




 **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**

**Integrating BCMA-Directed Bispecific Antibodies
Into the Treatment Algorithm for Multiple Myeloma**

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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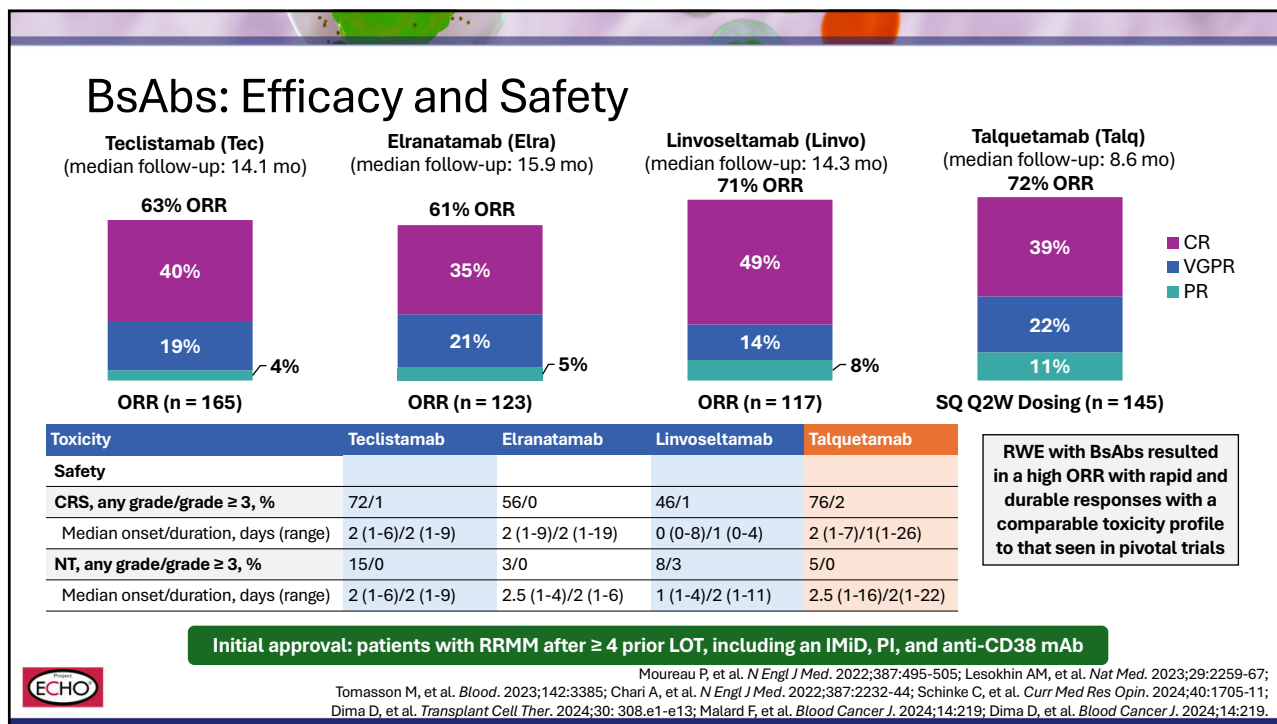
Approved Bispecific Therapies for Myeloma

BsAb	Teclistamab (BCMA x CD3) MajesTEC-1 (phase 1/2; n = 165)	Elranatamab (BCMA x CD3) MagnetisMM-3 (phase 1/2; n = 123)	Linvoseltamab (BCMA x CD3) LINKER-MM1 (phase 1/2; n = 117)	Talquetamab (GPC5D x CD3) MonumenTAL-1 (phase 1; n = 232)
Trial Population	≥ 3 LOT, including exposure to 1 PI, 1 IMiD, and 1 anti-CD38 mAb	Cohort A: Refractory to at least 1 PI, 1 IMiD, and 1 anti-CD38 mAb	≥ 3 LOT, including exposure to 1 PI, 1 IMiD, and 1 anti-CD38 mAb	RRMM w/intolerance to or progressed on established therapies (data for Q2W dosing)
ECOG PS > 1, %	67	63	85	Excluded PS ≥ 2
Prior BCMA therapy allowed	Not allowed	Cohort A: No		Yes
Age, median (range), years	64 (33-84)	68 (36-89)	70 (37-91)	64 (39-84)
Age > 65 years, %	48	NR	27	30 for > 70
EMD, %	17	32	16	32
High-risk cytogenetics, %	26	25	39	16
Median LOT	5	5	5	6
Triple-class refractory, %	78	97	82	79
Penta-drug refractory, %	30	42	28	30

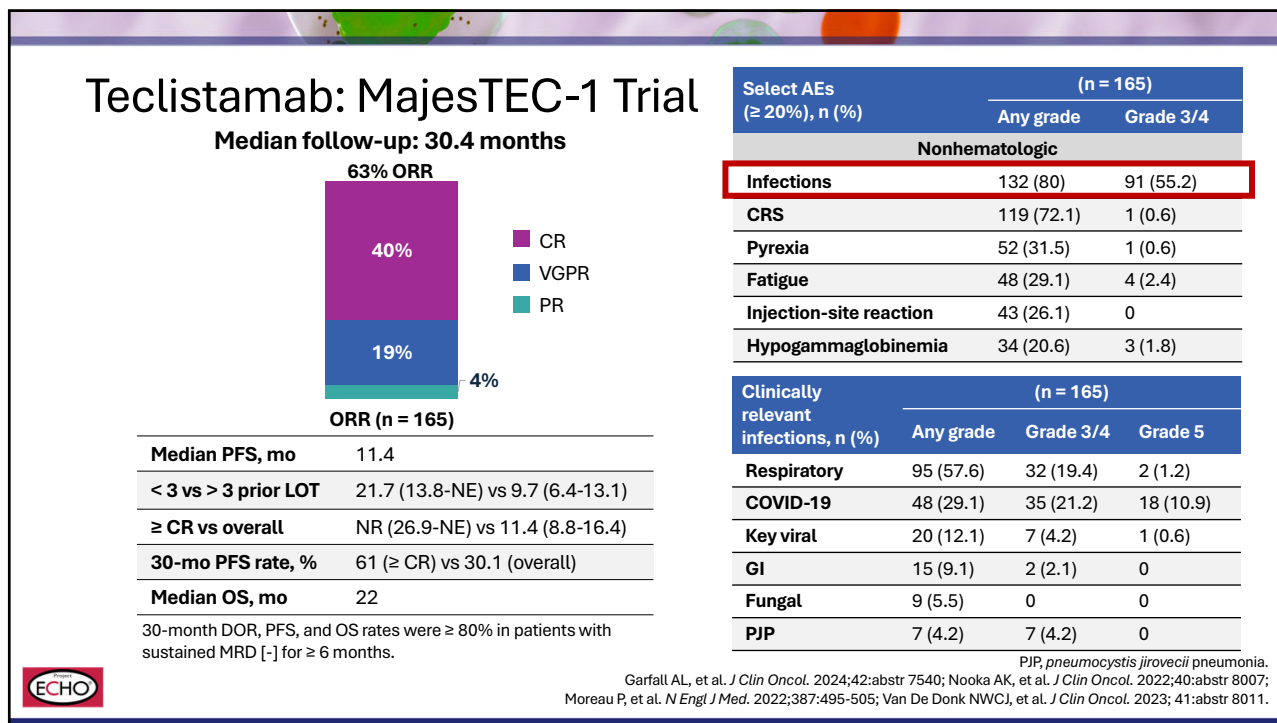


Moureau P, et al. *N Engl J Med.* 2022;387:495-505; Lesokhin AM, et al. *Nat Med.* 2023;29:2259-67; Bumma N, et al. *J Clin Oncol.* 2024;42:2702-12; Chari A, et al. *N Engl J Med.* 2022;387:2232-44.

