



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

**BCMA-Directed Bispecific Antibodies in Multiple Myeloma:
Mechanisms of Action, Clinical Efficacy, and Emerging Therapeutics**

Led by



Produced in collaboration with



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Learning Objectives

Upon completion, participants should be able to:

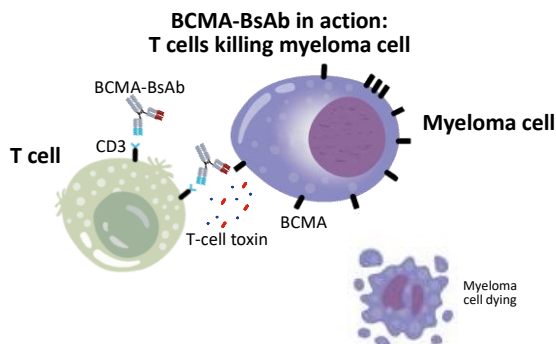
- Explain the mechanism of action of BCMA-directed BsAbs
- Characterize the safety and efficacy of BCMA-directed BsAbs for the treatment of multiple myeloma
- Appropriately incorporate BCMA-directed BsAbs into cases of patients with multiple myeloma that are representative of clinical practice



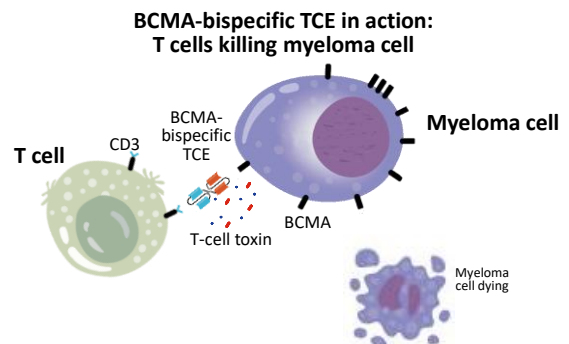
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Bispecific T-Cell Engagers

Bispecific Antibody Fab + Fc

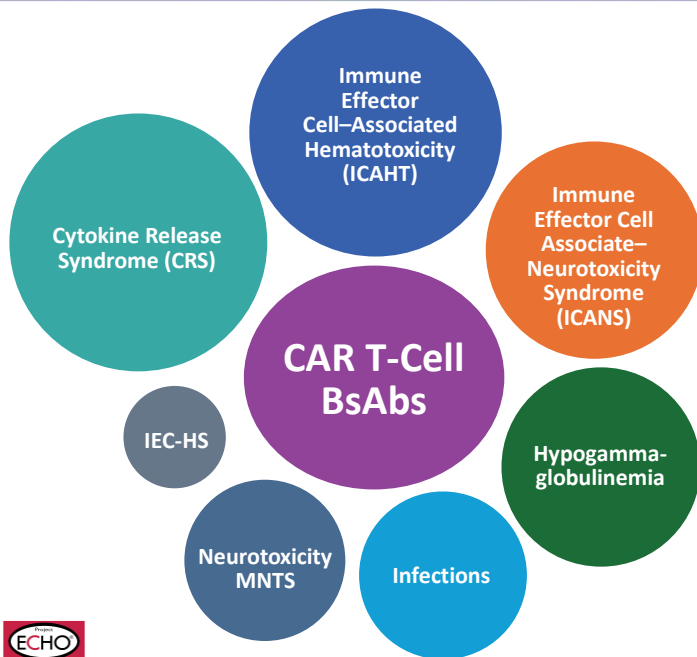


Bispecific T-Cell Engager (TCE) Fab only



Cho S, et al. *Front Oncol.* 2022;12:1032775.

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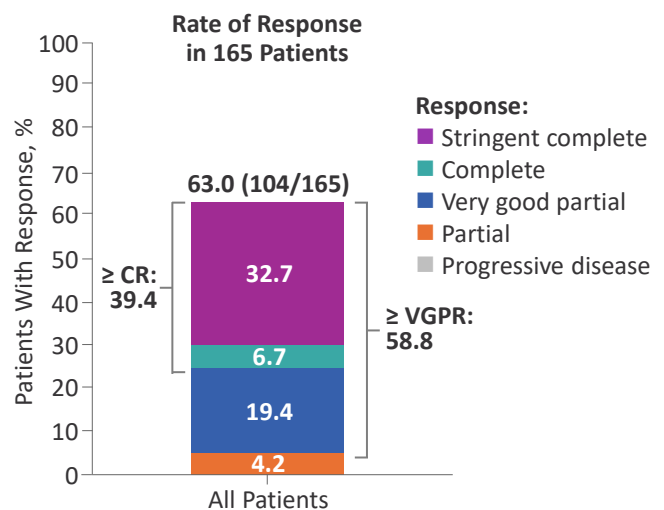
Common Adverse Events/Toxicities From T-Cell Therapies

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

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Teclistamab in RRMM: MajesTEC-1 Trial

- Phase 1/2 study; 165 RRMM patients whose prior therapies included an immunomodulatory drug, a proteasome inhibitor, and an anti-CD38 antibody
- ORR: 63% (95% CI, 55.2-70.4)
- $\geq$ CR: 39.4% (n = 65)
- MRD negative: 44 patients (26.7%; 95% CI, 20.1-34.1); MRD-negativity rate among the 65 patients with $\geq$ CR: 46%



From *N Engl J Med*, Moreau P, et al, Teclistamab in relapsed or refractory multiple myeloma, 387:495-505. © 2022 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

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MajesTEC-1 Trial: Demographics

