



Targeting BCMA:

A Giant Leap Forward in Myeloma Therapy

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Cancer Institute

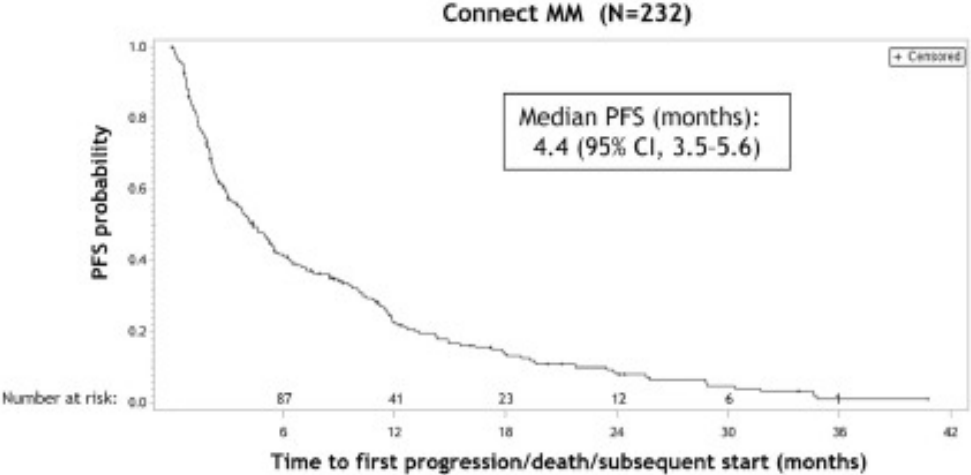
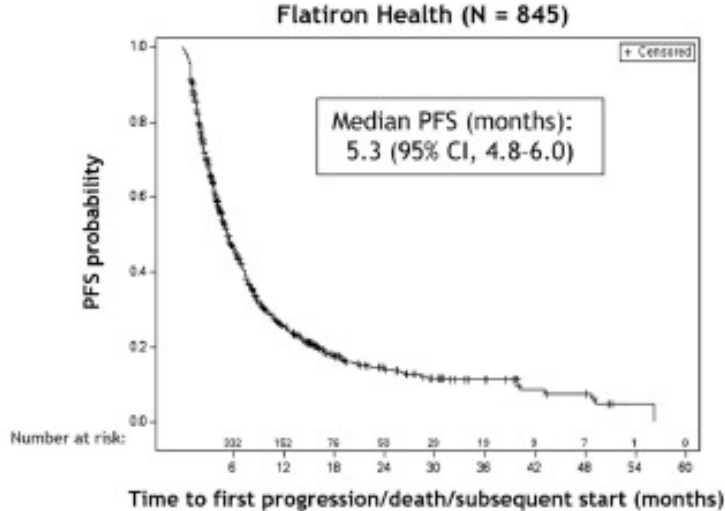
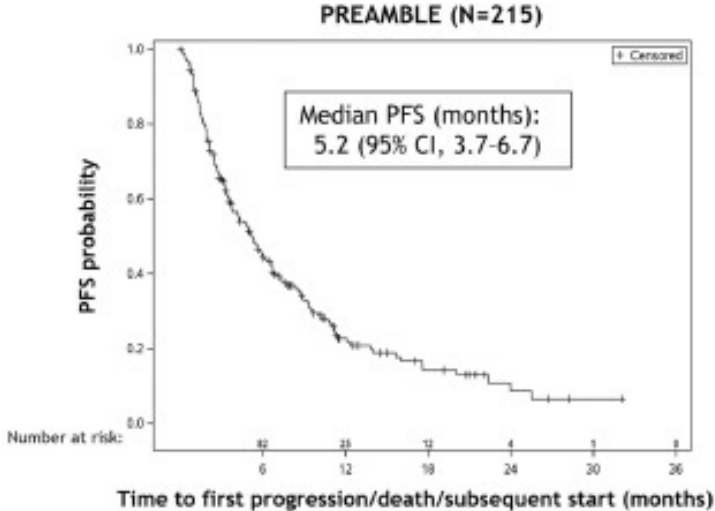
Disclosures

Advisory Boards: BMS, Janssen, GSK, Karyopharm, Sanofi, Pfizer, Regeneron

Consulting: AbbVie, Karyopharm, Janssen, Sanofi, GSK

Research Funding: BMS, Sanofi, Regeneron, Adaptive, NCGM

Background: Clearly, 2L+ Treatment with IMiD/PI/CD38 is insufficient



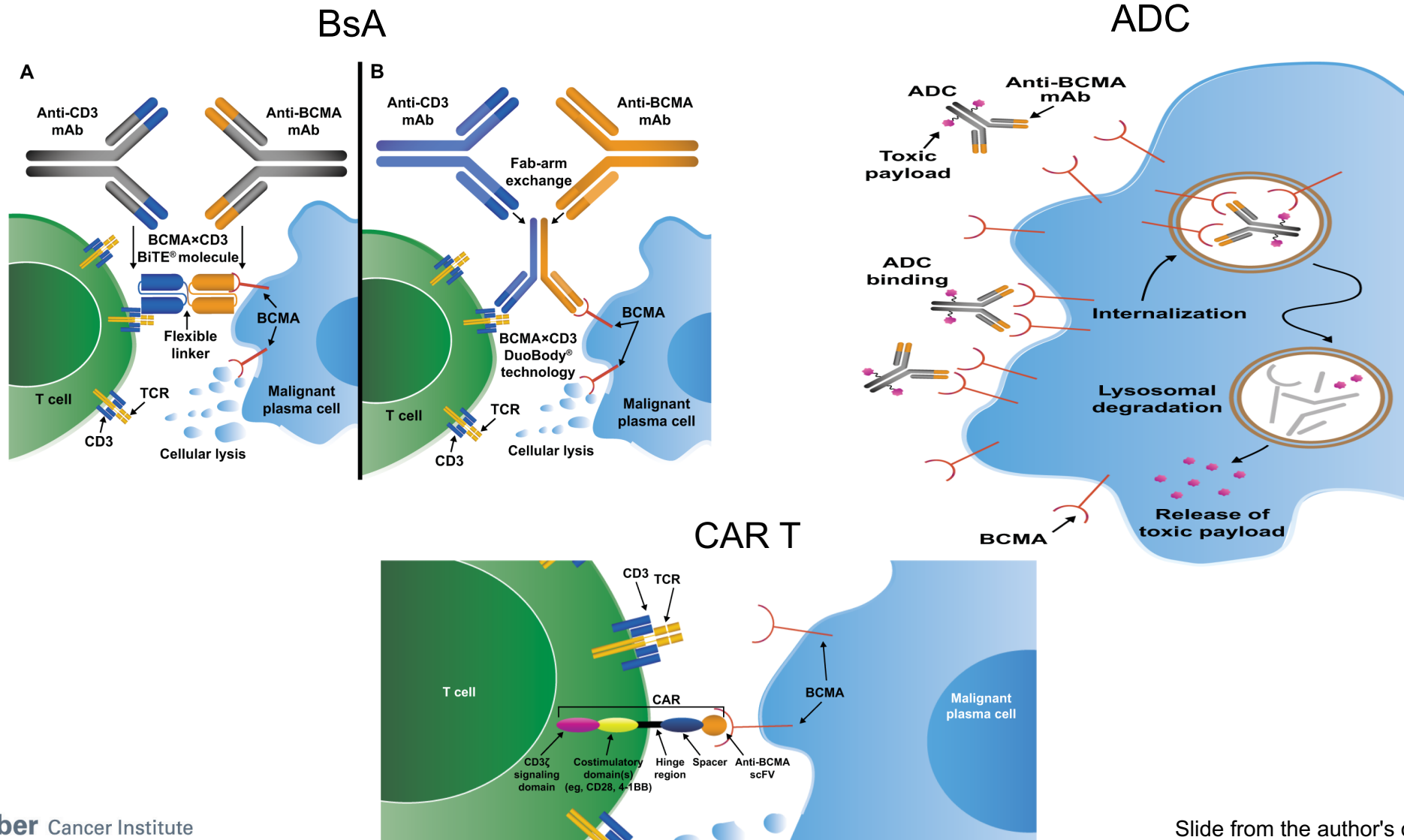


BCMA as a Target in MM

- almost universally expressed on MM cell surface
- natural ligands: APRIL, BAFF
- minimally expressed in hematopoietic cells
- expressed in pDCs (microenvironment)
- gamma secretase induces shedding/soluble form

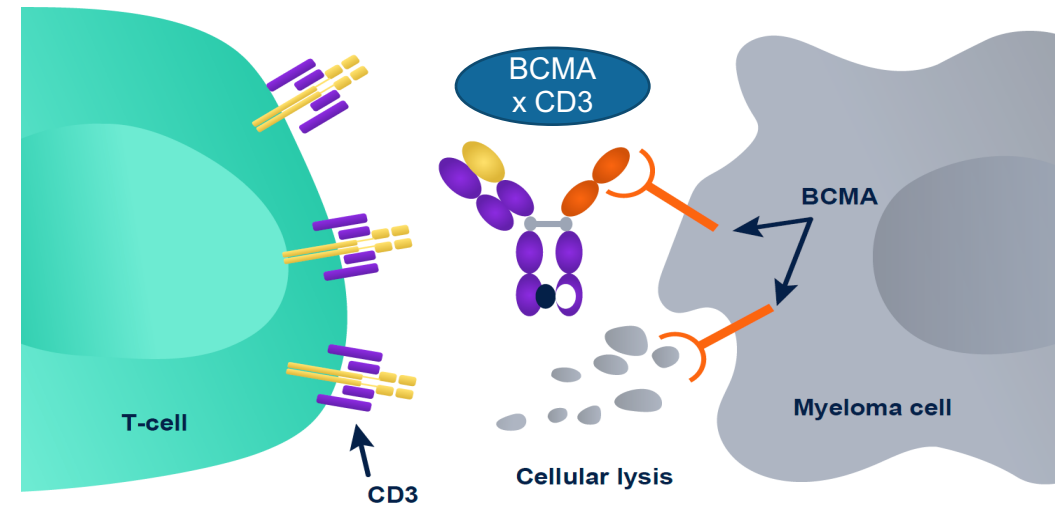


Current Targeting Mechanisms: TCEs and ADC



Bispecific T-cell-Engaging (TCE) Antibodies: US History

- December 2014: blinatumomab receives accelerated approval for B-ALL in the U.S.
- 8 years later: teclistamab approved for RRMM (8 months after cilta cel approved)
- BsA (vs CAR T):
 - off-the-shelf/greater access
 - generally less toxic



Currently 4 FDA-approved BsA in 5th Line or Later

Teclistamab¹
(MajesTEC-1)

Elranatamab²
(MagnetisMM-3)

Talquetamab³
(MonumenTAL-1)

Brazil: Tec, Elra, Talq all ANVISA approved for triple exposed patients

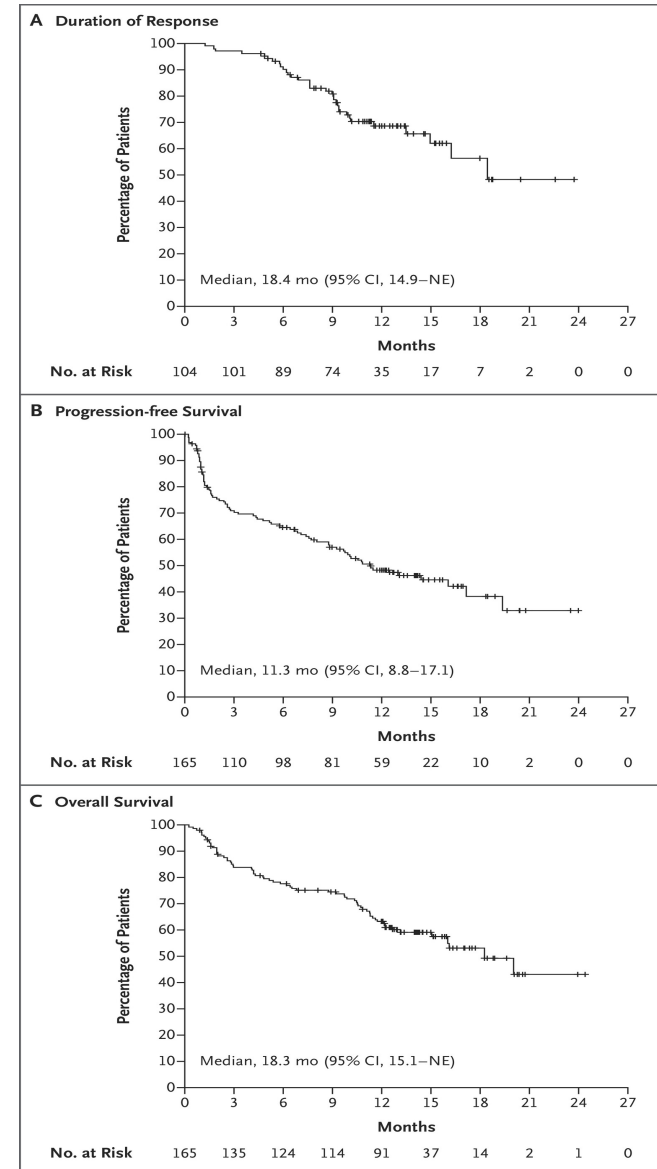
¹Moreau et al, NEJM 2022

²Cohen et al, ASCO 2023

³Chari et al, ASH 2023

Teclistamab MajesTec-1: Efficacy

- ORR: 63%
- MRD negativity: 81.5% (in evaluable patients)
- Lower response rate seen in patients with EMD and $\geq 60\%$ marrow plasmacytosis
- mDOR: 18.4 months
- mPFS: 11.4 months