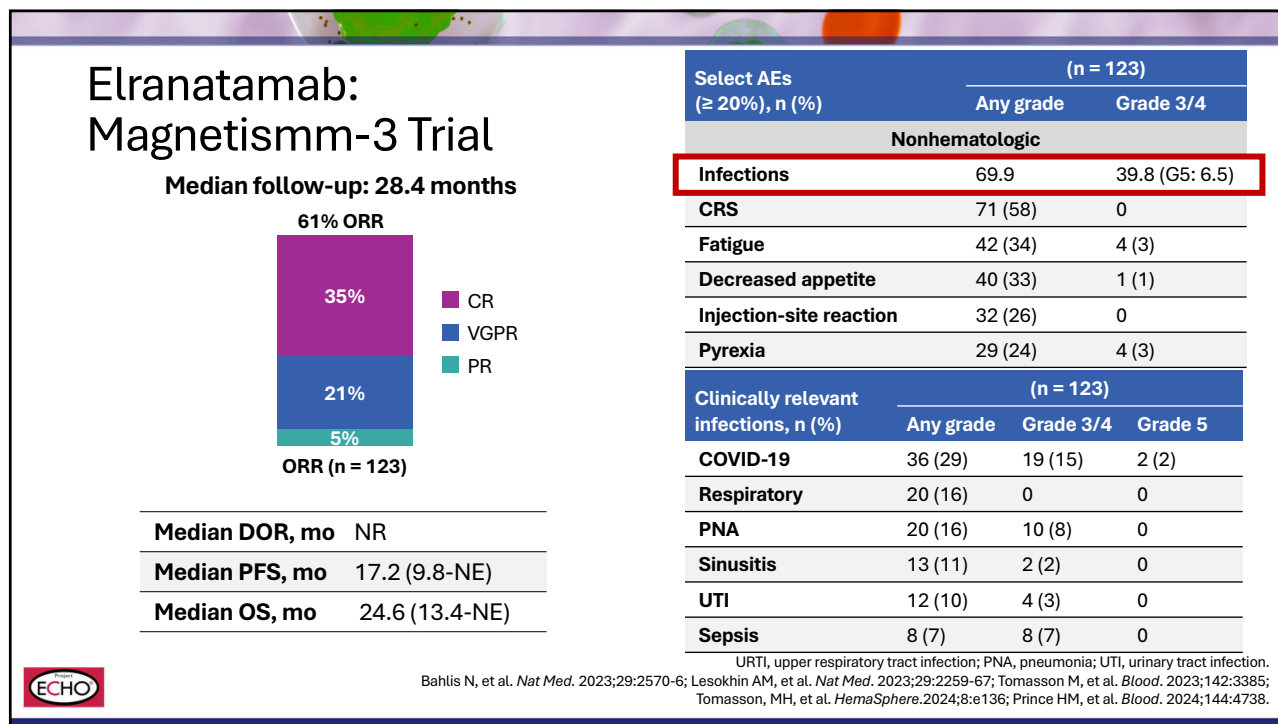
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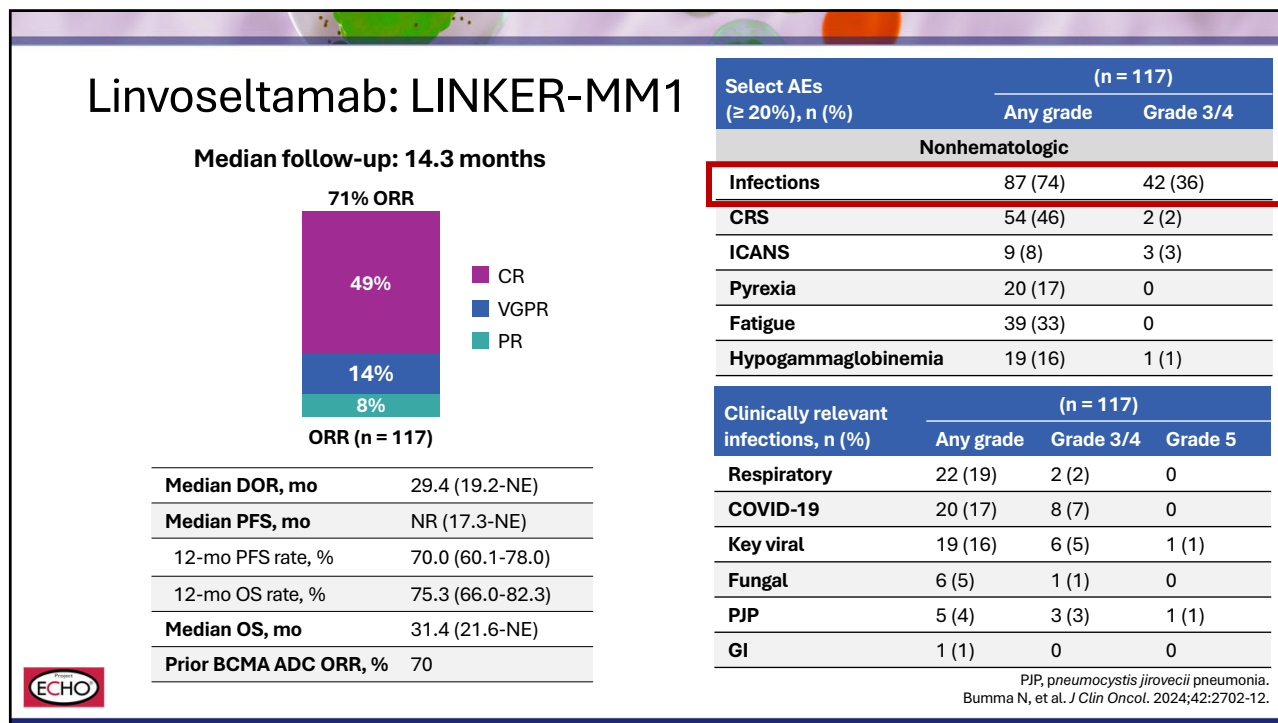
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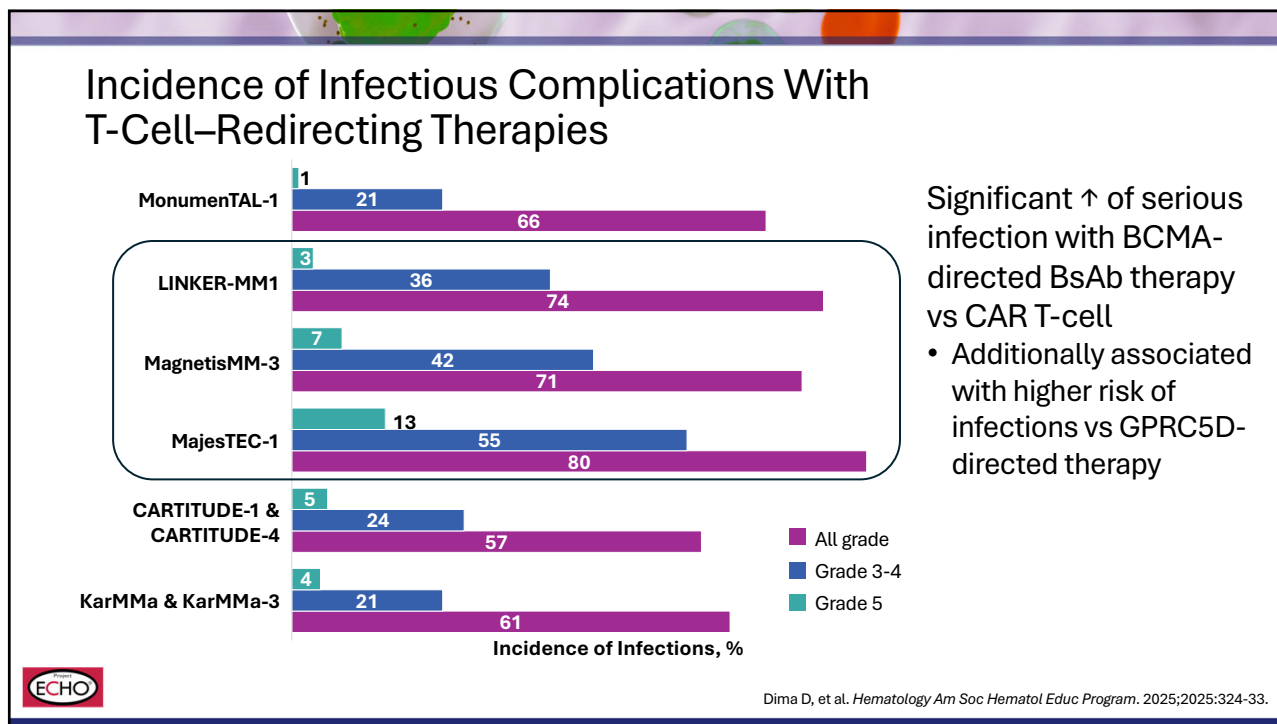
Jaime Symowicz, 2026-03-20T20:54:18.254