Patient Characteristics at Baseline

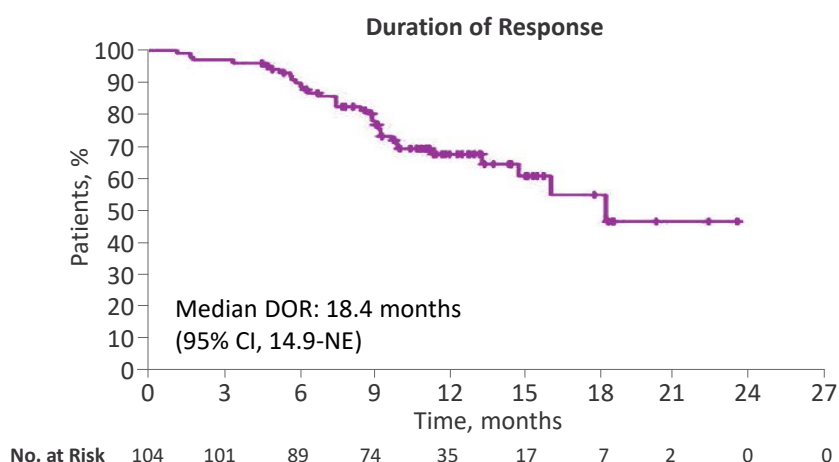
Characteristic	Total (N = 165)
Age	
Median (range), years	64.0 (33.0-84.0)
≥ 75 years, no. (%)	24 (14.5)
Race, no. (%)	
White	134 (81.2)
Black	21 (12.7)
Asian	3 (1.8)
Other	7 (4.2)
High-risk cytogenetic profile, no./total no. (%)	
del(17p)	23/148 (15.5)
t(4;14)	16/148 (10.8)
t(4;16)	4/148 (2.7)
Refractory status, no. (%)	
Immunomodulatory agent	152 (92.1)
Proteasome inhibitor	142 (86.1)
Anti-CD38 monoclonal antibody	148 (89.7)
Triple-class	128 (77.6)
Penta-drug	50 (30.3)
Refractory to the last line of therapy	148 (89.7)



Moreau P, et al. *N Engl J Med.* 2022;387:495-505.

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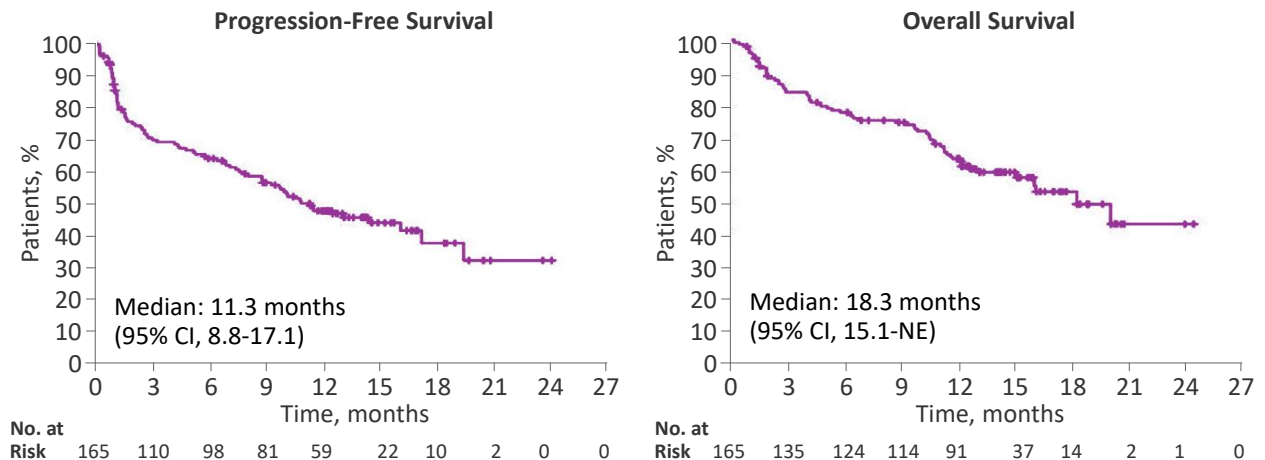
Teclistamab in RRMM: MajesTEC-1 Trial



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Teclistamab in RRMM: MajesTEC-1 Trial



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MajesTEC-1 Trial: Adverse Events in 165 Patients (Safety Population)

- Grade 3/4 in 156 patients (94.5%)
- 104 patients (63.0%) skipped a dose because of adverse events
- Most common adverse events were hematologic
- Infections occurred in 126 patients (76.4%), including 74 patients (44.8%) with grade 3/4
- Treatment was discontinued in 1 patient who developed grade 3 adenoviral pneumonia and 1 patient who developed grade 4 progressive multifocal leukoencephalopathy
- Hypogammaglobulinemia occurred in 123 patients (74.5%)

Event	Any Grade No. of Patients (%)	Grade 3/4
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)
Nonhematologic		
Cough	33 (20.0)	0
Pneumonia	30 (18.2)	21 (12.7)
COVID-19	29 (17.6)	20 (12.1)
CRS	119 (72.1)	1 (0.6) ^a
Neurotoxic event	24 (14.5) ^b	1 (0.6)
Infections	76.4	44.8%



^aNo grade 4.
^bIncluding ICANS in 5 patients (3%; all grade 1 or 2).
Moreau P, et al. *N Engl J Med*. 2022;387:495-505.

