Up-Front Treatment of Multiple Myeloma (MM) – Survey Questions

Module 2: Emerging Novel Therapies for Relapsed/Refractory (R/R) MM – Faculty Presentation

Module 3: Emerging Novel Therapies for R/R MM – Survey Questions

**Module 4:** Current Management of R/R MM – Faculty Presentation

**Module 5:** Current Management of R/R MM – Survey Questions

Module 6: ASCO and EHA 2025



- I need an update on the trials, I know nothing
- Would like to learn
- Do you see belantamab being used as part of first-line treatment in the future?



- Based on the latest Phase III data, in what clinical scenarios would belantamab mafodotin in combination therapy be preferable to bispecific antibodies in relapsed/refractory settings?
- Which is the best partner for belantamab and which is the best dosing schedule?
- How are you planning to space belamaf doses once it's approved DREAMM-8 protocol and beyond?



- How do community providers manage the occular toxicities of belantamab when local ophthalmologists have limited experience dealing with these side effects?
- I am only informed because my wife is an ophthalmologist, but in general how often is screening done and can an optometrist do it?



- In practice, it is very difficult to get patients to do their ocular screenings how do investigators get their patients (not on trial, where there is a lot of support) to the eye specialist and communicate what needs to be done to clear for therapy? The eye specialist has no knowledge of the therapy, and communication is very challenging between providers because it goes through multiple levels of phone trees and providers.
- Would you be comfortable giving belantamab if you did not have rapid access to optho?



## Questions from General Medical Oncologists — CELMoDs

• What do you see as the future role of iberdomide and mezigdomide? How do they differ from lenalidomide and pomalidomide?



## Agenda

## **Introduction: ASCO 2025 Showstoppers**

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**Module 5:** Current Management of R/R MM – Survey Questions

Module 6: ASCO and EHA 2025



## Current Management of Relapsed/Refractory (R/R) Multiple Myeloma (MM)

Ajay K Nooka, MD, MPH Professor, Department of Hematology and Medical Oncology Director, Myeloma Program Associate Director of Clinical Research Winship Cancer Institute Emory University School of Medicine Atlanta, Georgia Research database documenting the effectiveness of idecabtagene vicleucel (ide-cel) and ciltacabtagene autoleucel (cilta-cel) in patients with heavily pretreated MM

- Chimeric antigen receptor T-cell (CAR-T) therapies, idecabtagene vicleucel (IC) and ciltacabtagene autoleucel (CC) are approved for specific indications in RRMM patients.
- Comparative real-world (RW) efficacy data are limited.
- Evaluated overall survival (OS) and time to next treatment (TTNT) for IC versus CC in a RW setting using the TriNetX, a global RW data platform, providing insights to inform therapeutic decision-making.
- Adult RRMM pts (ICD-10 code C90.0) treated with IC (n=485) or CC (n=392) between 2021 and 2024 were included in analysis.

Khan E, Ilyas R, Jin M, Ramesh N, Mewawalla P, Sadashiv S, et al. Comparative efficacy of idecabtagene vicleucel and ciltacabtagene autoleucel in relapsed/refractory multiple myeloma: Real-world analysis of overall survival and time to next treatment. Journal of Clinical Oncology. 2025;43(16\_suppl):e19532-e.

# Propensity score matching with 37 variables (demographic, patient and disease characteristics) balanced cohorts

Characteristic	Ide-cel (IC) (252)	Cilta-cel (CC) (252)	P-value
Age at CAR-T (mean +/-SD yrs)	65.3 +/-9.4	65.2 +/-9.5	0.94
Female vs Male (%)	42 vs 58	44 vs 56	0.65
White and African American race (%)	76 vs 15	76 vs 17	1.0/0.46
Bortezomib/Carfilzomib/Ixazomib (%)	37/28/8	38/30/8	0.93/0.62/0.87
Lenalidomide/Pomalidomide/Thalidomide (%)	50/44/8	51/45/7	0.72/0.86/0.50
Daratumumab/Isatuximab/Elotuzumab (%)	36/4/6	36/4/6	0.85/1.0/0.71
Belantamab/Teclistamab/Talquetamab (%)	4/4/4	4/4/4	1.0/1.0/1.0
Elevated LDH (>220U; %)	75	75	0.92
Albumin ≥3.5 g/dL/ β2-microglobulin ≥5.5 mg/L	95/15	95/15	0.69/1.0

Khan E, Ilyas R, Jin M, Ramesh N, Mewawalla P, Sadashiv S, et al. Comparative efficacy of idecabtagene vicleucel and ciltacabtagene autoleucel in relapsed/refractory multiple myeloma: Real-world analysis of overall survival and time to next treatment. Journal of Clinical Oncology. 2025;43(16\_suppl):e19532-e.

- Median follow up (f/u) was 14.2 months for IC and 8.5 months for CC.
- Median OS was not reached (NR) in either group.
  - 48 patients in IC and 32 patients in CC died during f/u.
  - Estimated 2-year survival probabilities IC vs CC: 77% vs 73% (HR: 1.051; 95% CI: 0.636–1.734; p=0.847).
- Median TTNT was 17.7 months for IC and NR for CC.
  - 118 pts in IC and 58 pts in CC had a TTNT event.
  - At 2 years, TTNT probabilities IC vs CC: 36% vs 52% (P<0.0001; HR for CC vs IC: 0.60; 95% CI: 0.44-0.83).</li>
- In this RW analysis, CC showed improved durability in delaying subsequent therapy compared to IC.
- This advantage did not translate into improved OS, likely from shorter follow-up period.
- Differences in follow-up duration and RW data limitations, including potential missing data, may have influenced outcomes.

