POST-ORLANDO 2025
Novità dal Meeting della Società Americana di Ematologia

Novità dal Meeting della Società Americana di Ematologia

Torino
Centro Congressi Lingotto
19-21 febbraio 2026

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MIELOMA MULTIPLO *Terapia alla ricaduta*

Dipartimento di Medicina dell'Università di Padova- Ematologia

DICHIARAZIONE Renato Zambello

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Janssen						x	
Sanofi						x	
GSK						x	
Amgen					x	x	
Pfizer						x	
Menarini					x	x	

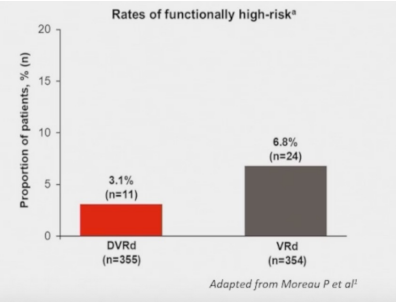
Outline

Prima/seconda ricaduta

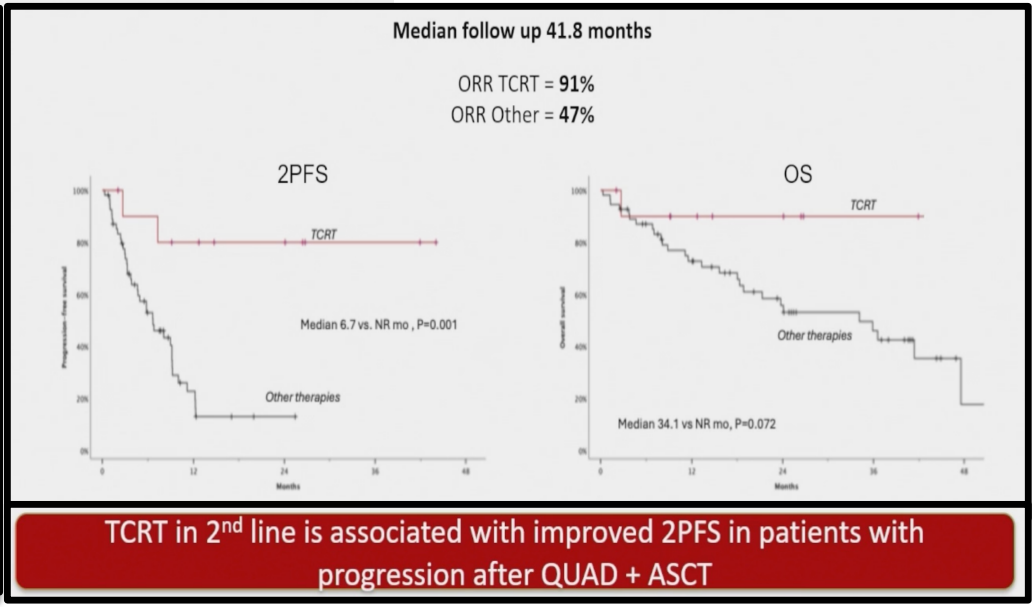
Ricadute successive

Condizioni difficili da trattare

Redefining Functional High-Risk (FHR) Multiple Myeloma (MM) in the Context of Upfront Quadruplet (QUAD) Therapy and Autologous Stem Cell Transplantation (ASCT)



FHR36 identifies a population with expected OS ~24 months



TCRT in 2nd line is associated with improved 2PFS in patients with progression after QUAD + ASCT

Costa L. ASH 2025

In conclusion, in NDMM treated with QUAD+ ASCT:

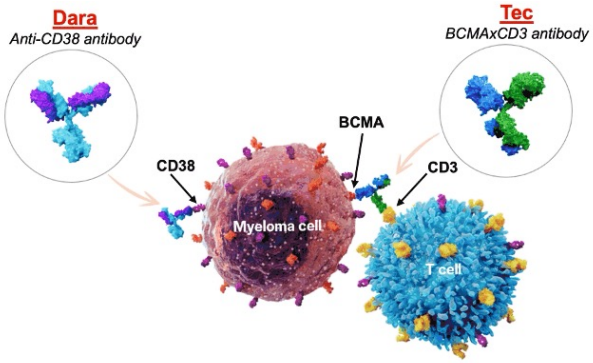
FHR36 identifies a population with expected OS 24 months (new definition of FHR)