JS1 0 Not finding all data in the Bumma ref

Jaime Symowicz, 2026-03-20T21:00:03.252

AN1 1 <https://ascopubs.org/doi/10.1200/JCO.24.01008>

Nooka, Ajay, 2026-04-11T17:02:17.773



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Major Toxicities of T-Cell-Redirecting Therapies

CRS

- The main symptom is fever
- Severe cases: hypotension and hypoxia

Cytopenias

- Most common AE with CAR T-cell and BsAb
- Grading per CTCAE version 5.0 or ICAHT

Infections

- Most common cause of non-relapse mortality
- Prophylaxis is crucial

Other Neurotoxicity

- Nerve palsies, Guillain-Barré syndrome, Parkinsonism
- Mainly seen with cilta-cel

ICANS

- Confusion, delirium, dysgraphia, word-finding difficulties
- Severe cases: seizures

IEC-HS

- Hyperinflammatory syndrome
- Hyperferritinemia, hepatic dysfunction, coagulopathy, cytopenias

Skin, Nail, Mouth (GPRC5D only)

- On-target, off-tumor toxicities
- Dry mouth, stomatitis, dysgeusia
- Weight loss
- Nail changes, dry skin, rashes

ECHO

Dima D, et al. *Hematology Am Soc Hematol Educ Program*. 2025;2025:324-33.

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Emerging BCMA-Targeted BsAb Combination Regimens for RRMM

Treatment	Tec + Dara + Len ^a (MajesTEC-2)		Tec + Dara (MajesTEC-3)		Etra + Dara ^a (MagnetisMM-5)	Linvo + Dara or Isa ^a (LINKER-MM2)			
	Tec 0.72 mg/kg + Dara + Len	Tec 1.5 mg/kg + Dara + Len	Tec 1.5 mg/kg or 3 mg/kg + Dara 1,800 mg	DPd/DVd premed	Etra 44 or 76 mg + Dara	DL1 Linvo 100 mg + Dara/Isa	DL1b Linvo 150 mg + Dara/Isa	DL2 Linvo 200 mg + Dara only	
N or n	13	19	291	296	34	18	16	8	
Median prior LOT (range)	2 (1-3)	2 (1-3)		1-3	4 (2-9)	3 (2-6)	3 (2-6)	4 (2-8)	
Triple-class refractory, %	Not reported		Not reported		17.6	3 (16.7)	5 (31.3)	1 (12.5)	
ORR, %	93.5		89.0	75.3	70.6	81	93	86	
mPFS, mo	Not reported		Not reached		18.1	Not reported		Not reported	
HR (95% CI)	Not reported		0.17 (0.12-0.23)		Not reported		Not reported		
mDOR, mo	Not reached		Not estimable		23.5	Not reported		Not reported	
HR (95% CI)	Not reported		Not reported		Not reported		Not reported		
Median f/u, mo	8.4		34.5		Not reported		17.4	10.1	8.8
Any grade AE (grade ≥ 3), %									
CRS	81.2 (0)		60.1 (0)		Not reported		41.7 (0)		
Infections	90.6 (37.5)		96.5 (54.1)		84.1 (43.4)		Not reported; COVID-19: 32.4 (2.9)		
Neutropenia	84.4 (78.1)		78.4 (75.6)		82.8 (78.6)		47.1 (47.1)		
Anemia	21.9 (12.5)		39.2 (20.5)		35.5 (17.2)		29.4 (26.5)		
Thrombocytopenia	25.0 (15.6)		36.4 (19.4)		43.4 (23.4)		20.6 (14.7)		
ICANS	0		1.1%		Not reported		0		
Deaths, n Due to AE/TEAE	2		7.1%		5.9%		15		
Hypogammaglobulinemia/IVIG	Not reported		84.5%		Not reported		Not reported		

Direct comparisons cannot be made between studies.

^aCombination is considered investigational and is not FDA approved.

