4th MEETING ON
INNOVATIVE IMMUNOTHERAPIES
FOR LYMPHOID MALIGNANCIES

Società Italiana di Ematologia

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Clinical Results in MM: BCMA, what's next?

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MILANO, STARHOTELS ROSA GRAND
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Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Janssen, takeda, roche,abbvie, kite,regeneron,BMS, Amgen,Sanofi, Astrazeneca, oncopeptides, menarini			x			x	x

New targets on myeloma cells and New drugs

BCMA

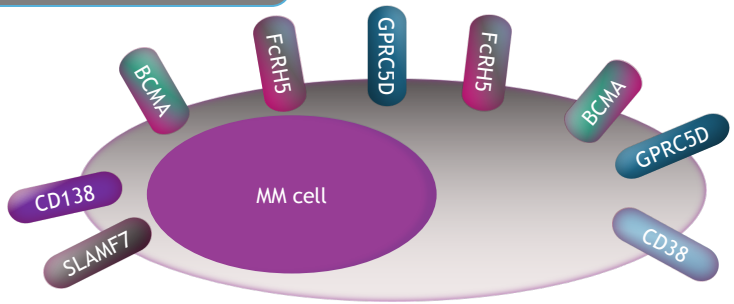
- BCMA is a member of the TNF receptor superfamily
- APRIL and BAFF are known ligands, leading to activation of the NF-κB pathway
- BCMA promotes plasma cell survival, growth, resistance to apoptosis, adhesion, and angiogenesis
- γ-secretase cleaving causes shedding of soluble BCMA
- BCMA is expressed on **malignant PCs, at low levels on normal PCs and mature B lymphocytes** and is absent in non-hematological tissues

FcRH5

- FcRH5 is a surface protein in the Ig superfamily
- It is expressed only in B cells, with increasing expression in **mature B cells and plasma cells**
- FcRH5 is involved in proliferation and isotype expression

GPRC5D

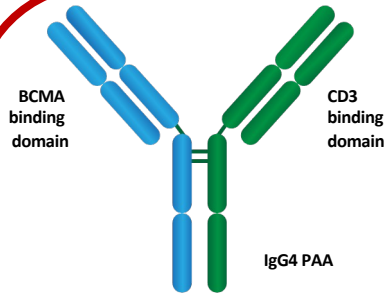
- GPRC5D is a member of the G protein-coupled receptor family with an **unknown function**
- It is highly expressed on **malignant PCs,** as well as hard **keratinized structures** (hair shaft, nail, and central region of the tongue)



Modality of targeting: ADC, Bispecific antibodies, CAR-T cells

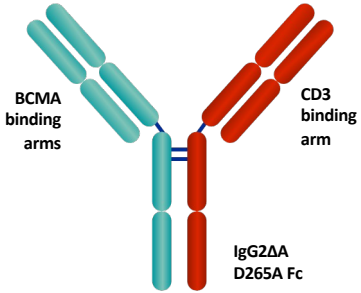
Image adapted from Verkleij CPM, et al. Curr Opin Oncol. 2020;32:664-71 and Bruins WSC, et al. Front Immunol. 2020;11:1155.
APRIL, a proliferation-inducing ligand; BAFF, B-cell activating factor; BCMA, B-cell maturation antigen; CD, cluster of differentiation; FcRH5, Fc receptor-like 5; GPRC5D, G-protein coupled receptor family C group 5 member D; Ig, immunoglobulin; MM, multiple myeloma; NF-κB, nuclear factor Bs; PC, plasma cell; SLAMF7, signaling lymphocytic activation molecule family member 7; TNF, tumor necrosis factor.
1. Rodríguez-Lobato LG, et al. Front Oncol. 2020;10:1243. 2. Pillarisetti K, et al. Blood Adv. 2020;4:4538–49. 3. Yu B, et al. J Hematol Oncol. 2020;13:125. 4. Verkleij CPM, et al. Blood Adv. 2020;5;2196-215. 5. Smith EL, et al. Sci Transl Med. 2019;11:eaau7746. 6. Li J, et al. Cancer Cell. 2017;31;383-95. 7. Bruins WSC, et al. Front Immunol. 2020;11:1155. 8. Lancman G, et al. Blood Cancer Discov. 2021;2:423-33.

T-Cell Redirecting Bispecific Antibodies approved by FDA and EMA for RRMM



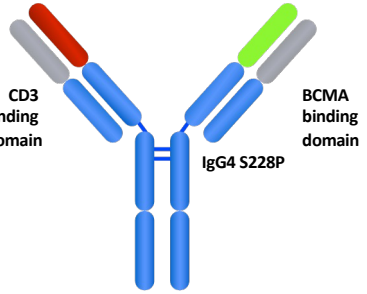
Teclistamab
BCMA x CD3 antibody

Anti-BCMA
MajesTEC-1[1]
Phase 1/2
(N=165)



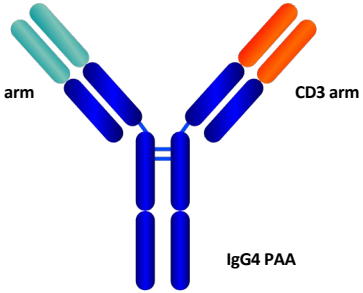
Elranatamab
BCMA x CD3 Antibody

Anti-BCMA
MagnetisMM-3[2]
Phase 2
(N=123)



Linvoseltamab
BCMA x CD3 Antibody

Anti-BCMA
LINKER-MM1[3]
Phase 1/2
(N=117)



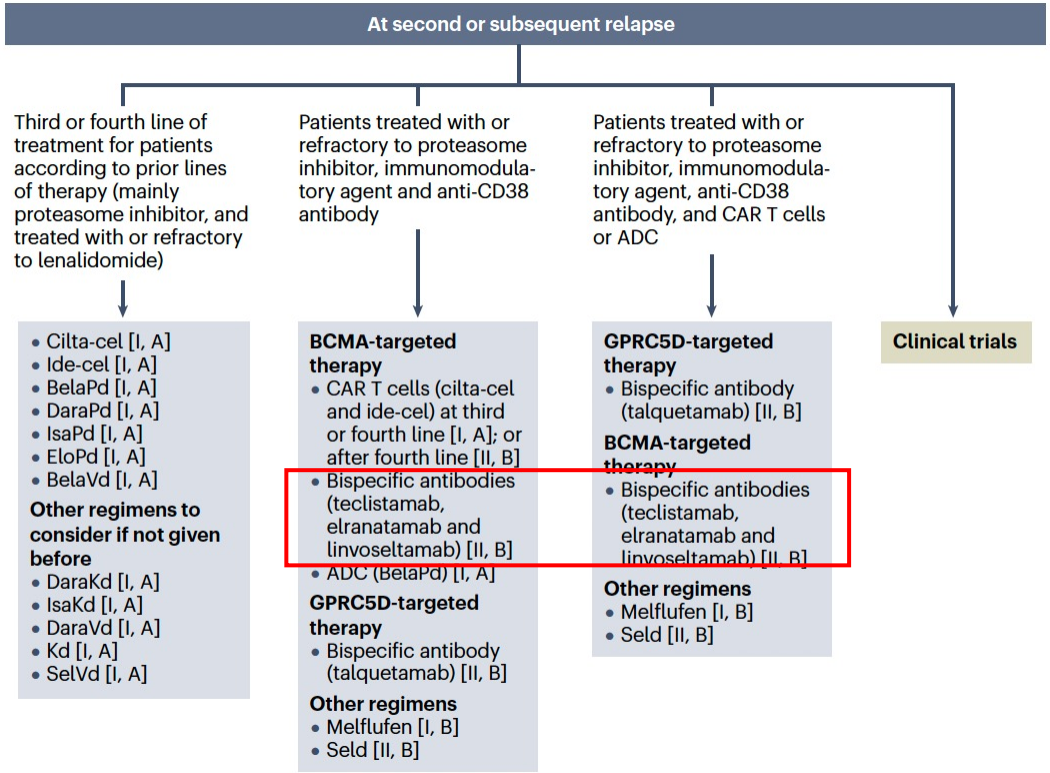
Talquetamab
GPRC5D x CD3 antibody

Anti-GPRC5D
MonumenTAL-1[4]
Phase 1/2
(N=375)

Approved for the treatment of RRMM exposed at Imid, PI and anti-CD38 MoAb

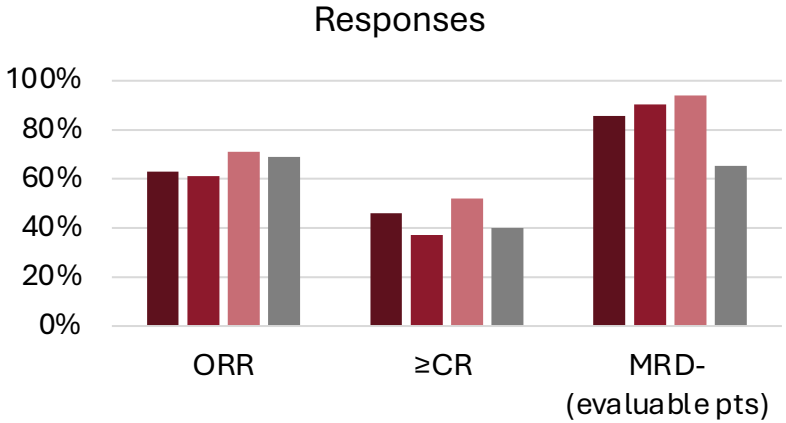
1. Moreau P, et al. *N Engl J Med*. 2022;387(6):495-505. 2. Lesokhin AM, et al. *Nat Med.* 2023;29(9):2259–2267. 3. Bumma N, et al. *J Clin Oncol*. 2024;42(22):2702-2712. 4. Chari A, et al. *Lancet Haematol*. 2025;12(4):e269-e281.