FHR36 is associated with worse response, 2PFS and OS in patients with progression after QUAD + ABMT

TCRT in second line is associated with improved 2PFS in patients with progression after QUAD + ABMT

Costa L. Ash 2025

Phase 3 Randomized Study of Teclistamab Plus Daratumumab Versus Investigator's Choice of Daratumumab and Dexamethasone With Either Pomalidomide or Bortezomib (DPd/DVd) in Patients With Relapsed Refractory Multiple Myeloma (RRMM): Results of MajesTEC-3



Dara PRIMES
the microenvironment by clearing immunosuppressive CD38+ T_{regs} and B_{regs}, in addition to Dara's direct on-tumor effects[2]

+

Tec + Dara ACTIVATE
CD8+ T cells for sustained immune enhancement

+

Tec REDIRECTS
activated CD8+ T cells to effectively kill myeloma cells

Key inclusion criteria
- RRMM
- 1-3 prior LOTs including a PI and lenalidomide
  - Patients with only 1 prior LOT must have been lenalidomide refractory per IMWG criteria
- ECOG PS score of 0-2

Key exclusion criteria
- Prior BCMA-directed therapy
- Refractory to anti-CD38 mAbs[a]

1:1 randomization N=587
22 Oct 2021 to 29 Sept 2023[b]

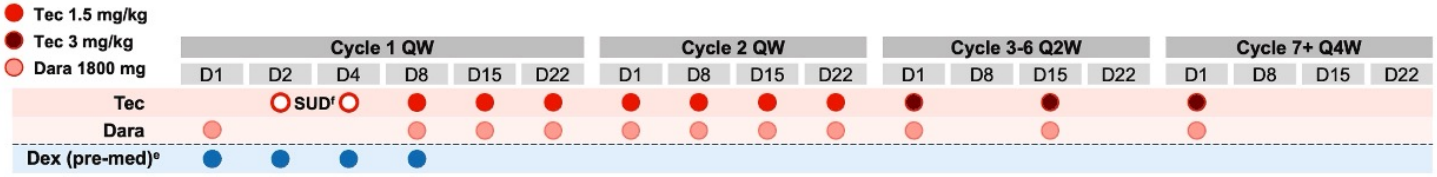
Tec-Dara
N=291
SC dosing following Dara schedule

DPd/DVd
N=296 (91% DPd)
by investigator's choice[c]

Primary endpoint
- PFS per IRC

Key secondary endpoints
- ≥CR[d] and ORR[d]
- MRD negativity (10^{-5})
- OS
- MySIm-Q Total Symptom score

Other secondary endpoints
- Safety
- PK and immunogenicity



Mateos MV et al, ASH, 2025; Costa LJ. et al, NEJM, 2025

MAJESTEC-3: TEC-DARA

Characteristic	Tec-Dara (n=291)	DPd/DVd (n=296)
Age		
Median (range), years	64 (36–88)	63 (25–84)
≥75 years, n (%)	31 (10.7)	25 (8.4)
Sex, n (%)		
Male	156 (53.6)	169 (57.1)
Female	135 (46.4)	127 (42.9)
Race, n (%)		
White	190 (65.3)	194 (65.5)
Asian	68 (23.4)	63 (21.3)
Black or African American	13 (4.5)	20 (6.8)