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MajesTEC-1 Trial: CRS

- CRS occurred in 119 patients (72.1%), with most events occurring after step-up and cycle 1 doses
- 6 patients (3.6%) had CRS during cycle 2 or later
- Median time to onset: 2 days (range, 1-6)
- Median duration: 2 days (range, 1-9)
- Most events of CRS were grade 1 or 2 in severity
- Supportive measures were provided to 110 patients (66.7%):
 - Tocilizumab in 60 patients (36.4%)
 - Low-flow oxygen by nasal cannula in 21 (12.7%)
 - Glucocorticoids in 14 (8.5%)



Moreau P, et al. *N Engl J Med.* 2022;387:495-505.

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MajesTEC-1 Trial: ICANS

- ICANS reported in 24 patients (14.5%), with most events being grade 1 or 2
- No patients discontinued therapy because of neurotoxic events
- Headache, which was the most frequent of the neurotoxic events, was reported in 14 patients (8.5%)
- 5 patients had a total of 9 ICANS events, all either grade 1 or 2; of these 9 events, 7 were concurrent with CRS, and all 9 events resolved without discontinuation or dose reduction
- Supportive treatment for neurotoxic events was provided to 14 patients (8.5%):
 - Tocilizumab (in 3 patients)
 - Dexamethasone (in 3 patients)
 - Levetiracetam (in 2 patients)
 - Gabapentin (in 1 patient)



Moreau P, et al. *N Engl J Med.* 2022;387:495-505.

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MajesTEC-1 Trial: Mortality and Infection

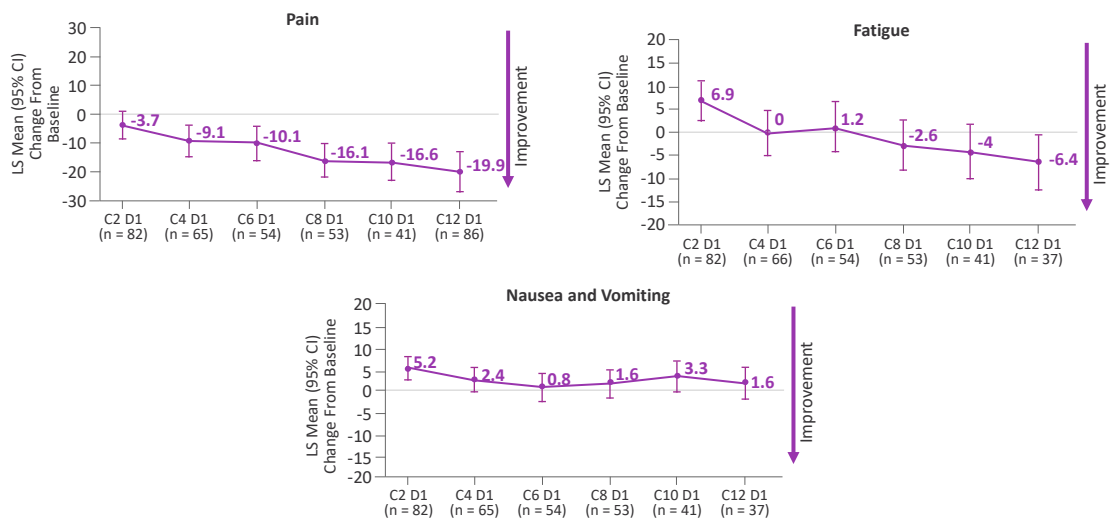
- A total of 68 patients (41.2%) died, with most deaths (41) attributed to progressive disease
- 19 patients died from adverse events, including 12 deaths from COVID-19
- 5 deaths were considered by investigators to be related to teclistamab:
 - 1 patient who had discontinued teclistamab due to progressive multifocal leukoencephalopathy
 - 2 patients who had contracted COVID-19
 - 1 patient who had hepatic failure
 - 1 patient who had streptococcal pneumonia



Moreau P, et al. *N Engl J Med.* 2022;387:495-505.

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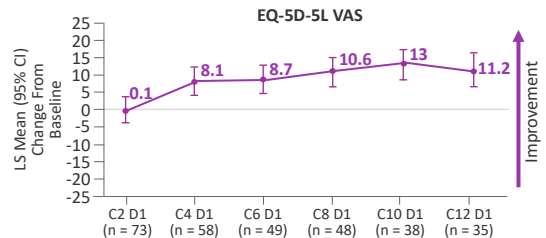
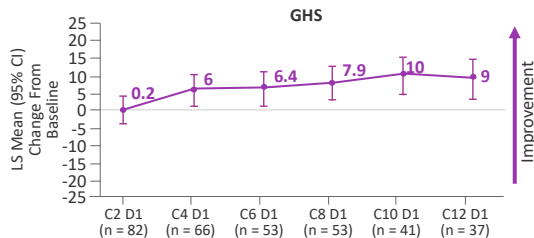
MajesTEC-1 Trial: Quality of Life



Martin TG, et al. *Clin Lymphoma Myeloma Leuk.* 2024;24:194-202.

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MajesTEC-1 Trial: Quality of Life



Martin TG, et al. *Clin Lymphoma Myeloma Leuk.* 2024;24:194-202.

