

Bispecific Antibodies and CELMoDs in Multiple Myeloma

Paul G Richardson, MD

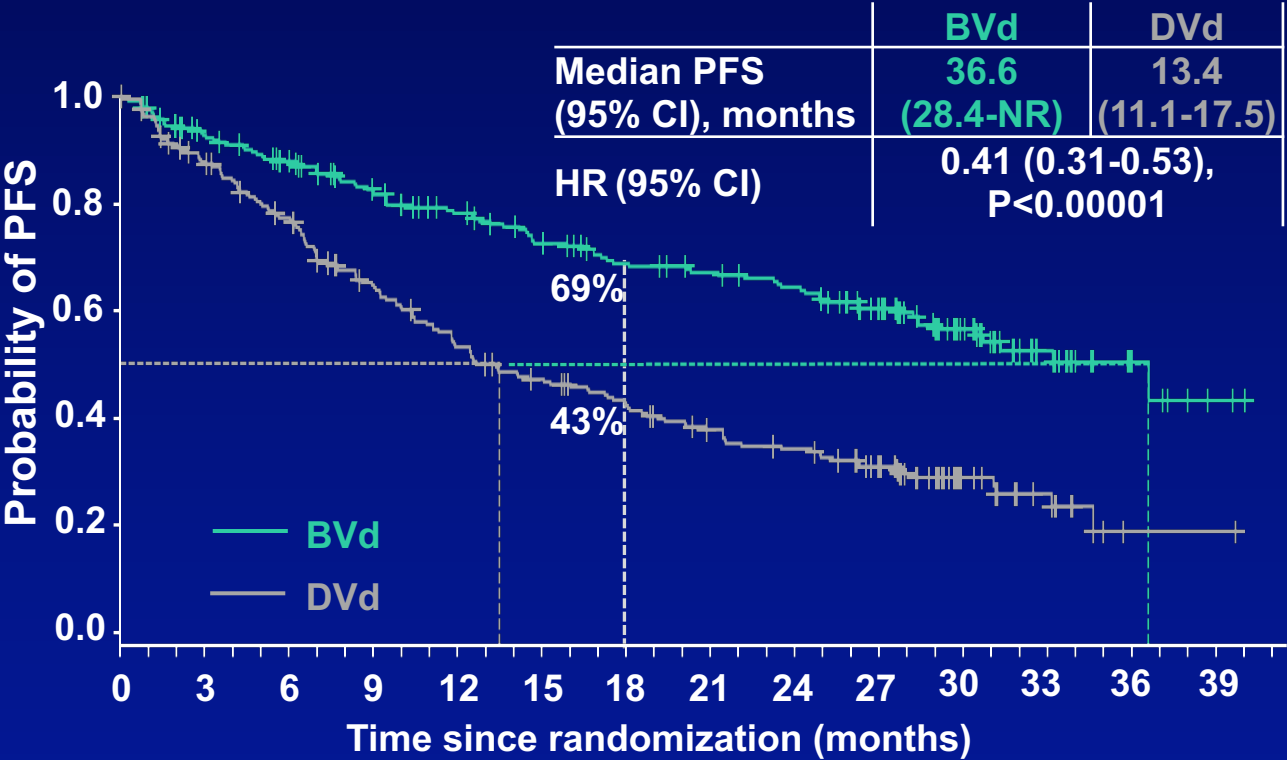
Belantamab mafodotin for early-relapse RRMM

DREAMM-7: Belantamab mafodotin + Vd vs Dara-Vd as ≥2nd-line therapy

Phase 3 DREAMM-7 study

- Belamaf+Vd x 8 cycles, then belamaf Q3W, N=243
- Dara-Vd x 8 cycles, then Dara Q4W, N=251

Patients	Belamaf-Vd, N=243	Dara-Vd, N=251
Median age, years	65	64
Age ≥75 years	15%	12%
High-risk cytogenetics	28%	27%
EMD	5%	10%
1 / 2-3 / ≥4 prior lines	51 / 36 / 12%	50 / 39 / 11%
Prior PI	90%	86%
Prior IMiD	81%	86%
R-refractory	33%	35%
Prior Dara	1%	2%
Prior ASCT	67%	69%



Outcomes

- Significant PFS benefit seen across prespecified subgroups, including R-refractory patients (HR 0.37), patients with high-risk cytogenetics (HR 0.36), and patients with prior V (HR 0.45)
- Early OS trend favoring belamaf-Vd – 18-month OS 84% vs 73% (HR 0.57)

Belantamab mafodotin for early-relapse RRMM

DREAMM-7: Belantamab mafodotin + Vd vs Dara-Vd as ≥2nd-line therapy



2026 ASCO
ANNUAL MEETING

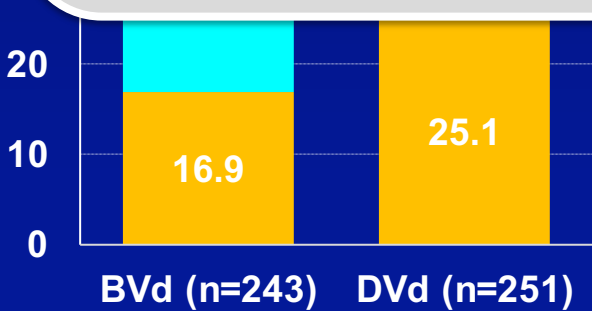
EHA2026
Congress

Sustained MRD status: Bela-Vd vs Dara-Vd

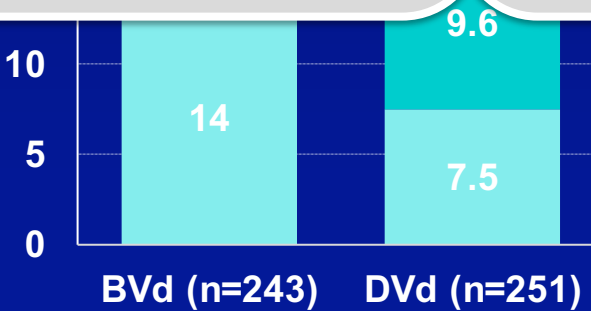
- Patients achieving **MRD-neg status**
 - Patients with CR: **70% vs 59% (10⁻⁵) / 45% vs 23% (10⁻⁶)**
 - ITT: **25% vs 10% (10⁻⁵) / 16% vs 4% (10⁻⁶)**
 - Median time to first MRD-neg status: 11.1 vs 17.0 months
- Patients achieving **sustained MRD-neg status (10⁻⁵)**
 - Patients with CR: **57% vs 42%**
 - ITT: **14% vs 4%**

Mateos M-V, et al. Blood 2025;146(Supplement 1):2265.

Patients, %



Median DOR 40.8 vs 17.8 months



Median PFS2 NR vs 33.4 months (HR 0.59)

Indirect comparisons: Bela-Vd vs SoC / Dara-Tec

- Indirect treatment comparisons of PFS and OS:
Bela-Vd vs Pom-Vd / Elo-Pom-dex / Isa-Pom-dex / ide-cel
 - PFS HRs **0.52 / 0.34 / 0.54 / 0.47**
 - OS HRs **0.60 / 0.41 / 0.35 / 0.51**
- Richter JR, et al. J Clin Oncol 2026;44(16_Suppl):7568.
- Matching adjusted indirect comparison of OS restricted mean survival time (RMST) and infections: **Bela-Vd vs Dara-Tec**
 - OS RMST ratio **1.01–1.04** at 1–3 years
 - Odds ratio for infections **0.24**

Richter J, et al. HemaSphere 2026;10(S1):PS1933.