Teclistamab MajesTec-1: Safety

- CRS: 72% (<1% grade 3, no grade 4)
- Neurotoxicity: 14.5% (only 1 grade 4 event)
 - Mostly headache
 - Only 3% ICANS
 - 1 grade 4 seizure in context of meningitis
- **Grade 3+ infections: 55% (bacterial, viral, fungal, PJP, COVID-19)**
- **22 (13%) fatal infections (18 from COVID-19)**

Table 2. Adverse Events in 165 Patients (Safety Population).*

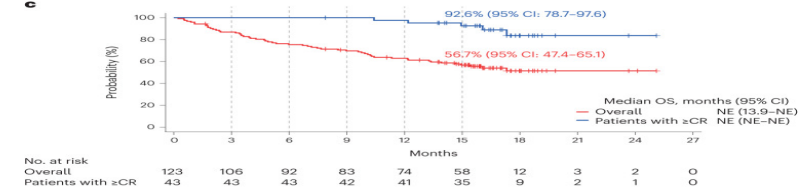
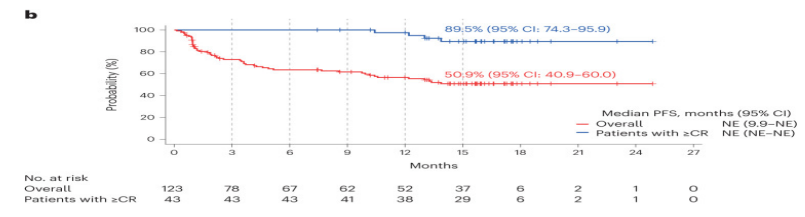
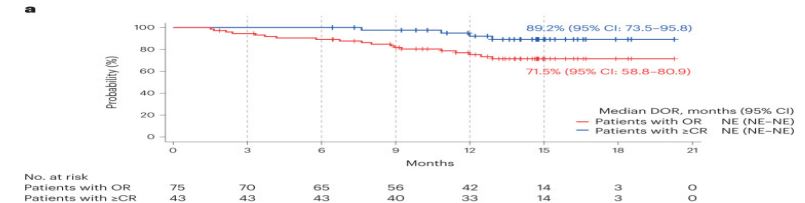
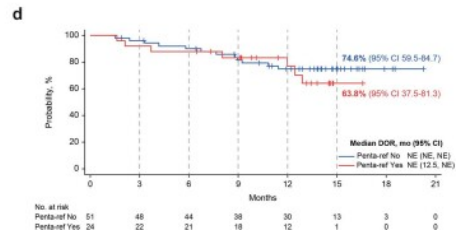
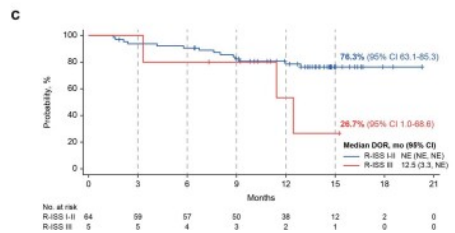
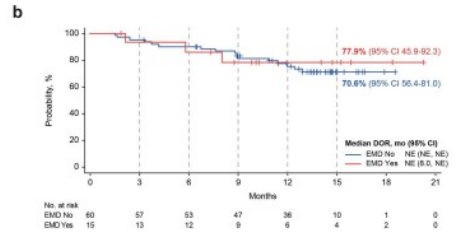
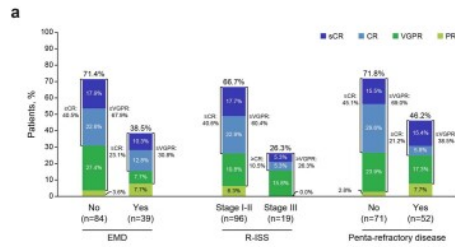
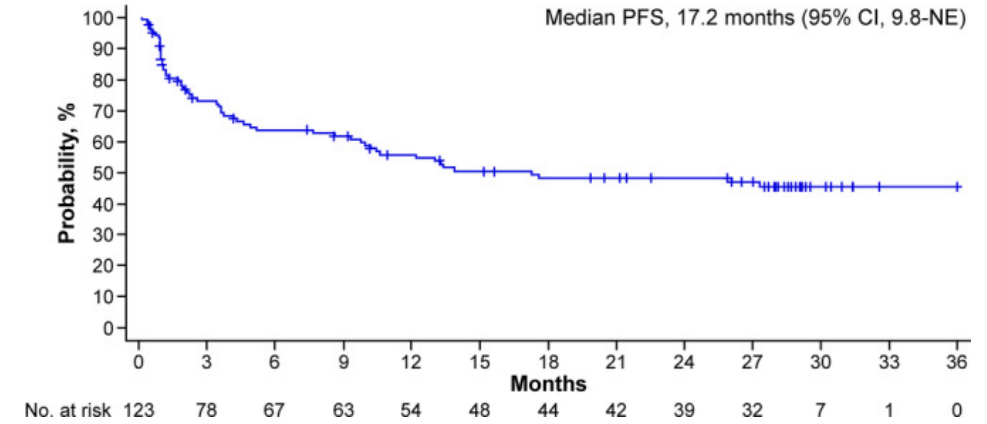
Event	Any Grade <i>no. of patients (%)</i>	Grade 3 or 4 <i>no. of patients (%)</i>
Any adverse event	165 (100)	156 (94.5)
Hematologic		
Neutropenia	117 (70.9)	106 (64.2)
Anemia	86 (52.1)	61 (37.0)
Thrombocytopenia	66 (40.0)	35 (21.2)
Lymphopenia	57 (34.5)	54 (32.7)
Leukopenia	29 (17.6)	12 (7.3)
Nonhematologic		
Diarrhea	47 (28.5)	6 (3.6)
Fatigue	46 (27.9)	4 (2.4)
Nausea	45 (27.3)	1 (0.6)
Injection-site erythema	43 (26.1)	0
Pyrexia	45 (27.3)	1 (0.6)
Headache	39 (23.6)	1 (0.6)
Arthralgia	36 (21.8)	1 (0.6)
Constipation	34 (20.6)	0
Cough	33 (20.0)	0
Pneumonia	30 (18.2)	21 (12.7)
Covid-19	29 (17.6)	20 (12.1)
Bone pain	29 (17.6)	6 (3.6)
Back pain	27 (16.4)	4 (2.4)
Cytokine release syndrome†	119 (72.1)	1 (0.6)
Neurotoxic event	24 (14.5)	1 (0.6)

* Listed are adverse events of any grade that were reported in at least 15% of the patients, as well as neurotoxic events. Covid-19 denotes coronavirus disease 2019.

† In this analysis, events associated with cytokine release syndrome were graded according to the criteria of the American Society for Transplantation and Cellular Therapy.

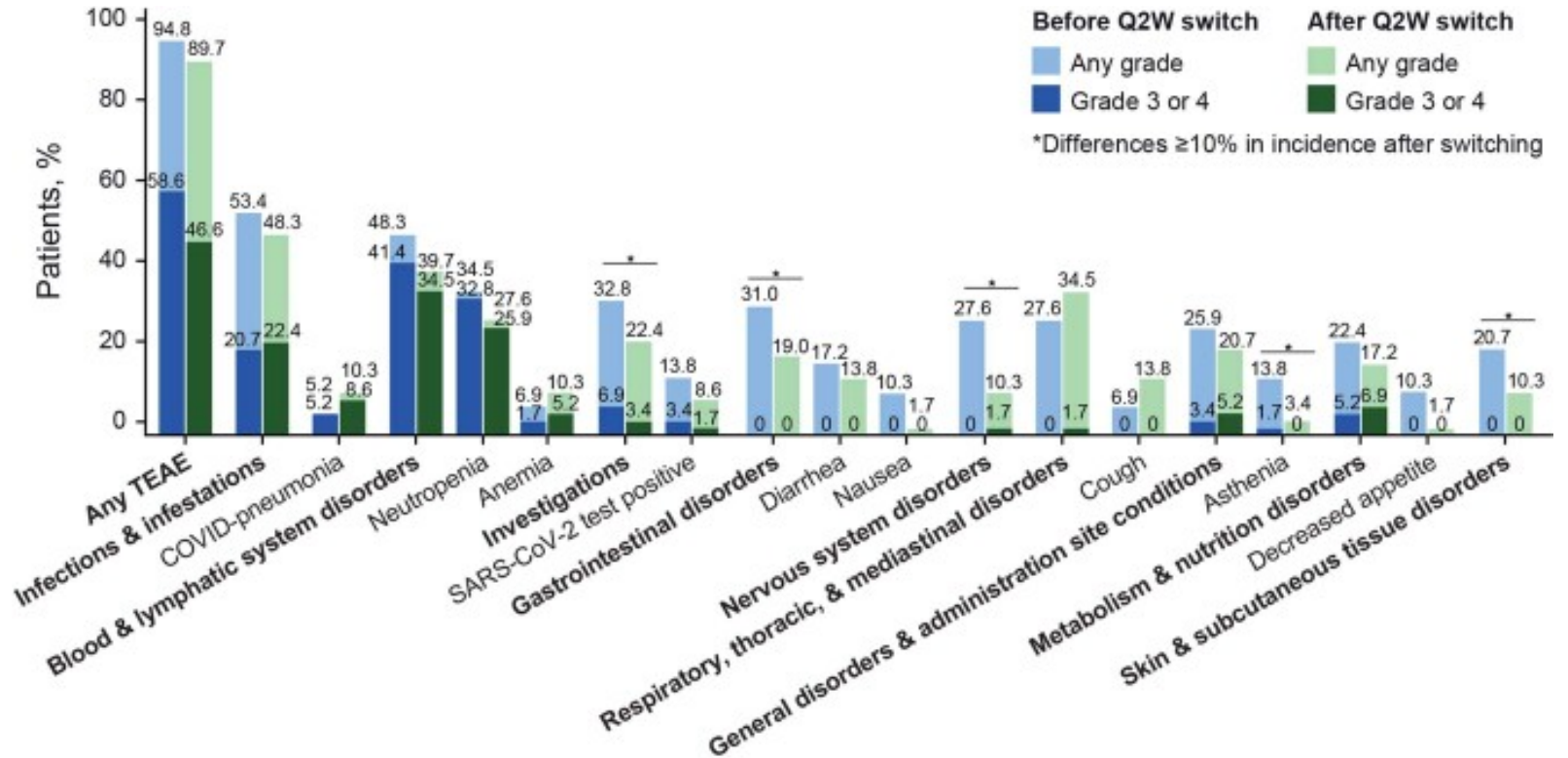
Elranatamab MagnetisMM-3: Efficacy

- ORR: 61%
- mPFS: 17.2 months
- mDOR: NR (as of 3/2024)
- mOS: 24.6 months



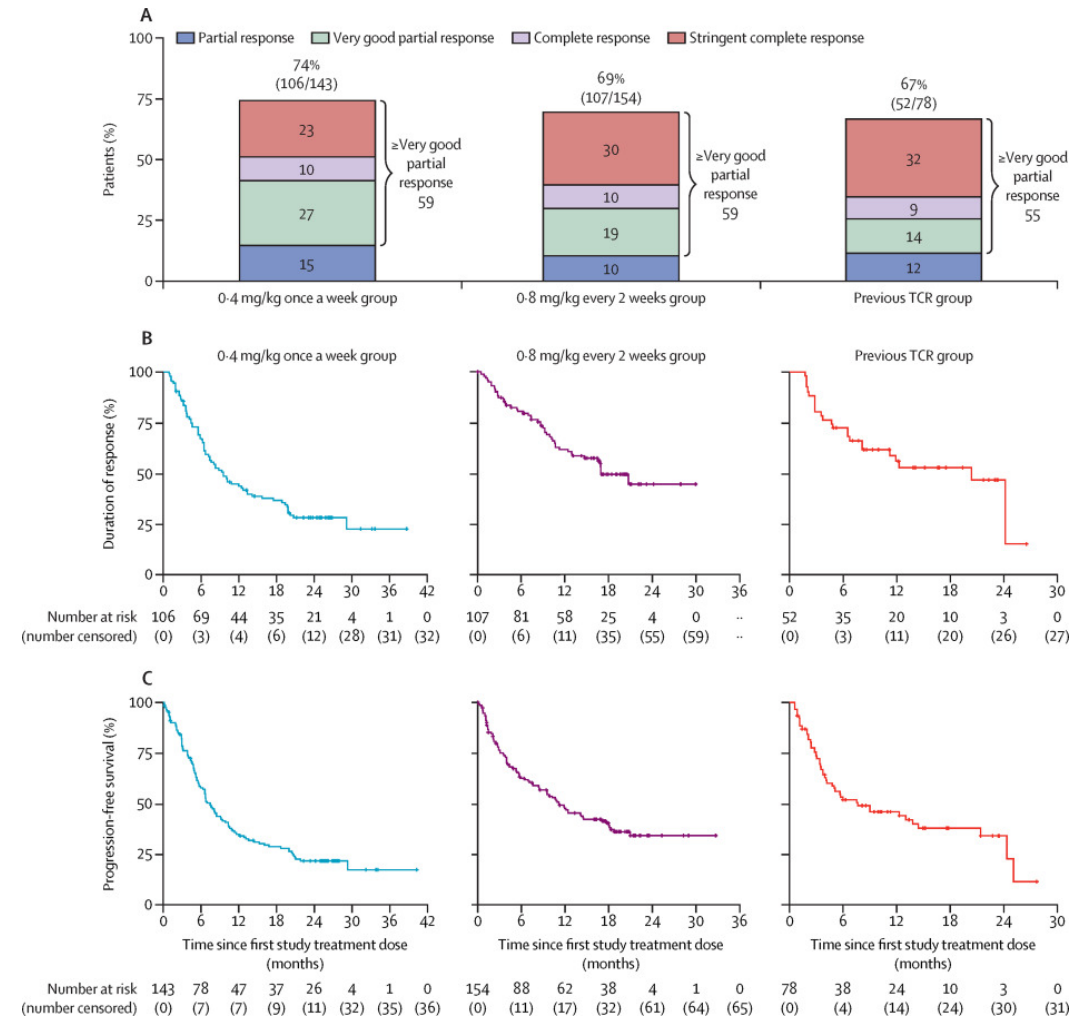
Elranatamab MagnetisMM-3: Safety

- CRS: 57% (all G1/2)
- ICANS: 5% (all G1/2)
- G3+ infection: 49%
- G5 infection: 6.5%