Khan E, Ilyas R, Jin M, Ramesh N, Mewawalla P, Sadashiv S, et al. Comparative efficacy of idecabtagene vicleucel and ciltacabtagene autoleucel in relapsed/refractory multiple myeloma: Real-world analysis of overall survival and time to next treatment. Journal of Clinical Oncology. 2025;43(16\_suppl):e19532-e.

#### Ide-cel in MM: Real world vs. Trial Data

	CIBMTR <sup>1</sup> N=821	US RWE <sup>2</sup> N=159	KarMMa <sup>3</sup> N=128
CRS - Any grade Grade 3 or higher	80% 3%	82% 3%	84% 5%
ICANS– Any grade Grade 3 or higher	28% 5%	18% 6%	18% 3%
Overall response rate	73%	84%	73%
Very good partial response rate	56%	62%	52%
Complete response rate	25%	42%	33%
Progression free survival, median	9.0 months	8.5 months	8.8 months
Median follow-up	11.6 months	6.1 months	13.3 months

Real world data: Most patients would not have met trial eligibility criteria

75% in the multi-center US MM consortium study did not meet eligibility criteria

CIBMTR study: 77% had significant comorbidities

#### Cilta-cel in MM: Real world vs. Trial Data

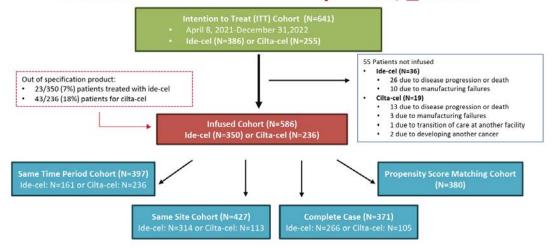
	US RWE <sup>1</sup> N=236	CARTITUDE-1 <sup>2-4</sup> N=97
CRS - Any grade; grade $\geq 3$	75%; 5%	95%; 4%
ICANS— Any grade; grade $\geq$ 3	14%; 4%	17%; 2%
Delayed neurotoxicity Parkinsonism Cranial nerve palsy	10% 2% 5%	12% 6%
Non-relapse mortality	10%	6%**
Second primary malignancy	8.5%*	1 y: 7%; 2 y:16.5%
Overall response rate	89% <sup>#</sup>	98%
Complete response rate	70%#	83%
Progression free survival	1 year: 68%#	1 year : 77% <sup>2;</sup> Median: 34.9 m <sup>4</sup>

DRR, CR rate and PFS: higher in patients receiving conforming products

PM excluding non-melanoma skin cancer: 13 (5.5%); Myeloid neoplasm/acute leukemia: 3 (1.3%); T cell lymphoma: \*\*NRM in CARTITUDE-1:16 deaths due to reasons other than progression. Only 6 of 16 deaths non-myeloma relate raths attributed to citia-cel per investigator assessment (6%).

1. Sidana et al. Blood. 2025;145(1):85-97; 2. Berdeja et al. Lancet 398:314-324, 2021. 3. Martin et al. J Clin Oncol 41:1265-1274, 2023. 4. Lin et al ASCO 2023