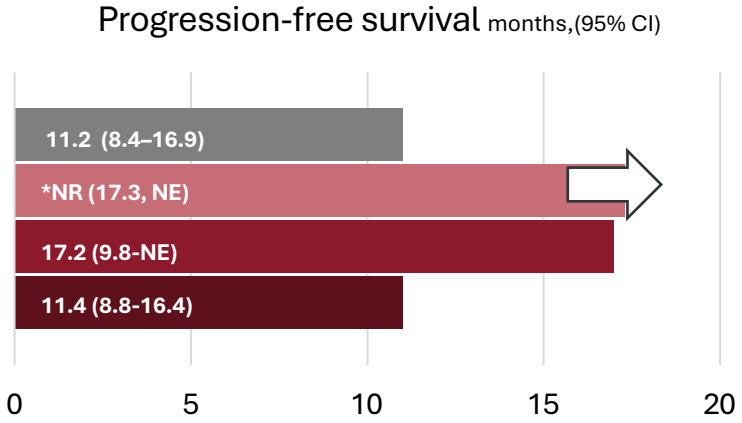
EHA-EMN 2025 guidelines for the treatment of 3xRRMM



Nature Reviews Clinical Oncology volume 22, pages680–700 (2025)

Efficacy data of T-Cell Redirecting Bispecific Antibodies for RRMM





Teclistamab Elranatamab Talquetamab Linvoseltamab

Teclistamab[1]	Elranatamab[2-4]	Linvoseltamab[5]	Talquetamab[6]
MajesTEC-1 Phase 1/2	**MagnetisMM-3** Phase 2	**LINKER-MM1** Phase 1/2	**MonumenTAL-1** Phase 1/2 (0.8 mg/kg Q2W)
mDOR 18.4 mo mOS 22.2 mo (mF/up 30.4 mo)	24-mo DOR 67% mOS 24.6 mo (mF/up 28.4 mo)	12- mo DOR 81% mOS NR (mF/up 14.3 mo)	mDOR 16.9 mo mOS NR (mF/up 19.4 mo)

MRD (10-5) among patients evaluable for MRD, ITT

Notes: *NR, Not reached (current follow up: 21.3 months)

1. Garfall et al., ASCO 2024 (Poster 7540). 2. Lesokhin AM, et al. Nat Med. 2023;29:2259–2267. 3. Mohty. EHA 2024. P932. 4. Prince. ASH 2024. Abstr 4738. 5. Lee et al. ASH 2024. Poster 3369. 6. van de Donk et al. ASCO 2025 (Abstract 7517).

T-cell redirecting and risk of infections[1-10]

	Bispecific antibodies			
Drug	**Teclistamab**	**Elranatamab**	**Linvoseltamab**	**Talquetamab** 0.8 mg/kg SC Q2W
Study	MajesTEC-1[6]	MagnetisMM-3[7]	**LinkerMM-1**	MonumenTAL-1[8–10]
Phase study	I/II	II	I/II	I/II
Target	BCMA/CD3	BCMA/CD3	**BCMA**	GPRC5D/CD3
Infections: All grade	80%	70%	74%	66%
Infections: Grade ≥3	55%	40%	36%	15%
Patients receiving IVIg during the study	46%	43%	64%	13%
Hypogammaglobulinemia	21%	NR	16%	68%
COVID, all grade	29%	29%		2%
CMV (%), all grade	1%	3%	10%	1%
PJP (%), all grade	4%	5%	4%	NR

BCMA, B-cell maturing antigen; CD, cluster of differentiation; CMV, cytomegalovirus; COVID, coronavirus disease; GPRC5D, G protein–coupled receptor class C group 5 member D; ICANS, immune effector cell-associated neurotoxicity syndrome; NR, not reported; PJP, *pneumocystis jirovecii* infection; SC, subcutaneous.

1. Munshi NC, et al. N Engl J Med 2021;384:705–716; 2. Logue JM, et al. Blood Adv 2022;6:6109–6119; 3. Rodriguez-Otero P, et al. N Engl J Med. 2023;388:1002–1014; 4. Berdeja JG, et al. Lancet 2021;398:1216; 5. San-Miguel J, N Engl J Med 2023;389:335–347; 6. Nooka AK, et al. Cancer 2024;130:886–900; 7. Lesokhin AM, et al. Nat Med 2023;29:2259–2267; 8. Touzeau CS, et al. EHA 2023 (Abstract No. S191 – presentation); 9. Rasche L, et al. EHA 2023 (Abstract No. P892 – poster); 10. Rasche L, et al. EHA 2023 (Abstract No. P892- poster, supplement).

Bispecific antibodies in MM: a roadmap

Triple—class RRMM (3+ lines)	Early lines RRMM	NDMM
	Single Agent/Combination	Single Agent/Combination
Teclistamab Talquetamab Linvoseltamab Elranatamab	Majestec-9: Tec vs SOc LinkerMM-3: Linvo vs SOc MagnetisMM-32: Elra vs SOc Majestec-3: Dara-tec vs SOc Monumental-6: Talq-Tec vs Talq-Pom vs SOc	TIE fist line EMN39: DRd → Linvo vs DRd Pre-ASCT Induction Majestec-5/GMMHD-10: Dara-Tec-R (+/- V) Post-ASCT maintenance Majestec-4/EMN30: Tec-R vs Tec vs R TIE fist line Majestec-7: Dara-Tec-R / Dara-Tal-R vs DRd

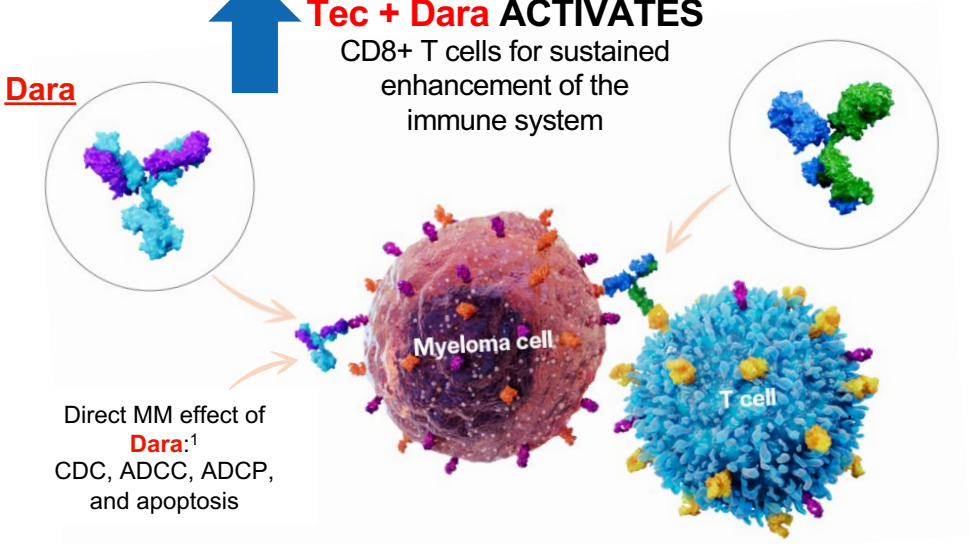
Early lines: RRMM

MajesTEC-3: Tec-Dara Synergistic MOA

Dara PRIMES
Clears immunosuppressive CD38+ B_{regs} and T_{regs}

Tec + Dara ACTIVATES
CD8+ T cells for sustained enhancement of the immune system

Tec REDIRECTS
functionally enhanced[a] CD8+ T cells

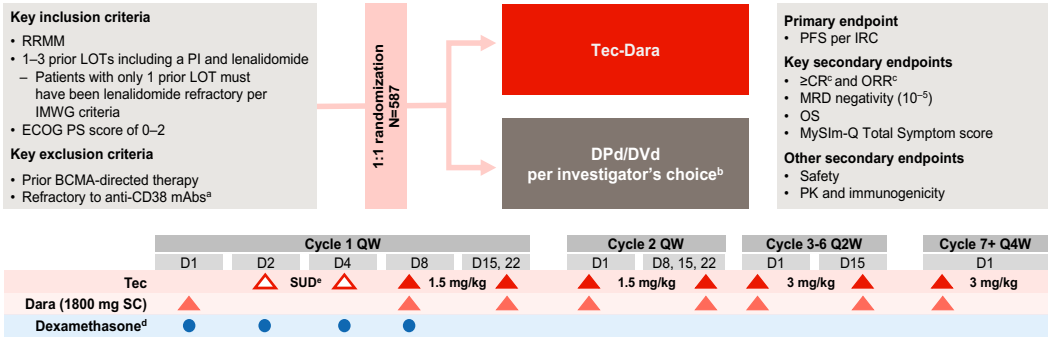


Tec + Dara synergistic immunotherapy combination EXTENDS PFS and OS through amplified Tec-mediated eradication of MM cells[2,3]

[a]Functional enhancement referring to the increase $CD8^+$ T-cell numbers and enhancement of their ability to proliferate, signal, secrete cytokines, and kill tumor cells by reducing immune suppression in the microenvironment.
ADCC, antibody-dependent cellular cytotoxicity; ADCP, antibody-dependent cellular phagocytosis; BCMA, B-cell maturation antigen; CDC, complement-dependent cytotoxicity; Dara, daratumumab; MM, multiple myeloma; MOA, mechanism of action; PFS, progression-free survival; OS, overall survival; Tec, teclistamab; Treg, regulatory T cell.
1. van de Donk NWCJ, et al. *Front Immunol.* 2018;9:2134. 2. Vishwamitra D, et al. Presented at: 66th American Society of Hematology (ASH) Annual Meeting and Exposition; December 7-10, 2024; San Diego, CA, USA. Oral 594.
3. Frerichs KA, et al. *Clin Cancer Res.* 2020;26:2203-2215.