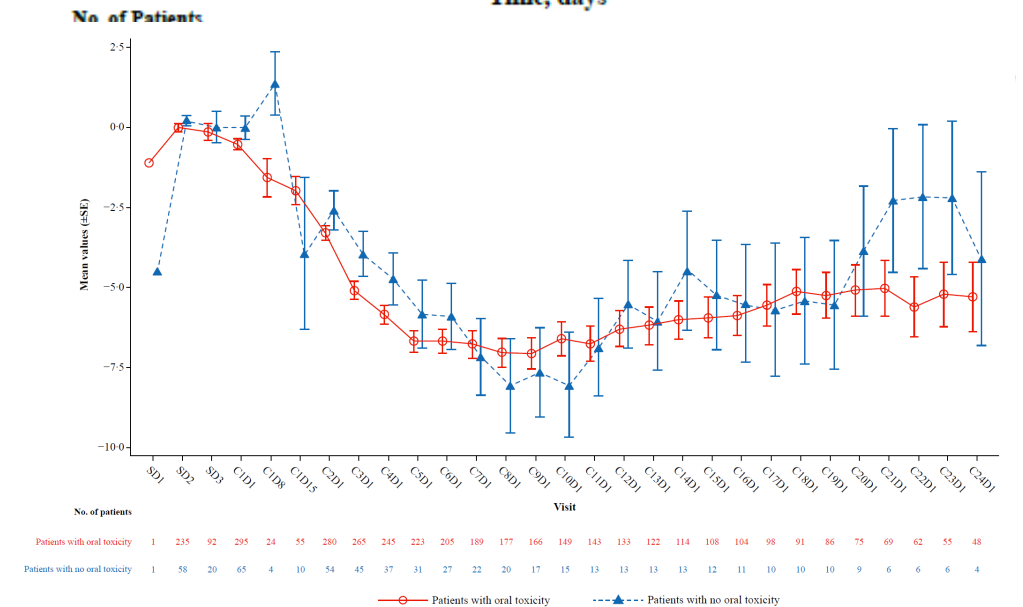
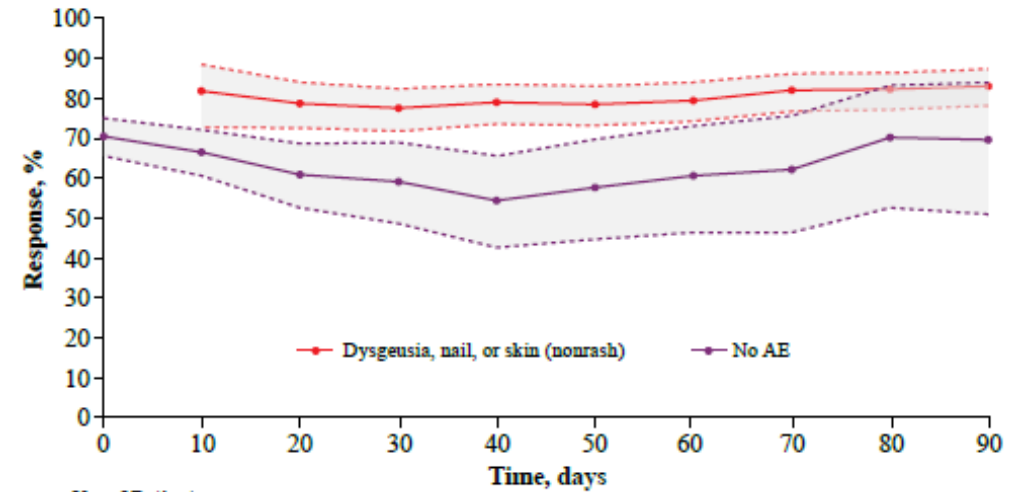
Talquetamab MonumenTal-1: Efficacy

- ORR: 74% (QW), 69%% (Q2W)
- mDOR: 9.5 months (QW), 17 months (Q2W)
- mPFS: 7.5 months (QW) 11.2 months (Q2W)
- Post-TCR patients: similar outcomes
 - ORR 74% in patients immediately post-CAR
 - ORR 29% vs 68% immediately vs not immediately post-BCMA BsA



Talquetamab MonumenTal-1: Safety

- G3/G4 infections: 17% (QW) 12% (Q2W)
- 20-30% high-grade cytopenias
- Skin/nail AEs: ~50-70%, almost all G1/2
- Dysgeusia: 71% (QW) 72% (Q2W) all low-grade
- Weight loss ~40%
- CRS 70-80% (1-2% grade 3/4)
- ICANS 10% (1-2% grade 3)



Current Unknowns/Dilemmas in TCR Therapy

- Sequencing (target BCMA or GPRC5D first?)
- Sequencing (CARs to BsA or vice versa?)
- Sequencing (one BsA right after another?)
- Dosing frequency (how often and for how long?)

T-cell exhaustion



Mitigating Risk with BsA

- Prophylactic tocilizumab
 - Being increasingly adopted
 - Data to support (e.g. Miami study)¹
 - 119 patients given single dose before step-up
 - 10% CRS incidence (G1 in 10/12 events)
 - 0% in linvo-treated patients*
 - NCCN listing
- IVIg
 - Grossly underreported/underappreciated in initial studies
 - IgG will drop to zero in BCMA BsA-treated patients if you let it
 - IVIg use associated with tenfold reduction in serious infections²
- Recognition of risk of opportunistic infections (e.g. CMV)

¹Kowalski et al, Blood Adv 2025

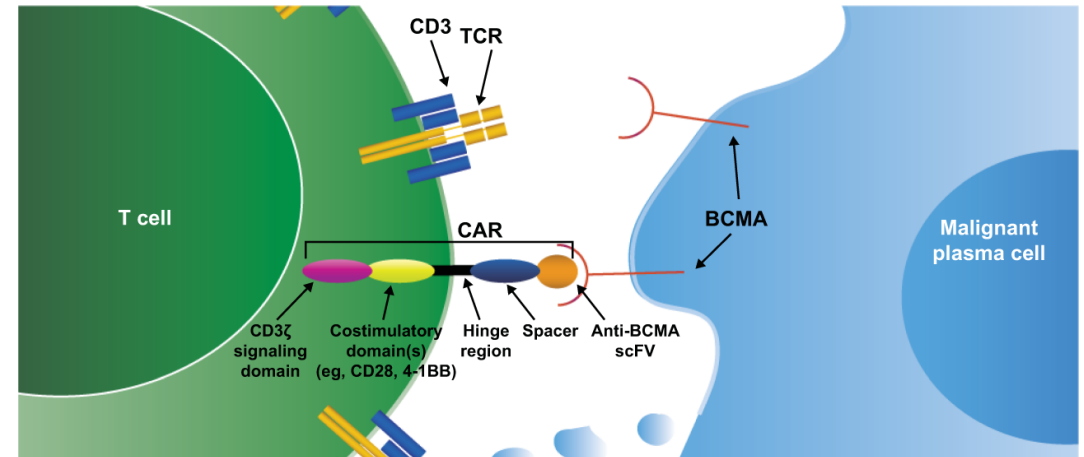
²Lancman et al, Blood Cancer Discov 2023

What will the Future Hold?

- Combination therapy
- Early lines for sure (but *how* early?)

CAR T cell Therapy: US History

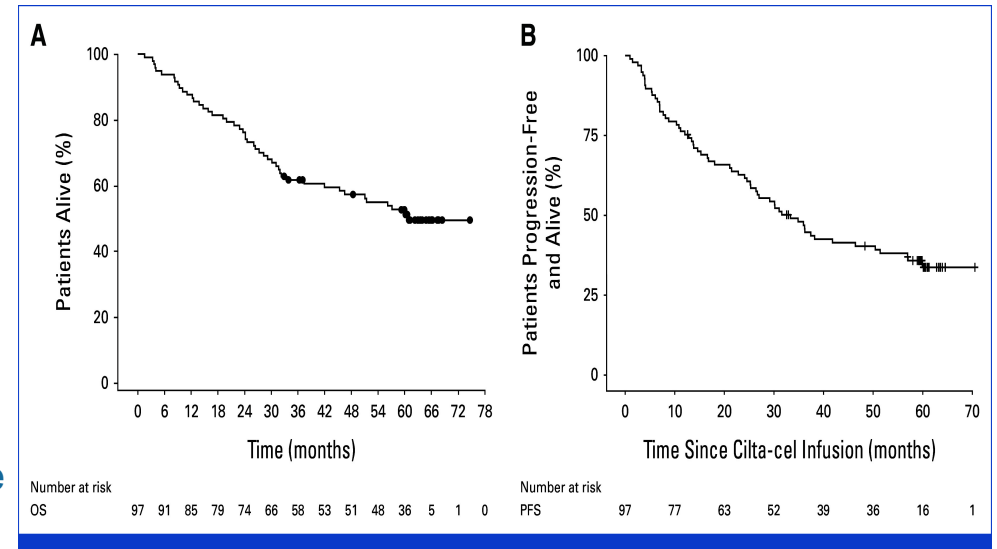
- March 2021: 1st CART cell approved for 5L+
- Feb 2022: cilta cel FDA approved for 5L+
 - ORR 98%
 - mPFS 35 mos
 - higher incidence of neurotox (Parkinsonism)
 - rare but fatal enterocolitis
- April 2024:
 - 1st CART cell now approved for 3L+
 - cilta cel approved for 2L+



Brazil: cilta cel ANVISA approved in Feb 2022 for triple class-exposed patients

Does CAR T-cell therapy have curative potential?

- I don't know
- I hope so (CARTITUDE-1)
- 1/3 patients progression-free at >5 years
- 12/12 MRD-negative and PET negative
- T-cell fitness and E:T ratio correlate with sustained response



Should we temper our excitement with caution?

- real-world patient:
 - 61F s/p three LoT to include HDM-ASCT x2
 - Bridging therapy to cilta cel (SD as best response)
 - day +13: ALC peaked at 5.1k/uL
 - day +21: severe tremor, bradykinesia, decreased speech, masked facies (cilta-cel Parkinsonism)
 - high-dose steroids x2: minimal/transient response
 - Cytosan precluded by severe cytopenias
 - IT MTX/cytarabine: no response
 - IT thiotepa: partial clinical response, now worsening ten months later

What I've been telling my patients

- *Maybe* this could cure you
- Low but non-zero chance of catastrophic and/or irreversible complications



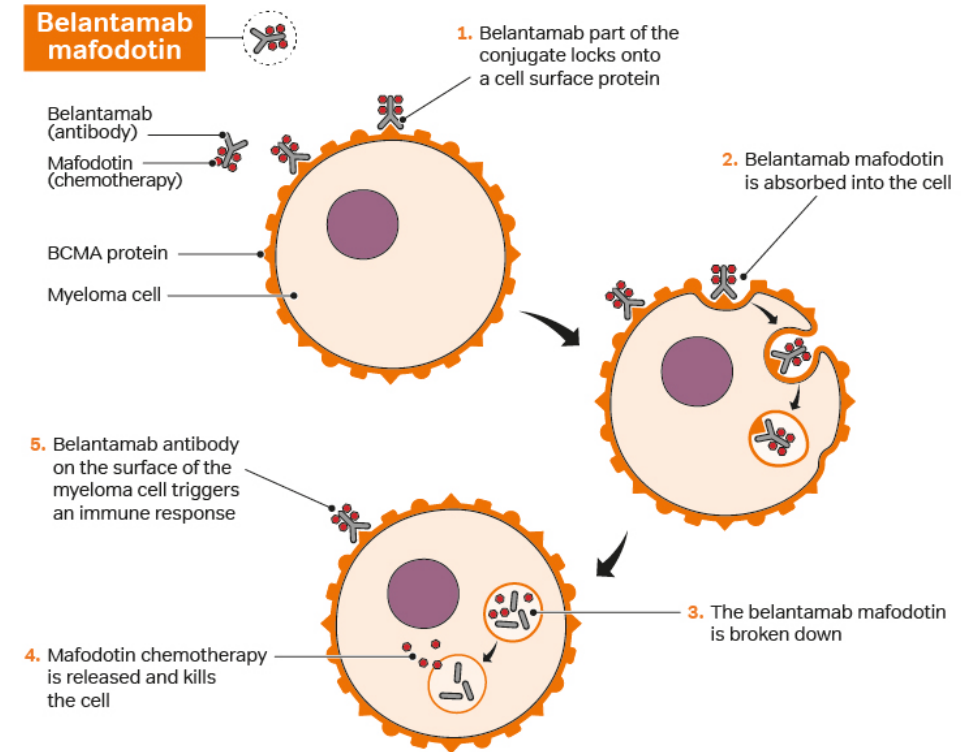
Antibody-Drug Conjugates: Rapidly Expanding Role in Oncology

- >400 ADC clinical trials
- 15 FDA-approved ADCs in the US
 - Solid tumors: breast, lung, gastric, urothelial, cervical, ovarian
 - Hematologic: MM, DLBCL, HL, AML, ALL
- projected global market of \$65 billion by 2030
- do not require cell apheresis, manipulation, or storage (unlike CAR)
- easily given in community settings (unlike BsA)