#### Ide-cel vs Cilta-cel: Retrospective, > 4 LOT

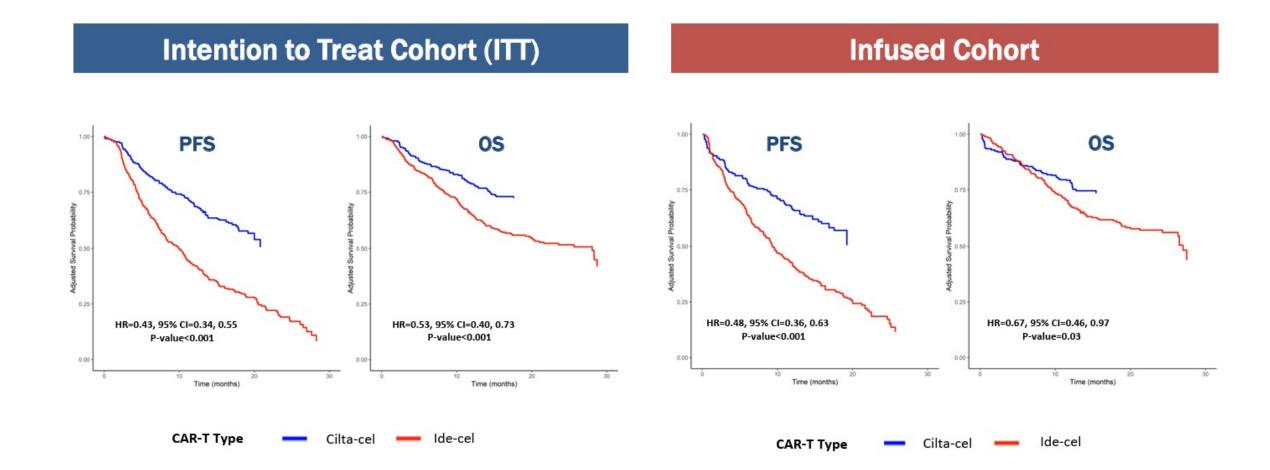


#### **Safety and Response**

		Ide-cel		Cilta-cel	
Outcomes	n (%)	OR (95% CI)	n (%)	OR (95% CI)	Р
Safety					
Any CRS	294 (84)	1.00 (Referent)	176 (75)	0.69 (0.45, 1.08)	0.10
Severe CRS (≥ Grade 3)	6 (2)	1.00 (Referent)	12 (5)	6.80 (2.28, 20.33)	< 0.001
Any ICANS	72 (22)	1.00 (Referent)	30 (14)	0.82 (0.49, 1.37)	0.4
Severe ICANS (≥ Grade 3)	14 (4)	1.00 (Referent)	8 (4)	1.54 (0.53, 4.48)	0.4
Delayed neurotoxicity	2 (0.6)	1.00 (Referent)	24 (10)	20.07 (4.46, 90.20)	< 0.001
Infections	122 (35)	1.00 (Referent)	112 (47)	2.03 (1.41, 2.92)	< 0.001
Second Malignancies (SPM)	18 (5)	1.00 (Referent)	20 (9)	1.77 (0.89, 3.56)	0.11
SPM: MDS, AML, lymphoma	6 (2)	1.00 (Referent)	4 (2)	0.94 (0.26, 3.47)	>0.9
Severe cytopenia, day 30	199 (58)	1.00 (Referent)	111 (50)	0.97 (0.68, 1.39)	0.9
Severe cytopenia, day 90	92 (31)	1.00 (Referent)	41 (25)	0.92 (0.61, 1.38)	0.7
Response					
Best ORR (≥ PR)	275 (79)	1.00 (Referent)	205 (89)	1.60 (0.90, 2.83)	0.1扣
Best CR or better	165 (47)	1.00 (Referent)	161 (70)	2.42 (1.63, 3.60)	<0.001

Models were fitted using IPTW weights

## **Cilta-cel vs Ide-cel: PFS and OS**



Hansen et al. J Clin Oncol. 2025

Published data from the Phase III KarMMa-3 and CARTITUDE-4 trials of ide-cel and cilta-cel, respectively, in earlier lines of treatment; recently presented overall survival findings from CARTITUDE-4

## KarMMa-3: Ide-cel vs SOC After 2-4 Lines

rial design	>	$\rightarrow$	$\Rightarrow$		Baseline characte	eristics
Key inclusion criteria	LDC Ide-cel Infusion		Survival	Primary endpoint	Median age	63 yrs
100-Ce	Leukapheresis	PFS follow-up: 3-month safety Follow up	safety > follow up · PFS (by	PFS (by IRC)	Median time since diagnosis	4.1 yrs
· ECOG 0-1	Optional bridging therapy			endpoints • ORR (by IRC), OS	Median prior therapies	N=3
2-4 prior regimens (IMID, PI, daratumumab)	_	el allowed after confirmed PD		Other secondary endpoints	Triple-class refractoriness	66%
Refractory to the last regimen	DPd, DVd, Int. Kd, or EPd)	Continuous SOC Isigimen ustili POD or unacceptable towofy, or withdrawal	Survival follow up	CR rate, DOR, TTR, MRD     Safety	Daratumumab refractoriness	95%
	file (26			A CONTRACT	High-risk cytogenetics	44%

Phase 3 KarMMa-3 study compared ide-cel vs SOC in R/R patients MM after 2-4 prior lines

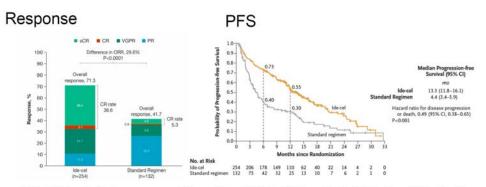
## CARTITUDE-4: Cilta-cel vs DPd/PVd After 1-3 Lines

Screening Key inclusion criteria:	Randomization	Randomization				Median age	61.5 yrs
Age ≥18 years with MM 1–3 prior LOT (including PI + IMID)	1:1 randomization	Eridging Day 1: Dita-cel	Day 1-112: Collect safety,		Median time since diagnosis	3 yrs	
Len refractory     ECOG PS x1	Stratified by:     Choice of     PVd/DPd     ISS stace	al cycle CAR+T cells/kg)	efficacy, PKPD duta every 28 days	falowap	Median prior therapies	N=2	
Key exclusion criteria: Prior CAR-T or BCMA-targeting therapy	Number of prior LOT	Aphanesis Aphanesis		Triple-class refractoriness	14.4%		
		T-cell transduction and expansion			Daratumumab refractoriness	23.1%	

Phase 3 CARTITUDE-4 compared cilta-cel vs SOC in R/R patients MM after 1-3 prior lines

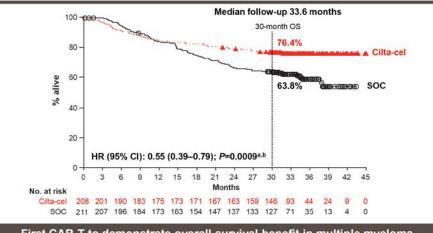
Sidana S, Martinez-Lopez J, Khan AM, Oriol A, Spencer A, Dhakal B, et al. Ciltacabtagene autoleucel (cilta-cel) vs standard of care (SOC) in patients (pts) with relapsed/refractory multiple myeloma (MM): CARTITUDE-4 survival subgroup analyses. Journal of Clinical Oncology. 2025;43(16\_suppl):7539-.

#### KarMMa-3: Response and PFS



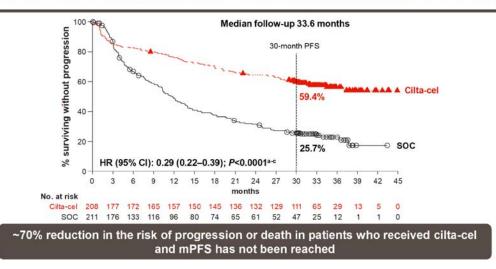
Phase 3 KarMMa-3 study compared ide-cel vs SOC in R/R patients MM after 2-4 prior lines

#### Long-Term CARTITUDE-4 Update (34 Months): Cilta-cel Significantly Improved Overall Survival

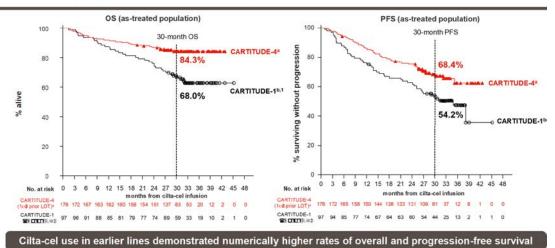


First CAR-T to demonstrate overall survival benefit in multiple myeloma

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



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



Sidana S, Martinez-Lopez J, Khan AM, Oriol A, Spencer A, Dhakal B, et al. Ciltacabtagene autoleucel (cilta-cel) vs standard of care (SOC) in patients (pts) with relapsed/refractory multiple myeloma (MM): CARTITUDE-4 survival subgroup analyses. Journal of Clinical Oncology. 2025;43(16\_suppl):7539-.