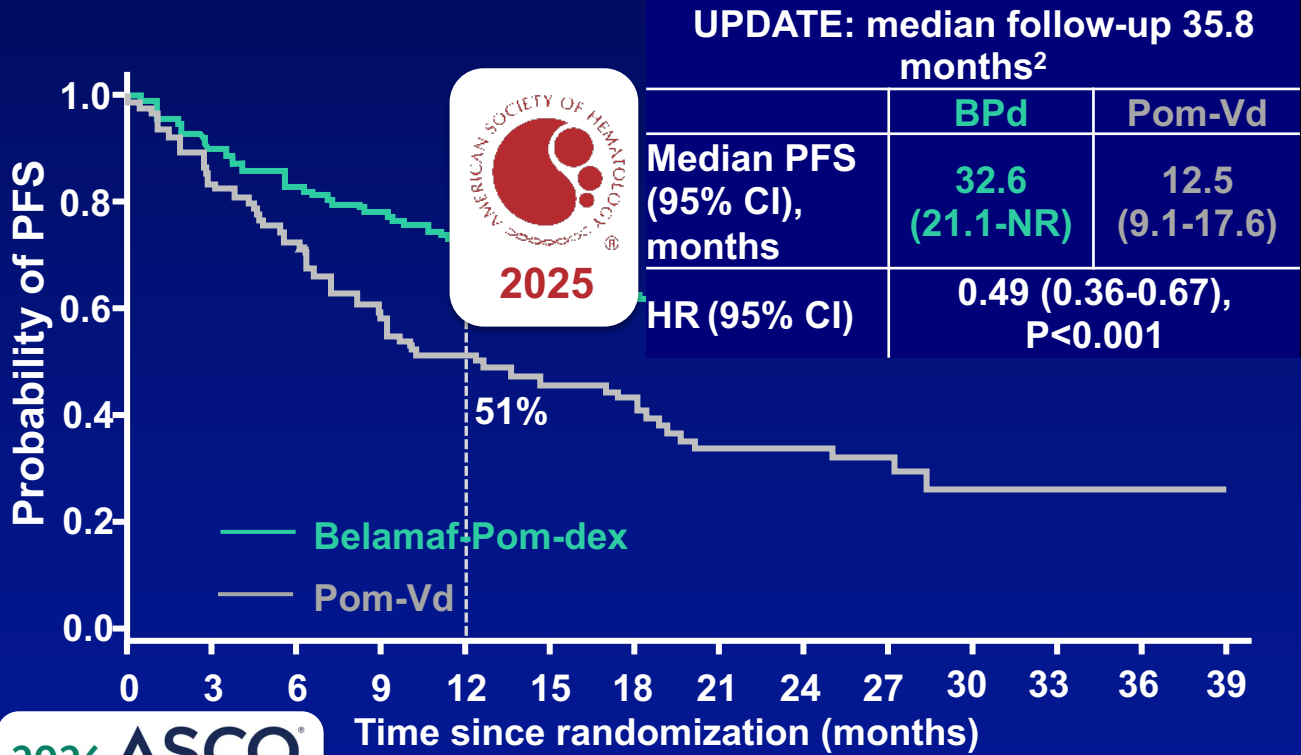
Grade ≥3	33%	20%
Pneumonia	12%	4%
Ocular AEs (Grade ≥3)	79% (34%)	29% (3%)
Vision blurred	68% (24%)	11% (<1%)
Dry eye	51% (7%)	7% (0)
Photophobia	47% (2%)	2% (0)
Eye irritation	43% (5%)	5% (0)

Belantamab mafodotin for early-relapse RRMM

DREAMM-8: Belantamab mafodotin + Pom-dex vs Pom-Vd as ≥2nd-line therapy

Phase 3 DREAMM-8 study ¹		
• Patients with ≥1 prior line, including lenalidomide • Belamaf-Pom-dex until PD/death, N=155 • Pom-Vd until PD/death, N=147		

Patients	Belamaf-Pom-dex, N=155	Pom-Vd, N=147
Median age, years	67	68
Age ≥75 years	12%	24%
High-risk cytogenetics	34%	32%
EMD	13%	7%
1 / 2 or 3 / ≥4 prior lines	53 / 35 / 12%	52 / 33 / 15%
Prior PI	90%	93%
Prior IMiD	100%	100%
IMiD-refractory	82%	76%
Prior CD38 mAb	25%	29%
CD38 mAb-refractory	23%	24%
Prior ASCT	64%	56%



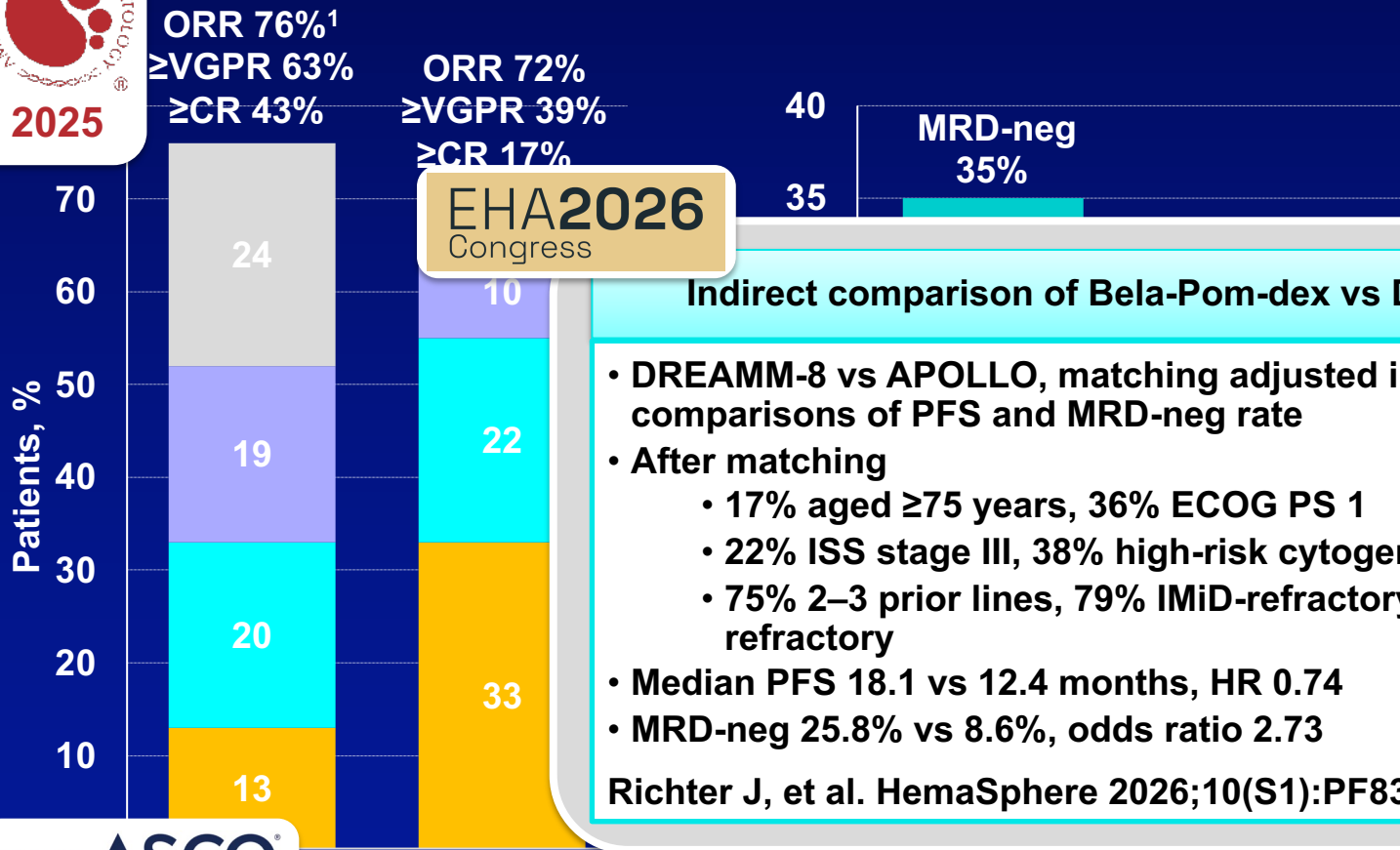
Outcomes
• Significant PFS benefit – seen across prespecified subgroups, including R-refractory patients (HR 0.45), CD38 mAb-refractory patients (HR 0.65), and patients with high-risk cytogenetics (HR 0.57)¹ • PFS2 benefit (median 47.1 vs 21.7 months, HR 0.52) seen across patient subgroups including R-refractory and CD38-exposed/refractory patients³ • Early OS trend favoring belamaf-Pom-dex – 12-month OS 83% vs 76% (HR 0.77)¹

1. Dimopoulos MA, et al. N Engl J Med 2024;391(5):408–421. 2. Trudel S, et al. Blood 2025;146(Supplement 1):2264.

3. Cengiz Seval G, et al. J Clin Oncol 2026;44(16_suppl):7566.

Belantamab mafodotin for early-relapse RRMM

DREAMM-8: Belantamab mafodotin + Pom-dex vs Pom-Vd as ≥2nd-line therapy



EHA2026 Congress

Indirect comparison of Bela-Pom-dex vs Dara-Pom-dex

- DREAMM-8 vs APOLLO, matching adjusted indirect comparisons of PFS and MRD-neg rate
- After matching
 - 17% aged ≥75 years, 36% ECOG PS 1
 - 22% ISS stage III, 38% high-risk cytogenetics
 - 75% 2–3 prior lines, 79% IMiD-refractory, 47% PI-refractory
- Median PFS 18.1 vs 12.4 months, HR 0.74
- MRD-neg 25.8% vs 8.6%, odds ratio 2.73

Richter J, et al. HemaSphere 2026;10(S1):PF832.

Safety ²	Belamaf-Pom-dex, N=155	Pom-Vd, N=147
Grade ≥3 AE	94%	76%
Related	80%	59%
to AEs	15%	12%
	63%	45%
	11%	11%
: AEs		
	24%	20%
	42%	28%
	10%	13%
	82%	68%
	49%	26%
ade ≥3 AEs, ≥10%)		
	79% (17%)	15% (0)
	61% (8%)	10% (0)
tion in eye	61% (6%)	6% (0)
	50% (4%)	9% (0)
Photophobia	44% (3%)	4% (0)
Eye pain	33% (2%)	5% (0)
Cataract	27% (6%)	10% (4%)
Reduced visual acuity	23% (13%)	6% (1%)



BPd (n=155) PVd (n=147)

24-month DOR 65% vs 40%¹
Long-term responders (PFS ≥30 months):
38% vs 15%³

BPd (n=155) PVd (n=147)

Sustained 12-month MRD-neg
≥CR 15% vs 3%¹

1. Trudel S, et al. Blood 2025;146(Supplement 1):2264. 2. Dimopoulos MA, et al. N Engl J Med 2024;391(5):408–421.
3. Dimopoulos MA, et al. J Clin Oncol 2026;44(16_suppl):7565.

