




 **Multiple Myeloma ECHO®** COMPLIMENTARY CME

**Advancing RRMM Care Through Communities of Practice:
Educating Community-Based
Hematologic/Oncologic Teams on
the Use of BCMA-Directed BsAbs**

**The Treatment Decision-Making Process:
When to Consider or Defer BCMA-Directed BsAbs
in a Patient's MM Treatment Journey**

Led by  **Chobanian & Avedisian**
School of Medicine

Produced in collaboration with    

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Faculty

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Learning Objective

Upon completion, participants should be able to:

- Appropriately incorporate BCMA-directed BsAbs into cases of patients with MM that are representative of clinical practice



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The Treatment Decision-Making Process in RRMM: It Is Not an Algorithm

Many of these variables change over time!

Patient-Related

- Age/frailty
- Performance status
- Drug metabolism
- Compliance/adherence
- Renal insufficiency
- Comorbidities
- Social support:
 - Preference/lifestyle
 - Caregiver support
 - Financial access
 - Logistical access

Disease-Related

- R-ISS
- Rate of growth
- Marrow burden
- CRAB symptoms:
 - Hypercalcemia
 - Renal failure
 - Anemia
 - Bone disease
- Extramedullary disease
- Molecular cytogenetics/genomics

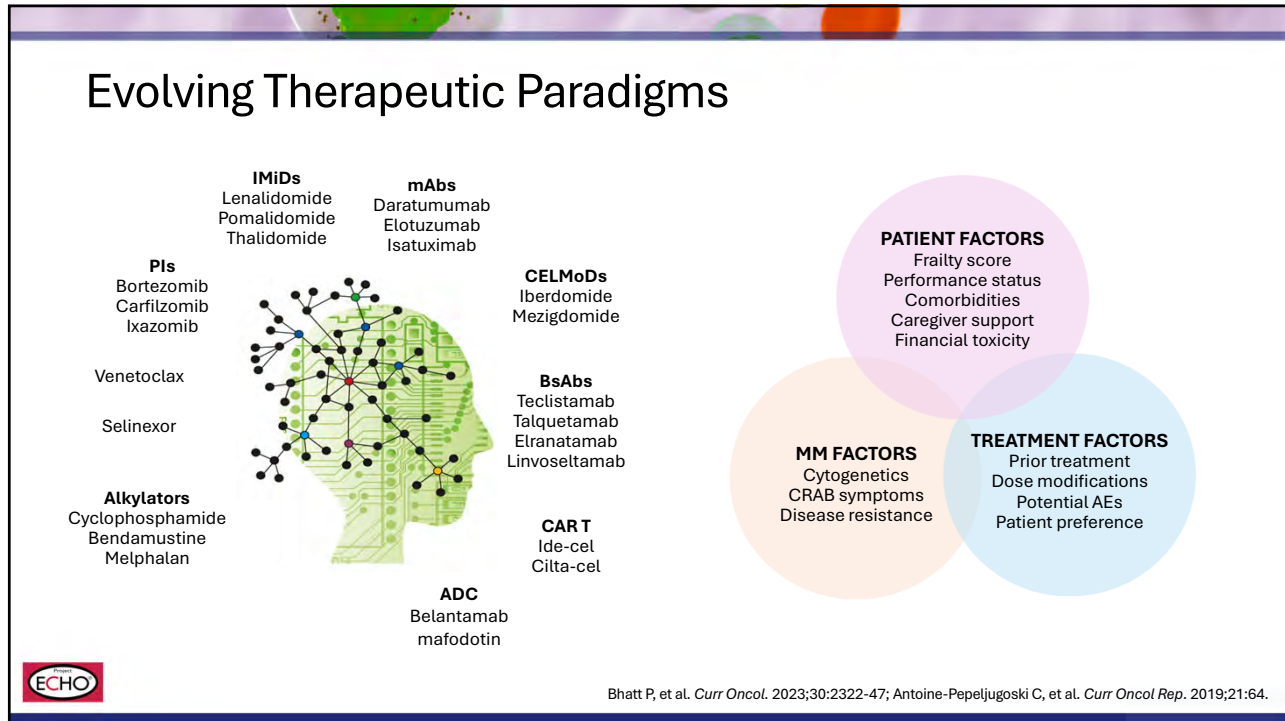
Treatment-Related

- Response to prior therapy
- Time to relapse
- Clinical trial availability
- Route of administration
- Adverse events/toxicity
- Single agent vs combination

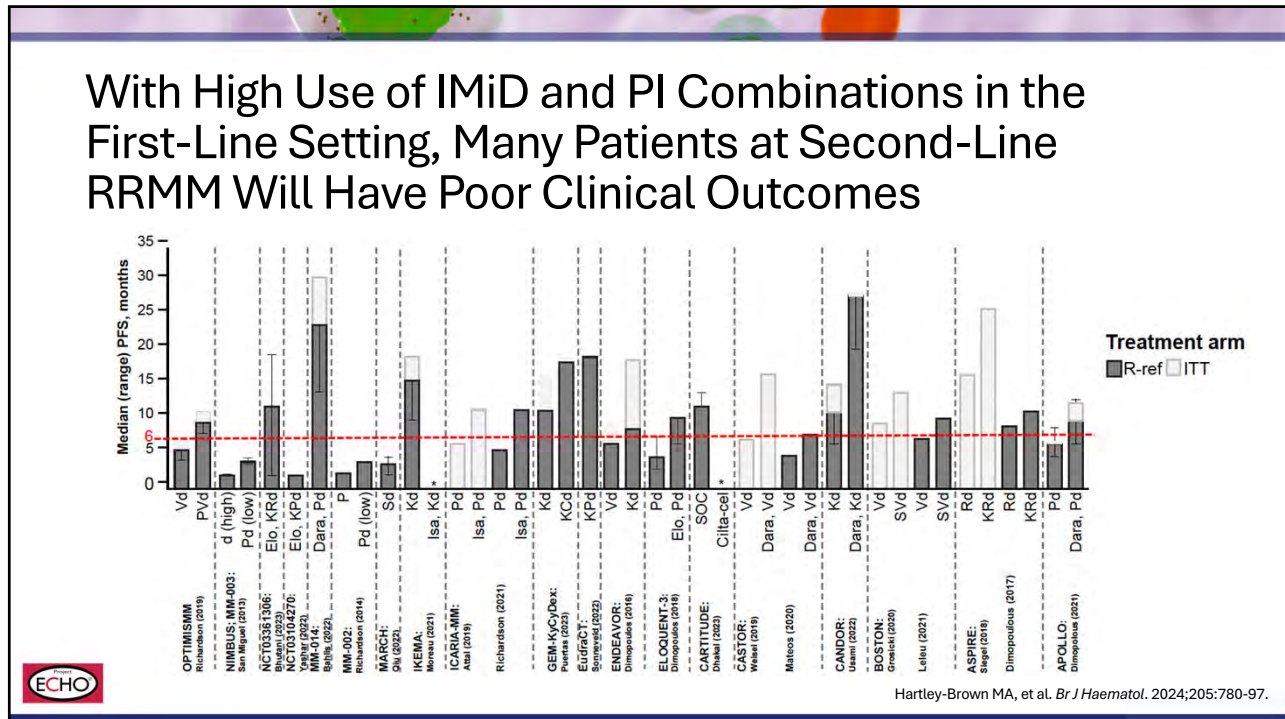


Kumar S, et al. *Clin Lymphoma Myeloma Leuk.* 2025;25:730-8; Gengenbach L, et al. *Cancers (Basel).* 2021;13:4320.