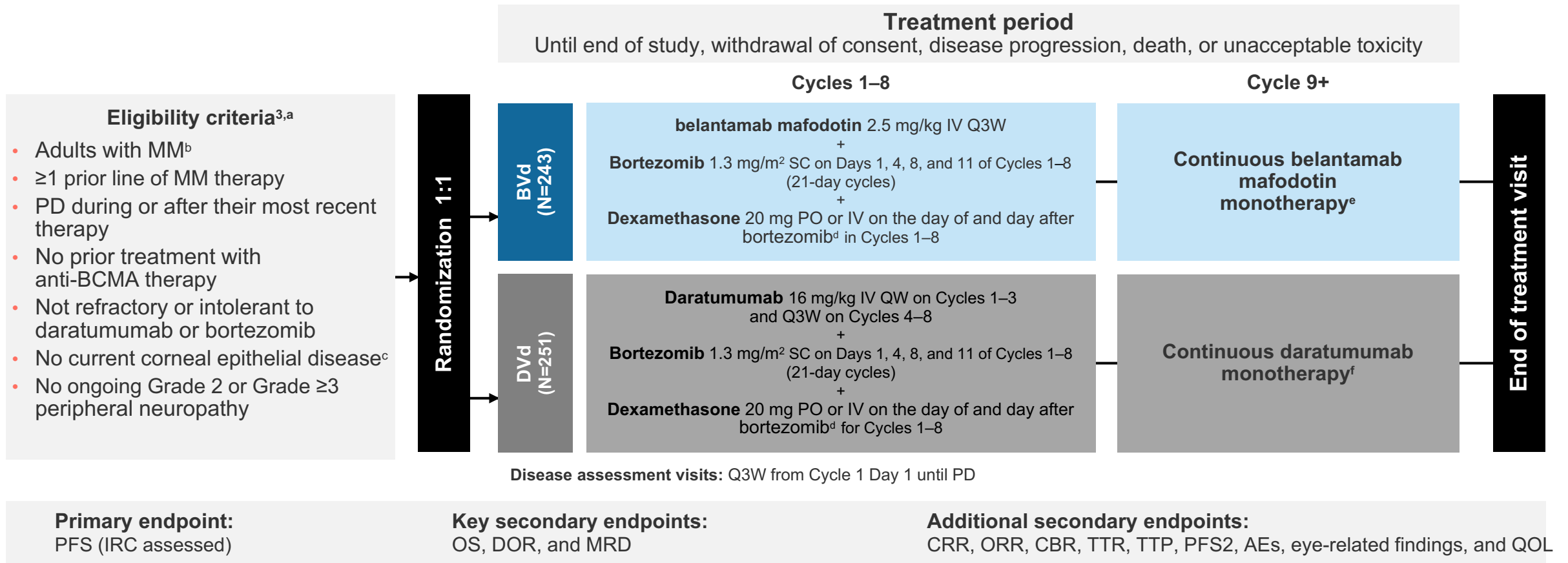


ADC in MM: belantamab mafadotin

- BCMA mAb carrying MMAF payload
- Multiple MoA to include:
 - receptor-mediated endocytosis →lysosomal cleavage →MMAF-induced microtubule disruption →cell cycle arrest and apoptosis (“Trojan Horse” chemotherapy)
 - ADCC via NK cells
 - ADCP via macrophages
 - immunogenic cell death (DAMP release)



DREAMM-7: global phase 3 trial of Bela-Vd versus Dara-Vd in patients with ≥ 1 prior line of MM therapy



1. belantamab mafodotin. Summary of Product Characteristics. GlaxoSmithKline; 2025; 2. Hungria V, et al. *N Engl J Med.* 2024;391(5):393–407; 3. Hungria V, et al. [Supplementary appendix]. *N Engl J Med.* 2024;391(5):393–407; 4. Hungria V, et al. *The Lancet.* 2025;26(8):1067–1080.



DREAMM-7: Patient Characteristics

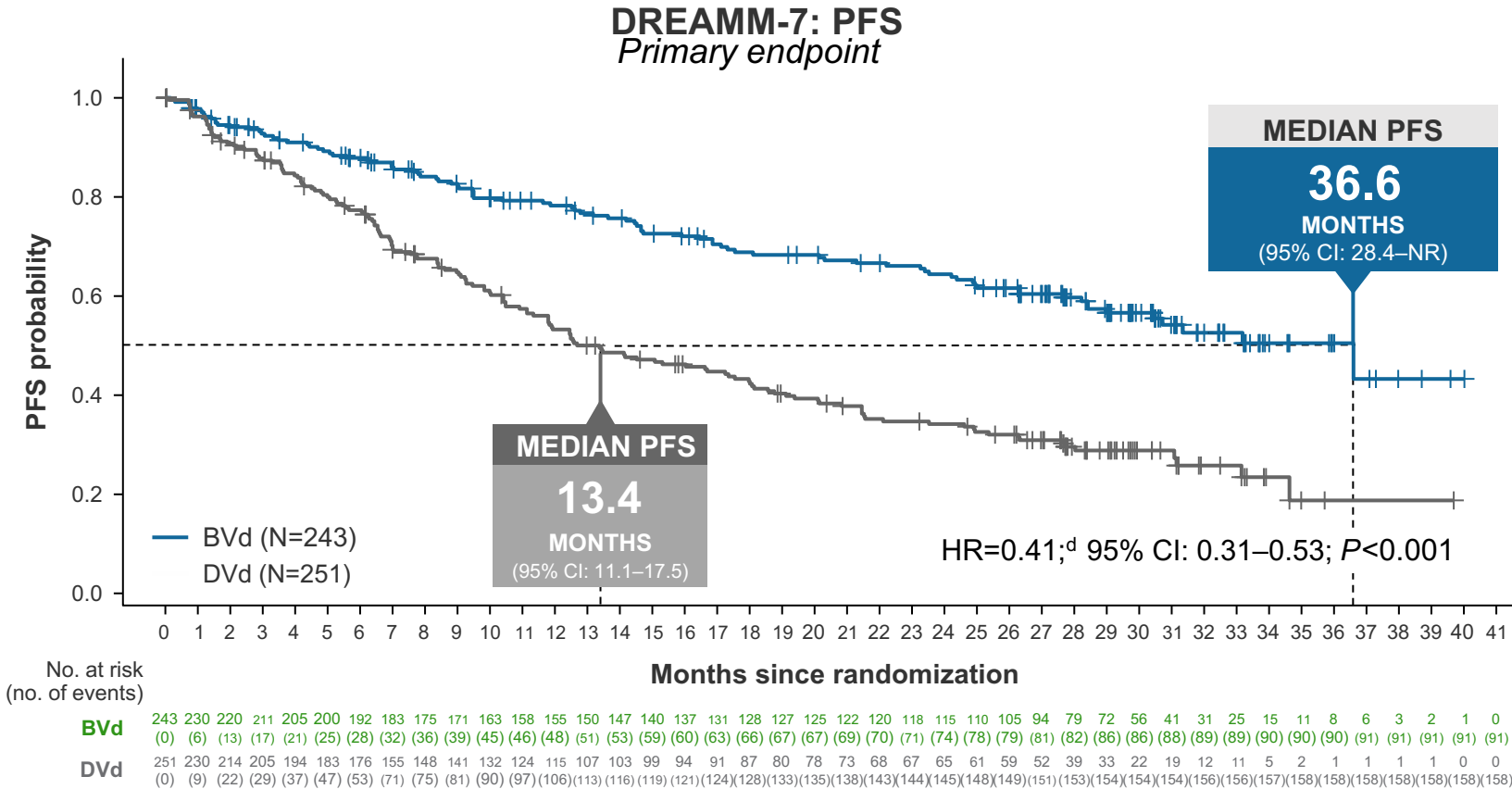
- ~30% high-risk cytogenetics
- ~50% one prior LoT
- ~80-90% PI-exposed
- ~50% Len-exposed
- only 1-2% CD38-exposed

Table 1. Baseline Demographic and Clinical Characteristics and Previous Therapies.*

Characteristics	BVd (N = 243)	DVd (N = 251)
Median age (range) — yr	65.0 (34.0–86.0)	64.0 (32.0–89.0)
Age category — no. (%)		
18 to <65 yr	121 (50)	126 (50)
65 to <75 yr	85 (35)	95 (38)
≥75 yr	37 (15)	30 (12)
Sex — no. (%)		
Male	128 (53)	144 (57)
Female	115 (47)	107 (43)
Race — no. (%)†		
White	206 (85)	203 (81)
Black	8 (3)	12 (5)
Asian	28 (12)	33 (13)
ECOG performance-status score ≤1 — no./total no. (%)‡	232/242 (96)	235/246 (96)
R-ISS stage at screening — no. (%)		
I	102 (42)	103 (41)
II	130 (53)	132 (53)
III	9 (4)	14 (6)
Unknown	2 (1)	2 (1)
Median time since diagnosis (range) — yr	4.3 (0.2–26.0)	3.9 (0.1–23.4)
Cytogenetic risk — no. (%)§		
Standard	175 (72)	175 (70)
High	67 (28)	69 (27)
t(4;14)	41 (17)	42 (17)
t(14;16)	8 (3)	6 (2)
del(17p13)	30 (12)	35 (14)
Missing or not evaluable	1 (<1)	7 (3)
Other cytogenetic abnormalities — no. (%)		
del(13)	18 (7)	28 (11)
del(1p)	22 (9)	31 (12)
Hyperdiploidy	33 (14)	28 (11)
t(11;14)	13 (5)	15 (6)
t(14;20)	1 (<1)	1 (<1)
1q21+	94 (39)	79 (31)
Other	30 (12)	24 (10)
Extramedullary disease — no. (%)		
Yes	13 (5)	25 (10)
No	230 (95)	226 (90)
Myeloma IgG — no. (%)	161 (66)	159 (63)
Previous lines of therapy — no. (%)		
1	125 (51)	125 (50)
2 or 3	88 (36)	99 (39)
≥4	30 (12)	27 (11)
Time to relapse after most recent therapy — no. (%)		
≤12 mo	49 (20)	50 (20)
>12 mo	194 (80)	201 (80)
Previous proteasome inhibitor — no. (%)		
Any	218 (90)	216 (86)
Bortezomib	210 (86)	211 (84)
Carfilzomib	31 (13)	35 (14)
Ixazomib	13 (5)	11 (4)
Previous immunomodulatory drugs — no. (%)		
Any	198 (81)	216 (86)
Lenalidomide	127 (52)	130 (52)
Thalidomide	121 (50)	144 (57)
Pomalidomide	25 (10)	19 (8)
Previous daratumumab treatment — no. (%)	3 (1)	4 (2)
Previous ASCT — no. (%)	164 (67)	173 (69)
Previous chemotherapy — no. (%)	198 (81)	206 (82)
Previous glucocorticoids — no. (%)	241 (>99)	247 (98)

* Percentages may not total 100 because of rounding. ASCT denotes autologous stem-cell transplantation, BVd belantamab mafodotin, bortezomib, and dexamethasone, DVd daratumumab, bortezomib, and dexamethasone, and R-ISS Revised International Staging System.
† Race was reported by the investigators.
‡ The Eastern Cooperative Oncology Group (ECOG) performance-status scores range from 0 to 5, with higher scores indicating greater disability.
§ Standard cytogenetic risk was defined by negative results for all high-risk abnormalities: t(4;14), t(14;16), and del(17p13). High cytogenetic risk was defined by the presence of at least one high-risk abnormality. High-risk abnormalities were assessed by means of interphase fluorescence in situ hybridization with the following central laboratory thresholds: 2% for t(4;14), 2% for t(14;16), and 5% for del(17p13). Local laboratory thresholds were based on local standards. Details are provided in the Supplementary Appendix.

Striking Improvement in mPFS with BelaVd



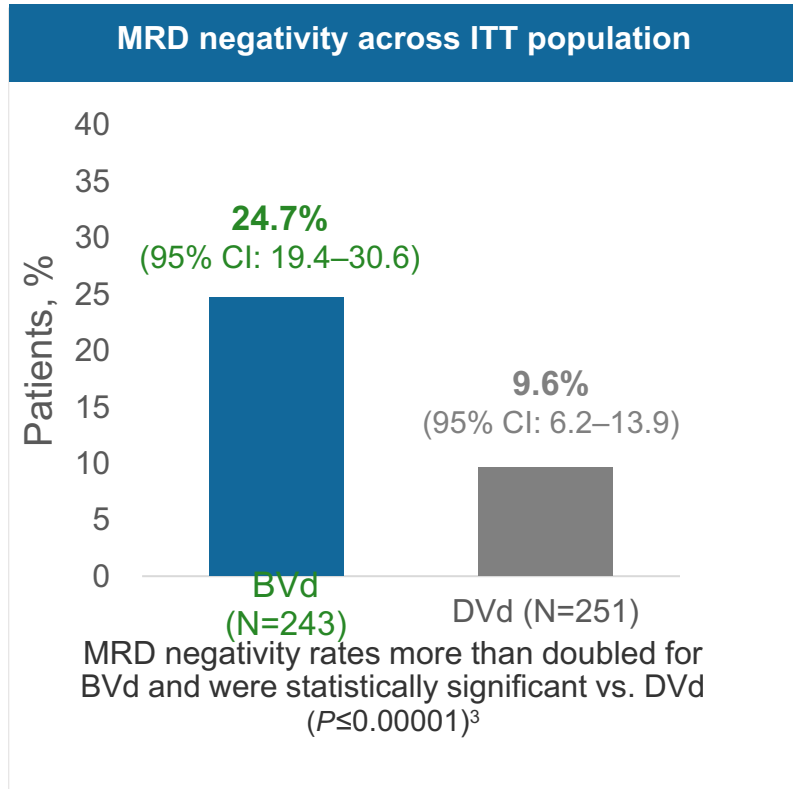
- Median PFS of **36.6 months for BVd** vs. 13.4 months for DVd

- Median follow-up: **28.2 months** (range: 0.1–40.0)
- Events, n (%): **BVd, 91 (37); DVd, 158 (63)**

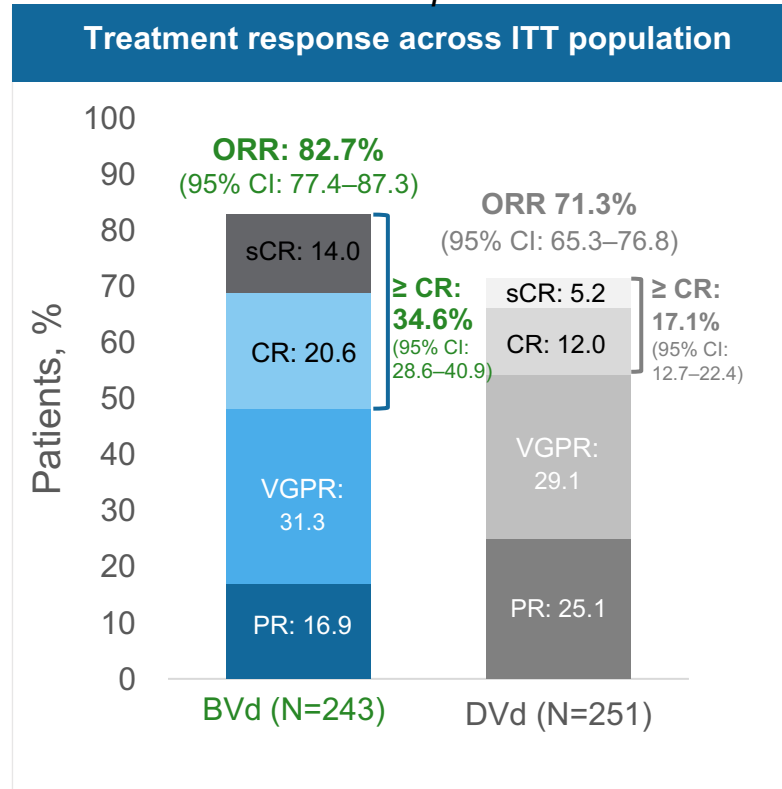
Hungria V, et al. *N Engl J Med.* 2024;391(5):393–407.