Belantamab mafodotin for early-relapse RRMM

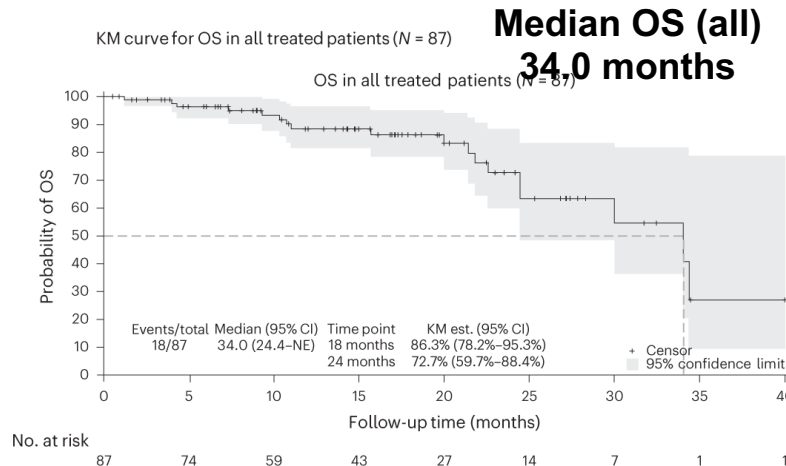
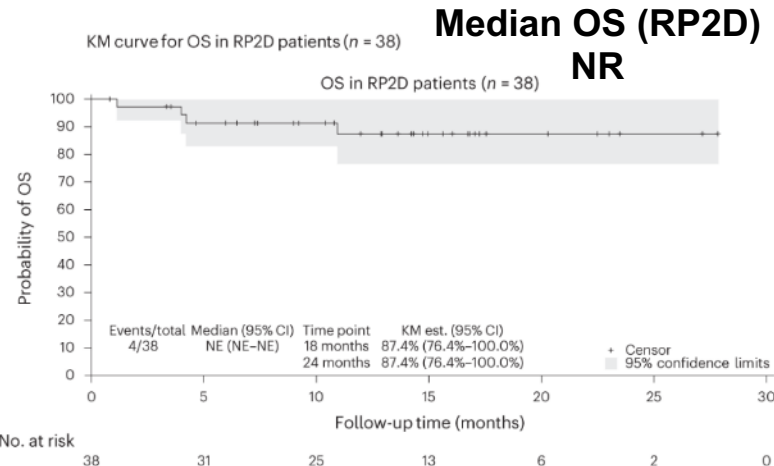
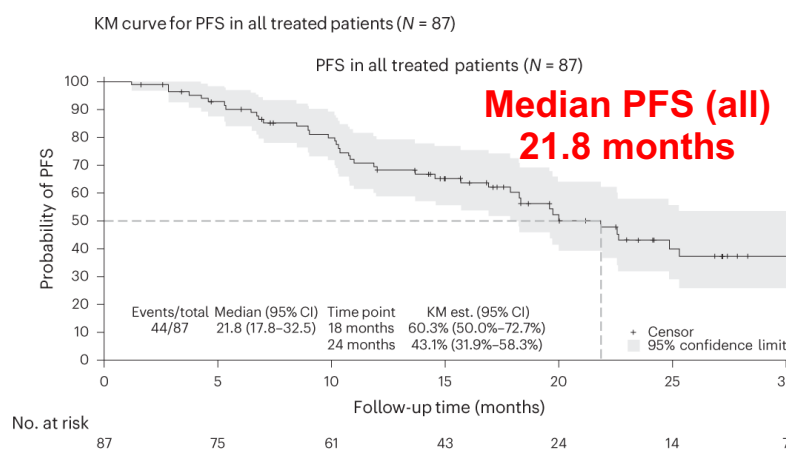
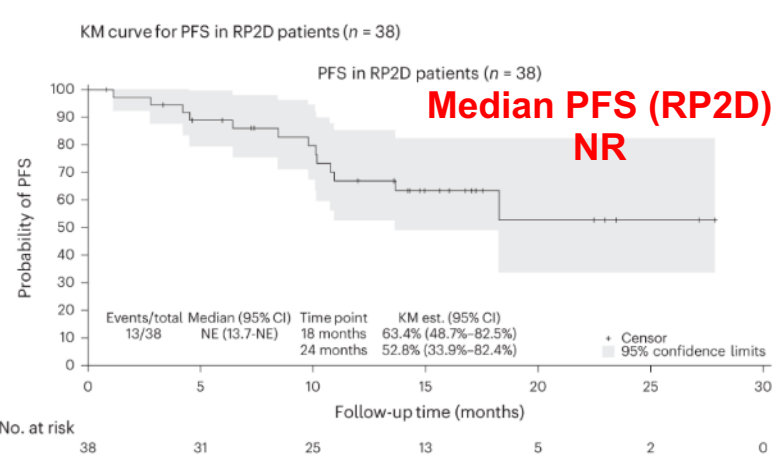
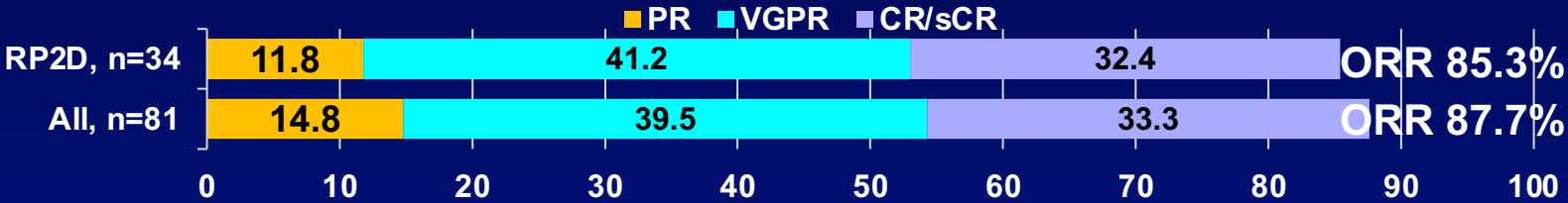
ALGONQUIN: supportive findings from a phase 1/2 study of Bela-Pom-dex

RP2D Bela 2.5 mg/kg Q8W + Pom-dex
Other Bela doses 1.9/2.5 mg/kg Q4W, 2.5 mg/kg Q12W, 2.5 mg/kg loading/split, 3.4 mg/kg split

Patients	RP2D, N=38	All, N=87
Median age, years	71	67
High-risk cytogenetics	18.5%	18.4%
Median prior lines	3	3
Prior PI	100%	100%
Prior R	100%	100%
Prior CD38 mAb	78.9%	66.7%
Prior ASCT	47.4%	69.0%
PI-refractory	84.2%	86.2%
R-refractory	94.7%	96.6%
CD38-refractory	78.9%	66.7%
Triple-class refractory	63.2%	55.2%

AE (grade 3/4), %	RP2D, N=38	All, N=87
Keratopathy	65.8 (52.6)	71.3 (55.2)
Decreased visual acuity	71.1 (39.5)	78.2 (43.7)
Fatigue	57.9 (5.3)	59.8 (11.5)
Infection	47.4 (7.9)	50.6 (20.7)
Neutropenia	39.5 (36.8)	49.4 (41.4)
Thrombocytopenia	39.5 (34.2)	43.7 (33.3)

Trudel S, et al. Nat Med 2024;30(2):543–51. Figures reproduced under Creative Commons CC BY 4.0 license.



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

Phase 1/2 study

- Belamaf + Kd
- N=70, median age 69
- 27% high-risk cytogenetics
- 77% with 2 or 3 prior lines
- 11% double-class refractory
- 9% triple-class refractory



DREAMM-20: Belantamab (naked BCMA mAb) in RRMM

- 18 patients with RRMM after ≥ 3 prior lines
 - Median age 76 years
 - 17/18 triple-class exposed, 2/18 prior BCMA-targeted therapy
- ORR 28% (2 VGPR, 3 PR)
- Treatment-related AEs 67%
 - 4 infusion-related reactions, 4 neutrophil count decreased, 2 anemia, 2 vision blurred, 2 platelet count decreased
- **No belantamab-related grade ≥ 2 corneal events**

Quach H, et al. J Clin Oncol 2025;43(16_supplement):7550.