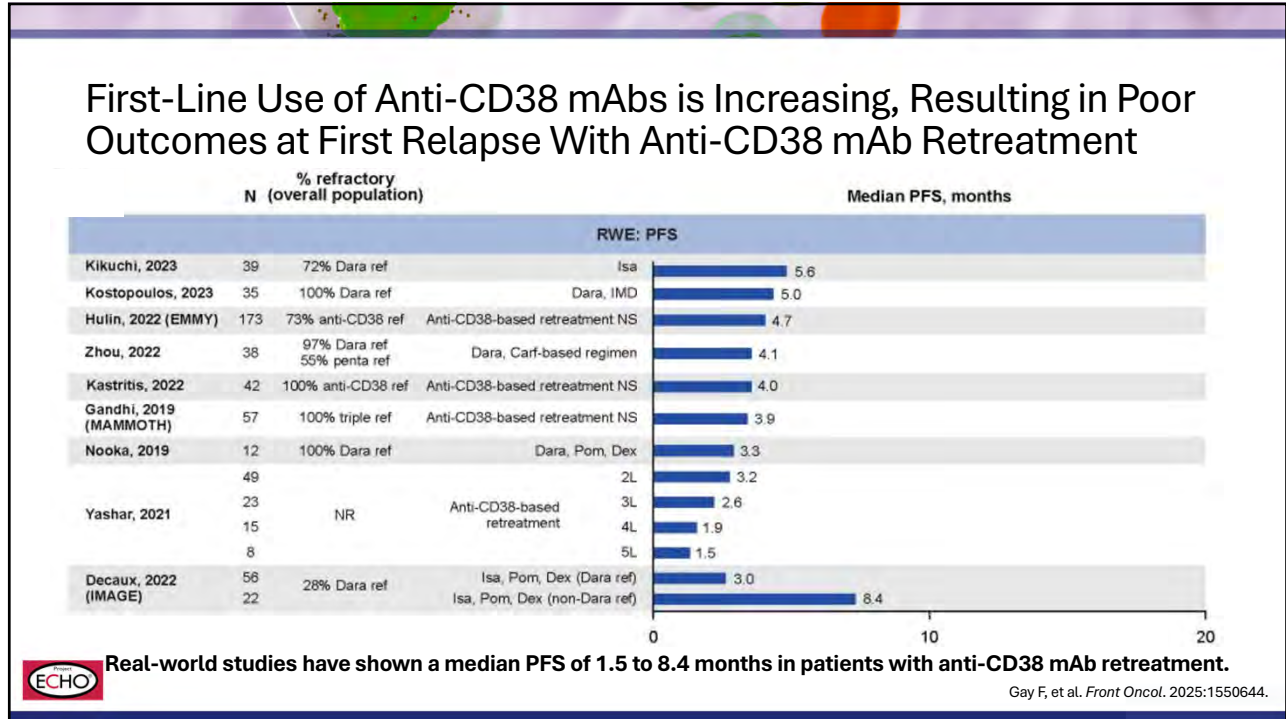
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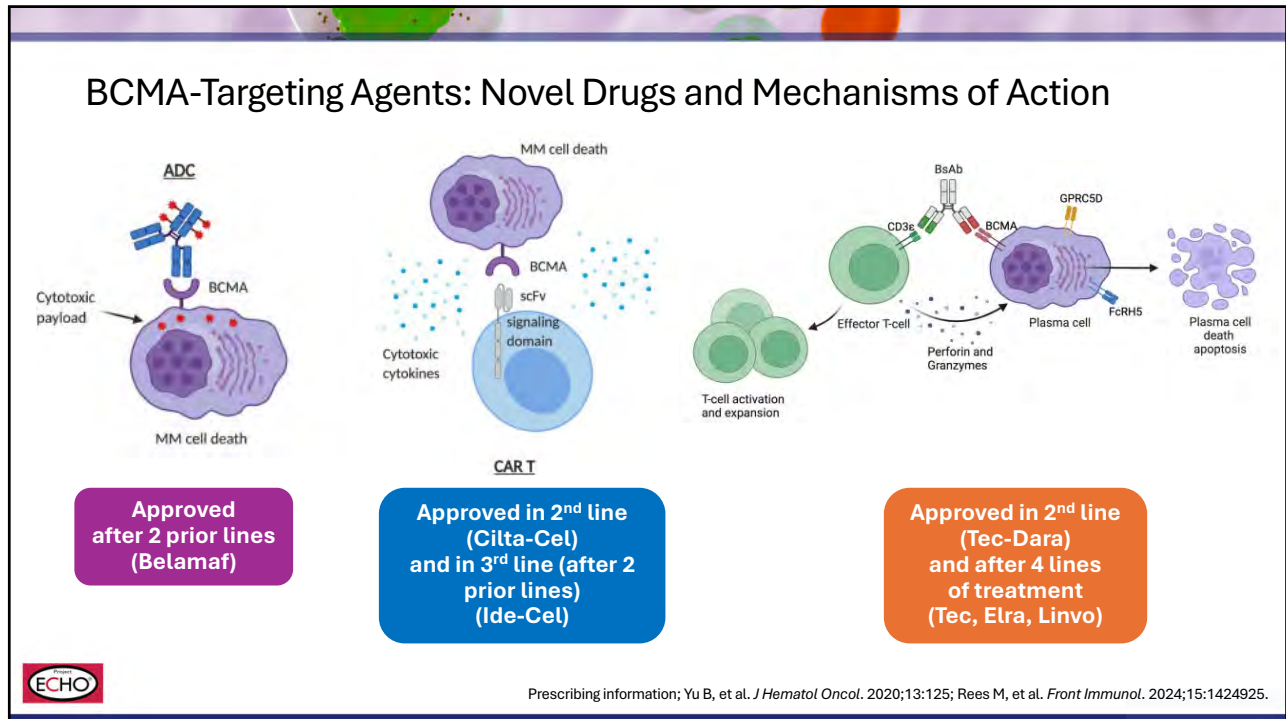
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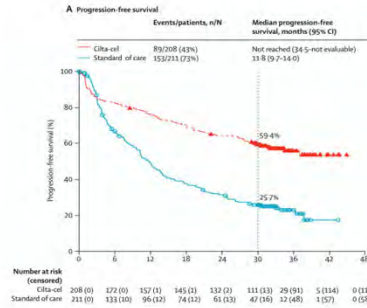
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BCMA-Directed Options in Early Relapsed MM

CARTITUDE-4 (34-mos follow-up) Cilta-Cel vs DPD/PVD



Patient characteristics (n = 208; 176 tx)
 1-3 prior LOT (med 2)
 Len refractory: 100%
 Prior anti-CD38 (24% refractory): 25%
 High-risk cytogenetics (del(17p, t4;14), t(14;16)): 35.3%
 EMD: 21%

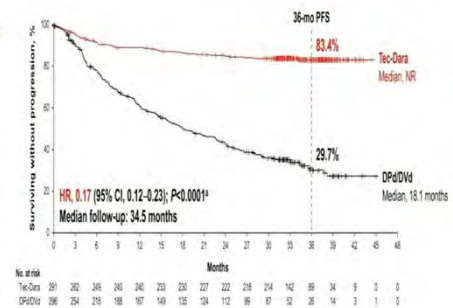


DREAMM-7 (28.2-mos follow-up), ITT Belamaf-Velc-Dex vs DVD



Patient characteristics (n = 243)
 ≥ 1 prior LOT (med 1)
 Len refractory: 33%
 Prior Dara: 1%
 High-risk cytogenetics: 28%
 EMD: 5%