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Teclistamab: Real-World Efficacy

	MajesTEC-1 N = 165	Riedhammer et al. N = 123 7/2022-10/2023	Dima et al. N = 106 8/2022-8/2023	Mohan et al. N = 110 1/2023-8/2023	Perrot et al. N = 303 10/2022-9/2023	Tan et al. N = 223 5/2022-1/2024
Demographics	mLoT 5 0% prior BCMA Median f/u 30 mos	mLoT 6 37% prior BCMA Median f/u 5.5 mos	mLoT 6 53% prior BCMA Median f/u 3.8 mos	mLoT 6 35% prior BCMA Median f/u 3.5 mos	mLoT 4 14% prior BCMA Median f/u 11.9 mos	mLoT 6 42% prior BCMA Median f/u 14 mos
ORR	63%	59% (65% BCMA naïve)	66%	62% (n = 98)	69%	66%
CRR	46%		29%	20%		25%
ORR (Prior BCMA)		55% (Ide-cel 33%, ADC 74%)	59% (57% CART, 50% ADC)	54%		55% (CRR 21%)
mPFS	11 mos	8.7 mos	5.4 mos	NR (6-mos PFS 52%)	11.3 mos	8.8 mos (DOR 17 mos)
mOS	22 mos	NR	NR (10-mos estimate 67%)	NR (6-mos OS 80%)	17 mos	20 mos
mPFS (prior BCMA)		1.8 mos				
Ineligible for MajesTEC-1	N/A	39%	83%		46%	76%



Moreau P, et al. *N Engl J Med.* 2022;387:495-505; Garfall AL, et al. *J Clin Oncol.* 2024;42:7540; Riedhammer C, et al. *Leukemia.* 2024;38:365-71; Dima D, et al. *Transplant Cell Ther.* 2024;30:308.e1-13; Mohan M, et al. *Blood Cancer J.* 2024;14:35; Perrot A, et al. *Haematologica.* 2025;110:990-4; Tan CR, et al. *Blood.* 2024;144:5166.

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Teclistamab: Real-World Safety

	MajesTEC-1	Riedhammer et al. N = 123 7/2022-10/2023	Dima et al. N = 106 8/2022-8/2023	Mohan et al. N = 110 1/2023-8/2023	Perrot et al. N = 303 10/2022-9/2023	Tan et al. N = 223 5/2022-1/2024
CRS	72% (0.6%)	59%	64% (1%)	56% (3.6%)		54% (1 grade 4)
ICANS	15% (0.6%)	7%	14% (3%)	11% (4.5%) (1 death)		8% (grade 3/4: 3%)
Tocilizumab		24%	41%	36%	36%	
Dexamethasone		16%	33%	17%	22%	
Infections (≥ G3)	79% (55%)	55% (27%)	31% (17%) (3 deaths)	40% (26%)		58% (25%) (10 deaths)
IVIG			42%	43%	61%	70%
Neutropenia (≥ G3)	72% (65%)	55% (38%)	42% (15%)			
GCSF			21%			
Inpatient/Outpatient	Inpatient	Inpatient	Inpatient	9% Outpatient	Both	26%
Schedule	1, 4, 7	Same as TEC-1	1, 3, 5 (more CRS after SUD#2) 1, 4, 7	1, 3, 5 1, 4, 7	Same as TEC-1	

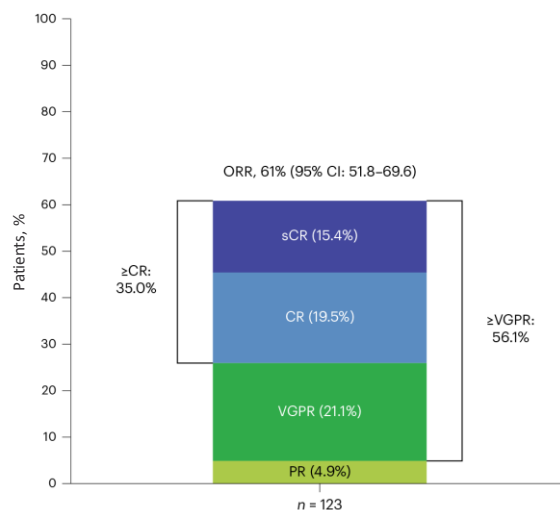


Moreau P, et al. *N Engl J Med.* 2022;387:495-505; Garfall AL, et al. *J Clin Oncol.* 2024;42:7540; Riedhammer C, et al. *Leukemia.* 2024;38:365-71; Dima D, et al. *Transplant Cell Ther.* 2024;30:308.e1-13; Mohan M, et al. *Blood Cancer J.* 2024;14:35; Perrot A, et al. *Haematologica.* 2025;110:990-4; Tan CR, et al. *Blood.* 2024;144:5166.

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Elranatamab in RRMM: MagnetisMM-3 Trial

- Phase 2 trial
- Patients with relapsed or refractory MM treated with subcutaneous elranatamab once weekly after 2 step-up priming doses
- After 6 cycles, persistent responders switched to biweekly dosing
- Results from cohort A, which enrolled patients without prior BCMA-directed therapy:
 - ORR of 61.0% (75/123); 35.0% ≥ CR
 - With a median follow-up of 14.7 months, median duration of response, progression-free survival, and overall survival (secondary endpoints) have not been reached



Lesokhin AM, et al. *Nat Med.* 2023;29:2259-67.

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Elranatamab in RRMM: MagnetisMM-3 Trial