Mateos M et Al. ASH 2025, LBA

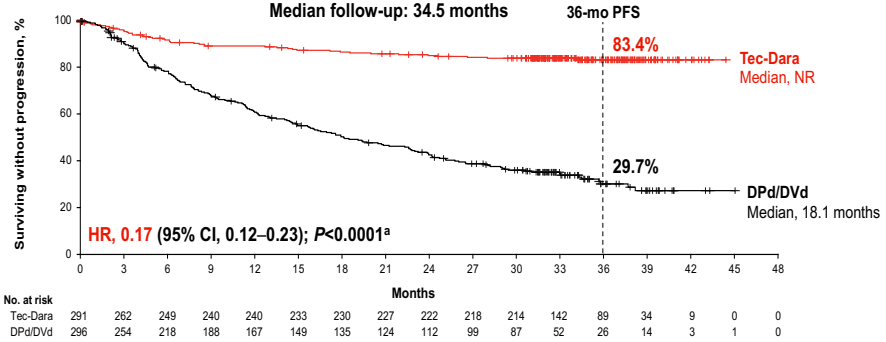
MAJESTEC-3 trial: Teclistamab-Daratumumab vs DVd/DPd



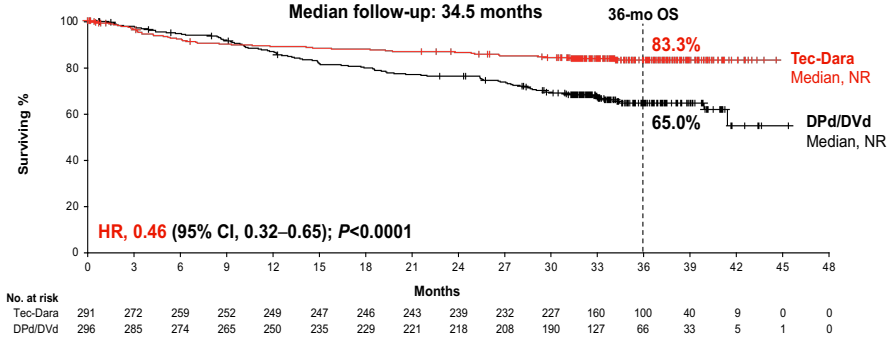
Tec-Dara was dosed using an established Dara SC schedule; steroid free after Cycle 1 Day 8

- **Median age 64-63 y (10-8%>75y)**
- **Median n of prior lines 2**
- **Prior exposure to Dara: 5%**

- **MRD neg 58.4% vs 17%**



Tec-Dara significantly improved PFS versus DPd/DVd, with 83% of patients alive and progression free at 3 years



Tec-Dara significantly improved OS versus DPd/DVd, with an emerging plateau from 6 months and 83% patients alive at 3 years

Mateos M et Al. ASH 2025, LBA

MAJESTEC-3 trial: Teclistamab-Daratumumab vs DVd/DPd

TEAE, n (%)[b]	Tec-Dara (n=283)		DPd/DVd (n=290)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Any TEAE	283 (100)	269 (95.1)	290 (100)	280 (96.6)
Hematologic				
Neutropenia	222 (78.4)	214 (75.6)	240 (82.8)	228 (78.6)
Anemia	111 (39.2)	58 (20.5)	103 (35.5)	50 (17.2)
Thrombocytopenia	103 (36.4)	55 (19.4)	126 (43.4)	68 (23.4)
Lymphopenia	63 (22.3)	59 (20.8)	50 (17.2)	32 (11.0)
Leukopenia	51 (18.0)	30 (10.6)	61 (21.0)	46 (15.9)
Nonhematologic[c]				
CRS	170 (60.1)	0	0	0
Diarrhea	147 (51.9)	10 (3.5)	89 (30.7)	7 (2.4)
Cough	136 (48.1)	1 (0.4)	66 (22.8)	0
Pyrexia	104 (36.7)	4 (1.4)	55 (19.0)	1 (0.3)

- Of CRS events, most were grade 1 (44.2%)
- ICANS was low (1.1%); all resolved
- TEAE profile was comparable
  - Leading to discontinuation: 4.6% vs 5.5%, respectively
  - Serious AEs: 70.7% vs 62.4%

TEAE, n (%)[d]	Tec-Dara (n=283)		DPd/DVd (n=290)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Any infection	273 (96.5)	153 (54.1)	244 (84.1)	126 (43.4)
Treatment-emergent infection or infestation[c]				
COVID-19	124 (43.8)	17 (6.0)	97 (33.4)	6 (2.1)
URTI	115 (40.6)	12 (4.2)	88 (30.3)	7 (2.4)
Pneumonia	65 (23.0)	47 (16.6)	53 (18.3)	43 (14.8)
Nasopharyngitis	62 (21.9)	0	57 (19.7)	0
Sinusitis	52 (18.4)	5 (1.8)	17 (5.9)	3 (1.0)
Rhinovirus infection	44 (15.5)	5 (1.8)	10 (3.4)	1 (0.3)
Bronchitis	40 (14.1)	2 (0.7)	31 (10.7)	6 (2.1)
Influenza	38 (13.4)	8 (2.8)	43 (14.8)	10 (3.4)
COVID-19 pneumonia	34 (12.0)	32 (11.3)	12 (4.1)	7 (2.4)
Urinary tract infection	29 (10.2)	4 (1.4)	27 (9.3)	1 (0.3)

- Hypogammaglobulinemia[a] occurred in 84.5% of Tec-Dara patients; 87.3% received ≥1 dose of Ig
- Fatal infections occurred in 13 (4.6%) patients with Tec-Dara
  - 12 occurred <6 months prior to implementation of reinforced IgRT and prophylaxis guidance
  - 9 patients did not receive any IgRT

Mateos M et al. ASH 2025, LBA

Bispecific antibodies in MM: open questions

Early lines RRMM

Single Agent/Combination

Majestec-9: Tec vs SOc

LinkerMM-3: Linvo vs SOc

MagnetisMM-32: Elra vs SOc

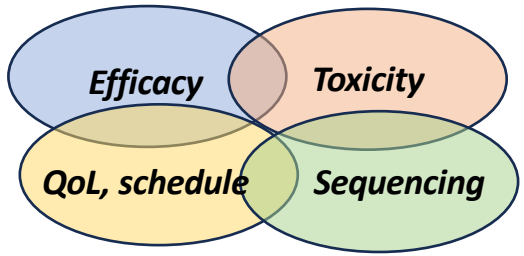
Majestec-3: Dara-tec vs SOc

Monumental-6:
Tal-Tec vs Talq-pom vs SOc

Phase 3 MajesTEC-9 study of TECVAYLI® (teclistamab-cqyv) monotherapy, showing a 71% reduction in the risk of disease progression or death and a 40% reduction in the risk of death in a patient population that was predominantly refractory to anti-CD38 therapy and lenalidomide. Data confirm superior progression-free survival (PFS) and overall survival (OS) with TECVAYLI® compared to standard of care as early as second line (press release)

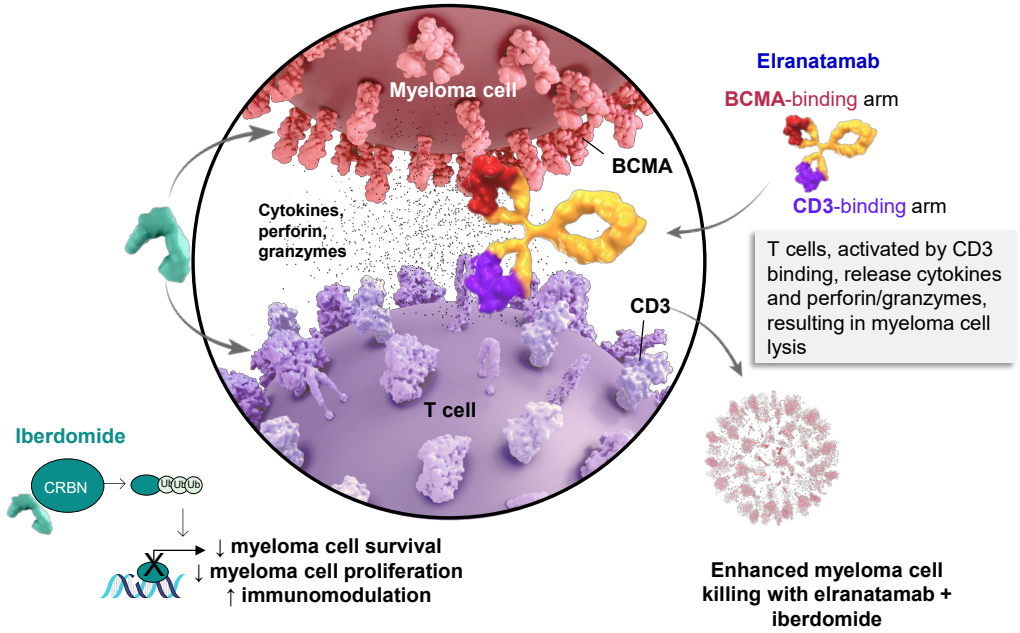
If yes, optimal combination? → trials with combo are ongoing