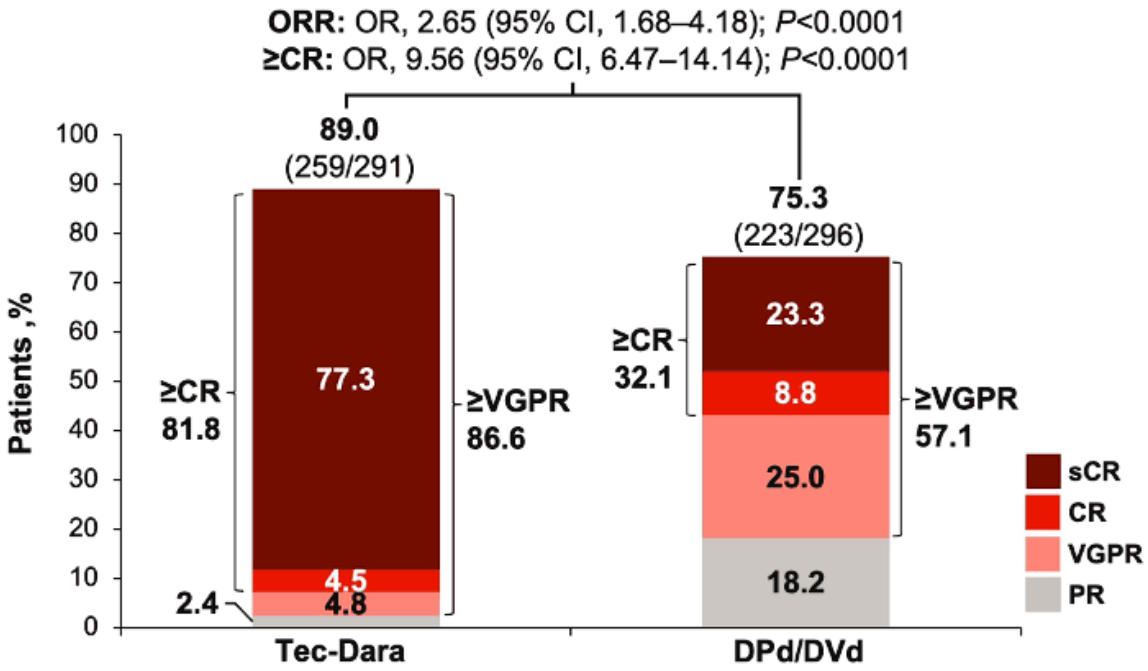
Characteristic	Tec-Dara (n=291)	DPd/DVd (n=296)
Prior LOTs, n (%)		
Median (range), n	2 (1–3)	2 (1–3)
1 prior LOT	108 (37.1)	114 (38.5)
2 prior LOTs	134 (46.0)	134 (45.3)
3 prior LOTs	49 (16.8)	48 (16.2)
Prior transplantation, n (%)	210 (72.2)	226 (76.4)

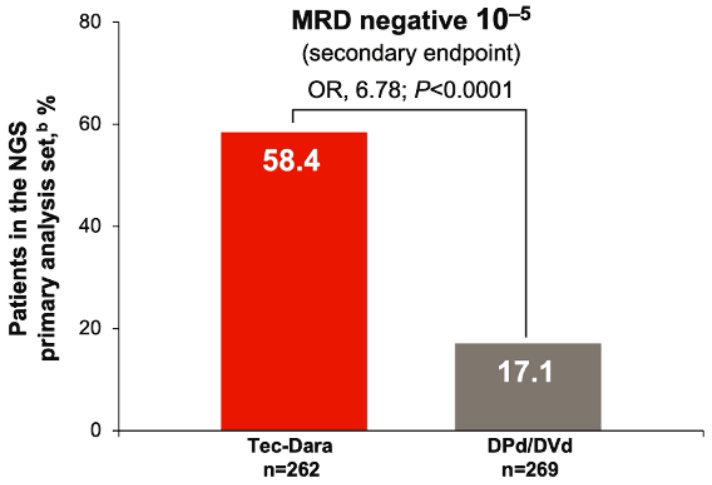
Characteristic	Tec-Dara (n=291)	DPd/DVd (n=296)
Baseline ECOG PS score, n (%)		
0	167 (57.4)	160 (54.1)
1	108 (37.1)	127 (42.9)
2	16 (5.5)	9 (3.0)
ISS stage, n (%)		
I	182 (62.5)	185 (62.5)
II	85 (29.2)	88 (29.7)
III	24 (8.2)	23 (7.8)
BMPCs ≥60%,[b] n/N (%)	28/286 (9.8)	24/293 (8.2)
Presence of soft-tissue plasmacytomas, n (%)	41 (14.1)	41 (13.9)
Extramedullary plasmacytomas[c]	14 (4.8)	17 (5.7)
Paraskeletal plasmacytomas	32 (11.0)	31 (10.5)
High-risk cytogenetics,[d] n/N (%)	104/285 (36.5)	104/294 (35.4)

Characteristic	Tec-Dara (n=291)	DPd/DVd (n=296)
Prior therapy exposure, n (%)		
PI	290 (99.7)	296 (100)
IMiD	291 (100)	296 (100)
Anti-CD38	15 (5.2)	16 (5.4)
Refractory status, n (%)		
To last prior LOT	250 (85.9)	251 (84.8)
Any PI	117 (40.2)	104 (35.1)
Any IMiD	247 (84.9)	253 (85.5)
Lenalidomide	240 (82.5)	251 (84.8)
Double (PI and IMiD)	99 (34.0)	88 (29.7)