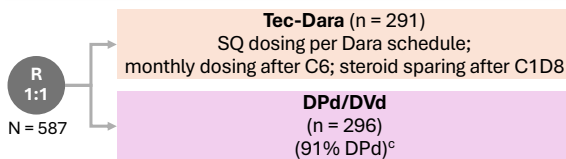
Searle E, et al. *Blood*. 2022;140:394-6; Mateos MV, et al. *Blood*. 2025;146:abstr LBA-6; Grosicki S, et al. *Blood*. 2022;140:4407-8; Dimopoulos MA, et al. *Blood*. 2025;146:2254.

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MajesTEC-3 Phase 3 Trial of Tec + Dara vs Investigator's Choice of Dara-Pd or Dara-Vd in RRMM: Study Design and Patients

Key Eligibility Criteria

- RRMM with 1-3 prior LOT (including PI + Len)
- Len refractory with 1 prior LOT^a
- ECOG PS 0-2
- No prior BCMA-directed therapy; not refractory to anti-CD38 mAbs^b



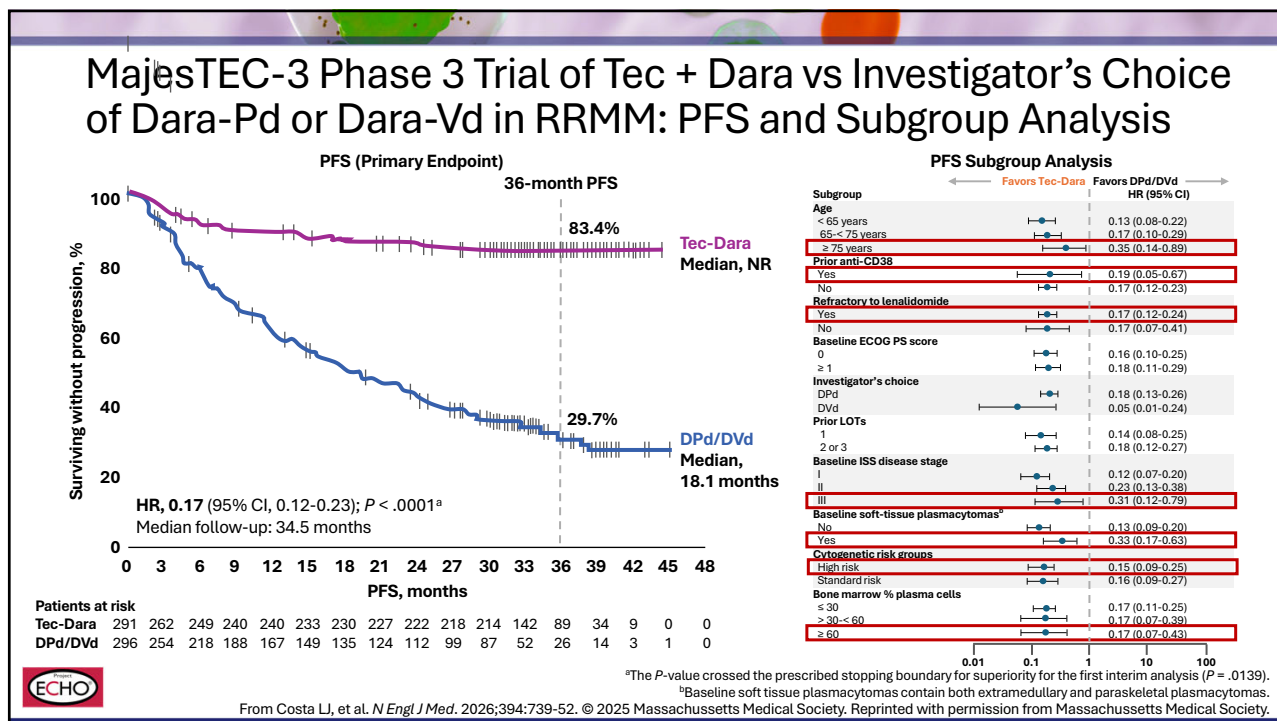
- Treatment (4-week cycles: cycles 1 and 2 QW; cycles 3-6 Q2W; cycles 7+ Q4W)
- Step-up dosing: Tec 0.06 mg/kg and 0.3 mg/kg on C1D2 and C1D4, respectively
- Tec 1.5 mg/kg; C1: D8, D15, D22; C2: D1, D8, D15, D22
- Tec 3 mg/kg; C3-6: D1, D15; C7+: D1
- Dara 1,800 mg; C1: D1, D8, D15, D22; C2: D1, D8, D15, D22; C3-6: D1; D15; C7+: D1dex (premed)^c; C1: D1, D2, D4, D8

Primary endpoint: PFS per IRC
Key secondary endpoints: ≥ CR^a and ORR, ^aMRD negativity (10⁻⁵), OS, My SIm-Q Total Symptom score

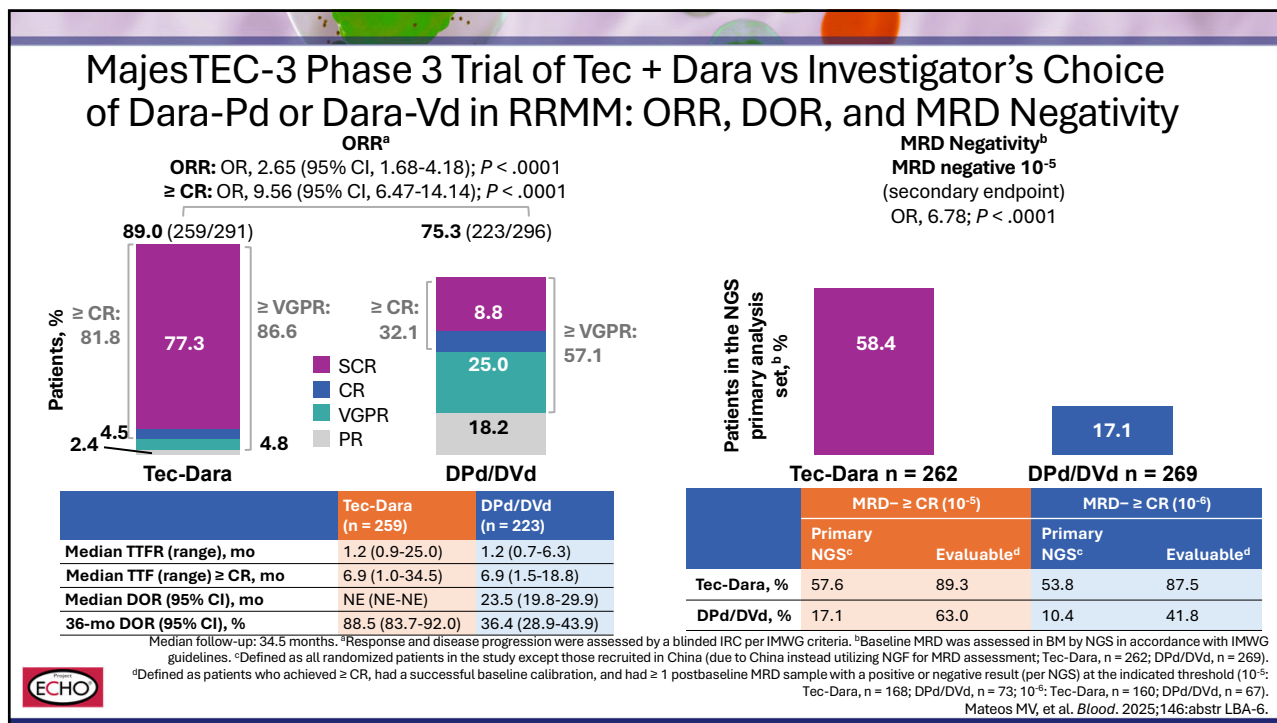
Patient Characteristics	Tec-Dara (n = 291)	DPd/DVd (n = 296)
Median age (range), years	64 (36-88)	63 (25-84)
≥75 years, n (%)	31 (10.7)	25 (8.4)
Baseline ECOG PS score, n (%)		
0	167 (57.4)	160 (54.1)
1	108 (37.1)	127 (42.9)
2	16 (5.5)	9 (3.0)
ISS stage, n (%)		
I	182 (62.5)	185 (62.5)
II	85 (29.2)	88 (29.7)
III	24 (8.2)	23 (7.8)
BMPCs ≥ 60%,^f n/N (%)	28/286 (9.8)	24/293 (8.2)
Soft tissue plasmacytoma, n (%)	41 (14.1)	41 (13.9)
Extramedullary plasmacytomas ^g	14 (4.8)	17 (5.7)
Paraskeletal plasmacytomas	32 (11.0)	31 (10.5)
High-risk cytogenetics,^h n/N (%)	104/285 (36.5)	104/294 (35.4)