Do we need a combination? → trials with single agent BsAb are ongoing



Phase I Magnetism-30 trial: Erlanatamab plus Iberdomide

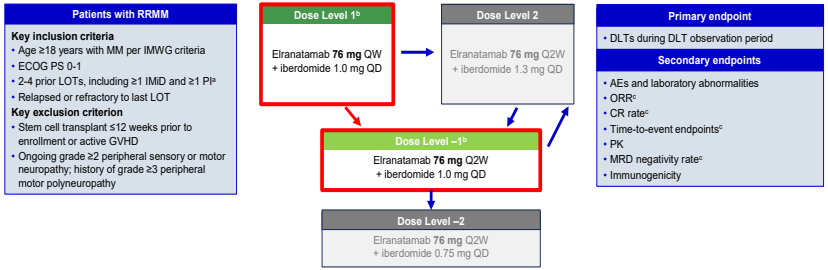
- **Elranatamab** is a BCMA-CD3 bispecific antibody approved as a monotherapy for patients with RRMM who have received ≥1 IMiD, ≥1 PI, and ≥1 anti-CD38 mAb[1-2]
  - Based on MagnetisMM-3 (NCT04649359), ORR was 61.0%, ≥CR rate was 37.4%, mPFS was 17.2 months, and mOS was 24.6 months[3,4]
- **Iberdomide** is an oral CELMoD™ with superior preclinical features than IMiDs, that:
  - Exhibits greater antiproliferative and proapoptotic activity in myeloma cells and immunomodulatory activity than the IMiDs class
  - Promotes activation and proliferation of T-cells, enhances T-cell engager function and prevents T-cell exhaustion in vitro and in vivo[5-7]

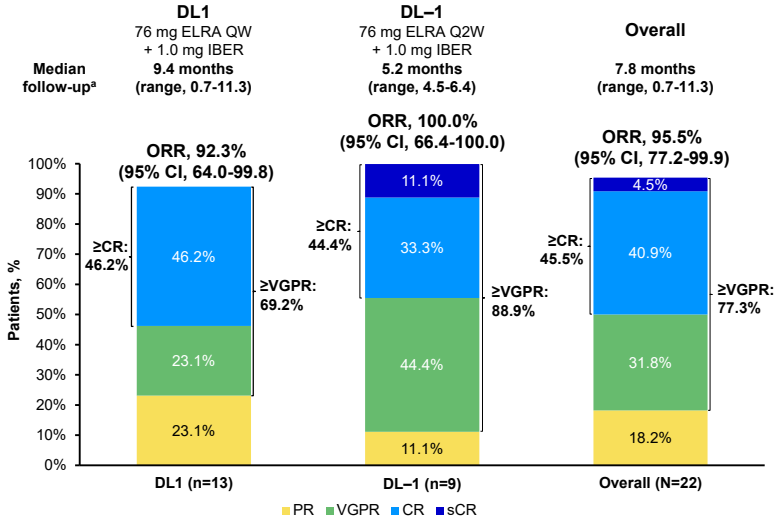


Elranatamab in combination with **iberdomide** may provide additional benefit to patients with RRMM based on the complementary mechanisms of action of this combination

1. Elrexfio (elranatamab-bcmm). Prescribing information. Pfizer Inc; 2025. **2**. Elrexfio (elranatamab-bcmm). Summary of product characteristics. Pfizer Europe MA EEIG; 2024. **3.** Lesokhin AM, et al. Nat Med 2023;29:2259-2267.
4. Tomasson MH, et al. Hemasphere 2024;8:e136 **5.** Lonial S, et al. Lancet Haematol 2022;9:e822-e832. **6**. Bjorklund CC, et al. Leukemia 2020;34:1197-1201. **7.** Paiva B, et al. Hemasphere 2023;7(suppl 3):P799.
BCMA=B-cell maturation antigen; CR=complete response; CELMoD=cereblon E3 ligase modulatory drug; IMiD=immunomodulatory drug; mAb=monoclonal antibody; mOS=median overall survival; mPFS=median progression-free survival; ORR=objective response rate; PI=proteasome inhibitor; RRMM=relapsed or refractory multiple myeloma

Phase I Magnetism-30 trial: Erlanatamab plus Iberdomide





N= 22 pts (Median age 68 y)

- **Median n of prior lines 2.5**
- **Triple Class refractory: 50%**

	N=22	
TEAE, n (%)[a]	**Any grade**	**Grade 3/4**
Any	22 (100.0)	19 (86.4)
Hematologic		
Neutropenia	17 (77.3)	16 (72.7)
Anemia	7 (31.8)	3 (13.6)
Lymphopenia	4 (18.2)	4 (18.2)
Nonhematologic		
CRS	15 (68.2)	0
Fatigue	14 (63.6)	0
Diarrhea	11 (50.0)	0
Headache	10 (45.5)	0
Cough	10 (45.5)	0
Nausea	9 (40.9)	1 (4.5)
Injection site reaction	9 (40.9)	0
Decreased appetite	8 (36.4)	1 (4.5)

Infections occurring in >5% of patients	**N=22**	
TEAE, n (%)[a]	**Any grade**	**Grade 3**
Infections[b]	9 (40.9)	2 (9.1)
Upper respiratory tract infection	6 (27.3)	0
Candida infection	3 (13.6)	0
Urinary tract infection	2 (9.1)	0

IVIG prophylaxis was administered approximately every 4 weeks to maintain IgG levels above 400 mg/dL

Elranatamab Combination: MagnetisMM-20 trial (Erla-Kd)

Median FUP: 8.9m

Key inclusion: RRMM 1-3 PL, K-sensitive. If prior K wash-out at least 6 months. No prior BCMA.
Median nºPL 2 (1-3); TCE 50%, only 1 prior K.
N=12

DL1 Elranatamab 12, 32 and 44mg QW until C7 then Q2W
DL2 12, 32 and 76mg QW until C7 then Q2W
+ Carfilzomib (K) 70mg/m2 weekly*

Safety

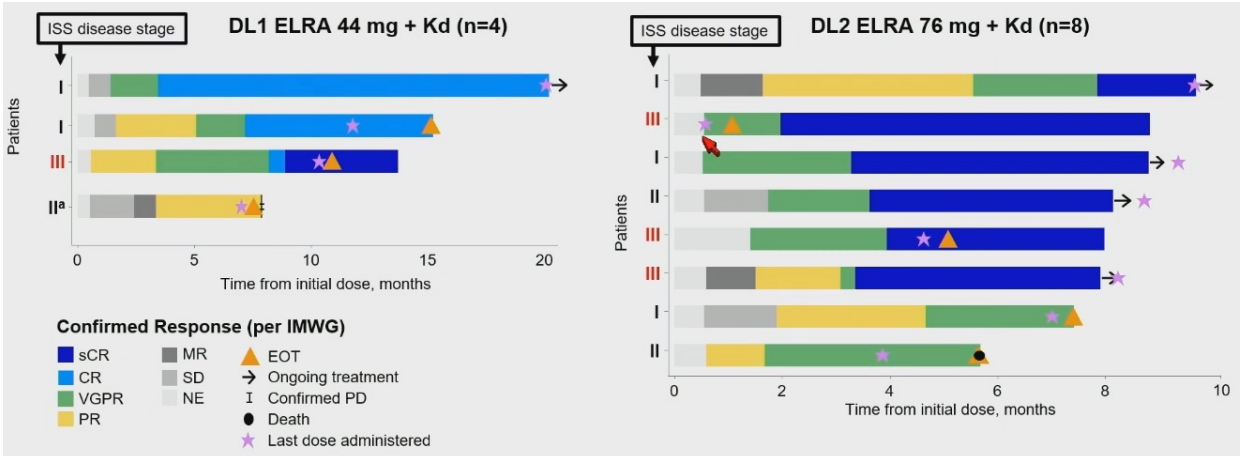
TEAEs	All grade	G3-4
Neutropenia	9 (75%)	9 (75%)
Thrombocytopenia	9 (75%)	5 (41.7%)
Infections	11 (91.7%)	2 (16.7%)
CRS	9 (75%)	0
Diarrhea	6 (50%)	1 (8.3%)
CMV reactivation	6 (50%)	1 (8.3%)

No ICANS was reported
No DLT in 10 evaluable patients

Response

ORR 100%; ≥CR 75%; ≥VGPR 91.7%

Swimmer plot of response per investigator



*If patients received 6 or more months of QW ELRA and achieved PR or better (lasting 2 or months), the could change to Q2W dosing at the same DL.
BsAbs, bispecific antibodies; (s)CR, (stringent) stable complete response; CMV, cytomegalovirus; CRS, cytokine release syndrome; D, dexamethasone; DL, dose level; DLT, dose-limiting toxicity; Elra, elranatamab; EOT, end of trial; G, grade; K, carfilzomib; ICANS, immune cell associated neurotoxicity syndrome; IMWG, International Myeloma Working Group; ISS, international staging system; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PL, prior lines; (VG)PR, (very good) partial response; QW, weekly; Q2W, every other week; SD, stable disease; TCE, triple class exposed; TEAE, treatment emergent adverse event.
Tomasson MH, et al. ASH 2024 (Abstract No. 1024 – oral presentation).

Linvoseltamab Combinations: phase I LINKER-MM2

Linvoseltamab (LINVO) + bortezomib (BTZ) in patients (pts) with relapsed/refractory multiple myeloma (RRMM): First results from the LINKER-MM2 trial

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Key takeaway points / conclusions

- **At a median follow-up of 9.3 months (range: 1–27), linvoseltamab (100–200 mg IV) in combination with bortezomib (1.3 mg/m^2 IV) has a generally manageable safety profile in patients with RRMM (N=24)**
  - One patient experienced a DLT: Grade 3 CMV reactivation
  - CRS, neutropenia, thrombocytopenia, and infection were among the most common TEAEs
- **Combination therapy with linvoseltamab and bortezomib resulted in an ORR* of 85% (17/20, 95% CI: 62–97), and ≥CR rate of 50% (10/20, 95% CI: 27–73)**
- **These encouraging data in PI-exposed or -refractory MM patients suggest the combination of linvoseltamab and bortezomib is feasible**

*≥PR as assessed by the investigator per IMWG criteria in the efficacy analysis set (N=20 patients who received at least one dose of the combination treatment and underwent at least one post-baseline response assessment after C1D1).
C, cycle; CI, confidence interval; CMV, cytomegalovirus; CR, complete response; D, day; DLT, dose limiting toxicity; IV, intravenous; MM, multiple myeloma; PI, proteasome inhibitor; PR, partial response; ORR, objective response rate; RRMM, relapsed/refractory multiple myeloma.