DREAMM-7: Significant Improvement in Depth and Duration of Response with BelaVd

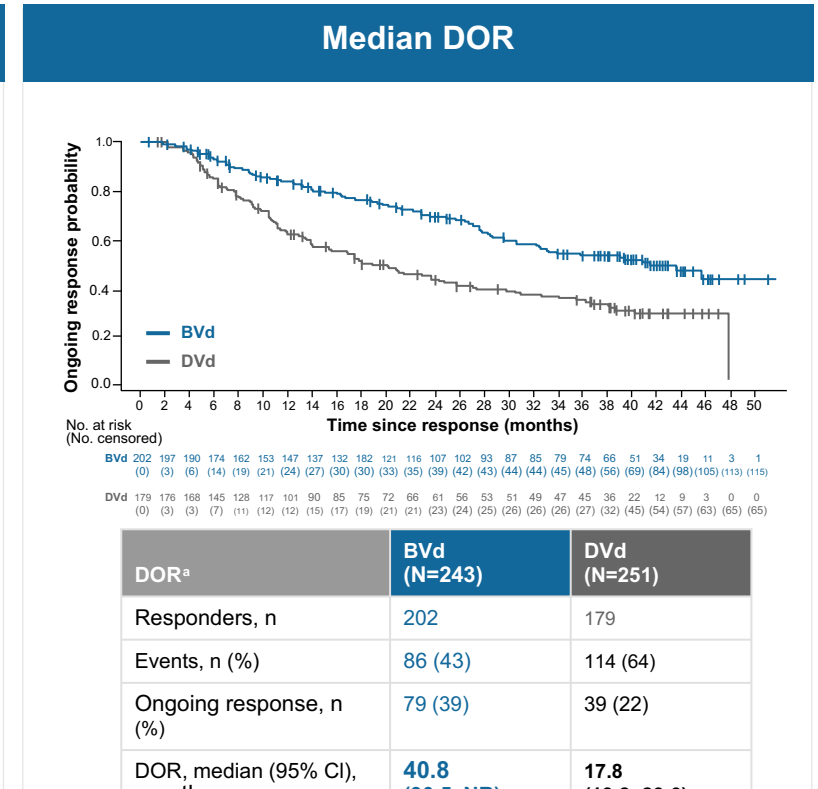
DREAMM-7: Secondary endpoints



Adapted from Hungria V, et al. Presented at: ASH 2024. Poster 3359.

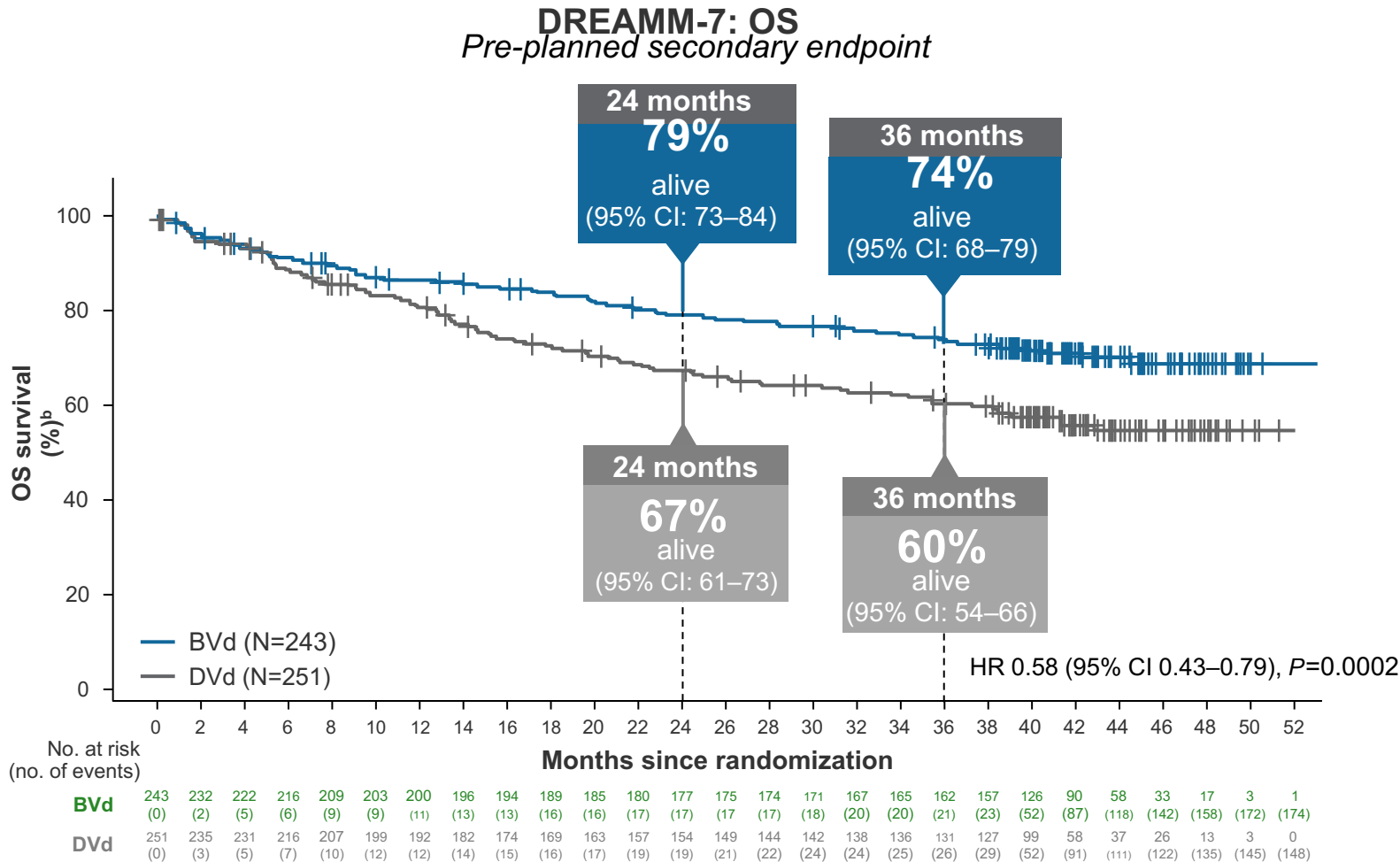


Adapted from Mateos MV, et al. Presented at: ASCO 2024. Poster 7546.



Adapted from Hungria V, et al. Presented at: ASH 2024. Oral 772.

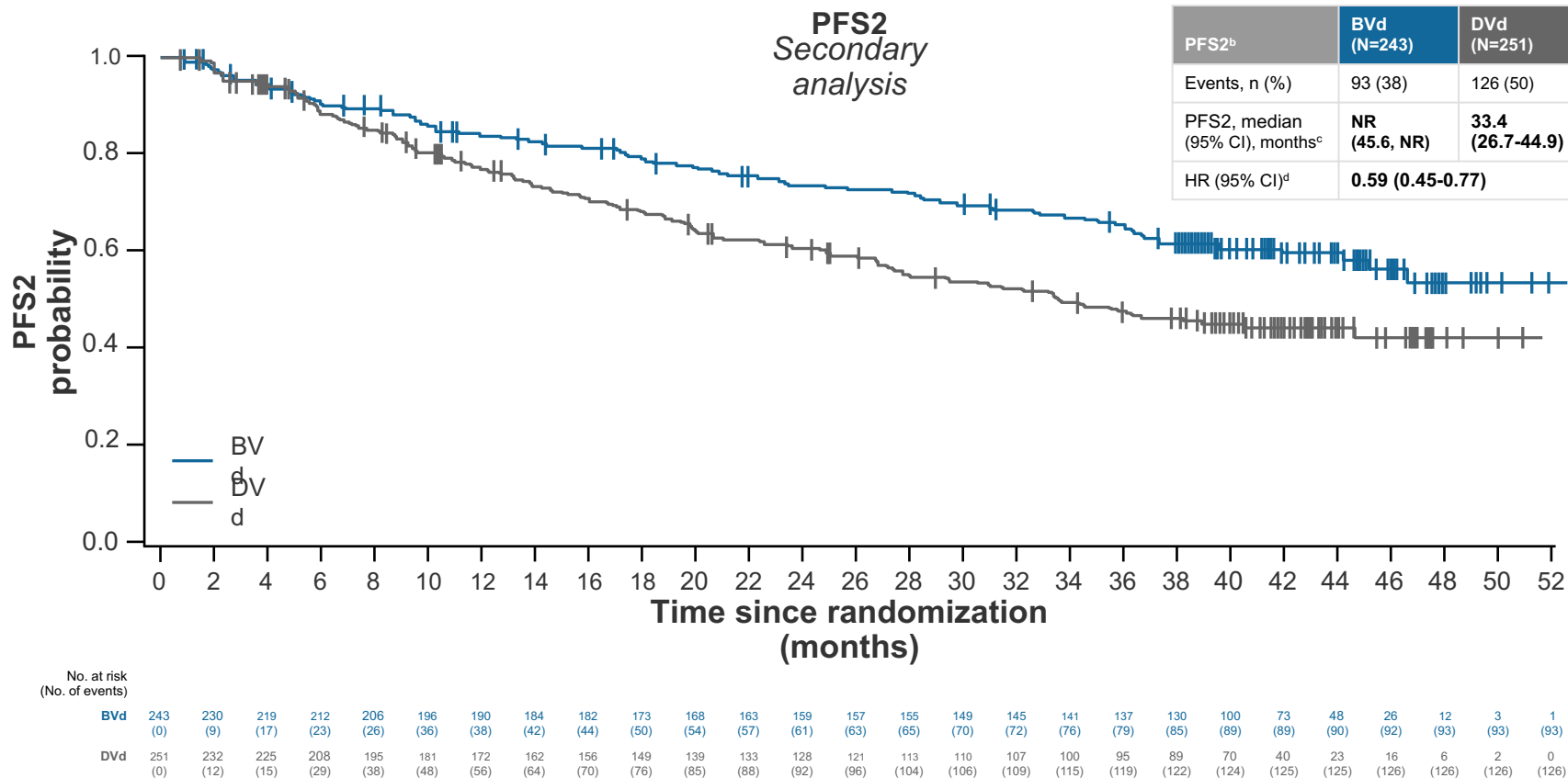
OS: significant 42% reduction in risk of death with BelaVd



- predicted mOS of 84 months with BVd and 51 months for DVd

Hungria V, et al. *Lancet Oncol.* 2025;26;1067–1080.