MajesTEC-3 (34.5-mos follow-up), ITT Tec-Dara vs DPD/DVD

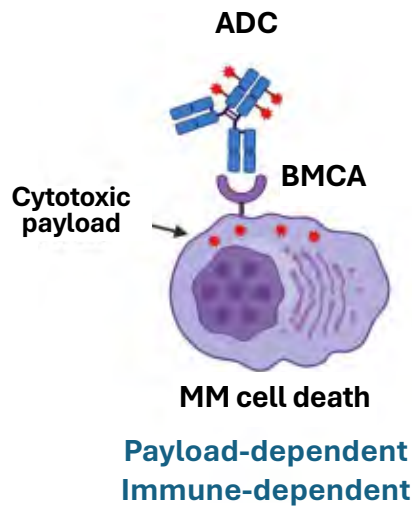


Patient characteristics (n = 291)
 1-3 prior LOT (med 2)
 IMiD refractory: 85%
 Prior Dara (0 refractory): 5%
 High-risk cytogenetics (del(17p, t4;14), t(14;16)): 36.5%
 EMD: 14%

Einslele H, et al. *Lancet Oncol.* 2026;27:254-68; Hungria V, et al. *N Engl J Med.* 2024;391:393-407; Costa LJ, et al. *N Engl J Med.* 2026;394:739-52.
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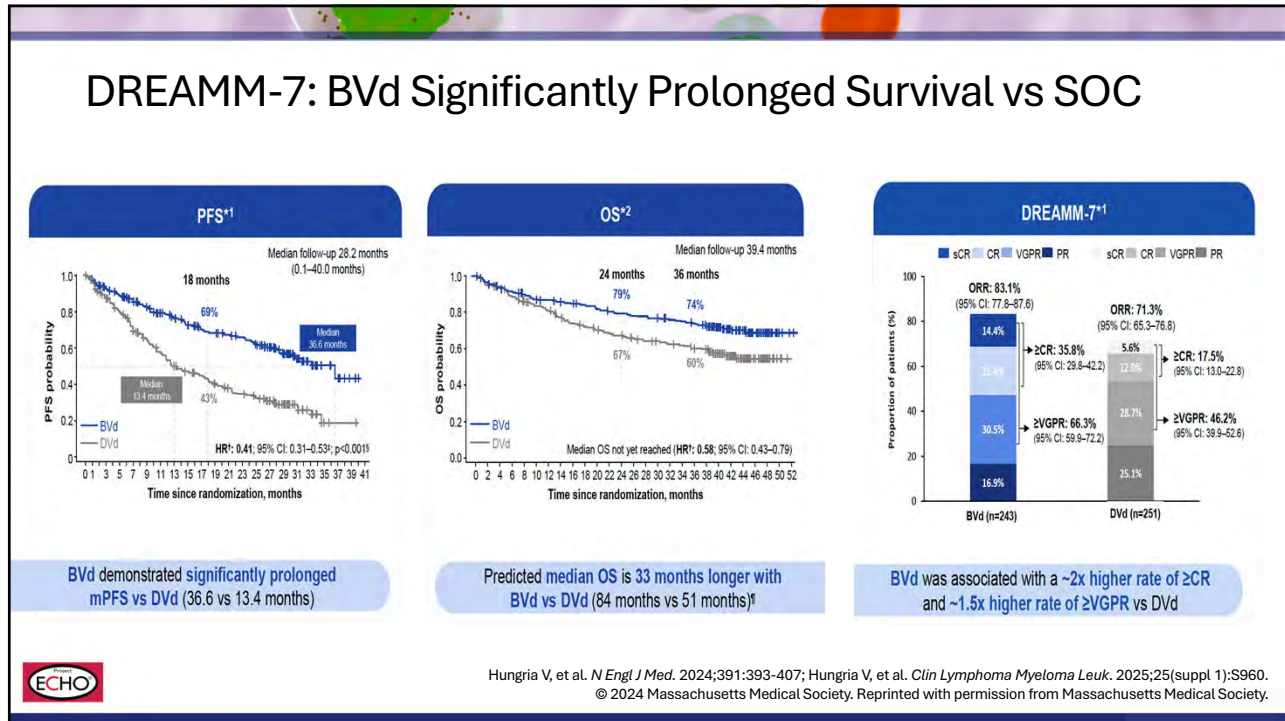
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Antibody-Drug Conjugate Targeting BCMA: Belantamab Mafodotin



Yu B, et al. *J Hematol Oncol.* 2020;13:125.

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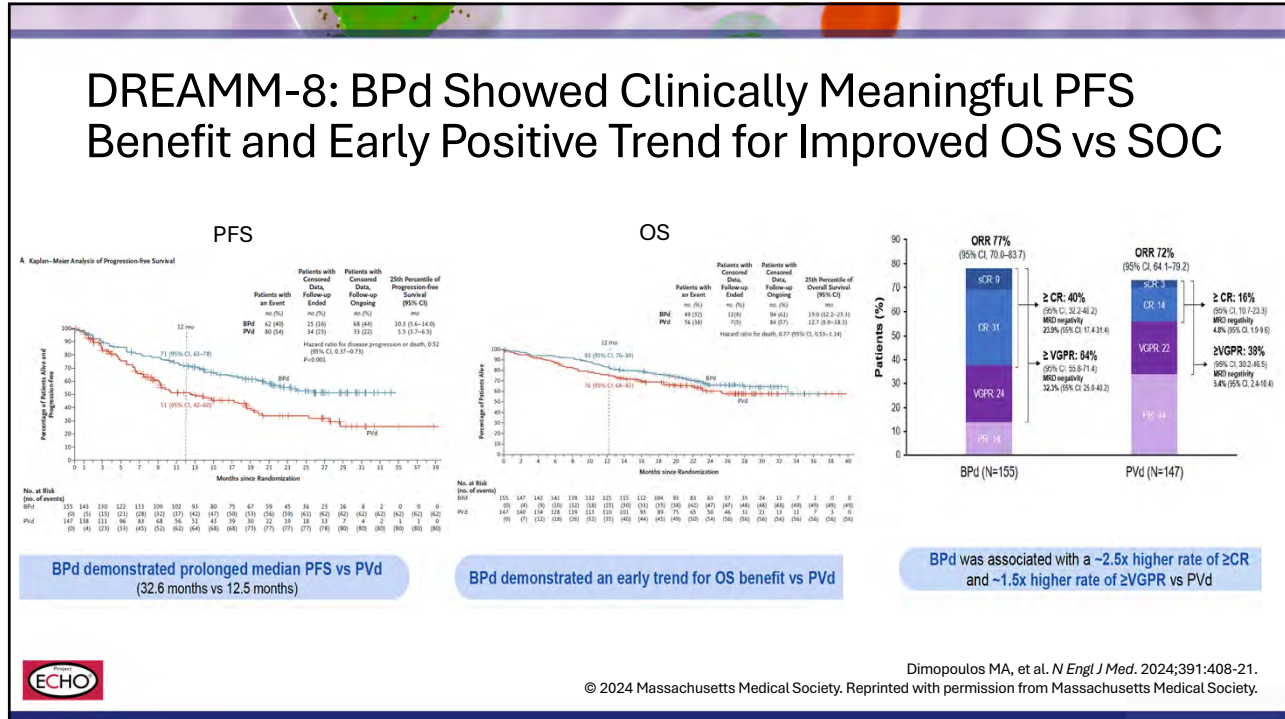
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DREAMM-7: BVd Significantly Improved PFS, OS, and Duration of Response vs SOC