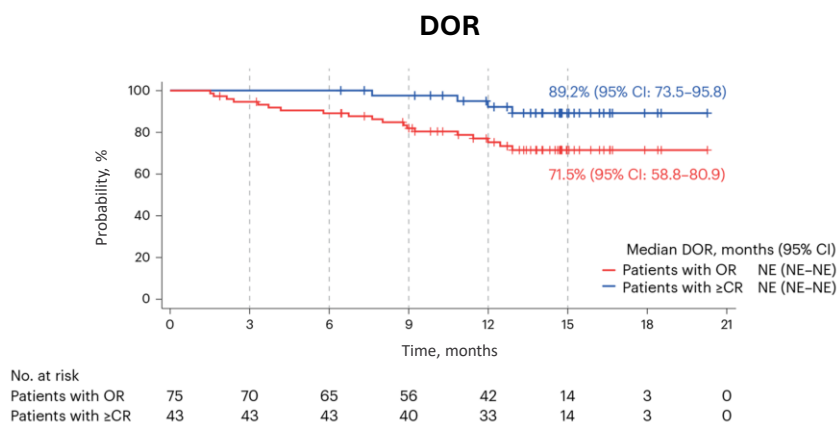
	Elranatamab SC Monotherapy (N = 123)
Median age, years	68.0 (36-89)
Race, no. (%)	
White	72 (58.5)
Black/African American	9 (7.3)
Asian	16 (13.0)
Not reported	26 (21.1)
Cytogenetic risk, no. (%)	
High	31 (25.2)
Standard	83 (67.5)
Unknown	9 (7.3)
Extramedullary disease by BICR, no. (%)	39 (31.7%)
Refractory status, no. (%)	
Triple-class	119 (96.7)
Penta-drug	52 (42.3)
Refractory to last line of therapy, no. (%)	118 (95.9)



Lesokhin AM, et al. *Nat Med.* 2023;29:2259-67.

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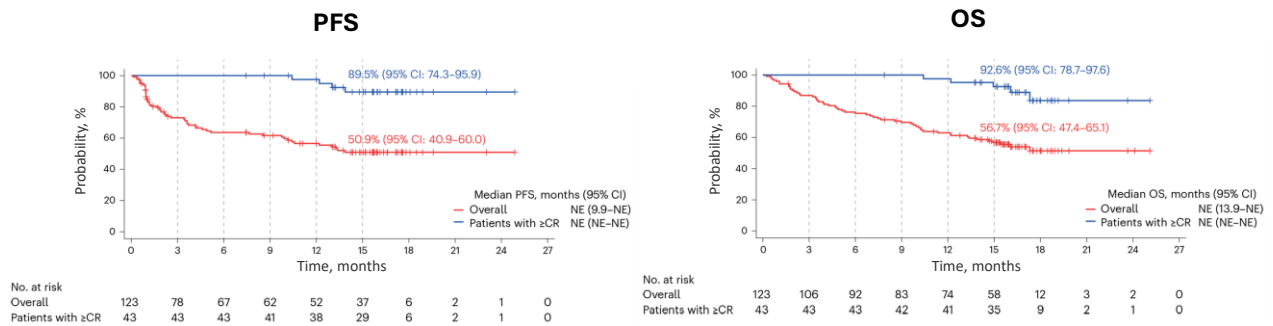
Elranatamab in RRMM: MagnetisMM-3 Trial



Lesokhin AM, et al. *Nat Med.* 2023;29:2259-67.

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Elranatamab in RRMM: MagnetisMM-3 Trial



Lesokhin AM, et al. *Nat Med.* 2023;29:2259-67.

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MagnetisMM-3 Trial: Safety Profile

Agent Target/Class (Trial)	Elranatamab BCMA BsAb (MagnetisMM-3)
Safety set, N	BCMA-naïve N = 123
CRS, %	
All grade	57.7
Grade 3/4	0
ICANS, %	
All grade	4.9
Grade 3/4	0
Grade 3/4 cytopenias, %	
Neutropenia	49.6
Anemia	37.4
Thrombocytopenia	23.6
Lymphopenia	25.2
Infections, %	
All grade	70.7
Grade 3/4	42.3

Median follow-up: 28.4 months^a



^aBy reverse Kaplan-Meier.
 Tomasson MH, et al. *Hemasphere.* 2024;8:e136.

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Elranatamab: Infection Incidence and Severity in MagnetisMM-3

Infections, %	MagnetisMM-3 BCMA-Naïve N = 123
Any grade	69.9
Grade 3/4	39.8
Grade 5	6.5
Most common infections, any grade	
COVID-19 related	29.3
Pneumonia	16.3
Upper respiratory tract infection	16.3
Sinusitis	10.6
Urinary tract infection	9.8
Sepsis	6.5
Bacteremia	5.7
CMV infection reactivation	5.7

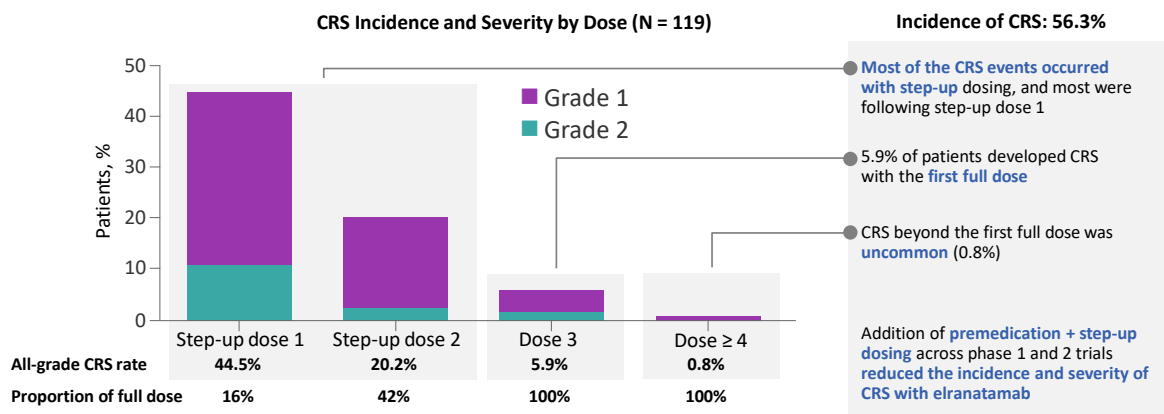
Opportunistic Infections in < 5% of Patients, Any Grade, %	MagnetisMM-3 BCMA-Naïve N = 123
<i>Pneumocystis jirovecii</i> pneumonia	4.9
Cytomegalovirus infection	3.3
Adenoviral hepatitis	0.8
Adenovirus infection	0.8
Pneumonia adenoviral	0.8
Pneumonia cytomegaloviral	0.8



Lesokhin AM, et al. *Nat Med.* 2023;29:2259-67.