^aPer IMWG. ^bPrior exposure to anti-CD38 mAbs was permitted. ^cDPd/DVd were administered per the approved schedules. ^dDex, Acetam, and diphenhydramine premedication was required for first 2 weeks; subsequent dexamethasone not required thereafter. ^eResponse and disease progression were assessed by blinded IRC per IMWG criteria. ^fMaximum value from BM biopsy or aspirate was selected if both were available. ^gFrom metastatic or hematogenous spread involving only soft tissues. ^hPresence of ≥1 of del(17p), t(4;14), or t(14;16). From Costa LJ, et al. *N Engl J Med*. 2026;394:739-52. © 2025 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

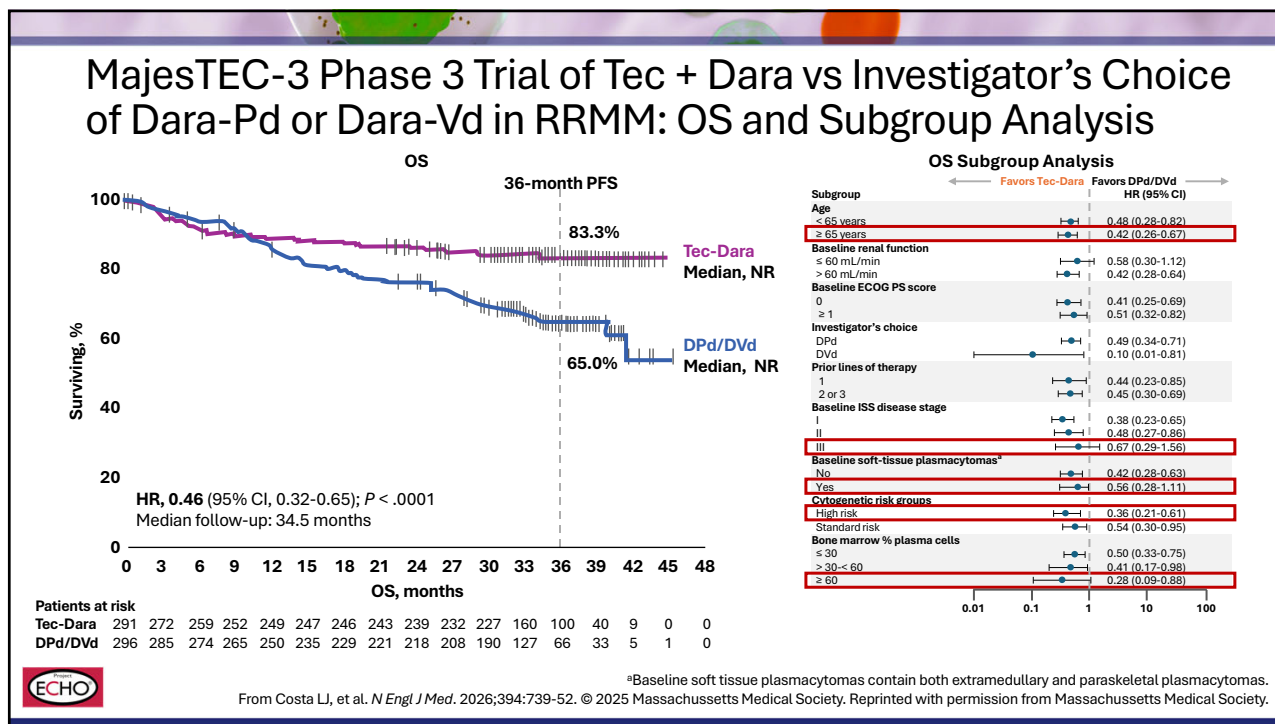
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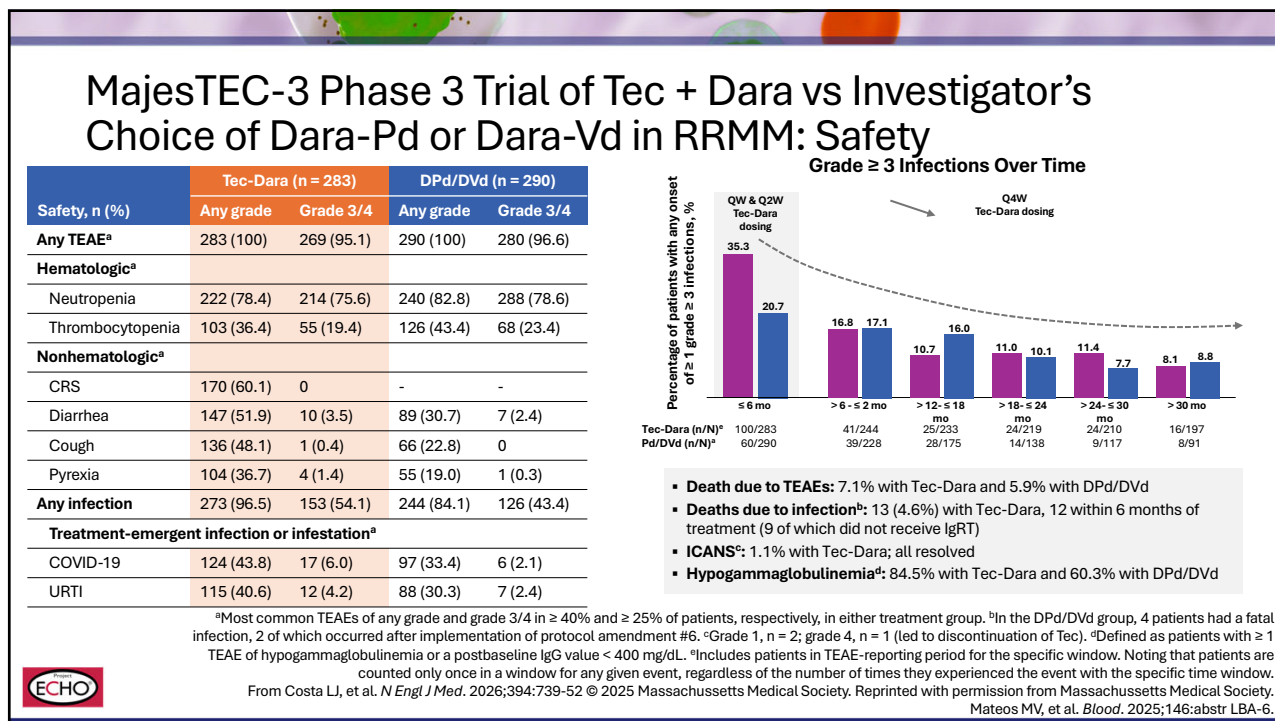
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Investigational Combinations of Approved BsAbs