Endpoint	BVd (n = 243)	DVd (n = 251)	Statistical Significance
PFS 2	NR (95% CI, 45.6 months-NR)	33.4 months (95% CI, 26.7-44.9)	HR, 0.59 (95% CI, 0.45-0.77)
OS	NR (95% CI, NR-NR)	NR (41.0 months-NR)	HR, 0.58 (95% CI, 0.43-0.79) P = .0002
ORR	83% (95% CI, 77.8%-87.6%)	71% (95% CI, 65.3%-76.8%)	
≥ CR and MRD negativity	25% (95% CI, 19.8%-31.0%)	10% (95% CI, 6.9%-14.8%)	
Duration of response to treatment	40.8 months (95% CI, 30.5 months-NR)	17.8 months (95% CI, 13.8-23.6)	

Hungria V, et al. *Lancet Oncol.* 2025;26:1067-80.

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DREAMM 7 & 8: Safety With Belantamab Combinations

DREAMM-7

AEs, n (%)	BVd (n=242)	DVd (n=246)
Any	242 (100)	246 (100)
Related to study treatment	242 (100)	234 (95)
Grade 3/4	229 (95)	187 (76)
Related to study treatment	219 (90)	164 (67)
Leading to treatment discontinuation	75 (31)	46 (19)
Related to study treatment	64 (26)	36 (15)
Leading to dose reduction	182 (75)	146 (59)
Leading to dose interruption/delay	228 (94)	185 (75)
Any SAE	121 (50)	90 (37)
Related to study treatment	47 (19)	30 (12)
Fatal SAEs	23 (10)	19 (8)
Related to study treatment	7 (3)	2 (<1)
Ocular AEs, n (%)	BVd (n=242)	DVd (n=246)
Vision blurred	53 (22)	2 (1)
Visual impairment	13 (5)	1 (<1)
Dry eye	17 (7)	0
Eye irritation	12 (5)	0

DREAMM-8

AEs, n (%)	BPd (n=150)	PVd (n=145)
Any	149 (>99)	139 (96)
Grade 3/4 AE	136 (91)	106 (73)
AEs leading to interruption/delay	136 (91)	109 (75)
Ocular events, n (%)	124 (83)	2 (1)
AEs leading to dose reduction	92 (61)	88 (61)
Ocular events, n (%)	88 (59)	0
AEs leading to discontinuation	22 (15)	18 (12)
Ocular events, n (%)	14 (9)	0
Any SAE	95 (63)	65 (45)
Fatal SAEs	17 (11) ^a	16 (11)
Ocular AEs, n (%)	BPd (n=150)	PVd (n=145)
Any	133 (89)	44 (30)
Grade 3/4	65 (43)	3 (2)

Mateos MV, et al. Abstract S214 presented at EHA 2024 Congress; Dimopoulos M, et al. Abstract LB3440 presented at EHA 2024 Congress.

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Therapeutic Revolution: T-Cell Engagers, BsAbs, and CAR T-Cell Therapies

A) IgG-like BsAbs

B) BsAb Mechanism

CAR T-cell Therapy

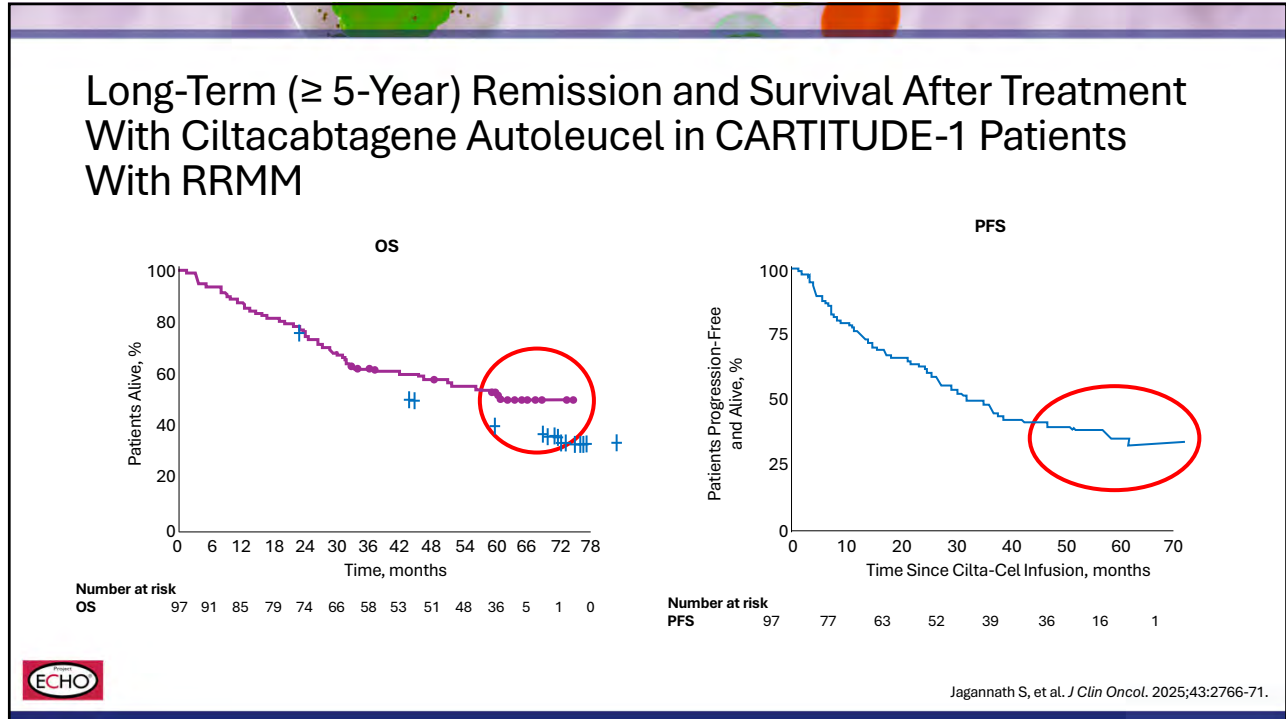
Rees M, et al. *Front Immunol.* 2024;15:1424925; Yu B, et al. *J Hematol Oncol.* 2020;13:125; National Cancer Institute. <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/car-t-cell-therapy>