Linvoseltamab (LINVO) + carfilzomib (CFZ) in patients (pts) with relapsed/refractory multiple myeloma (RRMM): Initial results from the LINKER-MM2 trial

Salomon Manier,[1] Enrique M. Ocio,[2] Carmen Martinez-Chamorro,[3] Sosana Delimpasi,[4] Albert Oriol,[5] Meletios A. Dimopoulos,[6] Xavier P. Leleu,[7] Samuel Rubinstein,[8] Nisha Joseph,[9] Mercedes Gironella Mesa,[10] Rajshekhar Chakraborty,[11] Carlos Fernández de Larrea,[12] Aurora Breazna,[13] James Drew,[13] Anita Boyapati,[13] Anasuya Hazra,[13]

Key takeaway points / conclusions

- **At a median follow-up of 14.8 months (range: 2–29), linvoseltamab (100–200 mg IV) in combination with carfilzomib (56 mg/m^2 IV) has a generally manageable safety profile in patients with RRMM (N=23)**
  - One patient experienced a DLT: Grade 4 thrombocytopenia in the setting of tumor lysis syndrome
  - CRS, neutropenia, and infection were among the most common TEAEs
- **Combination therapy with linvoseltamab and carfilzomib resulted in an ORR* of 90% (19/21, 95% CI: 70–99%), and ≥CR rate of 76% (16/21, 95% CI: 53–92%)**
  - 12-month DOR* rate was 87% (95% CI: 56–97%); 12-month PFS rate was 83% (95% CI: 55–94%)
- **These data support continued development of linvoseltamab in combination with carfilzomib for the treatment of patients with RRMM**

*≥PR as assessed by the investigator per IMWG criteria in the efficacy analysis set (N=21 patients who received at least one dose of the combination treatment and underwent at least one post-baseline response assessment after C1D1).
C, cycle; CI, confidence interval; CR, complete response; D, day; DLT, dose limiting toxicity; DOR, duration of response; IMWG, International Myeloma Working Group; IV, intravenous; ORR, objective response rate; PFS, progression-free survival; PI, proteasome inhibitor; PR, partial response; RRMM, relapsed/refractory multiple myeloma.

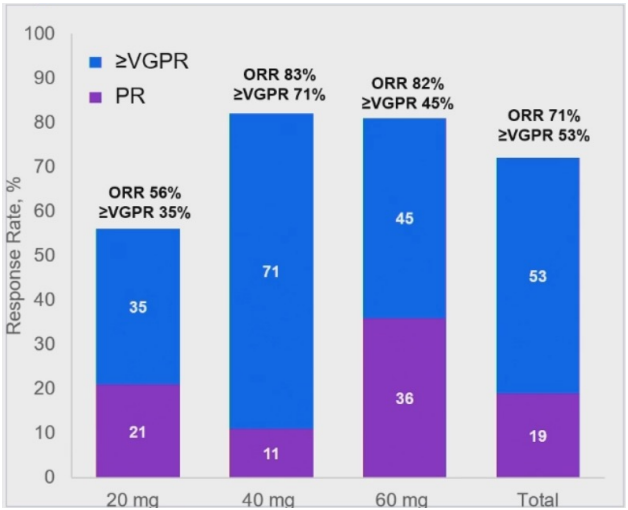
ABBV-383 (etentamig) combination + Dara + Dex

Phase 1b dose escalation and safety expansion study

ABBV-383 is composed of a ***bivalent BCMA-binding domain with high avidity, a low-affinity CD3-binding domain*** designed to mitigate cytokine release with potential for minimal T-cell exhaustion, and a present but silenced Fc tail resulting in an extended half-life and convenient dosing interval (every 4 weeks [Q4W]).

Median nº PL: 4 (3-10); Prior AntiCD38 was allowed with > 90 days wash-out; AntiCD38-refractory 56%. Triple-class exposed 70%. N=86

Efficacy



	Etentamig + Daratumumab-Dexamethasone			
	20 mg n=34[a]	40 mg n=35[a]	60 mg n=11	Total N=80
Median follow-up, months[b] (range)	4 (0–17)	8 (1–13)	8 (1–10)	7 (0–17)
Median time to first response, months (range)	1.1 (1–6)	1.0 (1–4)	1.0 (0–1)	1.0 (0–6)
Depth of response				
sCR/CR	5 (15)	14 (40)	3 (27)	22 (28)
MRD neg ($<10^{-5}$) among evaluable sCR/CR	1/2 (50)	12/12 (100)	3/3 (100)	16/17 (94)

Safety

Adverse events	*All grades*	*Grade 3-4*
Neutropenia	48%	44%
CRS	**29%**	**4%**
ICANs	4%	1%
Infections	67%	26%

- 10 patients (12%) discontinued due to AEs
- 12 TEAE leading to death (none deemed related to the study drug)

[a]Data combined for dose-escalation and safety expansion cohorts. [b]Based on N=86 total patients in the full analysis set. Median follow up is 16 months (1–17) and 4 months (0–5) for 20 mg dose-escalation and –expansion cohorts, respectively, and 13 months (9–13) and 7 months for 40 mg dose-escalation and –expansion cohorts, respectively.

(s)CR, (stringent) stable complete response; CRS, cytokine release syndrome; ICANS, immune cell associated neurotoxicity syndrome; MRD, minimal residual disease; ORR, objective response rate; (VG)PR, (very good) partial response; TEAE, treatment emergent adverse event.

1Rodriguez C, et al. ASH 2024 (Abstract No. 496 – oral presentation).

Bispecific antibodies in MM: open questions

Early lines RRMM

Single Agent/Combination

Majestec-9: Tec vs SOc

LinkerMM-3: Linvo vs SOc

MagnetisMM-32: Elra vs SOc

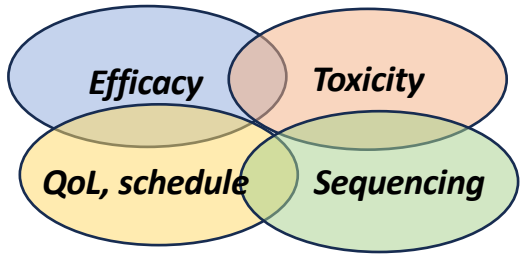
Majestec-3: Dara-tec vs SOc

Monumental-6:
Tal-Tec vs Talq-pom vs SOc

How to choose which anti-BCMA BsAb?

Do we need a combination? → trials with single agent BsAb are ongoing

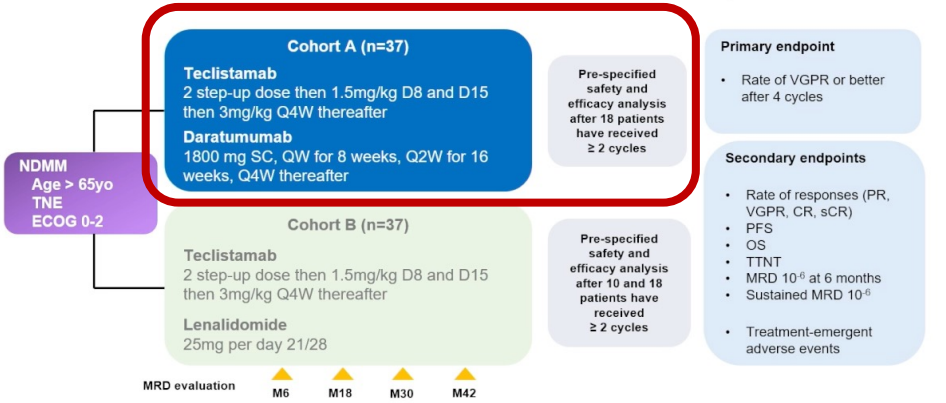
If yes, optimal combination? → trials with combo are ongoing



NDMM

IFM 2001-01: TEC-Lille TRIAL

Phase 2 study of Tec-Dara and Tec-Len in TNE NDMM (n = 74)



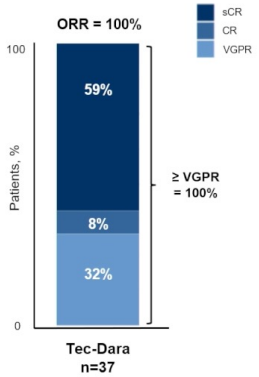
Current amendment:
Teclistamab 3mg/kg Q8W after C13 if CR or better and treatment interruption if 2-years sustained MRD -

NCT05

- **Median age 73 y (32%>75y)**
- **Frail 22%**

- **100% MRD neg on 27 evaluable patients**

Best response rate



Grade ≥ 3 AEs

AEs, n(%)	Tec-Dara (n=37) Grade ≥ 3
All grade ≥ 3 AEs	29 (78%)
All grade ≥ 3 SAEs	10 (27%)
Grade 5	-
Hematologic AEs	26 (70%)
Lymphopenia	21 (57%)
Neutropenia	16 (43%)
Anemia	2 (5%)
Thrombocytopenia	1 (3%)
Non-hematologic AEs	10 (27%)
Infection	5 (14%)
Hepatic cytolysis	2 (5%)
Skin rash	2 (5%)