Treatment exposure

- Median 11 cycles (range 1–38) received

Efficacy

- By end of cycle 2, ORR 83%, CR 41%
- Best ORR 83%, CR 41%
- Median follow-up 27.1 months
- Median PFS 22.6 months
- 24-month OS 70.5%

toxicity 41%, infections

ed vision, photophobia,

Grade 3 37%; Grade 4 1%)

3 51%; Grade 4 0%)

or worse (both eyes)

Real-world practical guidance for the clinical management of belantamab mafodotin-associated ocular events

Expert Experience Program

- Independent expert panel of hematologists and ophthalmologists

	Grade per KVA scale			
	Grade 1	Grade 2	Grade 3	Grade 4
Corneal examination finding(s)	Mild superficial keratopathy Mild superficial punctate keratopathy (documented worsening from baseline), with or without symptoms	Moderate superficial keratopathy Any/or a combination of: • Moderate superficial	Severe superficial keratopathy Any/or a combination of: • Severe superficial	Corneal epithelial defect Such as corneal erosion(s) or ulcer(s) ^b

Illustrative images of changes in visual acuity included in KVA scale

20/20



20/50



20/200



- Risk factors for ocular events
- Modifications of dose and/or treatment schedule
- Best practices for referral to and collaboration with an eye specialist
- Communication of benefits and risks

Grade 3	Corneal examination finding(s) • Severe superficial punctate keratopathy ^d Change in BCVA ^b • Decline from baseline by more than three lines (and Snellen Visual Acuity not worse than 20/200)	• Reduce belamaf dose ^e AND extend dose interval to at least 12 weeks and maintain at new dose interval, provided recovery to Grade 1 • If dose interval exceeds 16 weeks, further reduce belamaf dose ^e
Grade 4	Corneal examination finding(s) • Corneal epithelial defect Change in BCVA ^b • Snellen Visual Acuity worse than 20/200	• Consider treatment hold until Grade 1 • If continuing treatment with belamaf is being considered, reduce belamaf dose ^e AND extend dose interval to at least 12 weeks and maintain at new dose interval

Treatment sequencing of BCMA-targeted therapies

Feasibility of sequential use based on differing MOAs¹

BCMA-targeted ADCs

- e.g. belantamab mafodotin
- Eliminate myeloma cells via direct cell kill and through an anti-MM immune response
- Includes proposed mechanisms such as ADCC, ADCP,



T-cell-redirecting therapies post-Belamaf

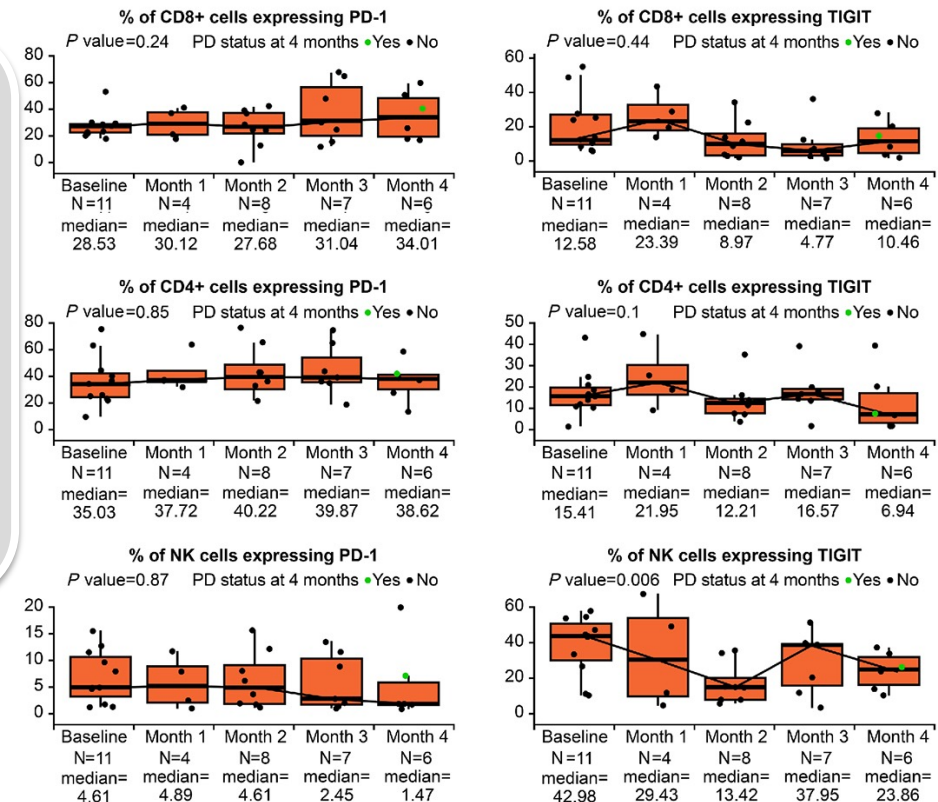
- 21 patients in DREAMM-7/DREAMM-8 received subsequent T-cell-redirecting therapies (TCRTs)
- Median 84.1 weeks from end of Belamaf to TCRT
- ORR 92%, including 46% sCR
- Median PFS on TCRTs NR (DREAMM-7 patients) and 6.6 months (DREAMM-8 patients)
- Among patients who received TCRTs immediately after Belamaf, all evaluable patients responded

Hajek R, et al. Clin Lymphoma Myeloma Leuk 2026;26(Suppl 2):S64, abstract PA-031.

- Near-baseline (s)BCMA levels at PD^{9,10}
- No evidence of T-cell exhaustion¹⁰
- No structural changes to BCMA binding site¹⁰



No impact of belantamab mafodotin on T-cell exhaustion markers PD-1 and TIGIT¹⁰



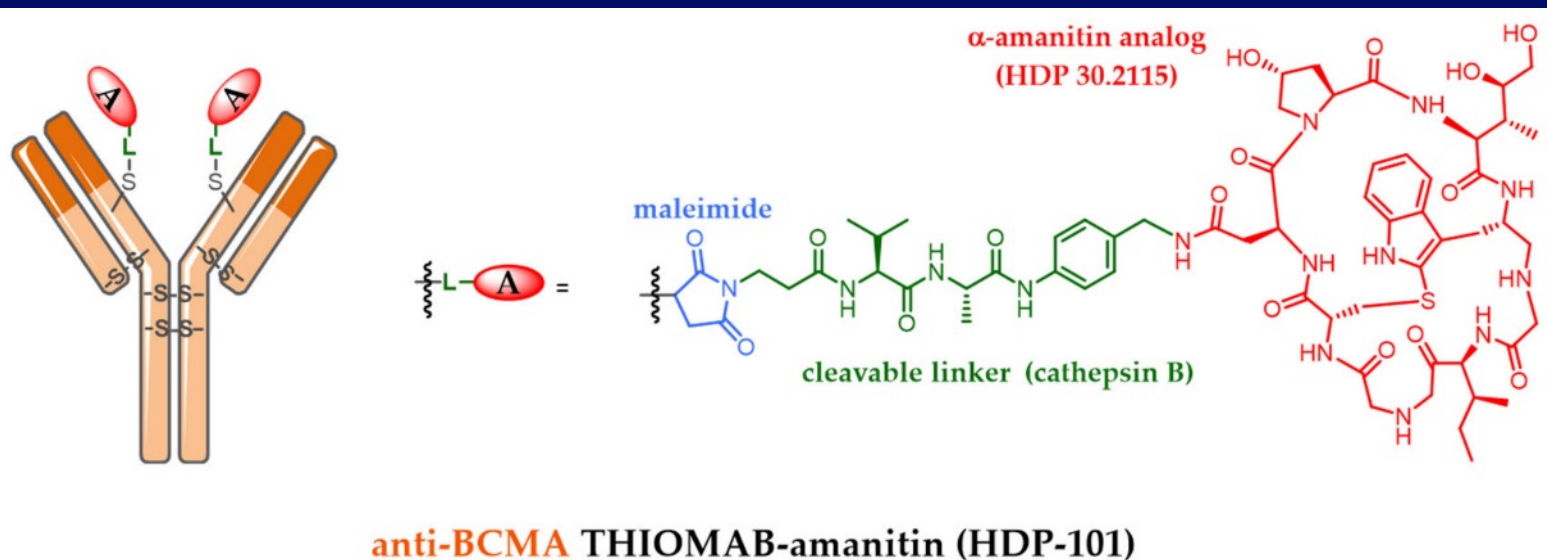
1. Quach H, et al. Blood 2024;144:2356–67. 2. Offidani M, et al. Drug Des Devel Ther 2024;18:1000000. 3. Offidani M, et al. Blood 2024;144:2356–67. 4. Rodriguez-Otero P, et al. N Engl J Med 2023;388:1002–14. 5. Berdeja JG, et al. Lancet 2021;398(10301):665–74. 6. Berdeja JG, et al. Lancet 2021;398(10301):665–74. 7. Lesokhin AM, et al. Nat Med 2023;29:2259–67. 8. Cho SF, et al. J Clin Invest 2023;133:1562–71. 9. Hengler V, et al. N Engl J Med 2024;391:393–407. 10. Musa H, et al. Haematologica 2026;111(2):665–78.