DREAMM-7: BVd efficacy following subsequent anti-myeloma therapy



In the **BVd arm**, the most common first subsequent therapies after study treatment were:

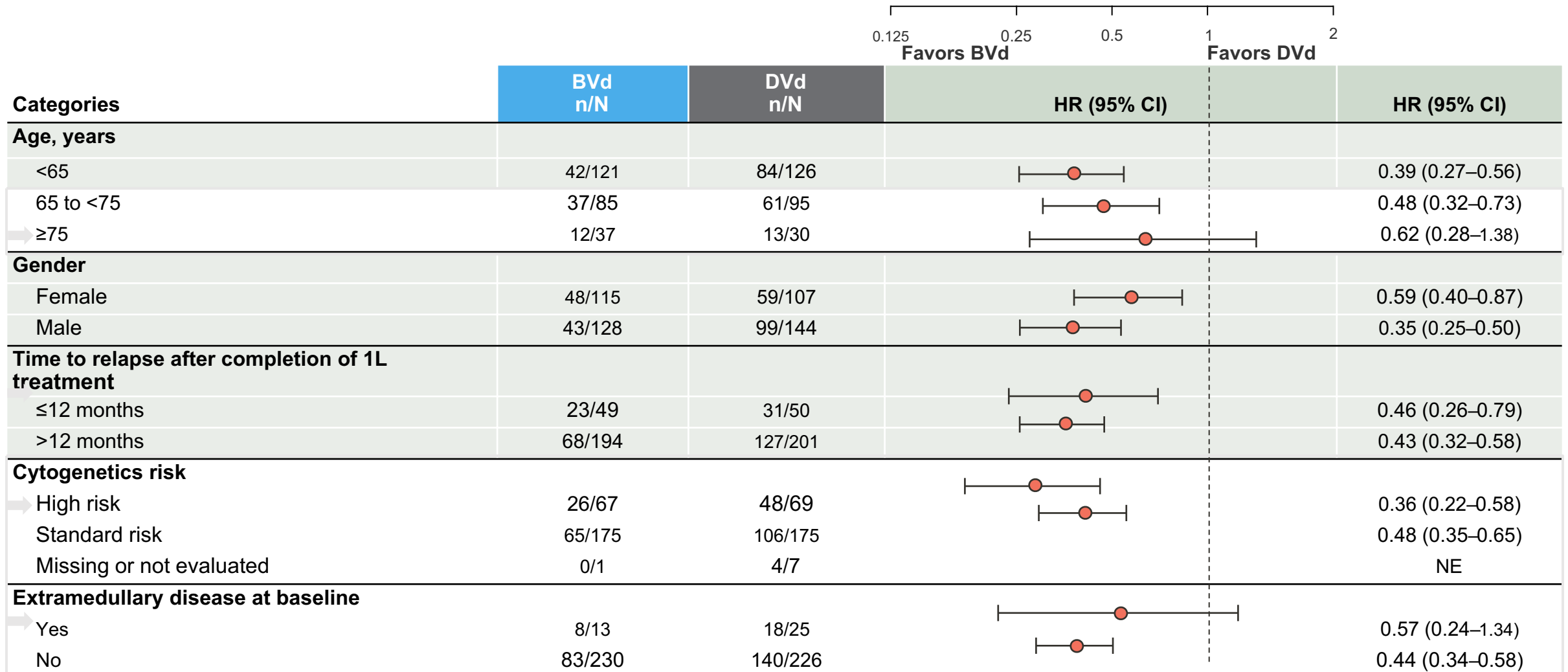
- Anti-CD38 monoclonal antibodies (daratumumab n=30/87, 34%) and isatuximab n=16/87, 18%)
- Pomalidomide (n=26/87, 30%)
- Lenalidomide (n=17/87, 20%)

In the **DVd arm**, they were:

- Lenalidomide (n=40/130, 31%)
- Carfilzomib (n=39/130, 30%)
- Pomalidomide (n=25/130, 19%)

Hungria V, et al. Presented at: 66th American Society of Hematology (ASH) Annual Meeting and Exposition; December 7–10, 2024; San Diego, CA and virtual. Presentation #772.

PFS benefit upheld in high-risk patients



1. Hungria V et al. [Supplemental appendix]. *N Engl J Med.* 2024;391(5):393-407; 2. belantamab mafodotin. Summary of Product Characteristics. GlaxoSmithKline; 2025.

Non-ocular toxicities in DREAMM-7

DREAMM-7 side effects of clinical interest (safety population) Updated analysis

Adverse event	BVd (N=242)		DVd (N=246)	
	n (%)	Patients/100 person-years	n (%)	Patients/100 person-years
Thrombocytopenia				
Any event	169 (70)	42	122 (50)	36
Grade ≥3	135 (56)	34	87 (35)	25
Neutropenia^b				
Any event	45 (19)	11	44 (18)	13
Grade ≥3	34 (14)	8	24 (10)	7
Infections and infestations				
Any event	176 (73)	44	167 (68)	49
Grade ≥3	80 (33)	20	49 (20)	14

The median duration of exposure to any trial drug was **15.9 months (range: 0.7–52.3 months)** for BVd and 12.8 months (range: 0.2–48.8 months) for DVd

No cases of ICANS or no fatal CRS observed in clinical trials

In DREAMM-7, patients on BVd experienced low rates of opportunistic infections (1%, n=3/242) and low use of IVIg (8%, n=19/242)

1. Hungria V, et al. *Lancet Oncol.* 2025;26:1067–1080; 2. Hungria V, et al. [Supplementary appendix]. *Lancet Oncol.* 2025;26:1067–1080; 3. belantamab mafodotin. UK Summary of Product Characteristics. GlaxoSmithKline; 2025; 4. belantamab mafodotin. Summary of Product Characteristics. GlaxoSmithKline; 2025; 5. Hungria V, et al. *N Engl J Med.* 2024;391:393–407; 6. Hungria V, et al. [Supplementary appendix]. *N Engl J Med.* 2024;391:393–407; 7. Hungria V, et al. Presented at: American Society of Hematology Annual Meeting and Exposition; December 7–10, 2024; San Diego, CA and virtual. Abstract 772.

Ocular Toxicities in DREAMM-7

DREAMM-7 eye-related side effects (by CTCAE) ≥15% of patients in either treatment group¹
Updated analysis

	BVd (N=242)		DVd (N=246)	
	Any Grade n (%)	Grade ≥3 n (%)	Any Grade n (%)	Grade ≥3 n (%)
Any event	191 (79)	82 (34)	72 (29)	7 (3)
Vision blurred	160 (66)	53 (22)	26 (11)	2 (1)
Dry eye	123 (51)	17 (7)	17 (7)	0
Photophobia	114 (47)	5 (2)	6 (2)	0
Foreign body sensation in eye	106 (44)	8 (3)	10 (4)	0
Eye irritation	103 (43)	12 (5)	13 (5)	0
Eye pain	77 (32)	2 (1)	8 (3)	1 (<1)

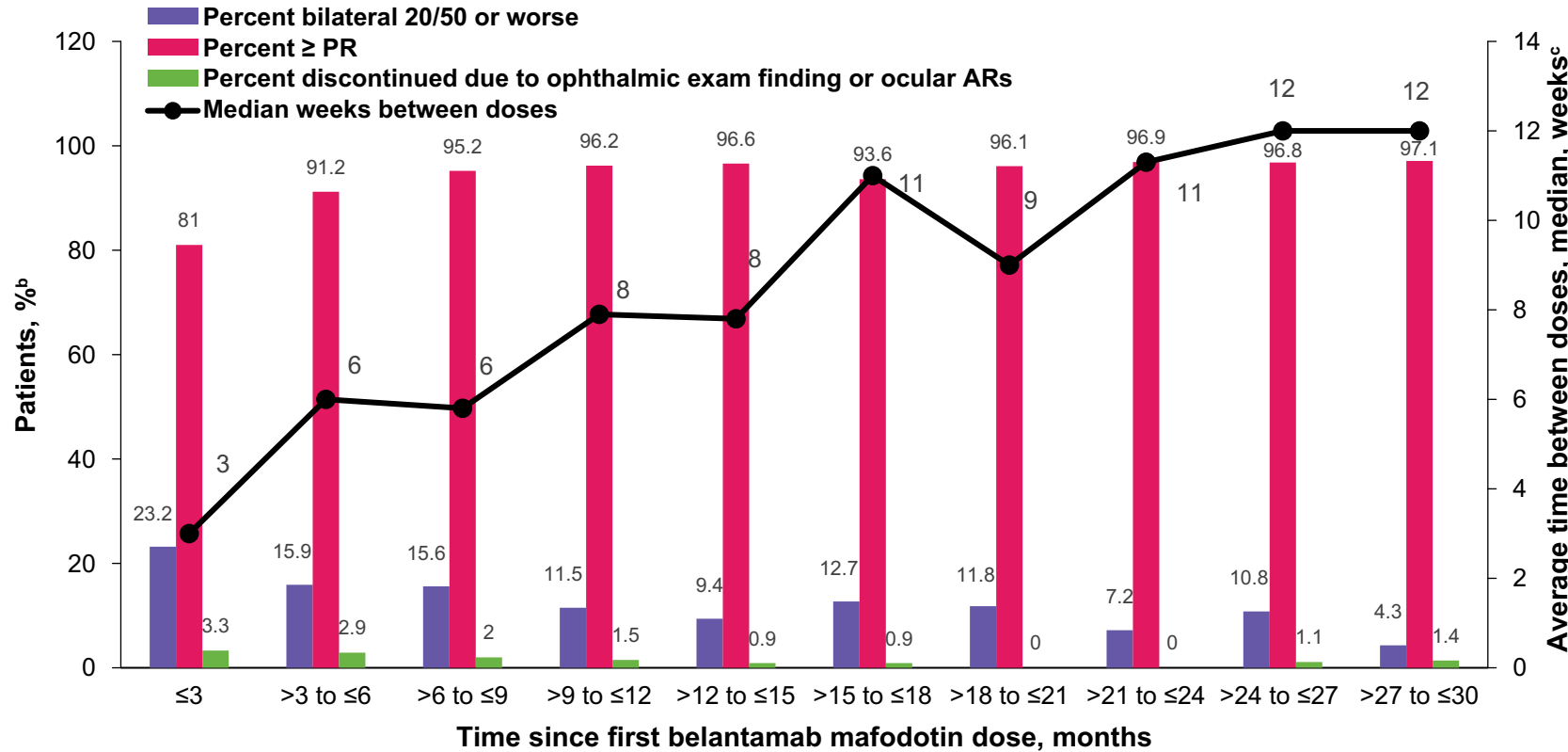
9% (n=22/242) of patients discontinued belantamab mafodotin due to eye-related AEs¹

- Throughout the study, **dose modifications managed adverse reactions** and enabled patients to continue treatment¹⁻³
- In the BVd arm, **34% of patients had a bilateral reduction in BCVA of 20/50 or worse; of those, 98% had improvement of first event¹**

Rare cases of corneal ulcer have been reported (<1% in the BVd arm of DREAMM-7). These should be managed promptly and as clinically indicated by an ECP. Treatment with belantamab mafodotin should be interrupted until the corneal ulcer has healed.^{1,2}

1. Hungria V, et al. *N Engl J Med*. 2024;391(5):393-407; 2. belantamab mafodotin. Summary of Product Characteristics. GlaxoSmithKline; 2025; 3. belantamab mafodotin. UK Summary of Product Characteristics. GlaxoSmithKline; 2025.

DREAMM-7: Median Dosing Interval, Response Rates, and Ocular Events



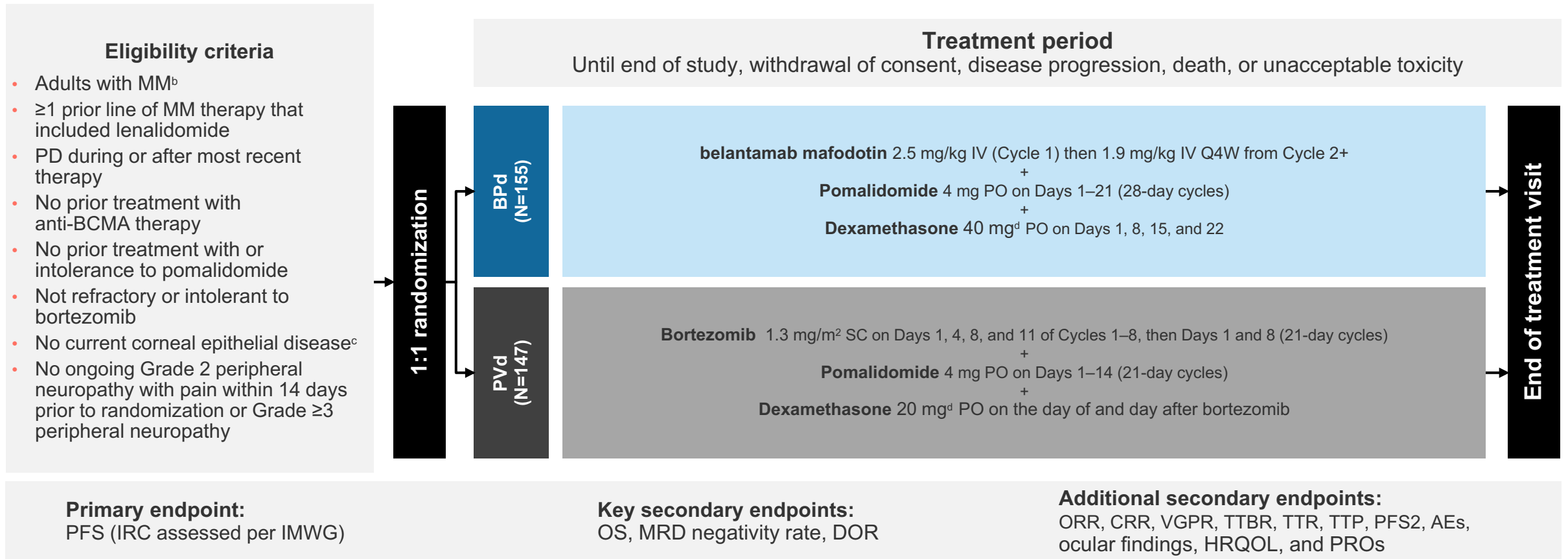
No. of patients on treatment: 211, 170, 147, 131, 117, 110, 102, 97, 93, 69

- Median time between doses increased with treatment duration
- Responses (Best Confirmed Response ≥ PR within each interval) remained high throughout treatment
- 23% of patients experienced 20/50 or worse events in the first 3 months; prevalence generally decreased thereafter
- The rate of treatment discontinuation due to ocular events was low

Results from the primary analysis (data cutoff, October 2, 2023)

1. Mateos MV, et al. ASCO 2024. Updates to abstract 439572. 2. Mateos MV, et al. EHA 2024. Abstract S214. 3. Hungria V, et al. IMS 2024. Poster P-396.