Mateos MV et a, ASH, 2025; Costa LJ. et al, NEJM, 2025

MAJESTEC-3: TEC-DARA

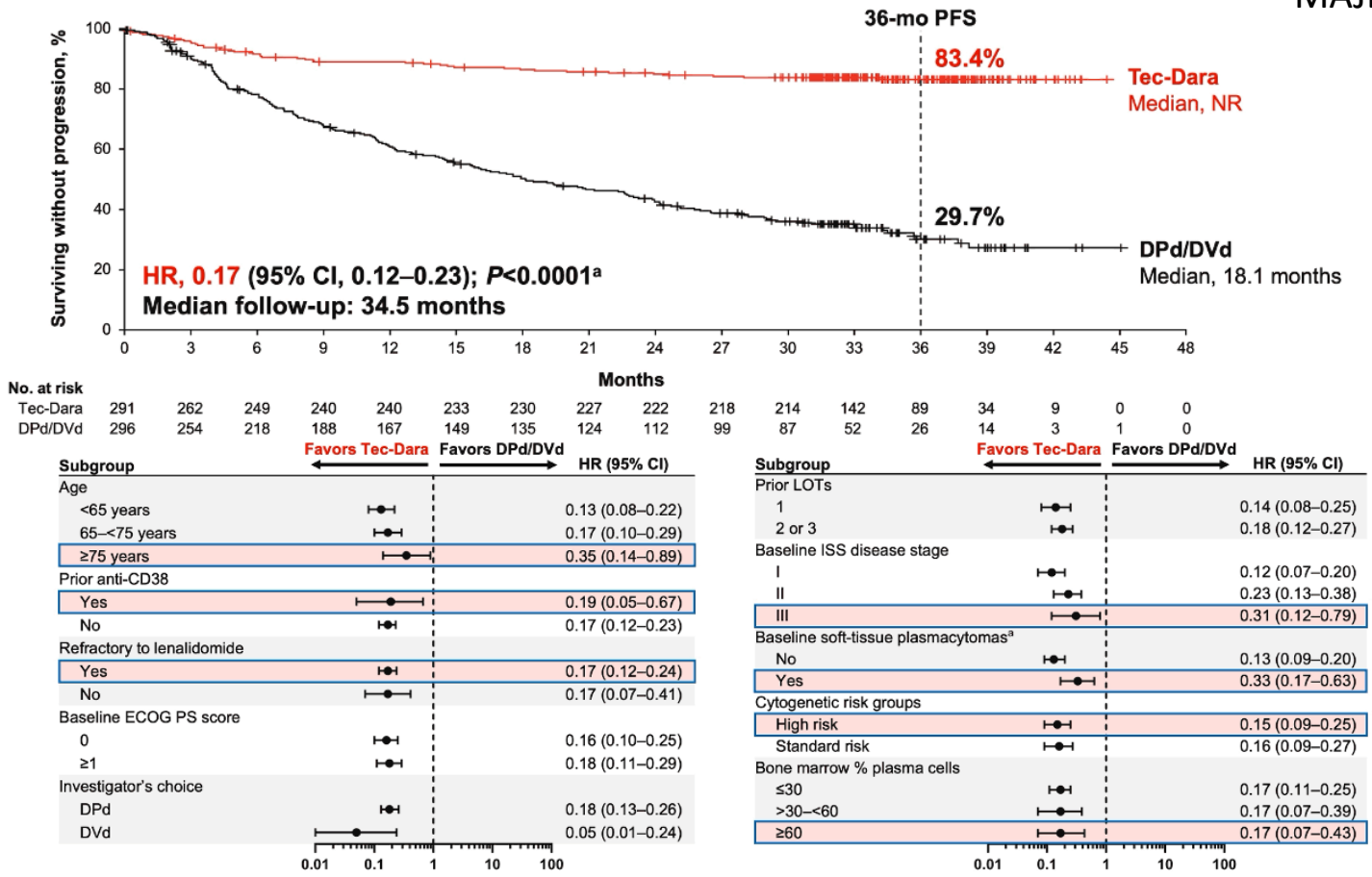




	MRD-negative ≥CR (10^{-5})	MRD-negative ≥CR (10^{-6})
Tec-Dara, %		
Primary NGS[b]	57.6	53.8
Evaluable[c]	**89.3**	**87.5**
DPd/DVd, %		
Primary NGS[b]	17.1	10.4
Evaluable[c]	63.0	41.8