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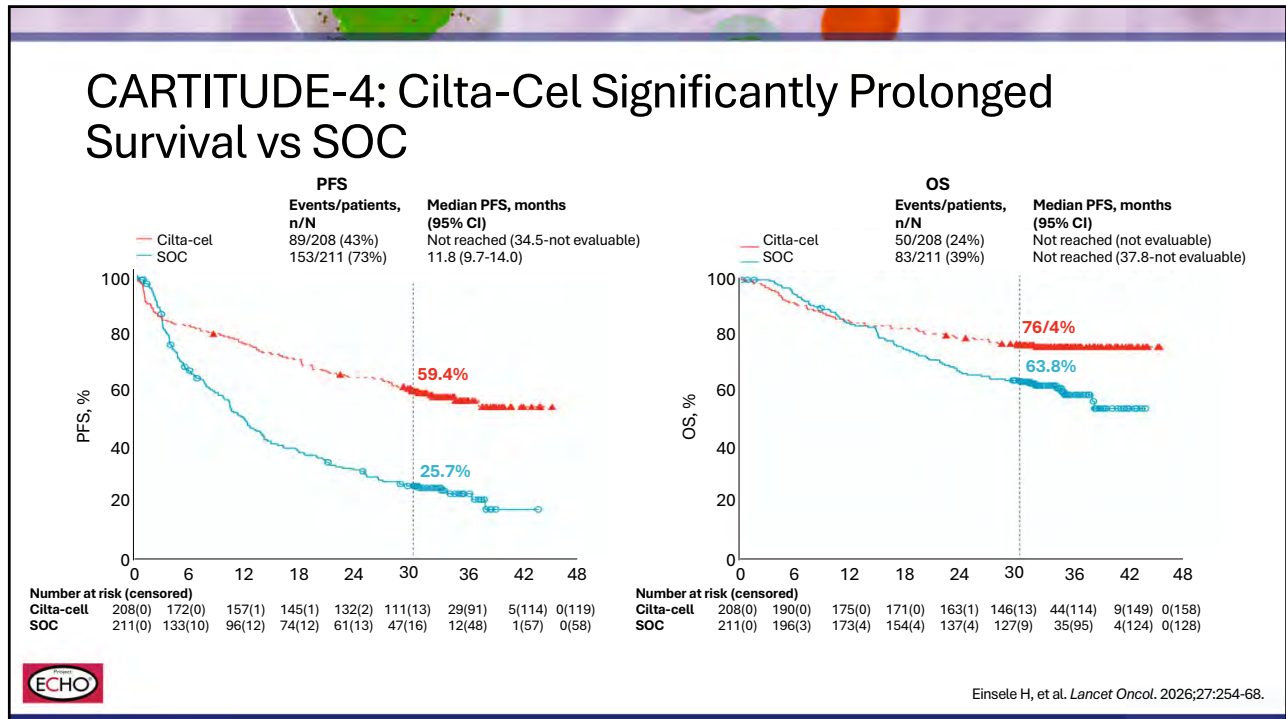
Specific Adverse Effects/Toxicities Associated With BsAbs and CAR T-Cell Therapies

IEC-HS = immune effector cell-associated HLH-like syndrome; MNTs = movement and neurocognitive treatment-emergent adverse events. Ludwig H, et al. *Lancet Oncol.* 2023;24:e255-69.

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Earlier Treatment With Cilta-Cel Is Safer

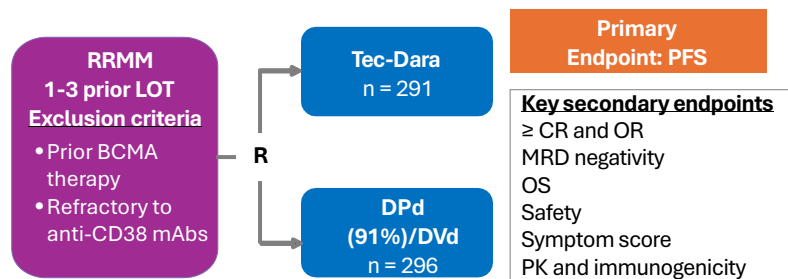
AE	CARTITUDE-1 (N = 97, ≥ 4L, median 6 prior lines)	CARTITUDE-4 (N = 176 treated with cilta-cel, 1-3L)
CRS — Any grade	95% (92/97)	76% (134/176)
CRS — Grade ≥ 3	4% (G3: 3%, G4: 1%, G5: 1%)	1.1% (G3-4; no G5)
CRS — Median onset	Day 7 (IQR 5-8)	Day 7 (IQR 5-8)
Tocilizumab use	69%	~53% (pooled CARTITUDE-1 + C4 label data)
ICANS — Any grade	17% (16/97)	4.5% (8/176)
ICANS — Grade ≥ 3	2%	0% (all G1-2)
Parkinsonism (MNTs)	5-6% (5-6/97)	0.6% (1/176)
Cranial nerve palsy	7% (7/97)	9.1% (16/176; G2: 8%, G3: 1.1%)
CAR-T peripheral neuropathy	12% (other neurotoxicities)	2.8% (G1-2: 2.3%, G3: 0.6%)
G3-4 Neutropenia	95% (92/97)	90% (187/208 safety pop)
G3-4 Thrombocytopenia	60% (58/97)	41% (86/208)
G3-4 Anemia	68% (66/97)	36% (74/208)
G3-4 Lymphopenia	50% (48/97)	21% (43/208)
Neutropenia recovery to ≤ G2 by d30	70%	Most recovered by d60
Thrombocytopenia recovery to ≤ G2 by d30	59%	Most recovered by d60
Infections — Any grade	58% (56/97)	62% (129/208)
Infections — Grade ≥ 3	20% (19/97)	27% (56/208)
Grade 5 infections	2% (2/97: sepsis/septic shock)	8% (16/208; includes COVID-19)
Second primary malignancies	7 pts (9 events: 5 MDS, 2 AML, 1 prostate, 1 BCC) at ~12 mo	4.3% (9/208) at ~16 mo; 4 new hematologic SPMs at ~34 mo
Treatment-related deaths	6/97 (6%)	6/208 (3%; 4 due to infection)



San-Miguel J, et al. *N Engl J Med.* 2023;389:335-47; Berdeja JD, et al. *Lancet.* 2021; 398:314-24; Einsele H, et al. *Lancet Oncol.* 2026;27:254-68.

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MajesTEC-3: Teclistamab + Dara, 1-3 Prior Lines



Dara

- Reduces CD38+ Treg, Breg & MDSC
- Activates CD8+ T effector cells
- Direct tumor cytolysis

Tec

- Activates CD8+ T effector cells
- Redirects T cells to BCMA+ tumor cells

Patient characteristics

- Median 2 prior LOT
- Stage 3: 8%
- BMPC ≥ 60%: ~10%
- EMD: 5%-6%
- High-risk cytogenetics: 36%
- **Prior anti-CD38: 5%**
- Refractory to last line: ~85%
- Len refractory: 82%-85%
- PI & Len refractory: 30%-34%



Costa LJ, et al. *N Engl J Med.* 2026;394:739-52; Mateos MV, et al. *Blood.* 2025;146:abstr LBA-6.

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Why Add Anti-CD38 mAb to a Bispecific?

- Clonal expansion of effector CD8+ T cells is a key immunologic driver of bispecifics
- Naive T cells need MHC class I signal to differentiate to effector
- Response failure with:
 - Increase in exhausted CD8+ clones
 - MHC-1 and BCMA loss

Activate CD8+ T cells

Reduce CD38+ T & B regulatory cells & MDSC

Reduce high tumour burden

Anti-CD38 mAb

Friedrich MJ, et al. *Cancer Cell*. 2023;41:711-25.