Novel BCMA-targeted ADC: HDP-101

EHA2025

Congress

June 12-15, 2025 | Milan, Italy



First-in-human phase 1/2a study⁴

34 RRMM patients

- Median age 69 years
- Median 6 prior regimens

Safety

- Grade 2–4 transient, asymptomatic thrombocytopenia in most patients at 100 µg/kg Q3W
- Reduced thrombocytopenia with 90 µg/kg Q3W + premedication, 30 µg/kg, days 1, 8, and 15, and 45 µg/kg, days 1 and 8
- No ocular toxicity to date

Efficacy

- 100 µg/kg Q3W: 1 sCR after 15 months on treatment (patient had prior BCMA CAR T and GPRC5D BsAb); 2 PRs; 1 SD (17 cycles)
- 90 µg/kg Q3W: 2 PRs, 2 SDs (n=10)

Antibody-targeted amanitin conjugate (ATAC; RNA polymerase II inhibitor)¹

ATAC mechanism based on internalization and lysosomal degradation in BCMA-positive tumor cells

HDP-101 resulted in complete tumor remissions in mice *in vivo*²

Favorable therapeutic window in mice and monkeys²

Potent anti-myeloma activity against cell lines³

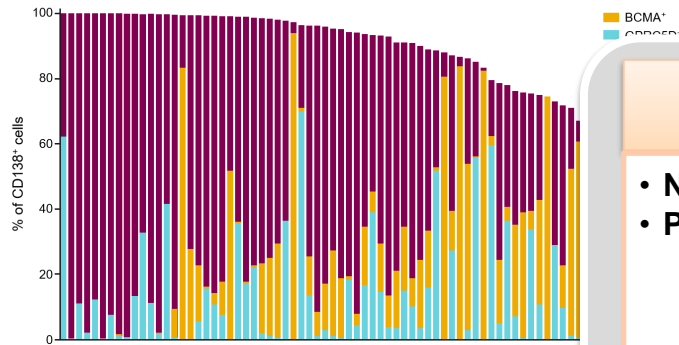
Potential activity (↑ belantamab mafodotin) in del17p MM models³

Novel ADCs for RRMM

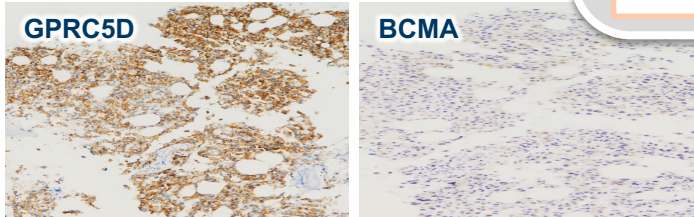
GPRC5D ADC for targeting RRMM

GPRC5D is a validated target in MM, expressed at all stages of disease^{1,2}

GPRC5D expressed in MM patient samples...



...including post-BCM.



AZD0305 is a GPRC5D-targeting ADC^{2,3}

Ongoing phase 1/2 study of AZD0305 in RRMM

- NCT06106945
- Patients with RRMM enrolled to three modules:
 - AZD0305 alone (≥ 3 prior lines)
 - AZD0305 + elranatamab (1–3 prior lines)
 - AZD0305 + Pom-dex (1–3 prior lines)
- Estimated enrolment: 226 patients
- Primary endpoints: DLTs, safety, tolerability
- Estimated primary completion date: August 2027

Rationale for GPRC5D-targeting ADC²

Activity may not rely on immune fitness in late-line patients

Potential for rapid administration

May be for use in orthogonal combination

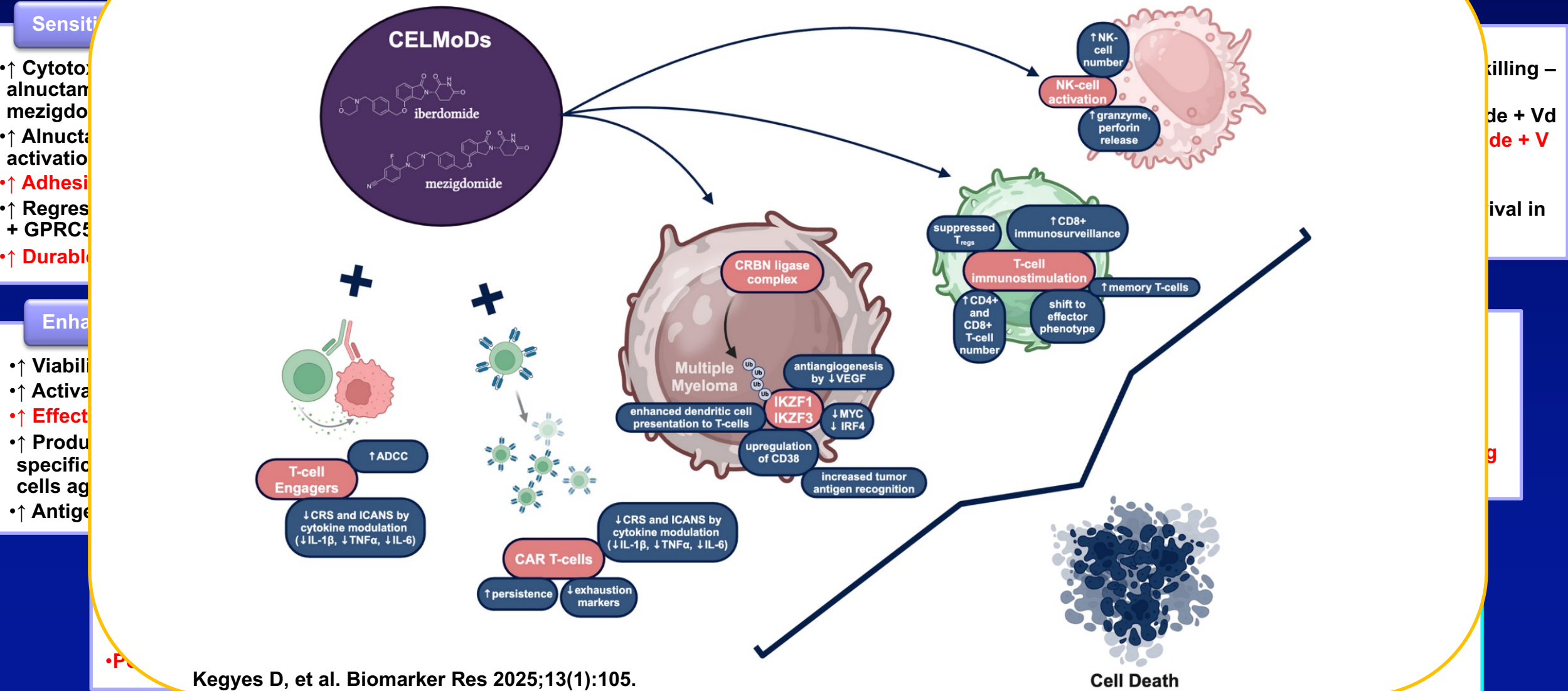
1. Smith EL, et al. Sci Transl Med 2019;11(485):eaau7746.
2. In-house data, AstraZeneca Pharmaceuticals LP.
3. Huang W, et al. Cancer Res 2022;82(12_Supplement):abstract 6020, poster presentation at AACR 2022.

ADC, antibody-drug conjugate; BCMA, B-cell maturation antigen; GPRC5D, G protein-coupled receptor, class C, group 5, member D; mAB, monoclonal antibody; (RR)MM, (relapsed/refractory) multiple myeloma; vc-MMAE, valine-citrulline monomethyl auristatin E.