At a median follow-up was 33.6 months, the PFS and OS benefit of cilta-cel over SOC in the ITT analysis was consistent across pts with standard-risk cytogenetics and high-risk cytogenetics, defined as del(17p), t(4;14), t(14;16), or gain/amp(1q)

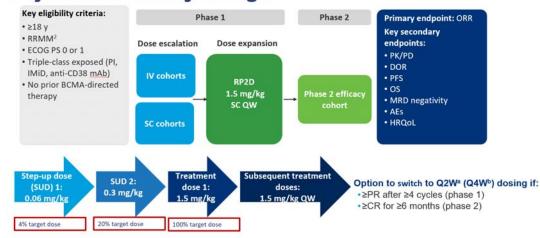
Cilta-cel, n	SOC, n	Median PFS cilta-cel, mo	Median PFS SOC, mo	HR (95% CI)	Median OS cilta-cel, mo	Median OS SOC, mo	HR (95% CI)
Standard-risk cytogenetics	69	70	NR	21	0.43 (0.26–0.72)	NR	NR
High-risk cytogenetics <sup>a</sup>	123	132	37	10	0.38 (0.27–0.52)	NR	38
del(17p)	49	43	30	9	0.40 (0.24–0.68)	NR	NR
t(4;14)	30	30	37	7	0.34 (0.17–0.68)	NR	27
gain/amp(1q)	89	107	37	10	0.39 (0.27–0.57)	NR	38
≥2 cytogenetic abnormalities <sup>ª</sup>	43	49	30	7	0.43 (0.25–0.73)	NR	23

Sidana S, Martinez-Lopez J, Khan AM, Oriol A, Spencer A, Dhakal B, et al. Ciltacabtagene autoleucel (cilta-cel) vs standard of care (SOC) in patients (pts) with relapsed/refractory multiple myeloma (MM): CARTITUDE-4 survival subgroup analyses. Journal of Clinical Oncology. 2025;43(16\_suppl):7539-.

- Comparing cilta-cel (n=21) vs SOC (n=18) in pts with extramedullary disease (EMD)
  - median PFS was 13 mo vs 4 mo (HR, 0.71 [95% CI, 0.34–1.49])
  - median OS was not reached (NR) vs 16 mo (HR, 0.61 [95% CI, 0.26–1.47])
- Comparing cilta-cel vs SOC by prior LOT
  - median PFS for 1 pLOT [Ciltacel (N=68) vs SOC (N=68)]: NR vs 17 mo (HR, 0.41 [95% CI, 0.25–0.67]), median OS NR vs NR
  - median PFS for 2 pLOT [Ciltacel (N=83) vs SOC (N=87)]: NR vs 12 mo (HR, 0.30 [95% CI, 0.19–0.49]), median OS NR vs NR
  - median PFS for 3 pLOT [Ciltacel (N=57) vs SOC(N=56)]: NR vs 8 mo (HR, 0.20 [95% CI, 0.11–0.34]), median OS NR vs 34 mo (HR, 0.49 [95% CI, 0.26–0.91])
- Compared with SOC, cilta-cel improved PFS and OS in pts with highrisk cytogenetics, suggesting it may overcome the poor prognosis associated with these high-risk features
- These data continue to support a positive benefit-risk ratio for cilta-cel in pts with lenalidomide-refractory MM as early as after first relapse

Sidana S, Martinez-Lopez J, Khan AM, Oriol A, Spencer A, Dhakal B, et al. Ciltacabtagene autoleucel (cilta-cel) vs standard of care (SOC) in patients (pts) with relapsed/refractory multiple myeloma (MM): CARTITUDE-4 survival subgroup analyses. Journal of Clinical Oncology. 2025;43(16\_suppl):7539-.

# Available efficacy and safety findings with the BCMA-directed bispecific antibodies teclistamab and elranatamab in R/R MM



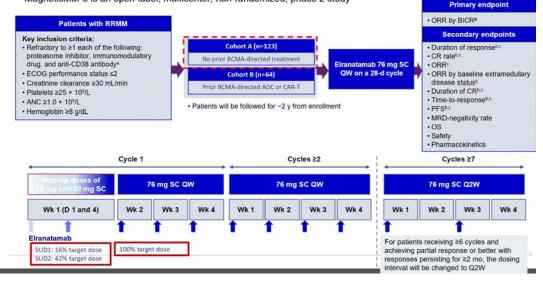
MajesTEC-1: Study Design<sup>1,a</sup>

#Phase 1, NCT03145181; phase 2, NCT04557098, AE, adverse event; ECOG PS, Eastern Cooperative Oncology Group performance status; HRQoL, health-related quality of life; IMID, immunomodulatory drug; IV, infravencus; mAb, monoclonal antibody; MRD, iminimal residual disease; PD; pharmacodynamics; PI, proteasome inhibitor; PK, pharmacokinetics; OW, weekiy; PR20, recommended phase 2 does; SC, subcutaneous.