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MajesTEC-3: Teclistamab + Dara, 1-3 Prior Lines

PFS

No. at Risk	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48
Teclistamab-daratumumab	291	262	249	240	240	233	230	227	222	218	214	142	89	34	9	0	0
DPd or Dvd	296	254	218	188	167	149	135	124	112	99	87	52	26	14	3	1	0

OS

No. at Risk	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48
Teclistamab-daratumumab	291	272	259	252	248	246	243	239	232	227	160	100	40	9	0	0	0
DPd or Dvd	296	285	274	265	250	235	229	221	218	208	190	127	66	33	5	1	0

Tec-Dara
OR: 89%; ≥ CR: 82%
MRD negative 10⁻⁵: 89% in evaluable pts

Safety Profile of Tec-Dara

- CRS only Gd 1-2 (60%)
- ICANS 1.1% (2 cases, 1 Gd 3, both resolved)
- **Hypogammaglobulinemia** 84.5%
- **Infection** – Gd 3-4 54.1%;
13 deaths (4.6%) in COVID era & prior to BsAb guidelines – 9/12 did not receive IVIG
- Since **reinforcement of IVIG** administration, only 1 infectious death

Costa LJ, et al. *N Engl J Med*. 2026;394:739-52.
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T-Cell–Redirecting BsAbs Approved for RRMM

Responses

Progression-free survival months, (95% CI)

Approved in the US for the treatment of RRMM exposed to IMiD, PI, and anti-CD38 mAb and at least 4 prior lines of therapy

Moreau P, et al. *N Engl J Med.* 2022;387:495-505; Lesokhin AM, et al. *Nat Med.* 2023;29:2259-67; Bumma N, et al. *J Clin Oncol.* 2024;42:2702-12; Chari A, et al. *N Engl J Med.* 2022;387:2232-44.

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BCMA-Directed BsAbs FDA Approved for MM

	Teclistamab (MajesTEC-1)	Etranatamab (MagnetisMM-3)	Linvoseltamab (LINKER-MM1)
ORR	~63% (≥ CR: 46%; ≥ VGPR: 59%)	~61% (≤ CR: ~35%; ~60.5% MRD neg among CRs)	~71% (≥ CR: ~50%; ≥ VGPR: ~63%)
MRD negativity	~81% (day 100, 10 ⁻⁵ sensitivity)	All evaluable CRs were MRD negative; ~62% sustained at > 6 mo	Not formally reported; deep CR rates suggest high MRD neg
Median duration of response	~22 months overall (CR or better: ~27 mo)	Not reached; ~71.5% at 15 mo	~29.4 months (200 mg cohort, median follow-up 14.3 mo)
Median PFS	~11 months overall (CR or better: ~27 mo)	Not reached; ~50.9% PFS at 15 mo	Not reached; ~72.7% PFS at 6 mo (200 mg cohort)
CRS (any grade)	~72% (mostly grade 1-2); grade 3 ~0.6%	~57.7% (mostly grade 1-2); no grade 3-4 reported	~46.2% (mostly grade 1; grade 2 ~10.3%; grade 3 ~0.9%)
ICANS (any grade)	~6% (grade 3-4 ~2.4%)	3.3% (no grade ≥ 3)	~7.7% (2.6% each grade 1, 2, 3)
FDA approval date (accelerated)	Oct 25, 2022	Aug 14, 2023	July 2, 2025
Approved label	RRMM after ≥ 4 prior lines, including PI, IMiD, anti-CD38	RRMM after ≥ 4 prior lines, including PI, IMiD, anti-CD38	RRMM after ≥ 4 prior lines, including PI, IMiD, anti-CD38
Key reference	Moreau P, et al. <i>N Engl J Med.</i> 2022;387:495-505.	Lesokhin AM, et al. <i>Nat Med.</i> 2023;29:2259-67.	Bumma N, et al. <i>J Clin Oncol.</i> 2024;42:2702-12.

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BsAbs and Infection Risk

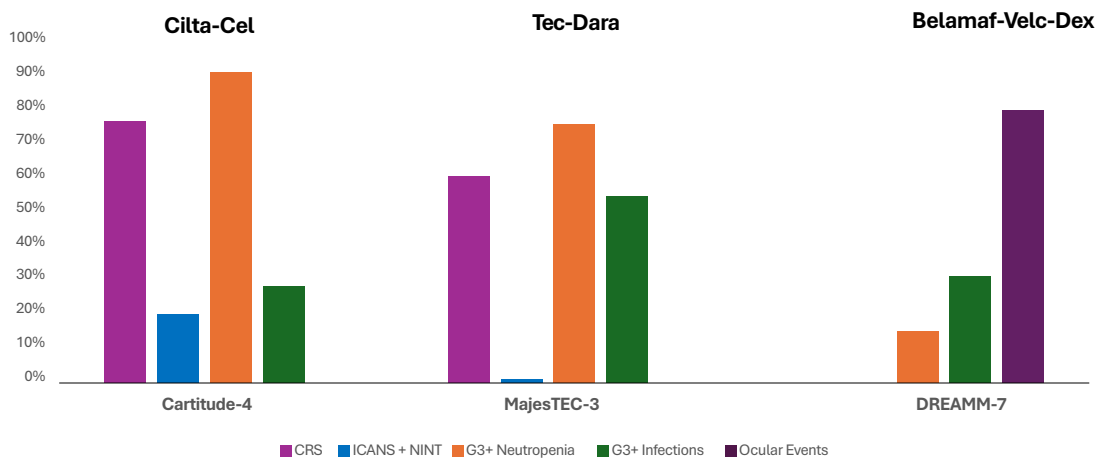
Drug	Teclistamab	Elranatamab	Linvoseltamab	Talquetamab 0.8 mg/kg SC Q2W
Study	MajesTEC-1	MagnetisMM-3	LinkerMM-1	MonumentAL-1
Phase study	I/II	II	I/II	I/II
Target	BCMA/CD3	BCMA/CD3	BCMA	GPRC5D/CD3
Median follow-up (months)	30.4	14.7	14.3	31.2
Infections: All grade	80%	70%	74%	68%
Infections: Grade ≥3	55%	40%	36%	18%
Patients receiving at least one does of IVIg during the study	46%	43%	64%	9%



Nooka AK, et al. *Cancer*. 2024;130:886-900; Lesokhin AM, et al. *Nat Med*. 2023;29:2259-67; Bumma N, et al. *J Clin Oncol*. 2024;42:2702-12; Chari A, et al. *Lancet Haematol*. 2025;12:e269-81.

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Toxicity Comparison for 3 BCMA-Directed Modalities



Berdeja JG. 7th Immune Effector Cell Therapies in Multiple Myeloma Workshop. March 27 - 28, 2026, Boston, MA; San-Miguel J, et al. *N Engl J Med*. 2023;389:335-47; Costa LJ, et al. *N Engl J Med*. 2026;394:739-52; Hungria V, et al. *N Engl J Med*. 2024;391:393-407.

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The Sequence of BCMA-Targeted Therapies Matters Significantly: Mechanisms of Resistance

Microenvironment

T-Cell Related

- T-cell exhaustion
- Poor T-cell fitness

Antigen escape or downregulation

- Mutations
 - Alterations preventing binding
- Biallelic loss or deletion of BCMA

Tedder B, et al. *Cells*. 2025;14:1077.