CELMoDs slides

CELMoDs: summary of pharmacodynamics

CELMDs: overview of immunologic effects



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

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

•High baseline EZH2 expression → poorer PFS

CELMoD doublet for later-relapse RRMM

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

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

Dose escalation

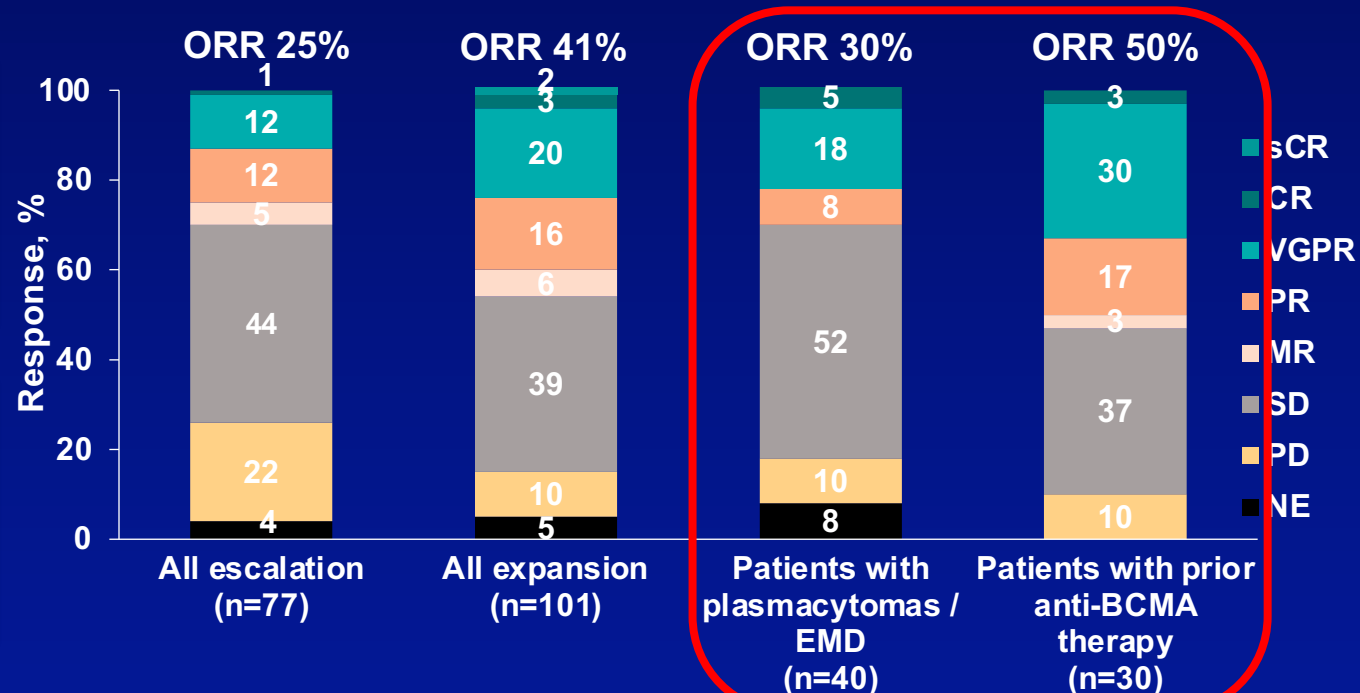
- 77 heavily pretreated RRMM patients
- 30% high-risk cytogenetics, 35% EMD
- **Median 6 prior therapies**
- **56% triple-class-refractory**

Dose expansion at RP2D

- 101 heavily pretreated RRMM patients
- 37% high-risk cytogenetics, 40% EMD
- **Median 6 prior therapies**
- **100% triple-class-refractory**

Efficacy in dose expansion cohort

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



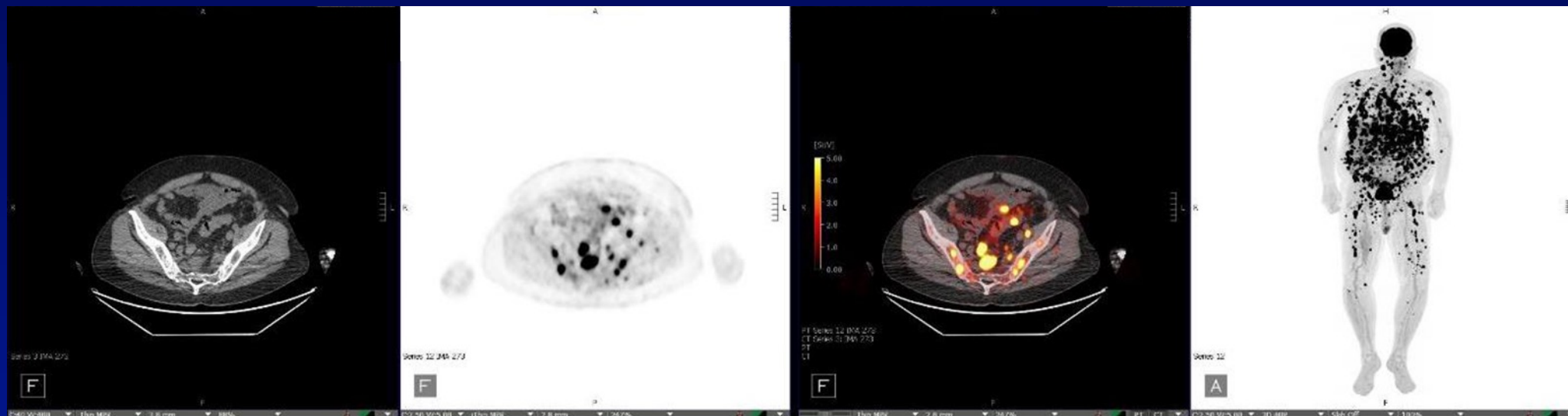
Safety in dose escalation/expansion cohorts

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

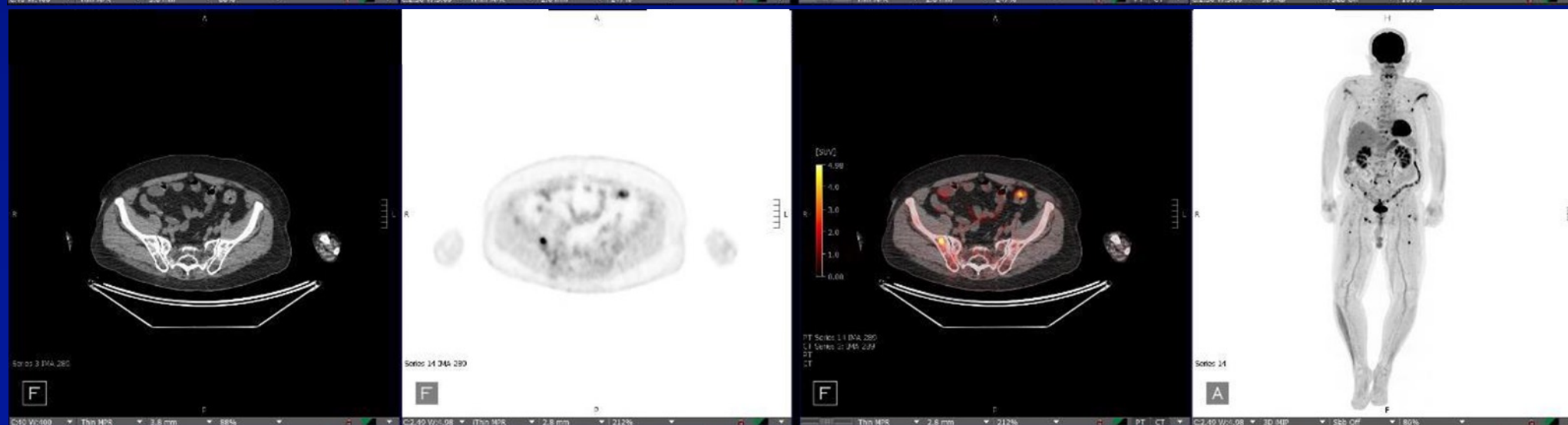
CELMoD doublet for later-relapse RRMM

Mezigdomide + dex induces responses in patients with EMD

At start of
treatment
(study entry)