1. Moreau P, et al. New Engl J Med 2022;387:495-505. 2. Rajkumar S, et al. Blood. 2011;117(18):4691-95.

#### **MagnetisMM-3 Study**

MagnetisMM-3 is an open-label, multicenter, non-randomized, phase 2 study



## Teclistamab and Elranatamab approvals

VOL. 387 NO. 6

## **MajesTEC-1**

ESTABLISHED IN 1812

The NEW ENGLAND JOURNAL of MEDICINE

## Teclistamab in Relapsed or Refractory Multiple Myeloma

P. Moreau, A.L. Garfall, N.W.C.J. van de Donk, H. Nahi, J.F. San-Miguel, A. Oriol, A.K. Nooka, T. Martin, L. Rosinol, A. Chari, L. Karlin, L. Benboubker, M.-V. Mateos, N. Bahlis, R. Popat, B. Besemer, J. Martínez-López, S. Sidana, M. Delforge, L. Pei, D. Trancucci, R. Verona, S. Girgis, S.X.W. Lin, Y. Olyslager, M. Jaffe, C. Uhlar, T. Stephenson, R. Van Rampelbergh, A. Banerjee, J.D. Goldberg, R. Kobos, A. Krishnan, and S.Z. Usmani

AUGUST 11, 2022

MagnetisMM-3

nature medicine

Article

https://doi.org/10.1038/s41591-023-02528-9

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## Elranatamab in relapsed or refractory multiple myeloma: phase 2 MagnetisMM-3 trial results

eceived: 18 June 2023	
ccepted: 1 August 2023	
ablished online: 15 August 2023	
Check for updates	

Alexander M. Lesokhin <sup>1</sup> A, Michael H. Tomasson<sup>2</sup>, Bertrand Arnulf<sup>3</sup>, Nizar J. Bahlis <sup>0</sup> <sup>4</sup>, H. Miles Prince <sup>0</sup> <sup>5</sup>, Ruben Niesvizky<sup>6</sup>, Paula Rodríguez-Otero<sup>7</sup>, Joaquin Martinez-Lopez <sup>0</sup> <sup>8</sup>, Guenther Koehne<sup>9</sup>, Cyrille Touzeau<sup>10</sup>, Yogesh Jethava<sup>11</sup>, Hang Quach<sup>12</sup>, Julien Depaus<sup>13</sup>, Hisayuki Yokoyama<sup>14</sup>, Afshin Eli Gabayan<sup>15</sup>, Don A. Stevens<sup>16</sup>, Ajay K. Nooka <sup>0</sup> <sup>17</sup>, Salomon Manier<sup>18</sup>, Noopur Raje<sup>19</sup>, Shinsuke Iida<sup>20</sup>, Marc-Steffen Raab <sup>0</sup> <sup>21</sup>, Emma Searle<sup>22</sup>, Eric Leip<sup>23</sup>, Sharon T. Sullivan<sup>23</sup>, Umberto Conte<sup>24</sup>, Mohamed Elmeliegy<sup>25</sup>, Akos Czibere<sup>24</sup>, Andrea Viqueira<sup>26</sup> & Mohamad Mohty<sup>27</sup>

EMA approval: Both teclistamab and elranatamab are indicated as monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma, who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy. FDA approval: Teclistamab and elranatamab are indicated as monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma, who have received at least four prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy.

# Key differences in study design and baseline characteristics

#### **Key differences**

#### MajesTEC-1

•≥3 prior lines of therapy Tripleclass exposed (proteasome inhibitor, immunomodulatory drug, and anti-CD38 antibody)

•ECOG PS 0 or 1

No prior BCMA-directed therapy

•Option to switch to Q2W (phase 1) or Q4W dosing (phase 2) if: •≥PR after ≥4 cycles (phase 1) •≥CR for ≥6 months (phase 2)

#### MagnetisMM-3

Refractory to ≥1 each of the following: proteasome inhibitor, immunomodulatory drug, and anti-CD38 antibody
ECOG performance status ≤2
Prior BCMA cohort (B) included
Q2W dosing if

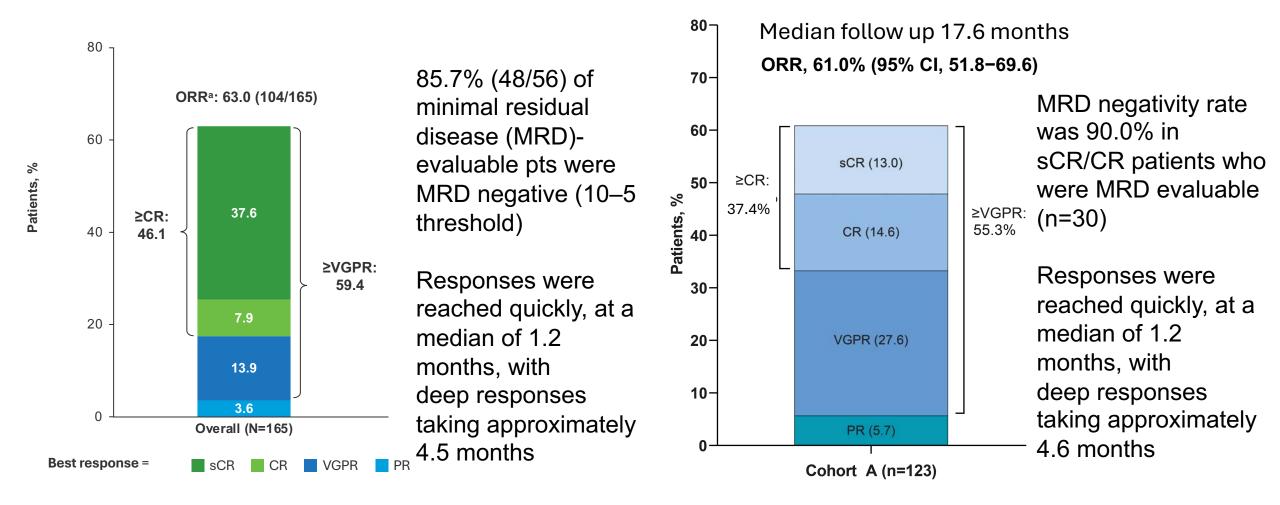
≥PR after ≥6 cycles, with responses persisting for ≥2 months