All grade AESI

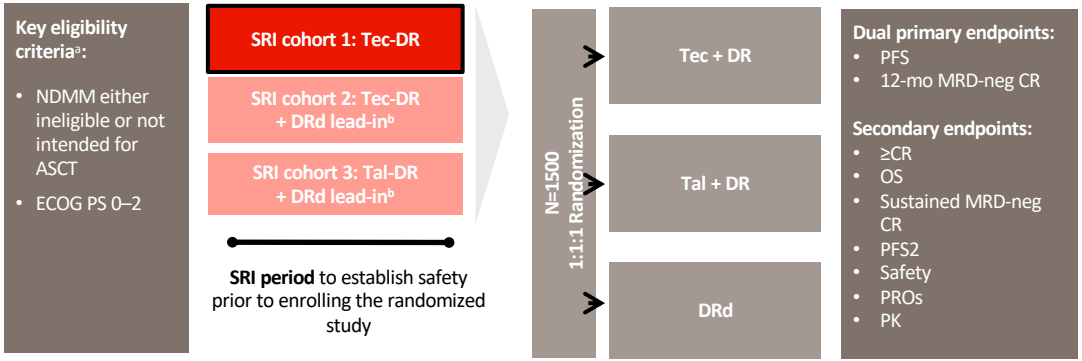
AESI, n(%)	Tec-Dara (n=37) All grade	Grade 1-2	Grade ≥ 3
Infections	24 (65%)	19 (52%)	5 (14%)
Bronchitis	6 (16%)	6 (16%)	-
COVID-19	5 (14%)	4 (11%)	1 (3%)
Urinary tract infection	5 (14%)	5 (14%)	-
Sinusitis	4 (11%)	4 (11%)	-
Pneumonia	3 (8%)	2 (5%)	1 (3%)
GI salmonella	1 (3%)	-	1 (3%)
Peritonitis	1 (3%)	-	1 (3%)
HHV6 infection	1 (3%)	-	1 (3%)
CRS	22 (59%)	G1: 13 (35%) G2: 9 (24%)	-
ICANS	-	-	-
Injection site reaction	7 (19%)	7 (19%)	-
Second primary malignancy	1 (3%)	1 (3%)	-

	Tec-Dara (n=37)
Treatment discontinuation due to AE*, n (%)	1 (3%)

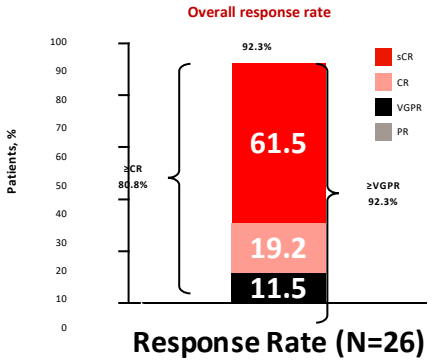
* GI infection to salmonella

Manier S. et Al. ASH 2025, Abstract 367

MajesTEC-7: SRI Cohorts Inform Phase 3 Design



Median age 72 years; 62% FIT



- SRI cohorts 2 and 3, with DRd lead-in strategy for debulking, were associated with an increased incidence of neutropenia, grade 3 CRS events, and serious/fatal infections (SRI cohort 2 only)
- Hypothesized that administering lenalidomide prior to and during the bispecific step-up schedule may have increased T-cell activation and bone marrow suppression
- SRI cohort 1 with the bispecific step-up schedule prior to the first dose of lenalidomide was not associated with similar risks
- DRd lead-in[a] strategy will not be adopted for the randomized phase of the study

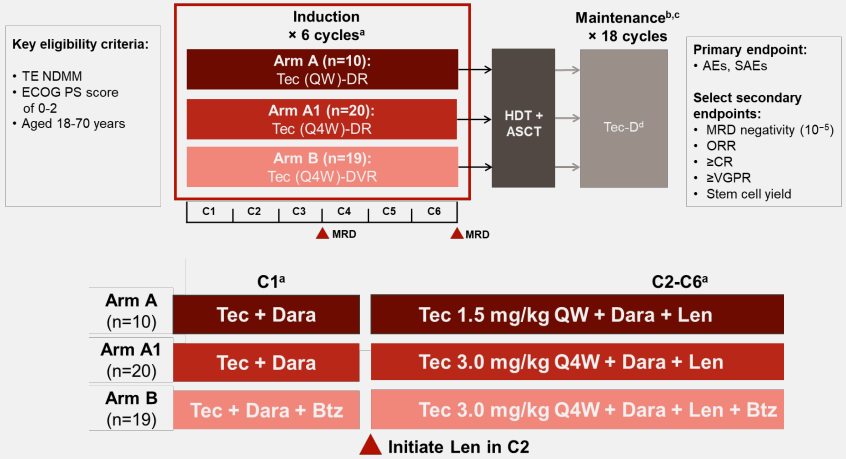
GRADE 3-4 Neutropenia 60%

Grade 3-4 Infections 30%

DRd, Daratumumab, lenalidomide, dexamethason; SRI safety run in
eVan de Donk, et al. P920 EHA 2024

Teclistamab based induction in TE-NDMM
GMMG-HD10/DSMM-XX/MajesTEC-5 (n=49)[1]

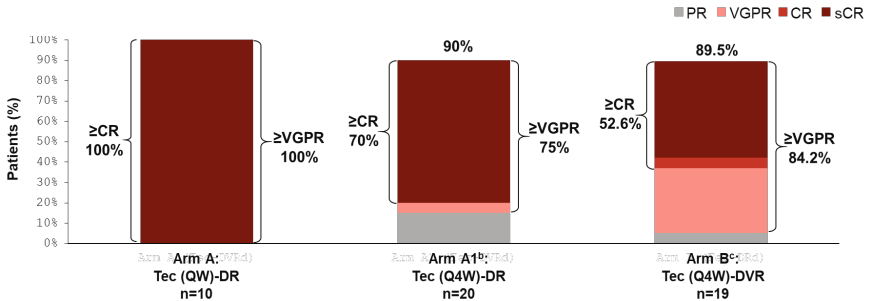
Study design



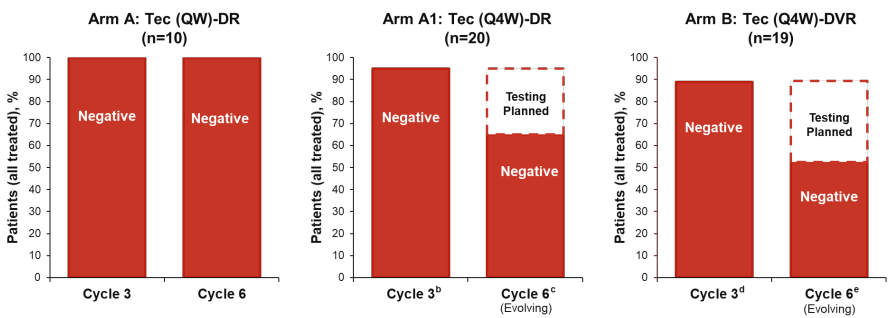
Primary endpoint: Safety

Overall incidence **of CRS 65.3% (all G1-2). No ICANs**
Neutropenia 63.3% (G3-4 57.1%)
Any grade **infection 79.6%** (G3-4 34.7%). 89.8% received IVIG

Secondary endpoint: Efficacy (ORR and MRD rates)



	Arm A: Tec (QW)-DR n=10	Arm A1[b]: Tec (Q4W)-DR n=20	Arm B[c]: Tec (Q4W)-DVR n=19
Induction complete, n	10	5[d]	8[e]
Induction ongoing, n	0	14	10



100% of evaluable patients achieved MRD negativity by C3; no patients were MRD positive

(S)AE, (serious) adverse event; ASCT, autologous stem cell transplant; C, cycle; (s)CR, stable complete response; CRS, cytokine release syndrome; D/Dara, daratumumab; ECOG PS, Eastern Cooperative Oncology Group Performance Status; G, grade; HDT, high dose therapy; ICANS, immune cell-associated neurotoxicity syndrome; IG, immunoglobulin; IV, intravenous; MRD, minimal residual disease; ORR, overall response rate; (VG)PR, (very good) partial response; QW, weekly; Q4W, every 4 weeks; Rz/Len, lenalidomide; Tec, teclistamab; V/Btz, bortezomib.

1. Raab M, et al. ASH 2024 (Abstract No. 493 – presentation)

Teclistamab-based combinations as maintenance post-ASCT
Run-in Results From the EMN30/MajesTEC-4 Trial (median FUP 21mo / 9mo / 9mo)[1]

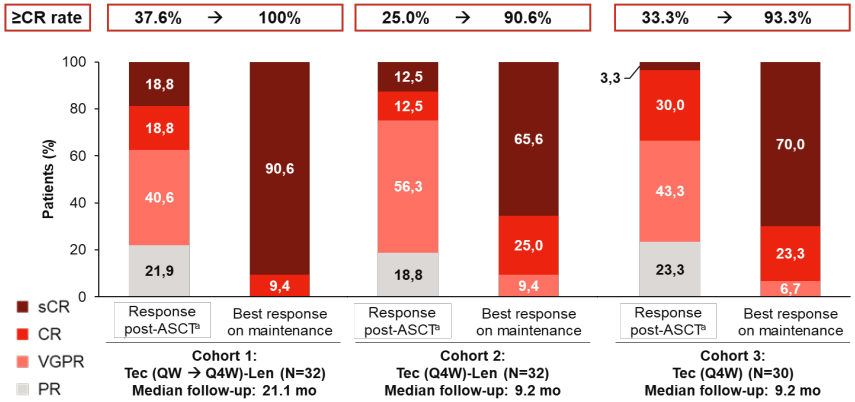
Study design

	Cycle 1	Cycle 2	Cycles 3-6	Cycles 7-26
Cohort 1: Tec-Len Tec QW → Q4W	Tec step up[a] + Tec 1.5 mg/kg on D8, D15, and D22	Tec 1.5 mg/kg QW + Len	Tec 3.0 mg/kg Q2W + Len	Tec 3.0 mg/kg Q4W + Len
Cohort 2: Tec-Len Tec Q4W	Tec step up[a] + Tec 1.5 mg/kg on D8 and D15	Tec 3.0 mg/kg Q4W + Len		
Cohort 3: Tec Tec Q4W	Tec step up[a] + Tec 1.5 mg/kg on D8 and D15	Tec 3.0 mg/kg Q4W		