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Timing of CRS With Step-Up Dosing



Lesokhin AM, et al. *Nat Med.* 2023;29:2259-67.

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Real-World Data: Elranatamab

	MagnetisMM-3 N = 123	Malard et al. n = 101 2022-2023
Demographics	mLoT 5 0% prior BCMA Median f/u 14.7 mos	mLoT 5 17% prior BCMA Median f/u 15.5 mos
ORR	61%	52%
CRR	35%	16%
ORR (Prior BCMA)		47%
mPFS	NR (15-mos PFS 51%)	1-year PFS 34%
mOS	NR (15-mos OS 57%)	1-year OS 42%
CRS	58% (0% grade 3 or 4)	45% (0%)
ICANS	3% (0% grade 3 or 4)	3% (0%)
Tocilizumab	22.7%	
Dexamethasone	8.4%	
Infections (≥ G3)	70% (40%; 7% deaths)	49% (24%)
IVIG	43%	50%
Neutropenia (≥ G3)	49% (49%)	

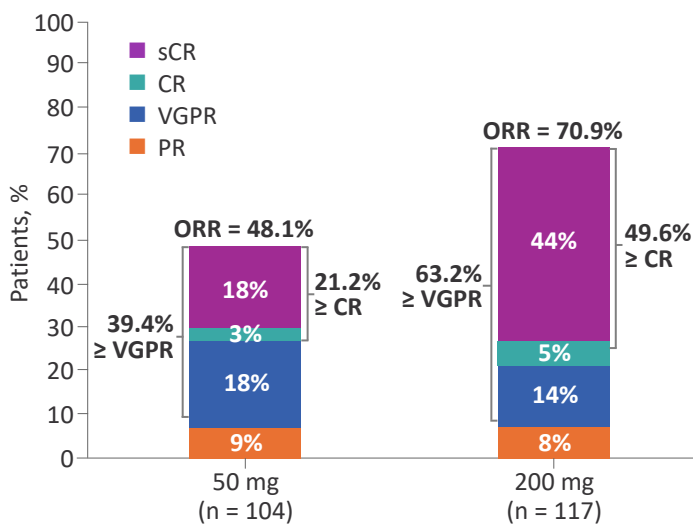


Lesokhin AM, et al. *Nat Med.* 2023;29:2259-67; Malard F, et al. *Blood Cancer J.* 2024;14:219.

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Linvoseltamab for RRMM: LINKER-MM1 Trial

- Phase 2 study; 221 RRMM patients whose prior therapies included an immunomodulatory drug, a proteasome inhibitor, and an anti-CD38 antibody
- Treatment was once a week through week 14 and then every 2 weeks; patients on 200 mg who achieved > VGPR by week 24 received linvoseltamab once every 4 weeks
- Primary endpoint was ORR



Bumma N, et al. *J Clin Oncol.* 2024;42:2702-12.

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LINKER-MM1 Trial: Demographics

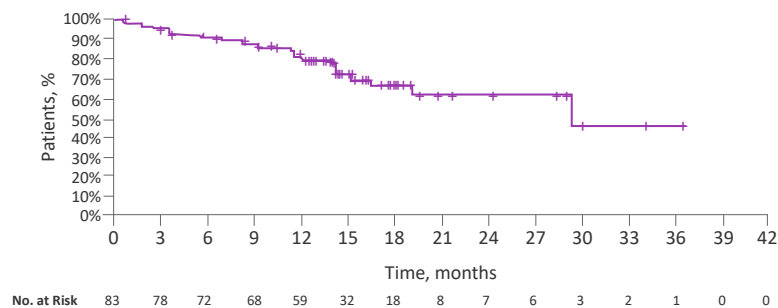
Patient and Disease Characteristics	50 mg (n = 104)	200 mg (n = 117)
Age		
Years, median (range)	65 (45-90)	70 (37-91)
≥ 75 years, no. (%)	17 (16.3)	31 (26.5)
Male, no. (%)	56 (53.8)	64 (54.7)
Race, no. (%)		
White	75 (72.1)	83 (70.9)
Black or African American	14 (13.5)	20 (17.1)
Asian	6 (5.8)	10 (8.5)
High-risk cytogenetics, no. (%)	28 (26.9)	46 (39.3)
Refractory status, no. (%)		
At least triple-refractory	97 (93.3)	96 (82.1)
At least quad-refractory	86 (82.7)	77 (65.8)
At least penta-refractory	56 (53.8)	33 (28.2)
Refractory to the last line of therapy, no. (%)	93 (89.4)	100 (85.5)

Bumma N, et al. *J Clin Oncol*. 2024;42:2702-12.