#### Similar inclusion/exclusion criteria

## **Baseline Characteristics**

	MajesTEC-1 (N=165)	MagnetisMM-3 (N=123)
Median age (range)	64 (33–84)	68 (36-89)
Males	96 (58.2)	68 (55.3)
Black	21 (12.7)	9 (7.3)
EMD	28 (17.0)	39 (31.7)
Prior lines of therapy	5 (2–14)	5 (2–22)
ISS*	52.5/35.2/12.3	22.8/55.3/15.4
High-risk cytogenetics	38 (25.7)	31 (25.2)
Triple class exposed	165 (100)	123 (100)
Penta drug exposed	116 (70.3)	87 (70.7)
Triple class refractory	128 (77.6)	119 (96.7)
Penta drug refractory	50 (30.3)	52 (42.3)
Prior stem cell transplant	135 (81.8)	87 (70.7)
Anti-CD38 refractory	148 (89.7)	118 (95.9)

## MajesTEC-1 and MagnetisMM-3: ORR

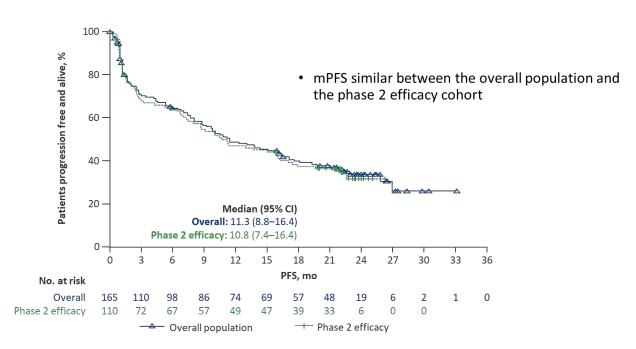


Usmani SZ, et al. Presented at ASCO; June 2–6, 2023; Chicago, IL, USA & Virtual. Poster # 8034.

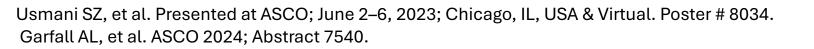
Garfall AL, et al. ASCO 2024; Abstract 7540.

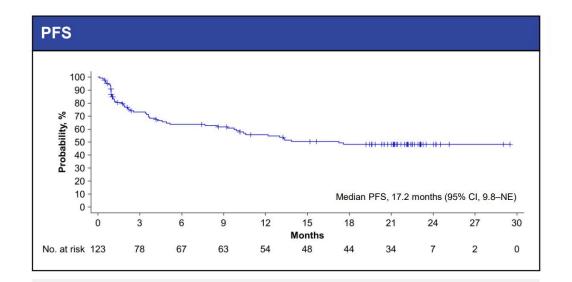
Tomasson MH, et al. ASH 2023 Blood (2023) 142 (Supplement 1): 3385.

## MajesTEC-1 and MAgnetisMM-3: PFS



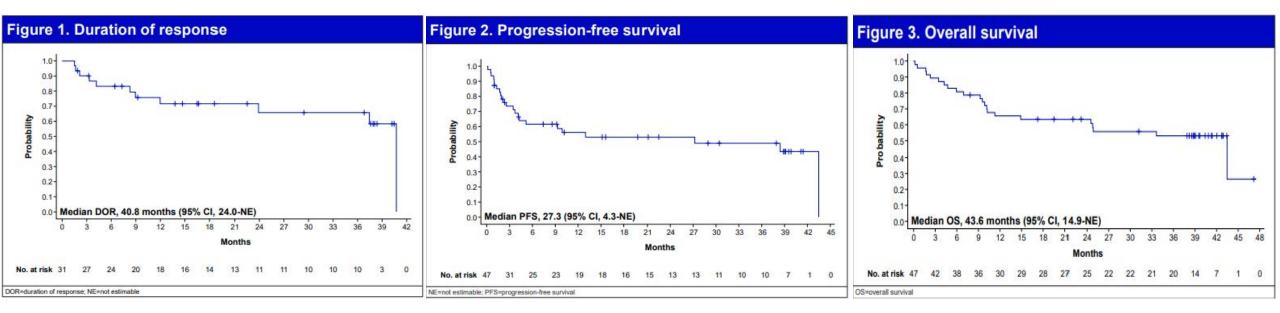
Median progression-free survival (mPFS): 11.4 months Median overall survival (mOS): 22.2 months





· Kaplan-Meier median PFS was 17.2 months

Efficacy and Safety of Less Frequent Dosing With Elranatamab in Patients With Relapsed or Refractory Multiple Myeloma: A US Subgroup Analysis From MagnetisMM-3



Among the 123 BCMA-naive patients in Cohort A, 47 were enrolled in the US

With a median follow-up of 39.6 months

Median ORR was 66.0%, median DOR was 40.8 months but may not yet be mature

Median PFS was 27.3 months

Median OS was 43.6 months but may not yet be mature

Nooka AK, Strouse CS, Larson SM, Lesokhin AM, Yanovsky AV, Vesole DH, et al. Efficacy and safety of less frequent dosing with elranatamab (ELRA) in patients with relapsed or refractory multiple myeloma (RRMM): A US subgroup analysis from MagnetisMM-3. Journal of Clinical Oncology. 2025;43(16\_suppl):7549-.