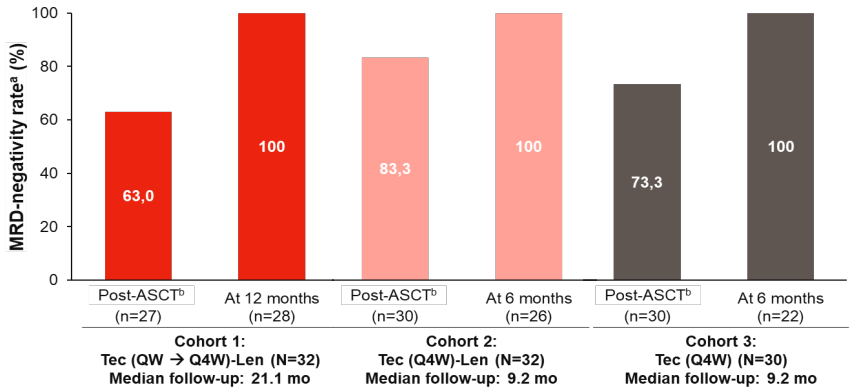
Safety

- Cumulative incidence of **grade 3/4 neutropenia at 6 months**: Cohort 1: 81.3%; Cohort 2: 56.3%; Cohort 3: 40.0%
- Low rates of discontinuation due to TEAEs (5.3% overall)
- **All CRS were G1/2.** CRS incidence by cohort: 50%, 40.6%, 43.3%.
- **No ICANS**.
- **All grade infections (G3-4)**: Cohort 1: 93.8% (37.5%); Cohort 2: 78.1% (28.1%); Cohort 3: 76.7% (20%). One grade 5 COVID-19 TEAE occurred in Cohort 2.

Efficacy: overall response rate and CR/sCR rate



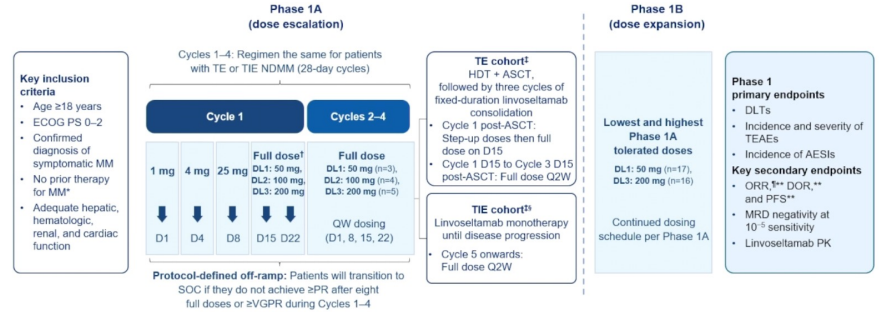
MRD negative rate (10^{-5})

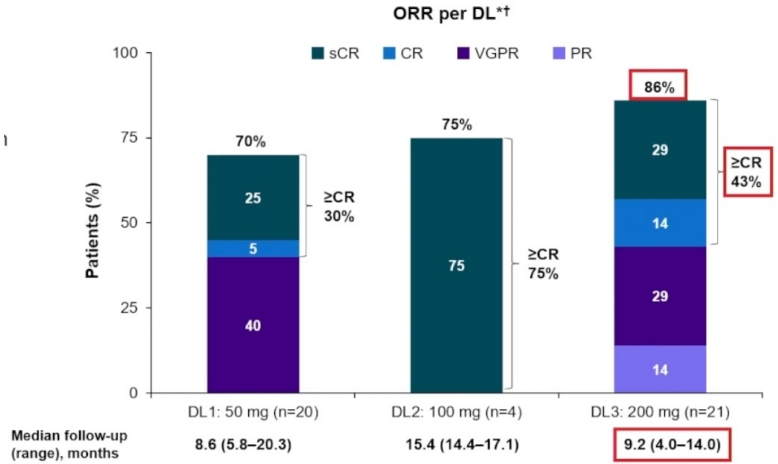


ASCT, autologous stem cell transplant; (s)CR, stable complete response; CRS, cytokine release syndrome; D, day; FUP, follow up; G, grade; ICANS, immune cell-associated neurotoxicity syndrome; Len, lenalidomide; mo, months; MRD, minimal residual disease; (VG)PR, (very good) partial response; QW, weekly; QxW, every x weeks; TEAE, treatment emergent adverse event; Tec, teclistamab.

1. Zamagni E, et al. ASH 2024 (Abstract No. 494 – presentation)

LINKER MM4: multicenter open label ph I/II study on linvoseltamab in NDMM





19/20 MRD evaluable pts were MRD neg

Event, n (%)	All doses: Phase 1 total (N=45) Any grade	Grade 3/4
Patients with any TEAE	45 (100)	39 (86.7)
Serious TEAE	30 (66.7)	23 (51.1)
TEAE leading to treatment discontinuation	1 (2.2)*	1 (2.2)*
Treatment-related TEAE	41 (91.1)	30 (66.7)
Infections†	38 (84.4)	15 (33.3)
Most common‡ hematologic TEAE		
Neutropenia§	17 (37.8)	15 (33.3)
Anemia§	12 (26.7)	8 (17.8)
Most common‡ non-hematologic TEAE		
CRS	20 (44.4)	0
Transaminase elevation§	14 (31.1)	6 (13.3)
Hypophosphatemia	14 (31.1)	3 (6.7)
Nausea	14 (31.1)	0
Diarrhea	13 (28.9)	4 (8.9)
Hypogammaglobulinemia	13 (28.9)	0
Infusion-related reactions	12 (26.7)	0

Incidence of AEs similar across DLs; no DLTs

Linvoseltamab 200 mg RP2D

Orlowki R et Al. ASH 2025, Abstract 697

The future of T-cell redirecting therapy in MM

LINKER-MM6/EMN39:
DRd followed by linvoseltamab in TIE-NDMM patients

Study design and population

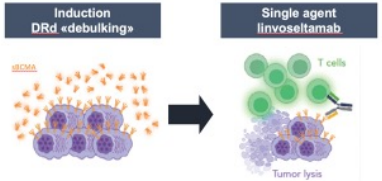
Patient Population
- Confirmed diagnosis of symptomatic MM per IMWG criteria
- Not considered candidate for HDT + ASCT due to advanced age or significant comorbidities
- ECOG ≤ 2

R 1:1
- DRd (until PD)
- DRd → Linvoseltamab (until PD)

Primary Endpoints
- MRD- CR status (10^{-5})
- PFS per IMWG response criteria

Key Secondary Endpoints
- OS

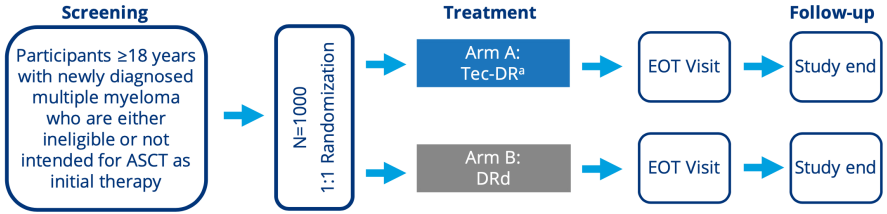
Rationale



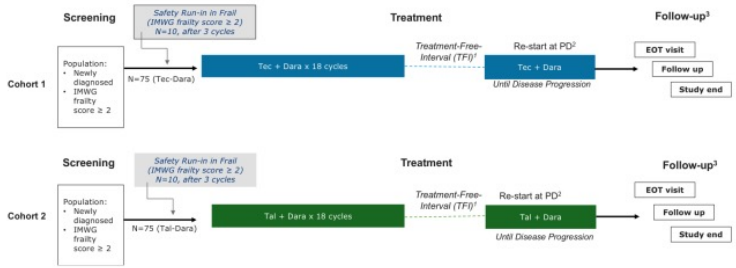
- E:T ratio → higher efficacy
- Deescalating dose intensity sooner vs RRMM dosing→ less dosing frequency
- Tumor burden: lower CRS/ICANS

Sources: EMN39/LINKER-MM6 data on file

MajesTec-7 (TNE)



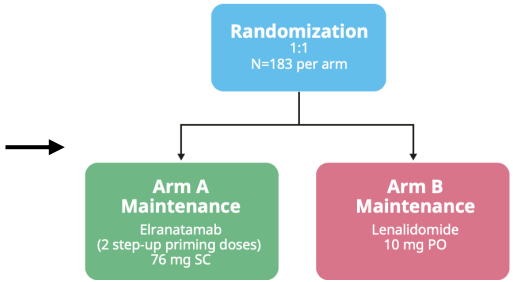
EMN 37 FITFIX FOR FRAIL trial



MagnetisMM-7

Patient Population:
- Newly diagnosed MM
- After induction + ASCT with or without consolidation
- PR or better
- MRD positive (≥1×10^{-5})

Stratification Criteria:
- Standard vs high-risk cytogenetics at diagnosis
- Induction regimen



Bispecific antibodies in MM: open questions

NDMM

Single Agent/Combination

TIE fist line
EMN39:
DRd → Linvo vs DRd

Pre-ASCT Induction
Majestec-5/GMMHD-10:
Dara-Tec-R (+/- V)

Post-ASCT maintenance
Majestec-4/EMN30:
Tec-R vs Tec vs R

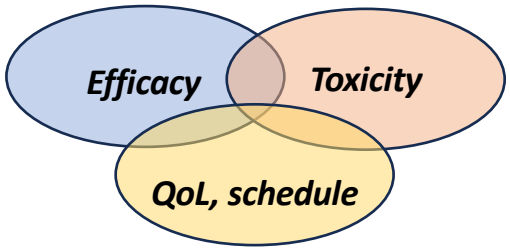
TIE fist line
Majestec-7:
Dara-Tec-R / Dara-Tal-R vs DRd

Single agents vs combo?