Combination	RedirecTT-1	MajesTEC-2A	TRIMM-2			
	Tec + Talq ^a	Tec + Dara-Pom ^a	Tec + Dara-Pom ^a	Talq + Dara-Pom ^a	Talq + Dara-Pom ^a	Talq + Dara ^a
Cohort size (n)	n = 94	n = 17	n = 10	0.4 QW n = 18	0.8 Q2W n = 59	n = 65
Median LOT (range)	4 (1-11)	1 (1-4)	4 (3-16)	6 (3-11)	6 (1-17)	5 (2-16)
High-risk cytogenetics (%)	41	27	33	22	28	18
EMD (%)	36	0	30	22	24	25
Triple-refractory (%)	86	0	70	83	76	58
Penta-refractory (%)	33	0	NA	22	34	NA
Prior BCMA therapy (%)	Allowed	30	11	72	68	54
ORR (≥ CR), (%)	78 (48)	94 (65)	70 (50)	100 (56)	76 (56)	78 (45)
PFS	65% at 18 mo	60 at 24 mo	47 at 24 mo	15.4 mo (m)	20.3 mo (m)	19.4 mo (m)
DOR	77% at 18 mo	60 at 24 mo	67 at 24 mo	13.8 mo (m)	26.4 mo (m)	93% at 12 mo
OS	NA	NA	NA	NA	NA	NA
Any CRS (grade ≥ 3), (%)	79 (2)	47 (0)	70 (0)	56 (0)	80 (0)	78 (0)
Any ICANS (grade ≥ 3), (%)	3 (1)	0 (0)	10 (0)	0 (0)	5 (2)	5 (0)
Any infections (grade ≥ 3), (%)	89 (64)	94 (65)	90 (60)	72 (17)	78 (37)	63 (25)

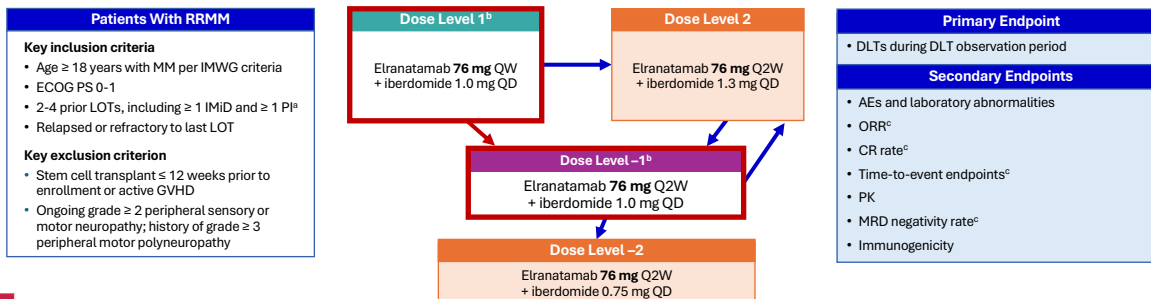


RedirecTT-1 visceral EMD: ORR 61% and 18-month DOR 82%.
^aCombination is considered investigational and is not FDA approved.
 Cohen YC, et al. *N Engl J Med.* 2025;392:138-49; D'Souza A, et al. *Blood.* 2024;144:495; Bahlis NJ, et al. *Hemasphere.* 2023;7:e90062ca.

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Safety and Efficacy of Elranatamab in Combination With Iberdomide^a in Patients With RRMM: Results From the Phase 1b MagnetisMM-30 Trial

- MagnetisMM-30 (NCT06215118) is a phase 1b, open-label, multicenter, prospective study
- **Part 1** (dose escalation) primary objective was to assess the tolerability and safety of elranatamab in combination with iberdomide to determine the recommended doses of the combination for evaluation in **Part 2** (randomized dose optimization)
 - A BOIN approach was used to guide dose escalation/de-escalation in **Part 1**



^aCombination is considered investigational and is not FDA approved. ^bIber was started after completion of the elra step-up dosing. Suvannasankha A, et al. *Blood.* 2025;46:100-1.

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MagnetisMM-30 Trial: ORR by Cytogenetic Risk

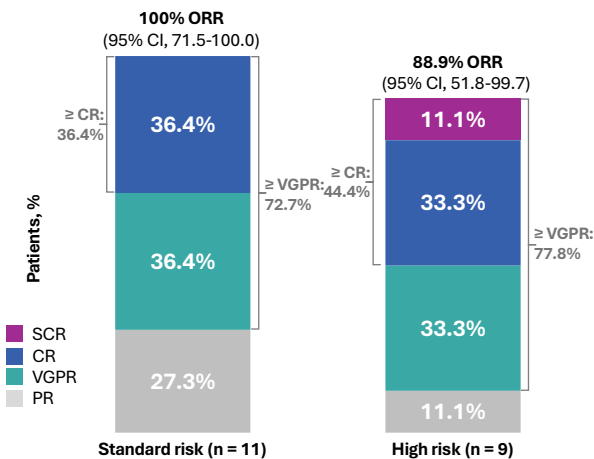
Confirmed ORR (95% CI) by investigator:

- Standard risk: 100% (71.5-100.0)
- High risk: 88.9% (51.8-99.7)

≥ CR rates (95% CI) were:

- Standard risk: 36.4% (10.9-69.2)
- High risk: 44.4% (13.7-78.8)

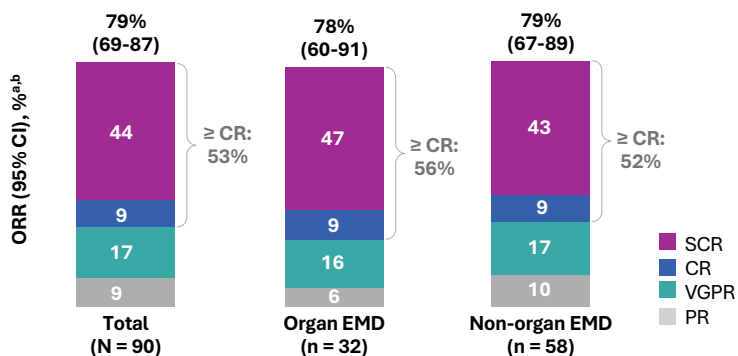
Two patients who had missing cytogenetic risk data both achieved CR



Suvannasankha A, et al. *Blood*. 2025;46:100-1.