# Extended follow-up from the pivotal Phase I/II MonumenTAL-1 study of talquetamab in R/R MM

- Talquetamab (Tal) is the first and only approved anti-GPRC5D bispecific antibody (BsAb) for relapsed/refractory multiple myeloma (RRMM)
  - Extended mFU of 30–38 mo at ASCO 2025
- 3 cohorts
  - Prior TCR naïve 0.4 mg/kg weekly (QW) (n=143) 38.2 months
  - Prior TCR naïve 0.8 mg/kg every other week (Q2W) (n=154) 31.2 months
  - Prior TCR exposed 0.4 mg/kg QW or 0.8 mg/kg Q2W (n=78) 30.3 months
- ORR unchanged (QW vs Q2W vs prior TCR) 74.1% vs 69.5% vs 66.7%
- mDOR (QW vs Q2W vs prior TCR) 9.5 vs 17.5 vs 19.2 months
- mPFS (QW vs Q2W vs prior TCR) 7.5 vs 11.2 vs 7.7 months
- mOS (QW vs Q2W vs prior TCR) 34.0 vs NR vs 28.3 months
- 36-month OS rates (QW vs Q2W vs prior TCR) 49% vs 61% vs 45%

Rasche L, Schinke CD, Touzeau C, Minnema M, Donk NWCJvd, Rodríguez-Otero P, et al. Efficacy and safety from the phase 1/2 MonumenTAL-1 study of talquetamab, a GPRC5D × CD3 bispecific antibody, in patients with relapsed/refractory multiple myeloma: Analyses at an extended median follow-up. Journal of Clinical Oncology. 2025;43(16\_suppl):7528

- Most common AEs
  - CRS all grades, unchanged (QW vs Q2W) 79% vs 72.4%
  - CRS grade 2, unchanged (QW vs Q2W) 14.7% vs 17.2%
  - GPRC5D-associated AEs (taste related) (QW vs Q2W vs prior TCR) 72% vs 71.4% vs 75.6%
    - rates of dose reductions due to taste related AEs 7 vs 3.9% vs 5.1%
    - rates of discontinuation due to taste related AEs 0 vs 1.9% vs 0%
  - GPRC5D-associated AEs (skin related) (QW vs Q2W vs prior TCR) 56.6% vs 73.4% vs 64.1%
    - rates of dose reductions due to skin related AEs 3.5 vs 0.6% vs 2.6%
    - rates of discontinuation due to skin related AEs 1.4 vs 0.6% vs 0%
  - GPRC5D-associated AEs (nail related) (QW vs Q2W vs prior TCR) 55.2% vs 53.2% vs 59%
    - rates of dose reductions due to nail related AEs 0.7 vs 0.6% vs 1.3%
    - rates of discontinuation due to nail related AEs 0 vs 0% vs 0%
  - GPRC5D-associated AEs (rash related) (QW vs Q2W vs prior TCR) 39.9% vs 29.9% vs 32.1%
    - rates of dose reductions due to rash related AEs 0.7 vs 0.6% vs 0%
    - rates of discontinuation due to rash related AEs 0 vs 0% vs 0%
  - Infections, any-grade (QW vs Q2W vs prior TCR) occurred in 61% vs 71% vs 78%
  - Infections, grade 3 and 4 (QW vs Q2W vs prior TCR) occurred in 23% vs 21% vs 26%
- A new safety signal, ataxia/balance disorders, was recently identified in association with Talquetamab and had low prevalence in MonumenTAL-1
- No death reported due to Talquetamab-related AEs

Rasche L, Schinke CD, Touzeau C, Minnema M, Donk NWCJvd, Rodríguez-Otero P, et al. Efficacy and safety from the phase 1/2 MonumenTAL-1 study of talquetamab, a GPRC5D × CD3 bispecific antibody, in patients with relapsed/refractory multiple myeloma: Analyses at an extended median follow-up. Journal of Clinical Oncology. 2025;43(16\_suppl):7528

#### Agenda

#### **Introduction: ASCO 2025 Showstoppers**

Module 1: Up-Front Treatment of Multiple Myeloma (MM) – Survey Questions

Module 2: Emerging Novel Therapies for Relapsed/Refractory (R/R) MM – Faculty Presentation

**Module 3:** Emerging Novel Therapies for R/R MM – Survey Questions

**Module 4:** Current Management of R/R MM – Faculty Presentation

Module 5: Current Management of R/R MM – Survey Questions

Module 6: ASCO and EHA 2025



 I live in an area where the nearest CAR T center is 1 hour away and crosses state lines. The closest within my state is 1-1/2 hours away. What can be done for community practice to be able to give cellular therapy and to increase access?



- How should we sequence CAR T-cell therapy relative to bispecifics and other novel agents in a patient with triple-class refractory MM and rapid disease progression?
- When should we be referring for CAR T? In the second line? What should we give to prepare for CAR T in terms of regimens that optimize CAR T and control disease?



- What are the most effective real-world strategies for mitigating prolonged cytopenias and neurotoxicity in patients post-CAR T-cell therapy for MM?
- What is the incidence of CAR T-associated secondary lymphomas and are there particular subsets of patients more likely to develop this complication?



- How to decrease incidence of neurotoxicity (Parkinsonism like) AEs for patients who received ciltacabtagene autoleucel)?
- How do you view the efficacy of Anito-Cel vs. ciltacabtagene autoleucel?



- Specific considerations of long term toxicities that should be considered after 1 year of therapy
- I have one patient developed CMV infection and severe fatigue after CART. No myeloma recurrence. CMV finally cleared but remains very fatigued and depressed. Other than providing IVIG and monitoring myeloma, what should a community oncologist do for post-CART patients?
- How can the community-based oncologist assist the academic center in the management of these patients? What can we be doing better?



## Questions from General Medical Oncologists — Bispecific Antibodies

- A significant barrier is access to timely CAR T-cell therapy or bispecifics for eligible patients due to insurance delays and logistical challenges at treatment centers, which can lead to disease progression before therapy initiation.
- What is the correct sequence?
- How do teclistamab and elranatamab compare in terms of response durability and infection risk, and what patient factors influence selection between them?