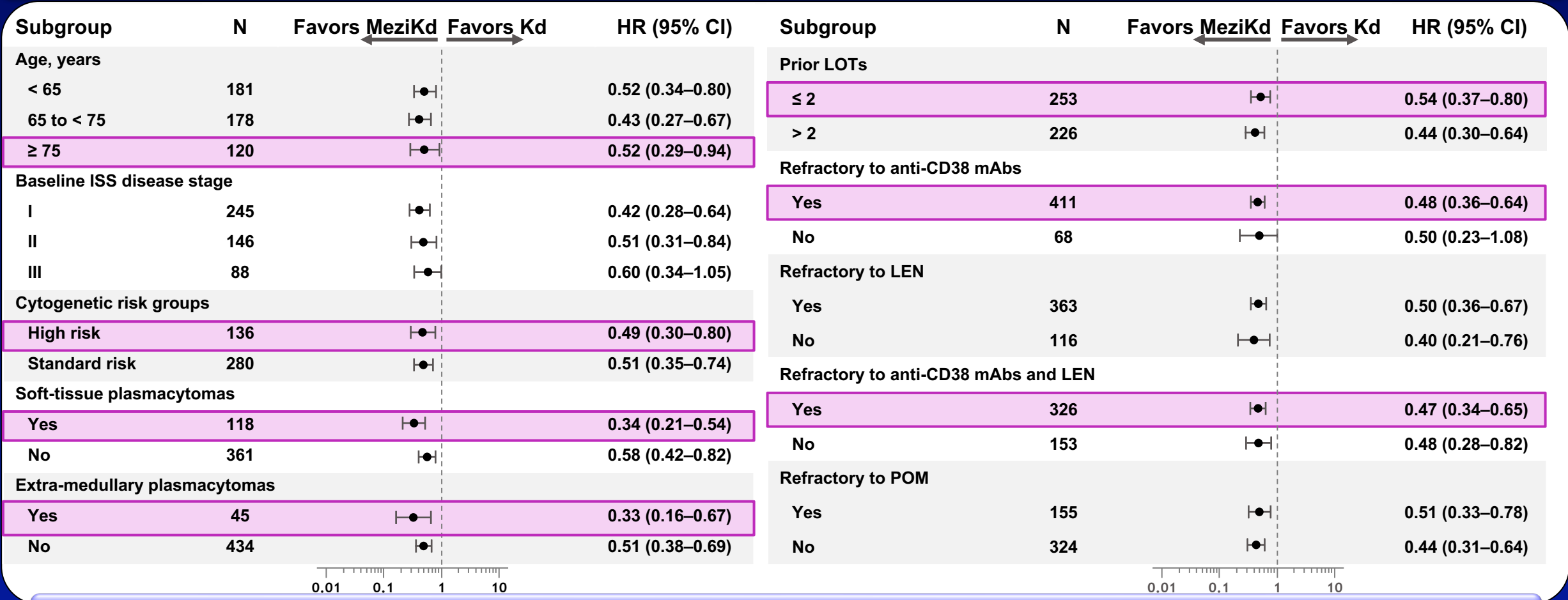


After 4 months of
treatment with
Mezi 1.0 mg,
D1–21 every 28
days, + Dex



SUCCESSOR-2: Subgroup analysis of PFS

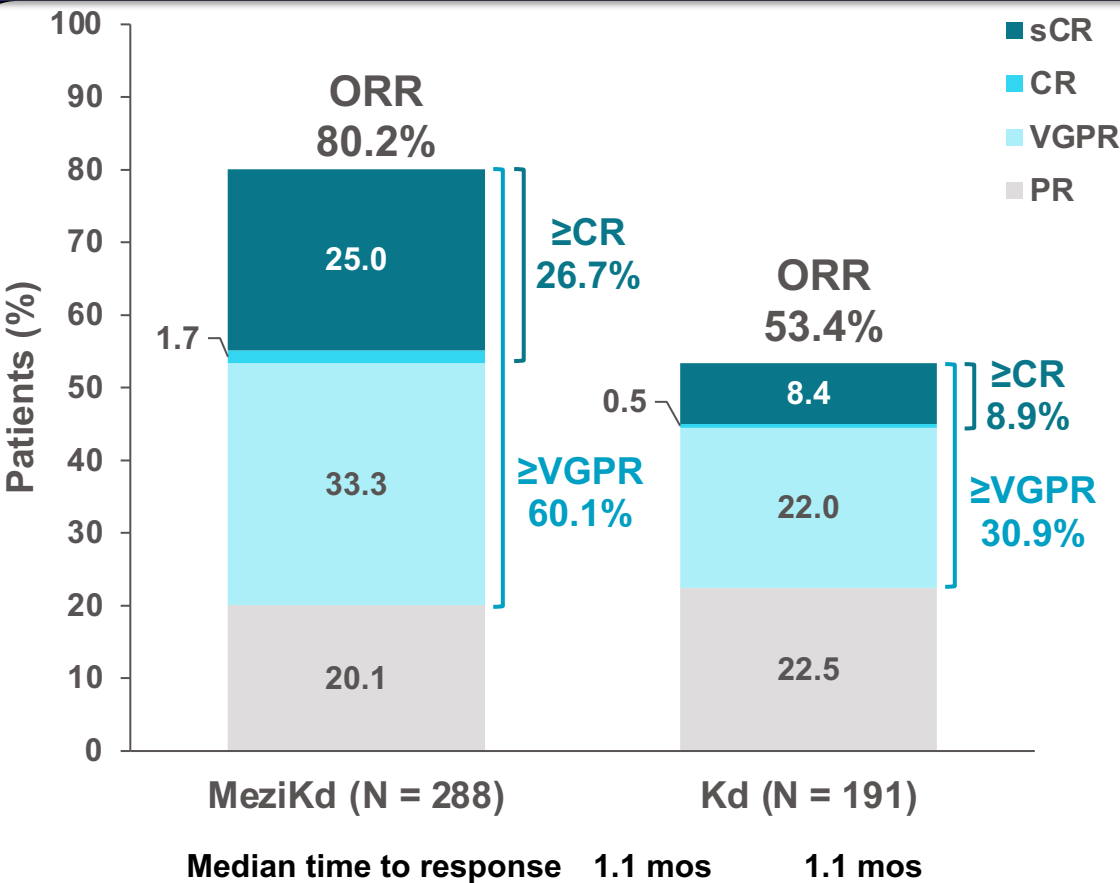
Subgroup analysis of PFS in confirmatory analysis group by ITT, n = 479



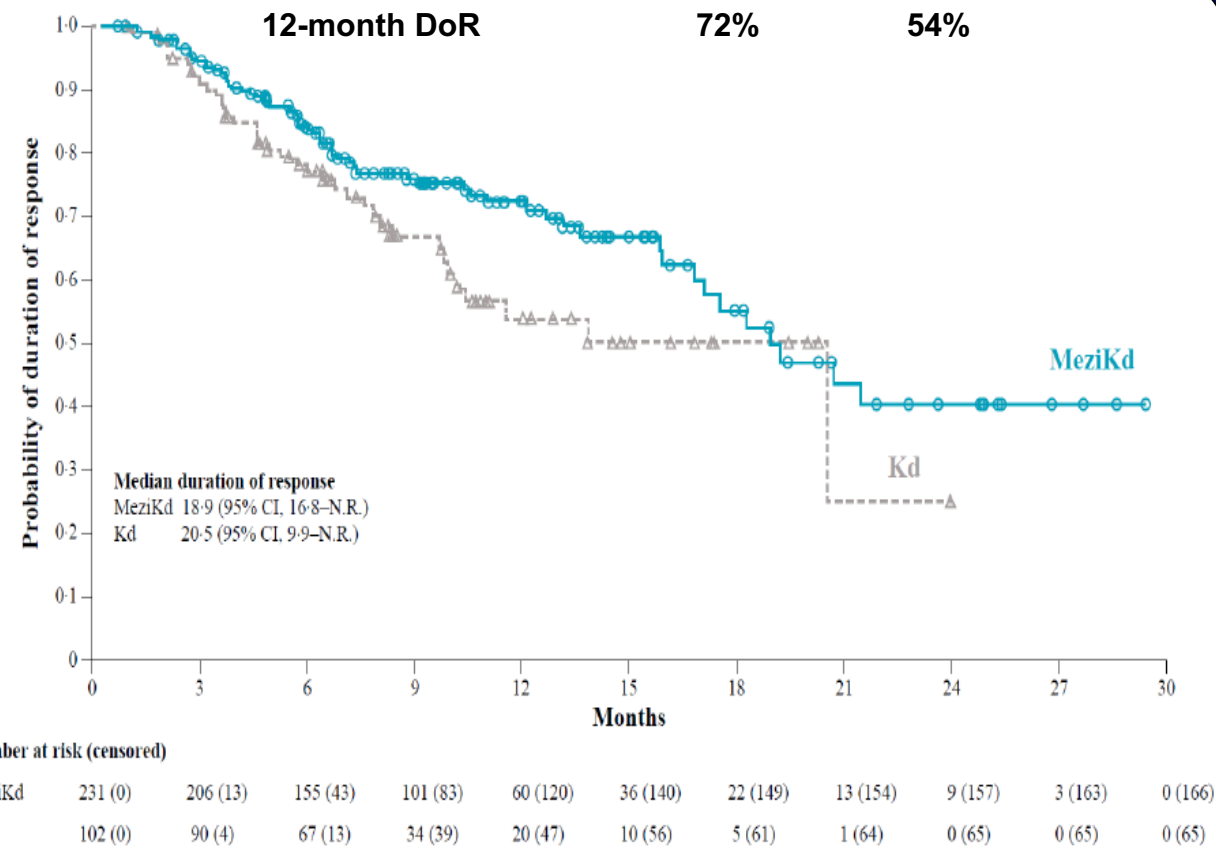
PFS survival benefit with MeziKd superior across all prespecified subgroups