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RedirecTT-1 Phase 2 EMD (Talq + Tec^a): High ORR Regardless of EMD Location



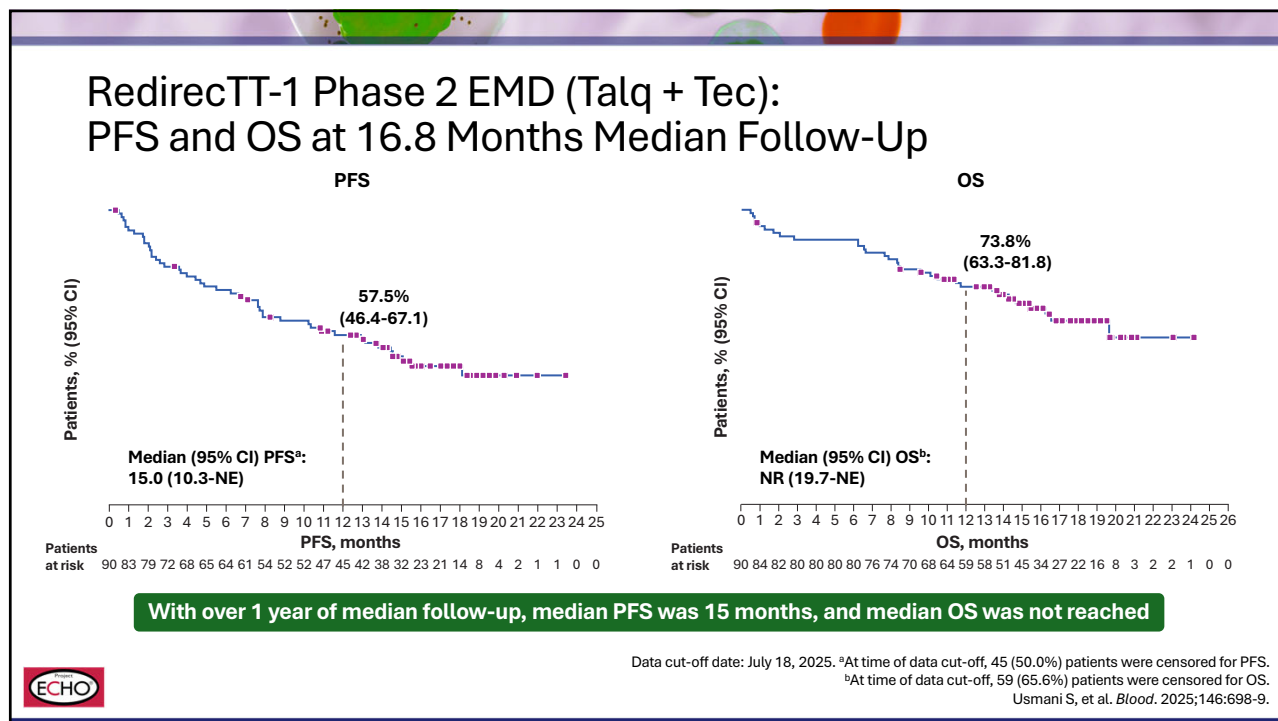
Patients with true EMD achieved deep responses with dual-antigen targeting Tal and Tec

- At an overall median follow-up of 16.8 months, median DOR was not reached in organ EMD and 15.4 months in non-organ EMD
- Organ EMD: kidney, liver, lung, and others
- Non-organ EMD: lymph node and soft tissue

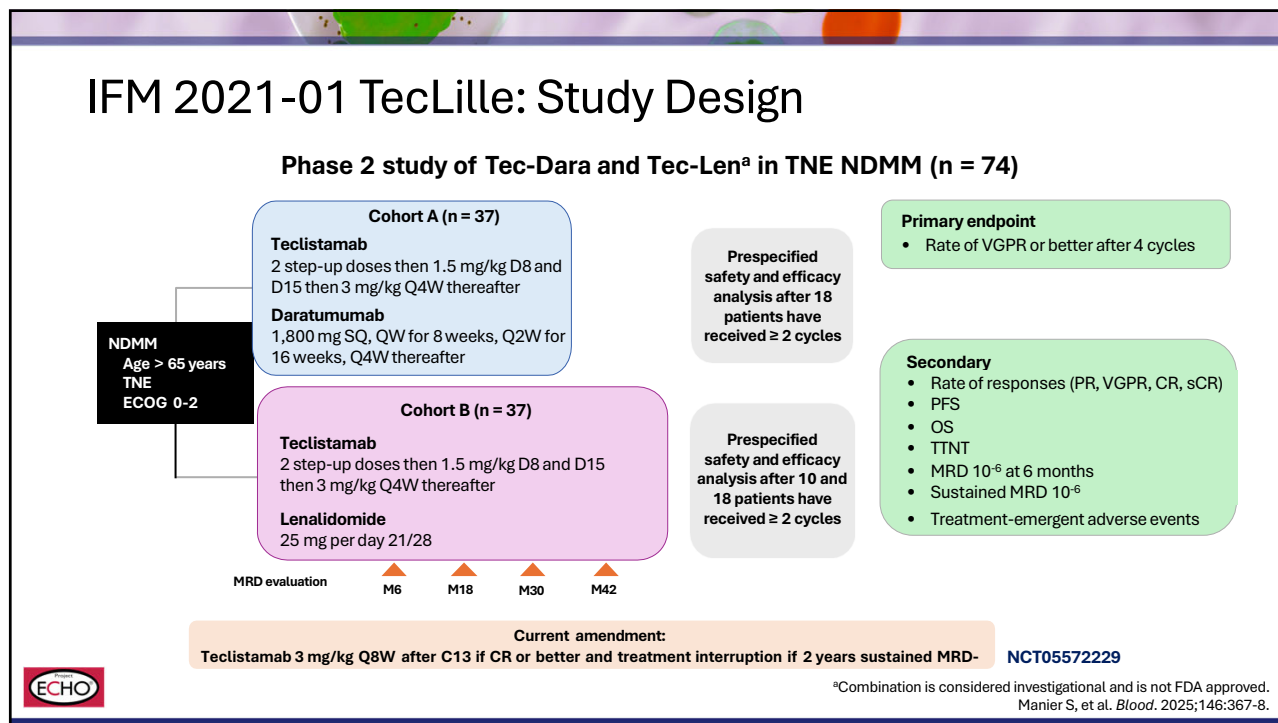


^aCombination is considered investigational and is not FDA approved. Usmani S, et al. *Blood*. 2025;146:698-9.