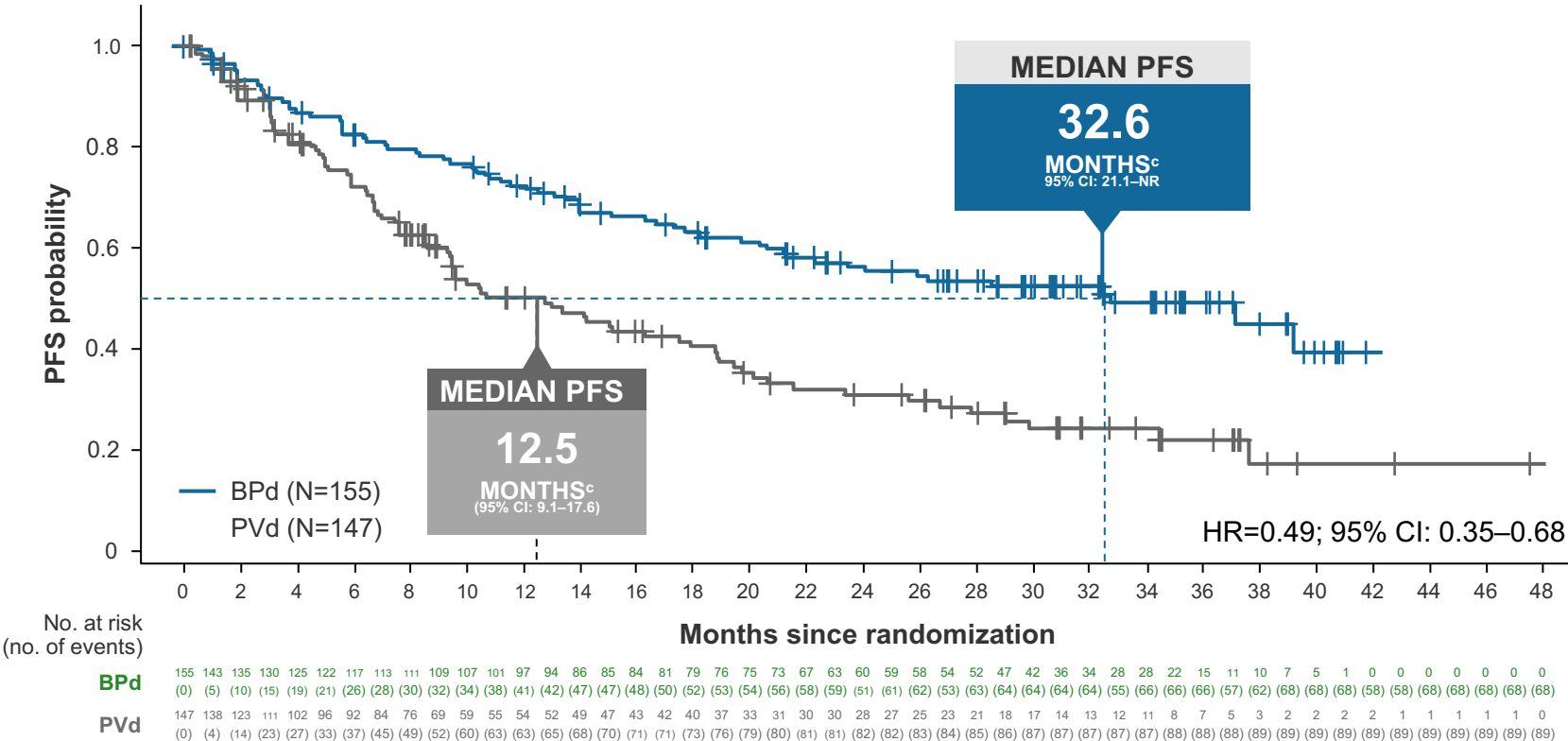
DREAMM-8: global phase 3 trial of Bela-Pd vs PVd in patients with ≥ 1 prior LoT and lenalidomide exposure



1. belantamab mafodotin. Summary of Product Characteristics. GlaxoSmithKline; 2025; 2. Dimopoulos MA, et al. *N Engl J Med.* 2024;391(5):408–421; 3. Dimopoulos MA, et al. [Supplemental appendix]. *N Engl J Med.* 2024;391(5):408–421; 4. Dimopoulos MA, et al. Presented at: European Hematology Association 2025 Congress; June 12–15, 2025; Milan, Italy. PF728; 5. Trudel S, et al. Presented at: 2024 American Society of Clinical Oncology (ASCO) Annual Meeting Annual Meeting; May 31–June 4, 2024; Chicago, IL.

DREAMM-8: Tripling of mPFS with Bela

DREAMM-8: PFS Pre-planned secondary endpoint

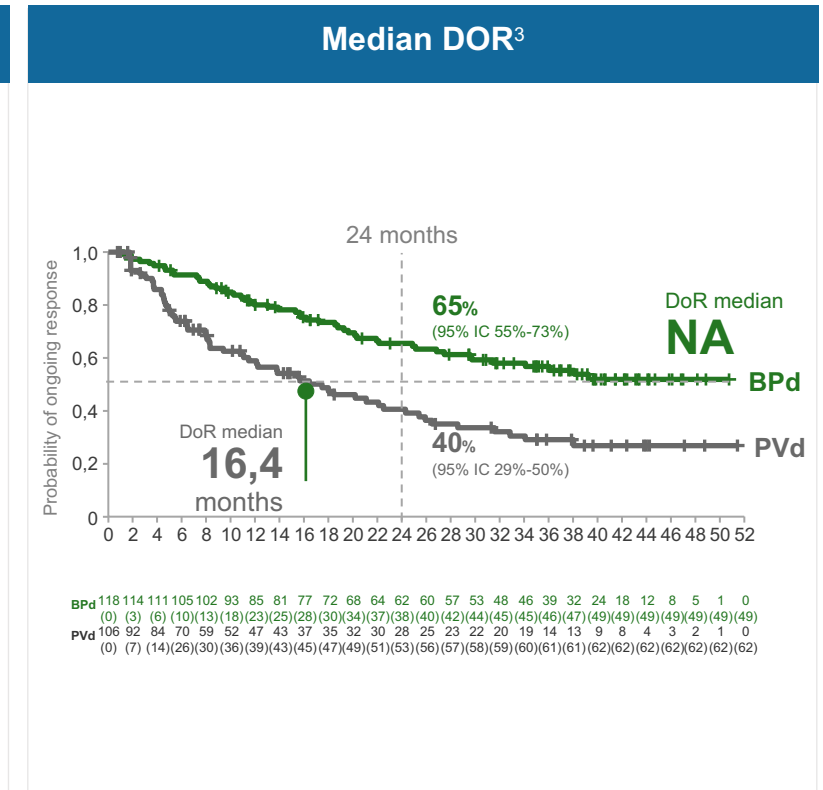
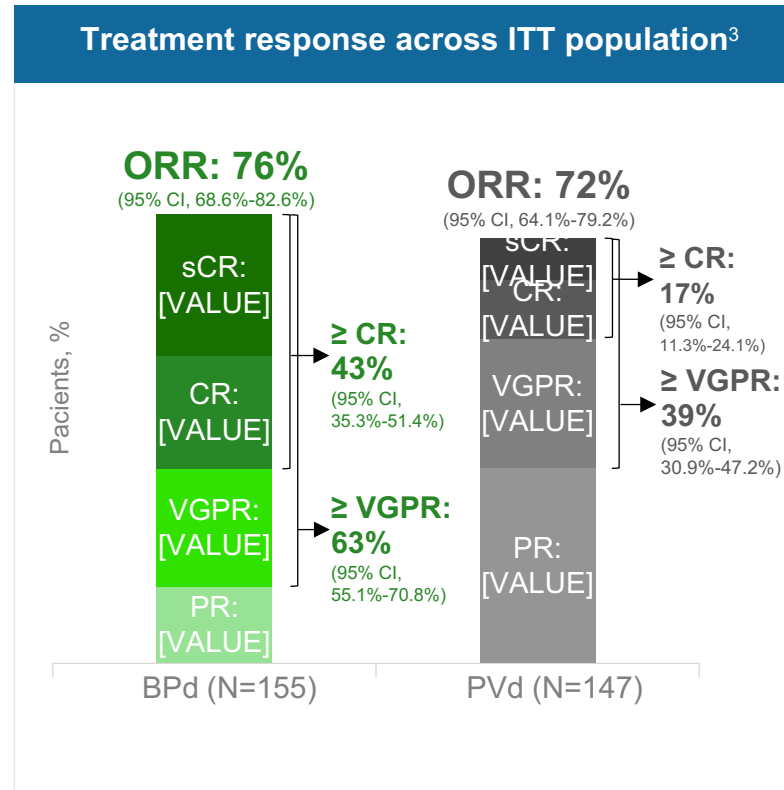
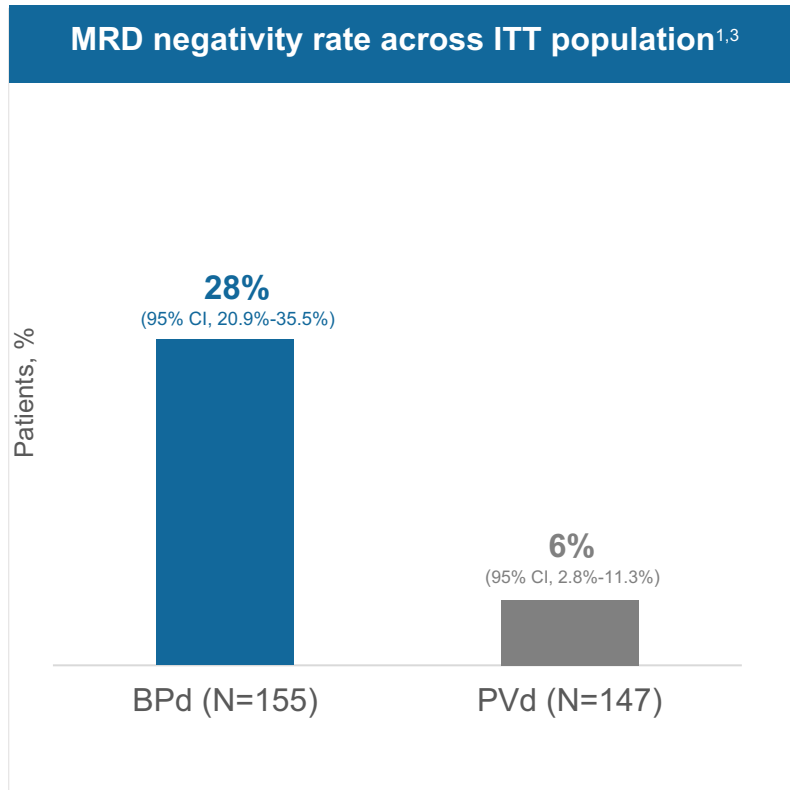


- Median PFS of **32.6 months** for BPd vs. **12.5 months** for PVd
- Median follow-up: **28.01 months** (range: 0.03–47.74)
- Events, n (%): **BPd, 68 (44); PVd, 89 (61)**

Adapted from Dimopoulos MA, et al. Presented at: EHA 2025. PF728.

DREAMM-8: Improvement in Depth and Duration of Response with Bela

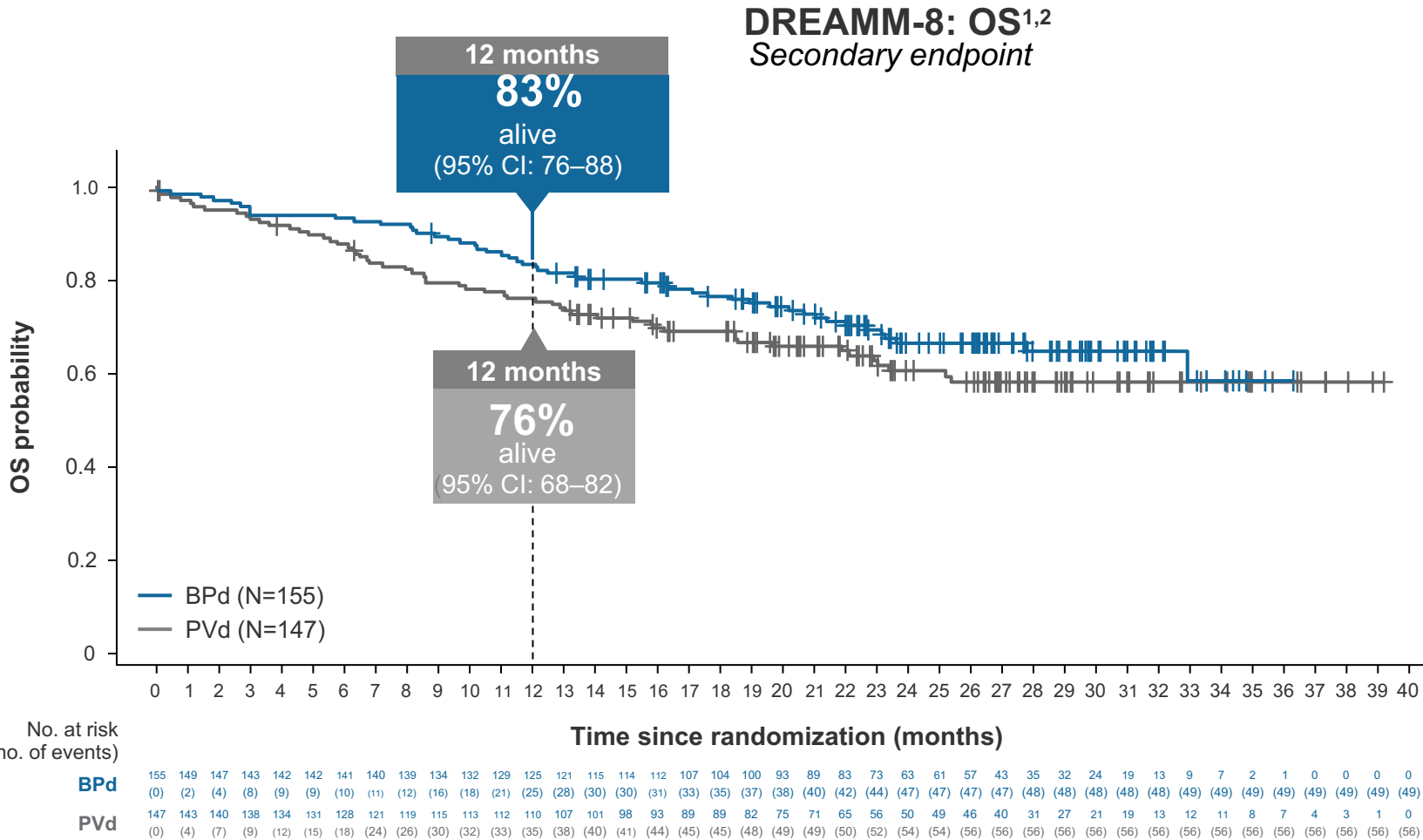
DREAMM-8 – Secondary endpoints



Adapted from Trudel S, et al. P2264 presented at ASH 2025.