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Linvoseltamab for RRMM: LINKER-MM1 Trial



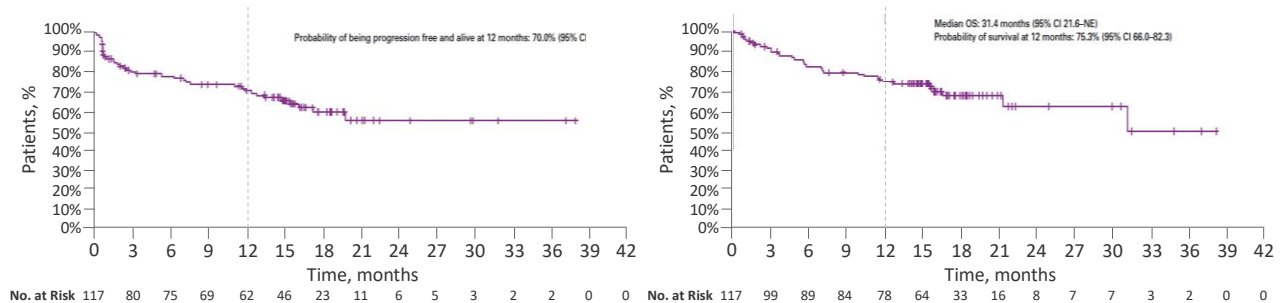
- Median DOR: 29.4 months (95% CI, 19.2-NE)
- Estimated probability of maintaining a response at 12 months: 80.9% (95% CI, 70.3%-88.0%)



Bumma N, et al. *J Clin Oncol*. 2024;42:2702-12.

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Linvoseltamab for RRMM: LINKER-MM1 Trial



- Median PFS: not reached (95% CI, 17.3 months NE)
- Probability of being progression free and alive at 12 months: 70.0% (95% CI, 60.1%-78.0%)
- Median OS: 31.4 months (95% CI, 21.6-NE)
- Probability of survival at 12 months: 75.3% (95% CI, 66.0%-82.3%)



Bumma N, et al. *J Clin Oncol.* 2024;42:2702-12.

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LINKER-MM1: Adverse Events

TEAEs in ≥ 20% of Patients

Treatment exposure and TEAEs	50 mg (n = 104)	200 mg (n = 117)
Treatment exposure, weeks, median (range)	13.9 (2.0-160.0)	53.0 (1.0-167.0)

TEAEs	Any Grade, No. (%)	Grade 3/4, No. (%)	Any Grade, No. (%)	Grade 3/4, No. (%)
Patients with TEAE	102 (98.1)	75 (72.1)	117 (100)	86 (73.5)
Hematologic TEAEs				
Neutropenia	30 (28.8)	28 (26.9)	50 (42.7)	49 (41.9)
Anemia	44 (42.3)	39 (37.5)	45 (38.5)	36 (30.8)
Nonhematologic TEAEs				
CRS	57 (54.8)	2 (1.9)	54 (46.2)	1 (0.9)
Cough	36 (34.6)	0	43 (36.8)	0
COVID-19	24 (23.1)	7 (6.7)	26 (22.2)	11 (9.4)



Bumma N, et al. *J Clin Oncol.* 2024;42:2702-12.

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LINKER-MM1: CRS and ICANS

CRS

- Shorter time to onset and resolution of CRS and an overall lower rate of CRS compared with teclistamab- and elranatamab-treated patients:
 - Median time to onset: 11 hours
 - Duration: 15 hours
 - Occurred in 46% of patients; majority being grade 1 (35% of patients) and a single case of grade 3
- Almost all CRS cases occurred during the first 2 doses of study drug
- Limited required duration of hospitalization or observation (24 hours on day 1 and 8)

ICANS

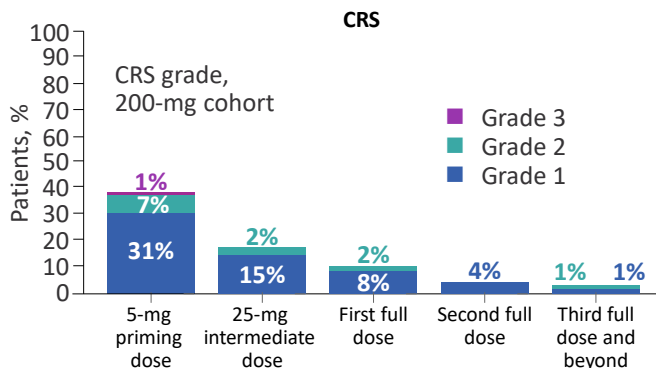
- The overall rate was 7.7% (grade 1-3, no grade ≥ 4 events occurred)
- Most patients experienced ICANS during step-up dosing (8/9 patients), and all cases occurred in the context of CRS or IRR



Bumma N, et al. *J Clin Oncol*. 2024;42:2702-12.

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Linvoseltamab for the Treatment of RRMM



Timing, duration, and management of CRS	200 mg (n = 117)
Time to first CRS onset, median (range), hours	11 (-1.1-183.6) ^a
Duration of CRS, median (range), hours	15.6 (1.0-96)
Patients with supportive measures to treat CRS, n (%)	29 (24.8)
Tocilizumab	22 (18.8)
Corticosteroids	13 (11.1)
Oxygen	9 (7.7)
Vasopressors	1 (0.9)
IV fluid bolus	11 (9.4)

- CRS, any grade, occurred in 46% of patients, with 35% grade 1, 10% grade 2, 1% (1 patient) grade 3, and no grade ≥ 4
- CRS occurred mostly during step-up dosing of linvoseltamab



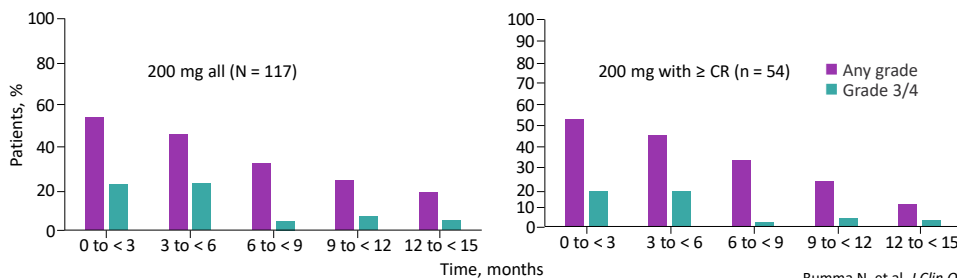
^aNegative numbers indicate CRS onset prior to the end of linvoseltamab administration.
Bumma N, et al. *J Clin Oncol*. 2024;42:2702-12.