SUCCESSOR-2: Response and DOR

Treatment response, n = 479



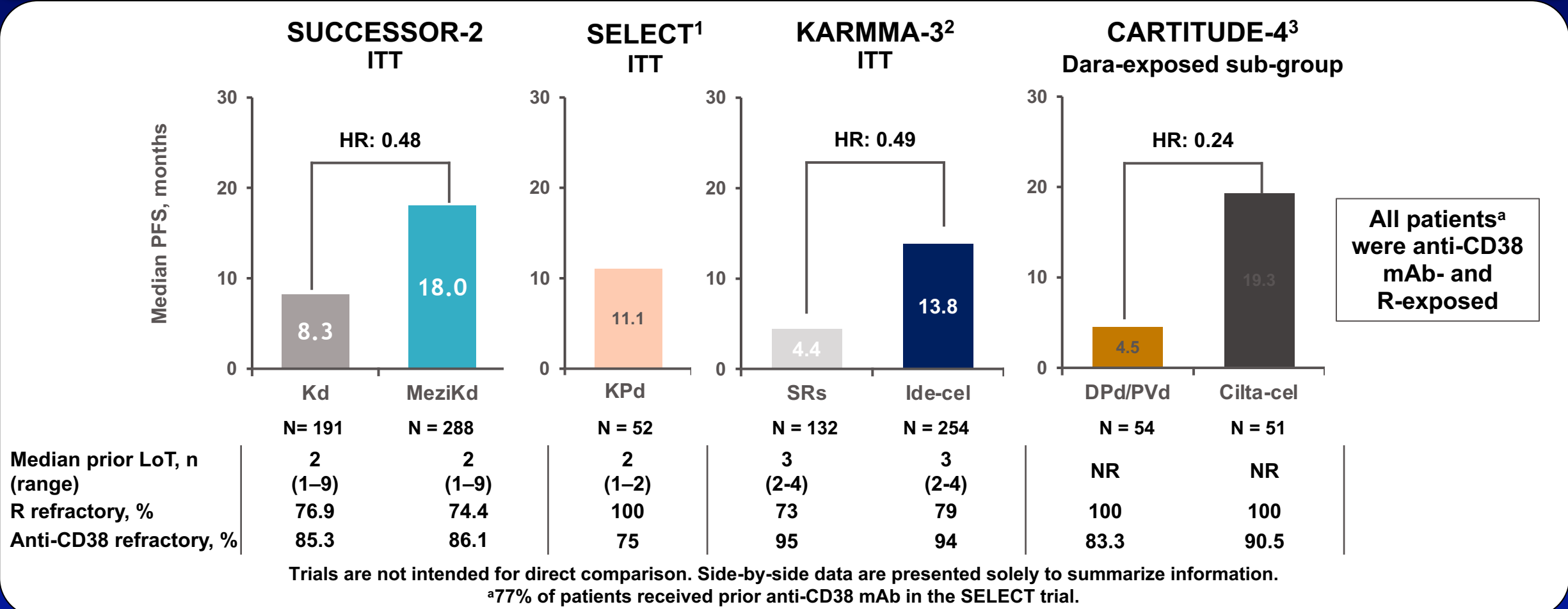
DOR, n = 333



Addition of Mezi to Kd deepened response, doubling the rate of ≥VGPR and tripling the rate of ≥CR

SUCCESSOR-2: How does it compare?

Contextualization of clinical benefit seen in SUCCESSOR-2 for anti-CD38 mAb- and R-exposed RRMM patients across multiple settings and implications for real-world practice¹



Richardson PG, et al. J Clin Oncol 2026;44(16_suppl):LBA7506. Dimopoulos MA, et al. HemaSphere 2026;10(S1):LB5004. Dimopoulos MA, et al. Lancet 2026;408(10551):219-33.
1. Richardson PG, et al. Blood Cancer J 2018;8(11):109. 2. Perrot A, et al. Leuk Lymphoma 2024;65(6):833-842; 3. Ailawadhi S, et al. Blood 2024;144(23):2389-2401;
4. Einsele H, et al. Lancet Oncol 2026;27(2):254-268.

EXCALIBER-RRMM: Dual primary endpoint

MRD-negative CR at any time – subgroup analysis

Subgroup	N	Favors DVd	Favors IberDd	MRD-neg CR rate, % IberDd	DVd
Age, years					
< 64	160			52.5	25.0
65 to 74	184			35.2	19.8
≥ 75	76			30.8	13.5
Baseline ISS disease stage					
I	265			46.8	27.7
II	103			37.3	9.1
III	52			20.8	3.6
Cytogenetic risk groups					
High risk ^b	92			27.1	15.9
Standard risk	267			45.5	24.1
Expanded cytogenetic risk groups					
High risk ^c	205			33.7	21.8
Standard risk	145			51.3	20.3
Soft-tissue plasmacytomas					
Yes	47			21.7	8.3
No	373			43.5	22.2

Subgroup	N	Favors DVd	Favors IberDd	MRD-neg CR rate, % IberDd	DVd
Renal function (eGFR), mL/min					
< 45	38			35.7	8.3
45 to < 60	59			46.9	18.5
≥ 60	322			40.4	23.0
Number of prior LOTs					
1	282			42.4	23.1
2	138			38.2	15.7
Previous LEN exposure					
Yes	292			40.1	18.7
No	128			43.1	25.4
Previous LEN exposure in the last prior LOT					
Yes	267			41.2	19.9
No	153			40.8	22.1
Refractory to LEN					
Yes	183			35.9	23.1
No	237			45.2	18.9
Refractory to LEN in the last prior LOT					
Yes	173			36.7	24.1
No	247			44.4	18.5

Treatment benefit with IberDd was consistent across prespecified subgroups, including LEN-exposed/-refractory patients

CELMoD triplets and quadruplets for RRMM: combination with mAbs or P Iberdomide + Isa-dex or Dara-Kd

Iberdomide + Isa-dex for functional high-risk RRMM IBIS AMaRC 20-01 study¹

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

- Median age 65 years (range 43–82)
- 24% R-ISS III
- **1 / 2 / 3 HRCAs in 32% / 16% / 12% (N=50)**
- Median time to IBIS salvage 6.3 months

Efficacy, follow-up ≥12 months

- **ORR 69%**
- Of 29 patients, 15 progression-free and alive, 8 alive with PD, 6 died
- 9-month PFS 51% / OS 82%

Safety

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

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

30 RRMM patients after 1–3 prior lines

- Median age 63 years (range 44–77); 33% high-risk (IMWG 2025); 16% EMD
- Median 1 prior line
- **93% R-refractory; 27% CD38 mAb-exposed; 30% prior K**
- 47% prior ASCT

Efficacy

- **ORR 92% (38% ≥CR, 35% VGPR)**
- **8/12 (67%) MRD-neg CR and PET-neg**
- 27 patients remain on treatment for up to 17 months

Safety

- Grade ≥3 hematologic AEs: 50% neutropenia, 10% thrombocytopenia, 3% anemia
- 6 (20%) SAEs, including 3 (10%) lung infections

Overcoming T-cell exhaustion

Improving CAR T-cell function with CELMoDs

EHA2025
Congress

Preclinical benefit of CELMoD-dex on TCE outcome

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

Mezigdomide EW, et al. Blood 2024;144(supplement 1):356.

Immune system reactivation with mezigdomide regimens

- Analysis of immune profiles in 56 patients with RRMM receiving mezigdomide-dexamethasone-based regimens
- 28 patients had T cell redirecting therapy (TCRT) in last regimen
- TCRT-treated patients had increases in immune cell subsets related to persistent activation and lower Treg counts
- Mezigdomide treatment resulted in increased proliferation levels, enhanced CD4+/CD8+ T cell and NK/NKT cell activation, and a shift to an effector memory phenotype, regardless of prior TCRT**

Kurtova A, et al. HemaSphere 2025;9(S1):PS1674.

Enhancing CAR T cells and immune effects with iberdomide

- Analysis of immunomodulatory effect of iberdomide-dex on CAR T cells in murine models and on the bone marrow compartment in patients with RRMM
- Iberdomide-primed CAR T cells had superior *in vivo* anti-MM activity versus non-primed CAR T cells
- In 21 patients progressing after BCMA therapy, iberdomide-dex resulted in:**
 - Significant increases in NK cells, $\gamma\delta$ T cells, and CD8+ T cells
 - Shift towards effector memory T cells and reduced naïve T cells
 - Increase in activated CD4+ and CD8+ T cells
- Findings consistent with previous report showing that **CAR T cells manufactured from iberdomide-treated patient samples had greater proliferative capacity, activation, and cytotoxicity**

Aleman A, et al. Clin Lymphoma Myeloma Leuk 2026;26(Suppl 2):S20–21, abstract OA-31.

2026 ASCO
ANNUAL MEETING

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

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

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

ASH 2025/IMS 2026: Novel combination studies in RRMM with CELMoDs and TCEs

MagnetisMM-30: Elranatamab + iberdomide¹

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

CA088-1005: Arlo-cel + mezigdomide³ or iberdomide

- Phase 1 study (NCT06121843) of arlo-cel plus novel therapies including mezigdomide and iberdomide
 - Dose-finding and dose-expansion study, with up to

CA057-1040: Elranatamab + mezigdomide⁴

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

CADMIUM (Alliance) Ide-cel + iberdomide



- Randomized Phase 2 study (NCT06121843) of iberdomide maintenance post ide-cel
- Patients with RRMM, ≥4 prior lines of therapy
- 6–12 patients in part 1 (safety run-in)
 - 60 patients in part 2, randomized to iberdomide or observation post ide-cel
- Primary endpoint: PFS
 - Secondary endpoints: OS, best response, deepening of response, including CR conversion

Mezi maintenance following ide-cel

- 7 patients; median age 81 years; median 5 prior lines
 - Median 108 days from ide-cel to mezi
 - ORR 85.7%, including 71.4% sCR – deepening of response to ide-cel seen in 5/6 (83.3%) responding patients
 - Median follow-up 17.9 months; median PFS 16.5 months
 - Most common grade ≥3 AE was neutropenia (85.7%)
 - No recurrent CRS, ICANS, or persistent cytopenias
- Janakiram M, et al. Clin Lymphoma Myeloma Leuk 2026;26(Suppl 2):S219, abstract PA-304.

CA057-1040: Elranatamab + mezigdomide⁵

- Phase 1b/2a study (NCT06645678) of elranatamab plus mezigdomide
- Patients receiving one of 3 dose levels of mezigdomide
- Patients with RRMM ≥2 prior lines of therapy, including an IMiD, a PI, and a CD38 mAb
- Patients enrolled to date: 7 at mezi 0.3 mg/kg; 7 at mezi 0.6 mg/kg; median 4 prior lines
- **ORR 100% (92.3% CR/sCR)**
- **7/8 evaluable patients (87.5%)**
- **7% (all grade 1/2), no ICANS**