1. belantamab mafodotin. Summary of Product Characteristics. GlaxoSmithKline; 2025; 2. Dimopoulos MA, et al. *N Engl J Med.* 2024;391(5):408–421; 3. TRUDEL, S. et al. Deep responses and durable outcomes in patients treated with belantamab mafodotin plus pomalidomide and dexamethasone from long-term follow-up of the Phase 3 dreamm-8 study. Presented at: 67th ASH Annual Meeting and Exposition. December 6-9. Orlando, FL, USA. Poster 2264

DREAMM-8: trend towards OS (data maturing)



mOS not reached at time of primary analysis^{1,2}

- Median follow-up: **21.8 months**^{1,2}
- Events, n (%): **BPd, 49 (32); PVd, 56 (38)**^{1,2}

Adapted from Dimopoulos MA, et al. *N Engl J Med.* 2024;391(5):408–421.

1. belantamab mafodotin. Summary of Product Characteristics. GlaxoSmithKline; 2025; 2. Dimopoulos MA, et al. *N Engl J Med.* 2024;391(5):408–421; 3. Trudel S, et al. Presented at: 2024 American Society of Clinical Oncology (ASCO) Annual Meeting Annual Meeting; May 31–June 4, 2024; Chicago, IL.

DREAMM-8: non-ocular toxicity

DREAMM-8 side effects of clinical interest (safety population) Updated analysis

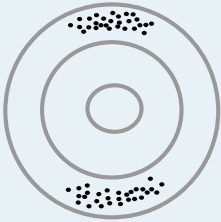
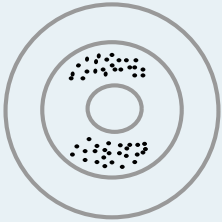
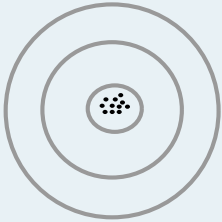
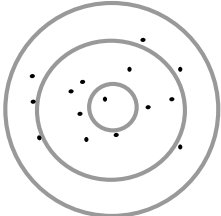
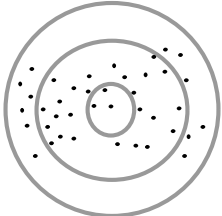
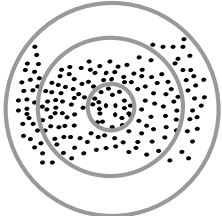
Adverse event	BPd (N=150)		PVd (N=145)	
	n (%)	Patients/100 person-years	n (%)	Patients/100 person-years
Thrombocytopenia				
Any event	81 (54)	33	60 (41)	39
Grade ≥3	57 (38)	23	42 (29)	27
Neutropenia				
Any event	97 (65)	39	69 (48)	45
Grade ≥3	87 (58)	35	60 (41)	39
Infections				
Any event	124 (83)	50	101 (70)	66
Grade ≥3	78 (52)	31	39 (27)	25

The median duration of exposure to any trial drug was **18.97 months (range: 0.92–43.47 months) in the BPd arm** and 8.51 months (range: 0.26–48.13 months) in the PVd arm¹

No cases of ICANS or no fatal CRS observed in clinical trials²

1. Dimopoulos MA, et al. Presented at: European Hematology Association 2025 Congress; June 12–15, 2025; Milan, Italy. PF728; 2. Dimopoulos MA, et al. [Supplemental appendix]. *N Engl J Med.* 2024;391(5):408–421; 3. belantamab mafodotin. UK Summary of Product Characteristics. GlaxoSmithKline; 2025; 4. belantamab mafodotin. Summary of Product Characteristics. GlaxoSmithKline; 2025.

What is keratopathy and how do we grade it?

	KVA grade 1	KVA grade 2	KVA grade 3	KVA grade 4
Snellen visual acuity scale	Decline of 1 line from baseline	Decline of 2 or 3 lines from baseline (not worse than 20/200)	Decline of ≥ 3 lines from baseline (not worse than 20/200)	Worse than 20/200
Slit lamp exam	Mild superficial keratopathy	Moderate superficial keratopathy Patchy microcyst-like deposits Peripheral subepithelial haze New peripheral stromal opacity	Severe superficial keratopathy Diffuse microcyst-like deposits Central subepithelial haze New central stromal opacity	Corneal epithelial defect (erosion or ulcer)
Slit lamp Location in eye				
Slit lamp Concentration in eye				

Important distinction: high-grade keratopathy ≠ severely blurred vision

Eye-related events reported in ≥15% of patients in the BPd treatment arm in DREAMM-8
Primary analysis

		BPd (N=242)	
		All grades	Grade 3/4
Eye-related side effects based on eye exam findings	Reduced visual acuity	91%	60%
	Corneal examination findings	87%	62%
Eye-related side effects graded according to CTCAE v5.0	Blurred vision	79%	17%
	Dry eye	61%	8%
	Foreign body sensation in eyes	61%	6%
	Eye irritation	50%	4%
	Photophobia	44%	3%
	Eye pain	33%	2%
	Visual impairment	15%	10%

- **8% (n=12/150) of patients discontinued treatment with belantamab mafodotin due to eye-related side effects**
- **Cases of corneal ulcer^d have been reported (2% in the BPd arm of DREAMM-8).** These should be managed promptly and as clinically indicated by an ECP. Treatment with belantamab mafodotin should be interrupted until the corneal ulcer has healed

1. belantamab mafodotin. UK Summary of Product Characteristics. GlaxoSmithKline UK Limited; 2025; 2. belantamab mafodotin. Summary of Product Characteristics. GlaxoSmithKline; 2025; 3. Dimopoulos MA, et al. *N Engl J Med.* 2024;391(5):408–421; 4. Dimopoulos MA, et al. [Supplementary appendix]. *N Engl J Med.* 2024;391(5):408–421.

So, where does this all leave us?

- BCMA-targeting therapy has been an enormous step forward in treatment of patients with RRMM
- BsA, CAR T, and Bela Maf all come with impressive efficacy and survival advantage over older drugs
- Safety and toxicity profiles are vastly different between BsA/CAR and Bela
 - cilta cel:
 - CRS, ICANS, cytopenias (common)
 - Parkinsonism, enterocolitis, MDS/AML (uncommon but devastating when it occurs)
 - T-cell lymphoma (rare but real)
 - BsA (Tec, Elra, Linvo, Talq)
 - CRS and neurotox (common but usually mild)
 - infections to include opportunistic (common)
 - dysgeusia, skin/nail tox, weight loss (Talq)
 - Bela Maf: ocular tox

How to make decisions for our patients?

- on an individual basis
- right answer for one patient may be wrong answer for next patient
- risk and benefit need to be considered in context of patient's comorbidities, complications of therapy, access to care, and most importantly their preferences and concerns
- for patients appropriate for all three (BsA, CAR, ADC), sequencing remains a largely unanswered question

Thoughts on sequencing

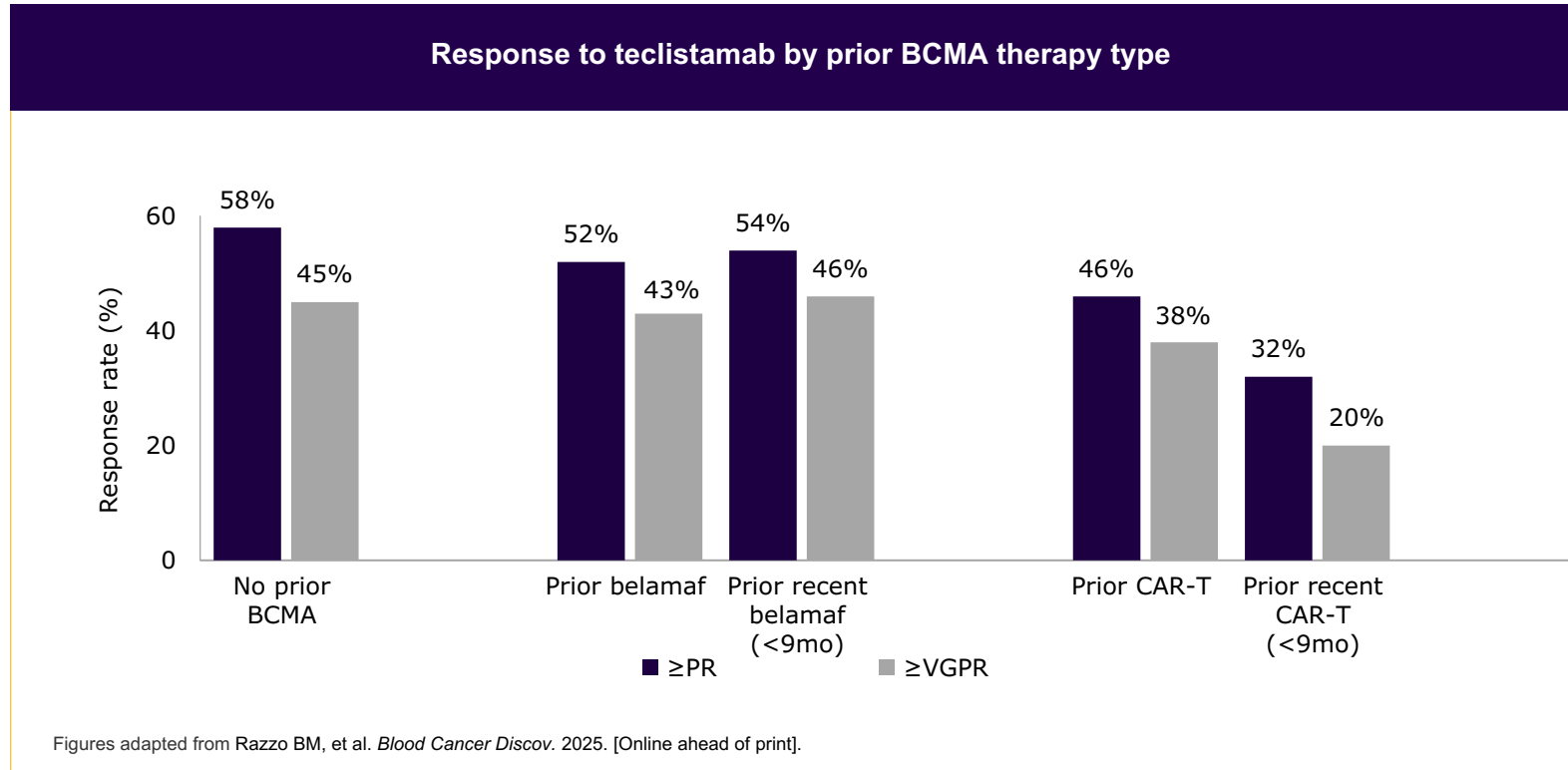
- between BsA and CAR T
 - generally preferable to select CAR before BsA in eligible patients given T-cell exhaustion with the latter
 - this may be changing though, e.g. fixed duration BsA studies showing good results
- between ADC and BsA/CAR: very limited data, but available data are mostly encouraging

Concerns have been raised based on very limited CARTITUDE-2 data

- 13 patients received ADC before cilta cel
- responses seen in 8/13 and mPFS
- one non-responder also had received another ADC prior to cilta cel
- I don't know that any recommendations re sequencing can be made from these data

The efficacy of bispecific antibody therapies following belantamab mafodotin treatment is studied in real-world

A retrospective study of post-approval, real-world outcomes with teclistamab in the US Multiple Myeloma Immunotherapy Consortium



- Of 509 patients treated with teclistamab, **59 had previously received belantamab mafodotin** as a BCMA-directed therapy^a

- Patients with recent belantamab mafodotin exposure had similar response rates to teclistamab as those without prior BCMA therapy (**≥PR: 54%**)

- Patients with **prior belantamab mafodotin only** had higher **≥PR** (partial response or better) and **≥VGPR** (very good partial response or better) to teclistamab (**≥PR: 52%**, **≥VGPR: 43%**) vs. those with **prior CAR-T** (**≥PR: 46%**, **≥VGPR: 38%**)

Shorter time since prior BCMA therapy (<9 months) was associated with inferior PFS to teclistamab, mainly driven by prior CAR-T. No strong association between PFS and time since belantamab mafodotin was detected.

This information is not included in the current EU/UK SmPC and should be interpreted with caution. The data are presented here for descriptive purposes only. ^a32 patients had received both idecabtagene vicleucel (CAR-T) and belantamab mafodotin.

BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T-cell; mo, months; PFS, progression-free survival; PR, partial response; VGPR, very good partial response.

Razzo BM, et al. *Blood Cancer Discov.* 2025. [Online ahead of print].

Musa et al, Haematologica 2026

- analysis of hundreds of marrow samples from multiple DREAMM studies
- BCMA loss was not seen
- reduced affinity of binding to sBCMA across time was not seen
- increase in T-cell exhaustion markers not seen
- decrease in T-cell proliferation/activation markers not seen

In Conclusion:

Let's keep practicing our art of oncology

And keep all the paints on our palette!





Perguntas/Obrigado!