### Questions from General Medical Oncologists — Bispecific Antibodies

- Given the proliferation of cellular/immunotherapies available across disease states, these are going to need to be given in the community. How can community docs team up better to be qualified and competent to choose and manage these medications?
- Have you used two different bsA molecules back-to-back (BCMA followed by GPRC5D or vice versa), and how have the outcomes been?
   I have a patient with RRMM who received BsA (Teclistamab) in the 5th line but had to be discontinued due to Grade 4 infections. For such patients with significant infection risk on 1 bsA, what do you recommend next to keep the disease in check and allow them to recover for the next line of different BsA, like Talquetamab?

#### Agenda

#### **Introduction: ASCO 2025 Showstoppers**

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**Module 5:** Current Management of R/R MM – Survey Questions

Module 6: ASCO and EHA 2025



Isatuximab (Isa) subcutaneous (SC) via an on-body delivery system (OBDS) vs Isa intravenous (IV), plus pomalidomide and dexamethasone (Pd) in relapsed/refractory multiple myeloma (RRMM): Results of the randomized, non-inferiority, phase 3 IRAKLIA study. Leleu XP et al. ASCO 2025; Abstract 7506

Belantamab mafodotin plus lenalidomide/dexamethasone in newly diagnosed intermediate-fit & frail multiple myeloma patients: Long-term efficacy and safety from the phase 1/2 BELARD clinical trial. Terpos E et al ASCO 2025; Abstract 7512

Design of the phase 3 DREAMM-10 study: Belantamab mafodotin plus lenalidomide and dexamethasone (BRd) vs daratumumab plus lenalidomide and dexamethasone (DRd) in transplant-ineligible, newly diagnosed multiple myeloma (TI-NDMM).

Lonial S et al

ASCO 2025; Abstract TPS7567

#### ASCO 2025 | ORAL ABSTRACT SESSION | JUNE 1-3



Long-term (≥5 year) remission and survival after treatment with ciltacabtagene autoleucel (cilta-cel) in CARTITUDE-1 patients (pts) with relapsed/refractory multiple myeloma (RRMM). Vorhees PM et al ASCO 2025; Abstract 7507

First-in-human study of JNJ-79635322 (JNJ-5322), a novel, next-generation trispecific antibody (TsAb), in patients (pts) with relapsed/refractory multiple myeloma (RRMM): Initial phase 1 results. Van de Donk N et al. ASCO 2025; Abstract 7505

ASCO 2025 | ORAL ABSTRACT SESSION | JUNE 1-3



#### EHA 2025 Upcoming Abstracts in MM June 12-15, 2025

**S201** Kaur G et al. Phase 2 registrational study of anitocabtagene autoleucel for relapsed and/or refractory multiple myeloma (RRMM): Updated results from iMMAGINE-1.

S203 Leleu X et al. Isatuximab subcutaneous via an on-body delivery system versus isatuximab intravenous, plus pomalidomide and dexamethasone, in relapsed/refractory multiple myeloma: The randomized phase 3 IRAKLIA study.

**S192** Jagannath S et al. Long-term (≥5 year) remission and survival after treatment with ciltacabtagene autoleucel in CARTITUDE-1 patients with relapsed/refractory multiple myeloma.

**S100** Popat R et al. First-in-human study of JNJ-79635322 (JNJ-5322), a novel, next-generation trispecific antibody, in patients with relapsed/refractory multiple myeloma: Initial phase 1 results.



#### EHA 2025 Upcoming Abstracts in MM June 12-15, 2025

**PS1793** Dimopoulos M et al. **Phase 3 DREAMM-10 study design: Belantamab mafodotin plus lenalidomide and dexamethasone vs daratumumab plus lenalidomide and dexamethasone in transplant-ineligible newly-diagnosed multiple myeloma.** 

PF733 Terpos E et al. Extended dosing schedule of belantamab mafodotin in combination with daratumumab, lenalidomide and dexamethasone in patients with newly diagnosed multiple myeloma: The phase 1/2 BELADRD study.

**PS1741** Cavo M et al **Real-world effectiveness and safety of belantamab mafodotin (belamaf)** monotherapy in patients (pts) with relapsed/refractory multiple myeloma (RRMM) treated in Europe.

**PS1752** Terpos E et al. Clinical management of belantamab mafodotin-associated ocular events: Practical guidance from the belamaf expert experience program.

PF783 Quach H et al. Belantamab for the treatment of multiple myeloma: Results from part 1 of the first-in-human phase 1/2 DREAMM-20 trial.



Consensus or Controversy? Clinical Investigators Provide Perspectives on the Current and Future Clinical Care of Patients with Metastatic Breast Cancer

> Monday, June 2, 2025 7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)

#### Faculty

Harold J Burstein, MD, PhD Javier Cortés, MD, PhD Rebecca A Dent, MD, MSc Kevin Kalinsky, MD, MS Joyce O'Shaughnessy, MD

Moderator Hope S Rugo, MD



#### **Dear Attendees,**

If you are interested in joining our Breast Cancer symposium webcast starting at 7:00 PM central time (8:00 PM ET), please use the link below to register on Zoom. THIS LINK IS ALSO POSTED IN THE ZOOM CHAT ROOM.

https://us02web.zoom.us/webinar/register/WN\_O9YZp8BaS2-uCMIWtthFg#/registration

If you have already registered for the Breast Cancer webcast, you should have received an email directly from Zoom with the viewing instructions for the webcast. If not, please use the link above to register again and you will be automatically redirected to the Zoom event.

Thank you for your participation!



## Thank you for joining us!

Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us. The survey will remain open for 5 minutes after the meeting ends.

Information on how to obtain CME credit is provided in the Zoom chat room. Attendees will also receive an email in 1 to 3 business days with these instructions.