TE: Induction? Comparison vs ASCT? Maintenance

Role in the elderly and frail

Continuous vs Fix duration



Conclusions

- **BsABs anti-BCMA: highly effective; manageble toxicity (risk of infections, IgIV)**
- **Moving to early lines as combo or single agents**

- **Optimal approach? work in progress…**

- **BsAB anti BCMA vs CAR-T cells vs ADC ??**

- **BsAbs anti BCMA vs BsABs anti GPRC5D/FcHR5??**

Back up slides

Anti-BCMA BsAbs: treatment optimization

- **802: Increased teclistamab dosing interval improves T-cell diversity and reduces infection risk, while T-cell exhaustion remains minimal irrespective of schedule**
  Afrin N, et al.

Method	Key finding
Flow cytometry	**Q4W vs QW:** elevated leukocytes counts and a higher number of T cells (median 1,292 vs 731, p=0.04)
ScRNA/CITE-sequencing	No significant difference in exhaustion signature across dosing schedules except for SLAMF6; terminally exhausted T cells were virtually absent
In vitro cytotoxicity assays	Similar killing capacity between T cells across dosing schedules
scTCR-sequencing	**Q4W vs QW:** greater clonotypic T-cell diversity (5,349 vs 2,172 clonotypes, p=0.02)
TCR sequence mapping to viral epitopes	**Q4W vs QW:** Broader viral TCR diversity (median SI [IQR]: 2.19 [1.52–2.86] vs 1.04 [0.17–1.86])
Tumour reactivity	Tumour-reactive T cells markedly increased from baseline to QW dosing (+27%), with a modest, non-significant decline with Q2W (+26%) and Q4W intervals (+22%)

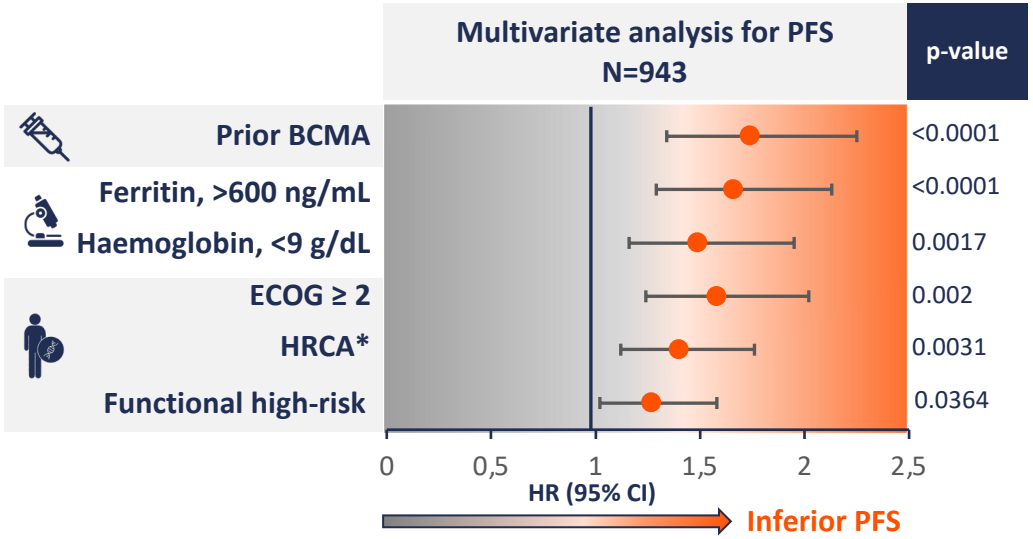
The study supports an initial dose-dense treatment phase, followed by extended dosing intervals to promote immune recovery, restore T-cell diversity and reduce infections without compromising anti-myeloma activity

CITE, cellular indexing of transcriptomes and epitopes; IQR, interquartile range; QW, every week; Q2W, every 2 weeks; Q4W, every four weeks; scRNA, single-cell RNA; scTCR, single-cell TCR; SI, Shannon Index; TCR, T-cell receptor.

Afrin N, et al. Presented at: ASH 2025, Orlando, FL, USA. 6–9 December 2025. Abstr. 802.

4069: Identifying high-risk profiles and adverse prognoses in RRMM treated with bispecific antibodies: A real-world analysis of 943 treatment initiations

Zanwar S, et al.



Prior BCMA exposure was associated with a markedly inferior PFS within the BCMA cohort (p<0.0001), but not the GPRC5D cohort (p=0.71)

- Number and type of prior BCMA therapy did not seem to impact PFS (p=0.76)

Platelet count and EMD were not significantly associated with inferior PFS

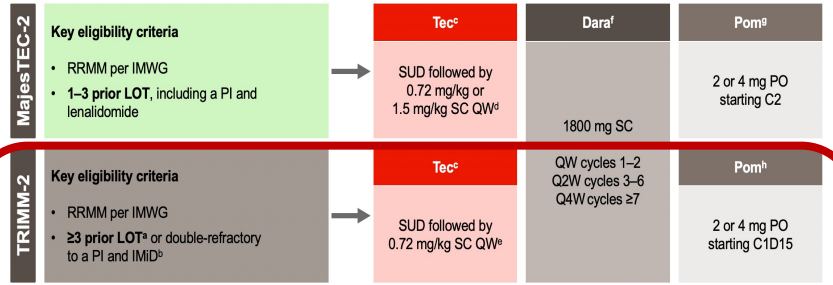
In this large real-world cohort of patients treated with TCEs, outcomes varied with fitness, disease biology and treatment history. Prior exposure to BCMA-directed therapy independently predicted inferior PFS for the cohort treated with BCMA-directed TCEs only.

*IMS/IMWG del(17p) or ≥2 HRCA, prior to infusion.
BCMA, B-cell maturation antigen; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group Performance Status; EMD, extramedullary disease; GPRC5D, G protein-coupled receptor, class C, group 5, member D; HR, hazard ratio; HRCA, high-risk cytogenetic abnormalities; IMS/IMWG, International Myeloma Society/International Myeloma Working Group; PFS, progression-free survival; RRMM, relapsed/refractory multiple myeloma; TCE, T-cell engager.
Zanwar S, et al. Presented at: ASH 2025, Orlando, FL, USA. 6–9 December 2025. Abstr. 4069.

touch HAEMATOLOGY

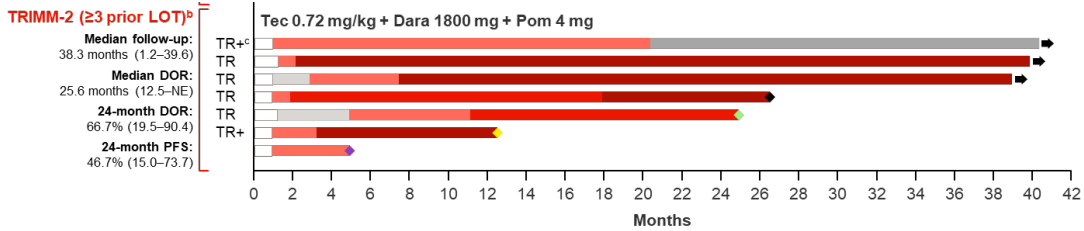
Teclistamab based Combinations: TRIMM-2 study
Teclistamab + daratumumab + pomalidomide

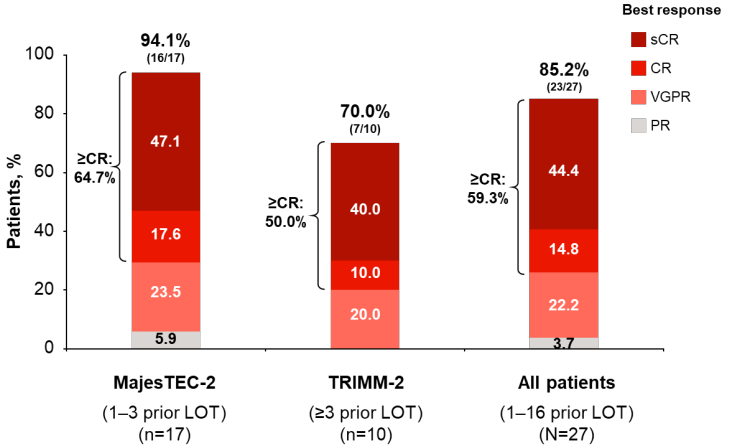
Study design



TRIMM-2: *≥3 PL or double-refractory.[a,b]*
N=10. Median of 4 PL.
70% Triple-class refractory. 30% prior BCMA

	TRIMM-2 (≥3 prior LOT); n=10	
	Any Grade	Grade 3/4
Any infection	9 (90.0)	6 (60.0)
Infections[a]		
Upper respiratory tract infection	4 (40.0)	0
Pneumonia	4 (40.0)	4 (40.0)
Sinusitis	4 (40.0)	1 (10.0)
COVID-19	4 (40.0)	1 (10.0)
COVID-19 pneumonia	1 (10.0)	1 (10.0)
Hypogammaglobulinemia		
Hypogammaglobulinemia[b]	10 (100)	
Received IVIG[c]	8 (80.0)	





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