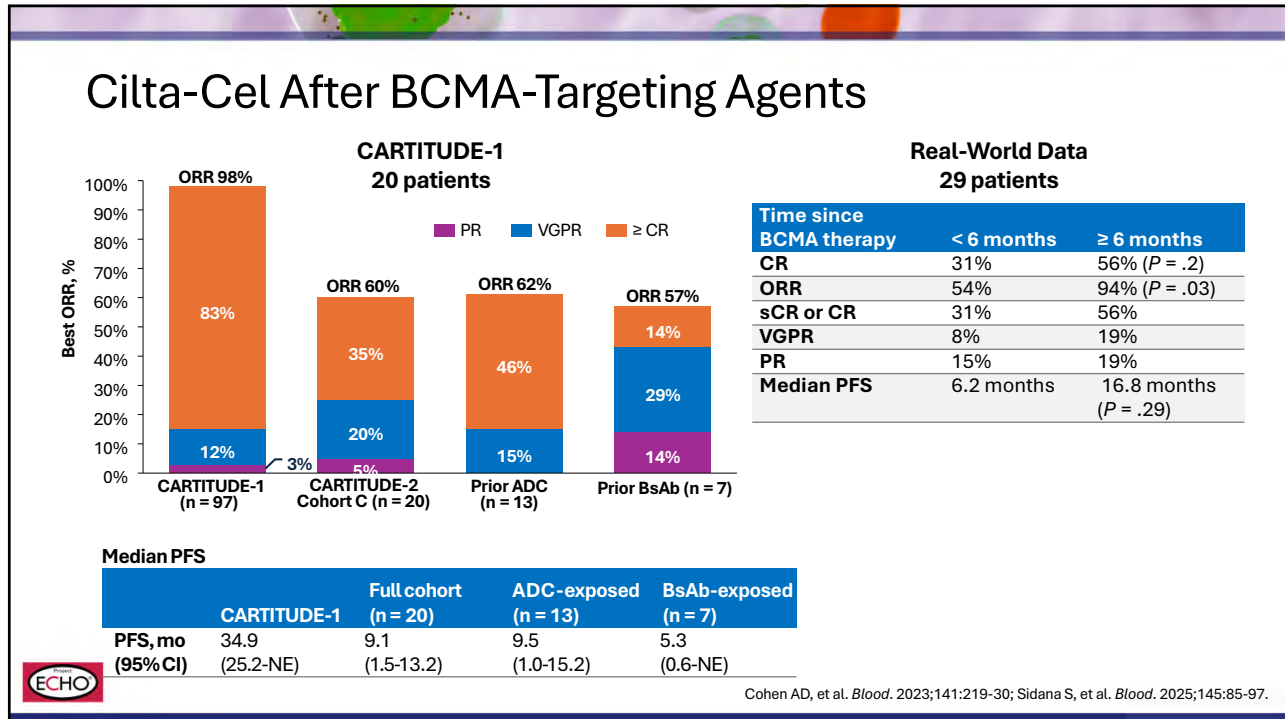
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The Sequence of BCMA-Targeted Therapies Matters Significantly

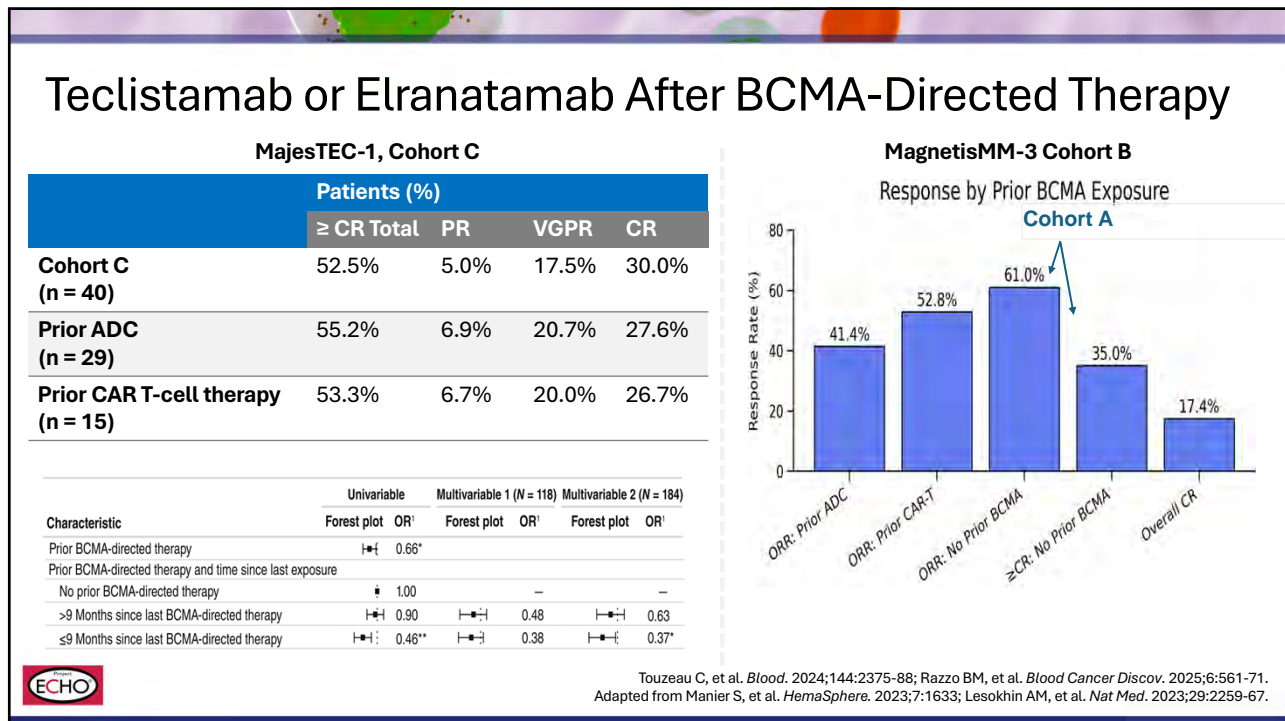
- **BsAbs before CAR T-cell therapy is detrimental:** Prior BCMA-targeting BsAb exposure causes **25%-40% manufacturing failure rates** and substantially impairs CAR T-cell efficacy (mPFS ~5.3 months for BsAb-exposed vs ~12+ months for BsAb-naïve); this effect is **target-agnostic** (even GPRC5D-targeting BsAbs impair CAR T-cell manufacturing)
- **CAR T-cell therapy before BsAbs is less detrimental:** The impact of prior CAR T-cell therapy on subsequent BsAb efficacy is more modest, likely because the treatment-free interval after CAR T-cell therapy allows T-cell recovery and BCMA antigen loss is rare (2%-4%) after CAR T-cell therapy
- **A BCMA-free interval > 6 months** between sequential BCMA-targeted therapies may improve outcomes of the second therapy

van de Donk NWCJ, et al. *Lancet Haematol*. 2024;11:e693-707; van de Donk NWCJ, et al. *HemaSphere*. 2025;9:e70260; Dima D, et al. *Hematology Am Soc Hematol Educ Program*. 2025;2025:324-33.