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Infection Frequency and Severity Over Time

Time period of onset of infections n/total (%)	200 mg (N = 117)		200 mg with ≥ CR (n = 54)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
0 to < 3 months	62/117 (53.0)	25/117 (21.4)	31/58 (53.4)	11/58 (19)
3 to < 6 months	37/82 (45.1)	18/82 (22.0)	25/56 (44.2)	10/56 (17.9)
6 to < 9 months	25/70 (35.7)	3/70 (4.3)	19/54 (35.3)	1/54 (1.9)
9 to < 12 months	18/64 (28.1)	5/64 (7.8)	14/54 (25.9)	4/54 (7.4)
12 to < 15 months	15/61 (24.6)	4/61 (6.6)	9/51 (17.6)	2/51 (3.9)

Infections occurred in 73% of patients, with grade 3/4 in 34% of patients



Bumma N, et al. *J Clin Oncol*. 2024;42:2702-12.



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FDA-Approved BCMA-Directed BsAbs for MM

	Teclistamab (MajestEC-1)	Elranatamab (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 mos	Not formally reported; deep CR rates suggest high MRD-neg
Median DOR	~24 months overall (CR or better: ~27 mos)	Not reached; ~71.5% DOR at 15 mos	~29.4 months (200-mg cohort, median follow-up 14.3 mos)
Median PFS	~11 months overall (CR or better: ~27 mos)	Not reached; ~50.9% PFS at 15 mos	Not reached; ~70% PFS at 12 mos (200-mg cohort)
CRS (any grade)	~72% (mostly grade 1/2); grade 3 ~0.6%	~56.3% (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 et al. <i>N Engl J Med</i> . 2022; Garfall et al. <i>J Clin Oncol</i> . 2024	Lesokhin et al. <i>Nat Med</i> . 2023 (MagnetisMM-3)	Bumma et al. <i>J Clin Oncol</i> . 2024 (LINKER-MM1 study)



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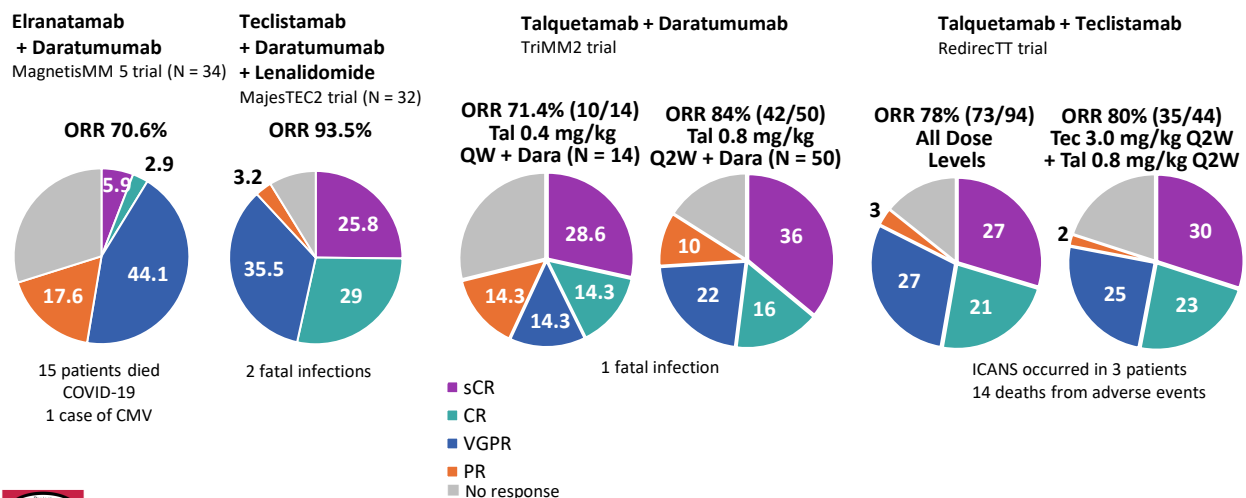
Long-Term Follow-Up Data for FDA-Approved BCMA-Directed BsAbs for MM

	Teclistamab (MajesTEC-1)	Elranatamab (MagnetisMM-3)	Linvoseltamab (LINKER-MM1)
ORR	~63% (≥ CR: 46%, ≥ VGPR: 59%)	~61% (≥ CR: ~37.4%; ~60.5% MRD-neg among CRs)	~71% (≥ CR: ~50%, ≥ VGPR: ~63%)
Median DOR	~24 months overall (CR or better: ~27 mos)	Not reached; ~66.9% DOR at 24 mos	
Median PFS	~11 months overall	17.2 mos	
Key reference	Garfall et al. <i>J Clin Oncol.</i> 2024	Tomasson MH et al. <i>Hemasphere.</i> 2024; 8:e136	Bumma et al. <i>J Clin Oncol.</i> 2024 (LINKER-MM1 study)



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New and Emerging Therapies for Multiple Relapsed MM: Clinical Data Combination Therapies With Bispecific T-Cell Engagers



Grosicki S, et al. *Blood.* 2022;140:4407-8; Searle E, et al. *Blood.* 2022;140:394-6; Dholaria BR, et al. *J Clin Oncol.* 2023;41:8003; Cohen YH, et al. *N Engl J Med.* 2025;392:138-49.

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