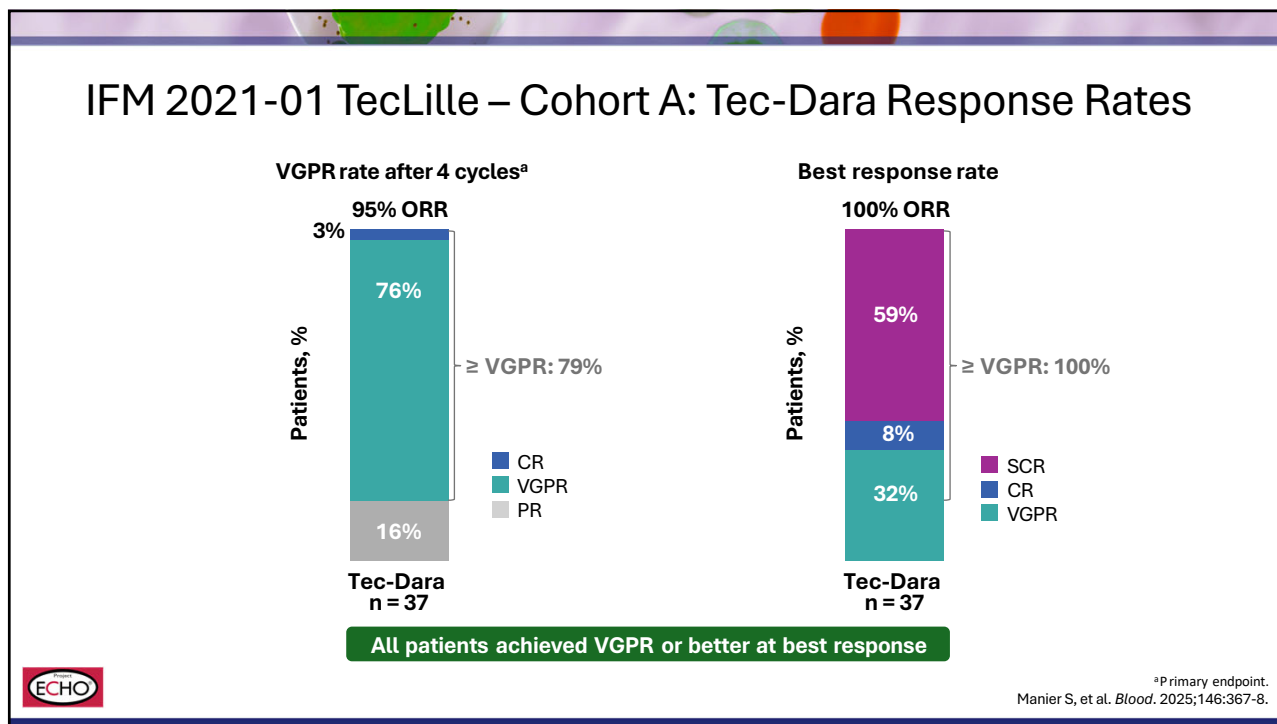
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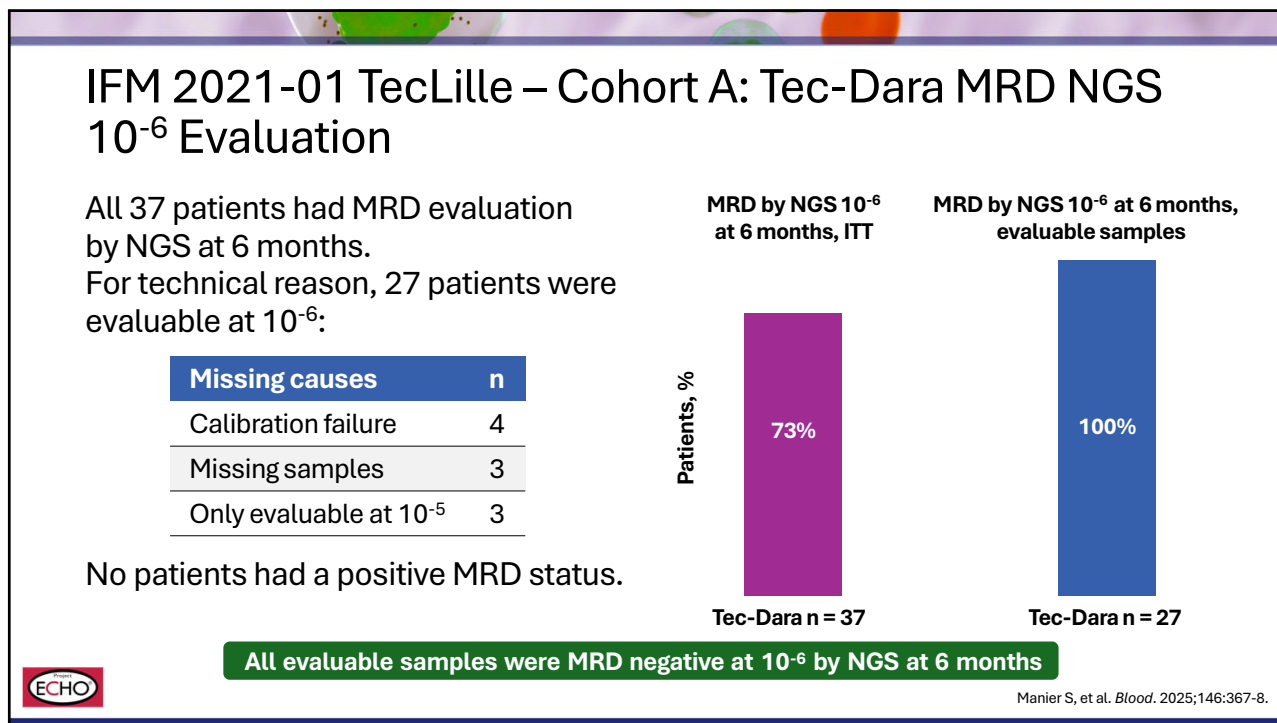
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Conclusions

- BsAbs have unprecedented activity as single agents in relapsed/refractory disease
- Established safety as single agents—CRS, ICANS, infections, cytopenias
 - CRS and ICANS in the first month of initiation of treatment
 - Infections and cytopenias after the first month of initiation of treatment
 - Grade ≥ 3 infection rates of close to 50% with BCMA-targeting BsAbs
 - Can be reduced with IVIG, antimicrobial prophylaxis, vaccinations, growth factors
- Proven efficacy as earlier lines of therapy in early relapsed disease
- Proven safety in combinations with IMiDs, CELMoDs, and other BsAbs
- Proven efficacy and safety as earlier lines of therapy in newly diagnosed myeloma