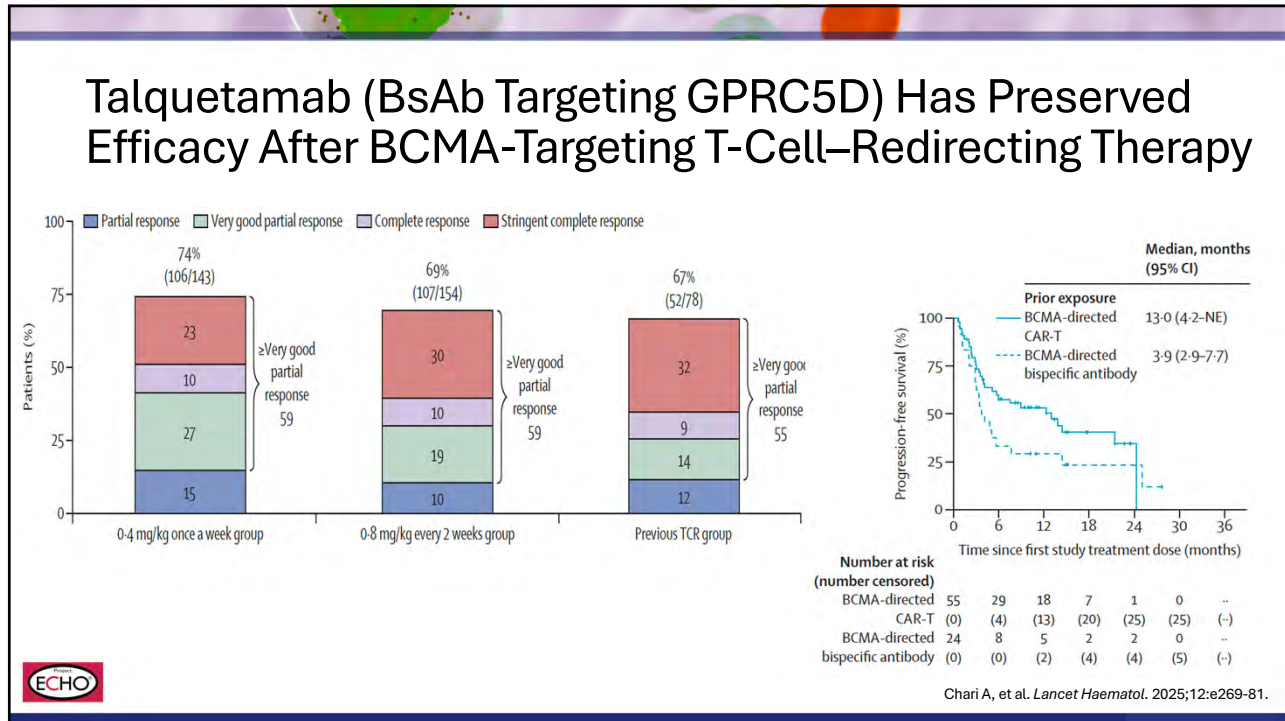
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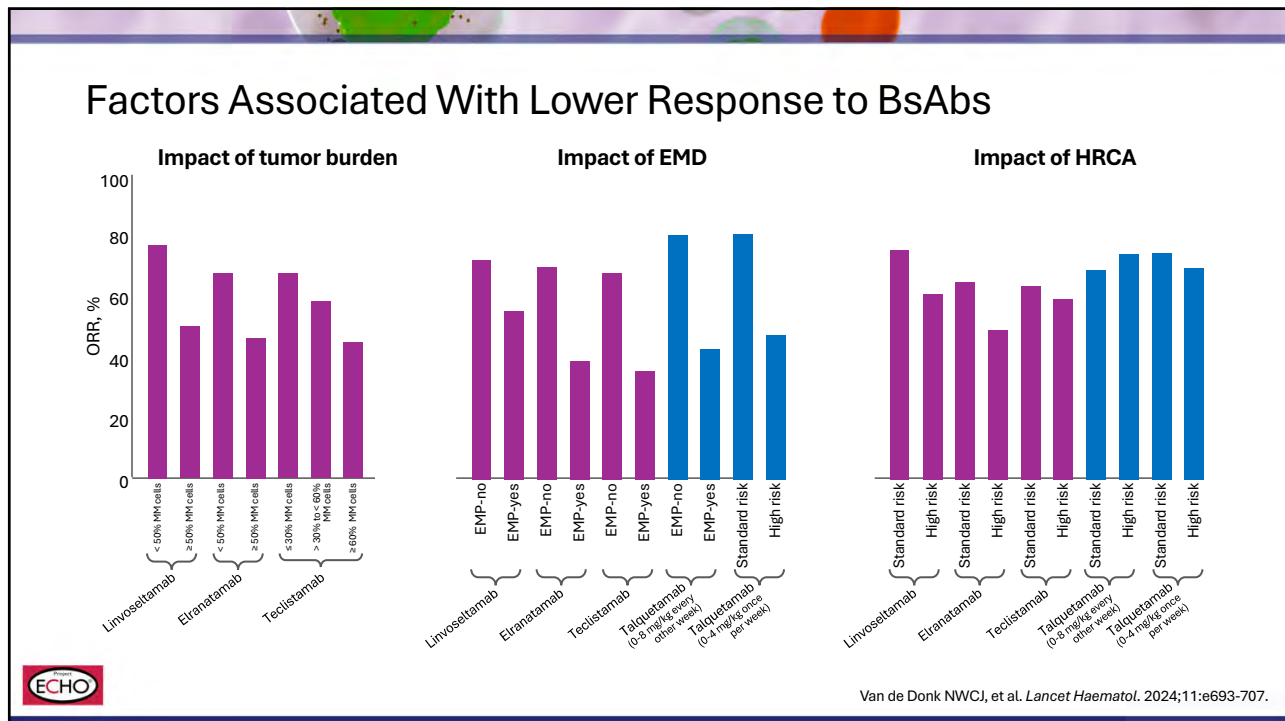
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How to Choose: Patient and Disease Characteristics to Consider

<p>CAR T-Cell Therapy</p> <p>Pro</p> <ul style="list-style-type: none"> • Fit • Adequate organ function • Has effective bridging options • Functional high risk • Wishes for treatment-free interval <ul style="list-style-type: none"> - One and done • Good social situation <p>Cons</p> <ul style="list-style-type: none"> • More difficult AE profile • Prior BCMA treatment • Requires specialty center <ul style="list-style-type: none"> - Logistical difficulty limits availability 	<p>BCMA-Directed BsAbs</p> <p>Pros</p> <ul style="list-style-type: none"> • Less fit • Permissive organ dysfunction <ul style="list-style-type: none"> - Likely safe even on HD • Off-the-shelf • Good social situation • May still have activity and support post CART or ADC <p>Cons</p> <ul style="list-style-type: none"> • Continuous therapy • High infection risk • May induce BCMA, difficult to sequence • Requires specialty center access 	<p>ADCs</p> <p>Pros</p> <ul style="list-style-type: none"> • Less fit/frail • Permissive organ dysfunction • Does not require proximity to specialty center • Off-the-shelf • Less likely to affect subsequent BCMA treatment adversely? <p>Cons</p> <ul style="list-style-type: none"> • Continuous therapy • Corneal toxicity <ul style="list-style-type: none"> - Eye exams • Seems less efficacious vs BsAb or CAR T
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Berdeja JG. 7th Immune Effector Cell Therapies in Multiple Myeloma Workshop. March 27 - 28, 2026, Boston, MA; van de Donk NWCJ, et al. *HemaSphere*. 2025;9:e70260; Dima D, et al. *Hematology Am Soc Hematol Educ Program*. 2025;2025:324-33.

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Conclusions: When to Consider Using or Not Using BCMA-Targeting BsAbs

<p style="color: blue; text-align: center;">When to consider using</p> <p style="color: purple; text-align: center; font-size: 1.2em;">Always</p>	<p style="color: blue; text-align: center;">When to consider deferring</p> <ul style="list-style-type: none"> • Patient eligible for CAR T-cell therapy • Prior BCMA-directed therapy (especially belantamab), BCMA-free interval < 6-9 months • Confirmed loss of BCMA expression • True extramedullary disease • High tumor burden • History of severe/recurrent infections or chronic lung disease • Poor baseline T-cell fitness (high Tregs, exhaustion markers, low T-cell counts); recent treatment with bendamustine, melphalan • Patient choice • Socioeconomic/geographic barrier
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