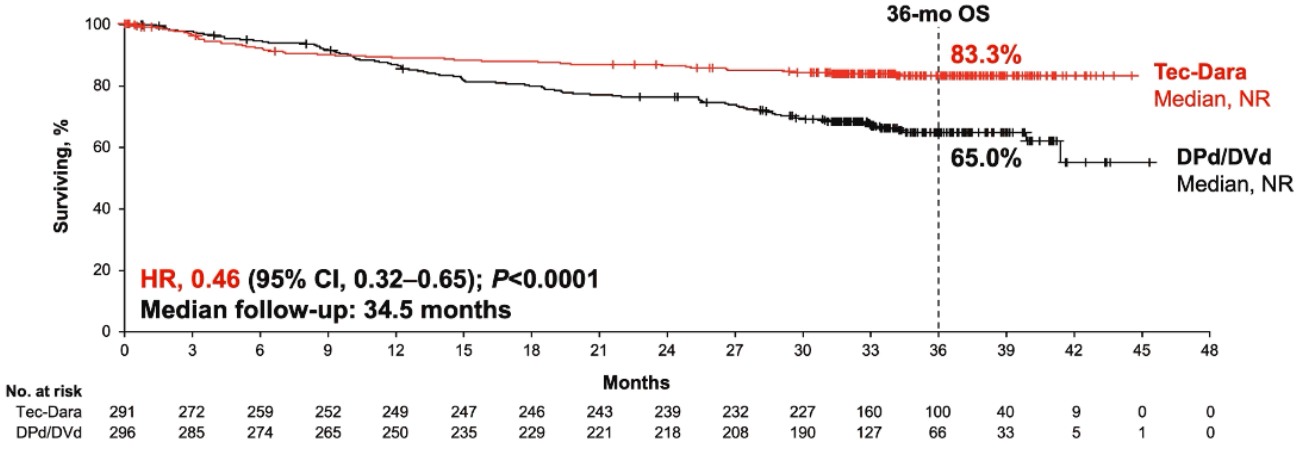
Mateos MV et a, ASH, 2025; Costa LJ. et al, NEJM, 2025

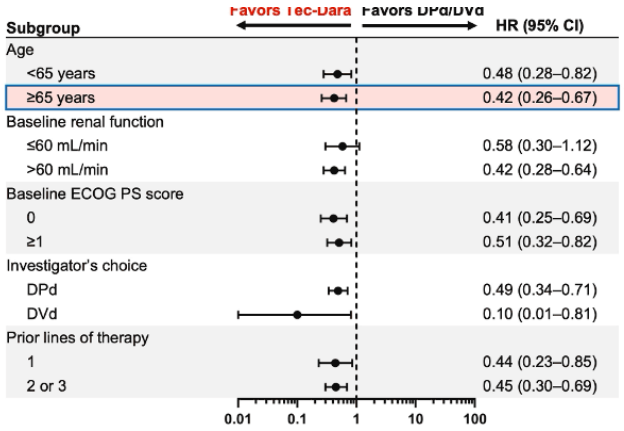
MAJESTEC-3: TEC-DARA

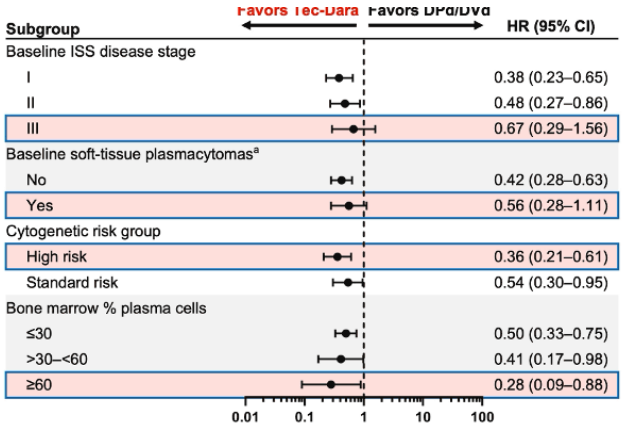


Mateos MV et a, ASH, 2025; Costa LJ. et al, NEJM, 2025

MAJESTEC-3: TEC-DARA





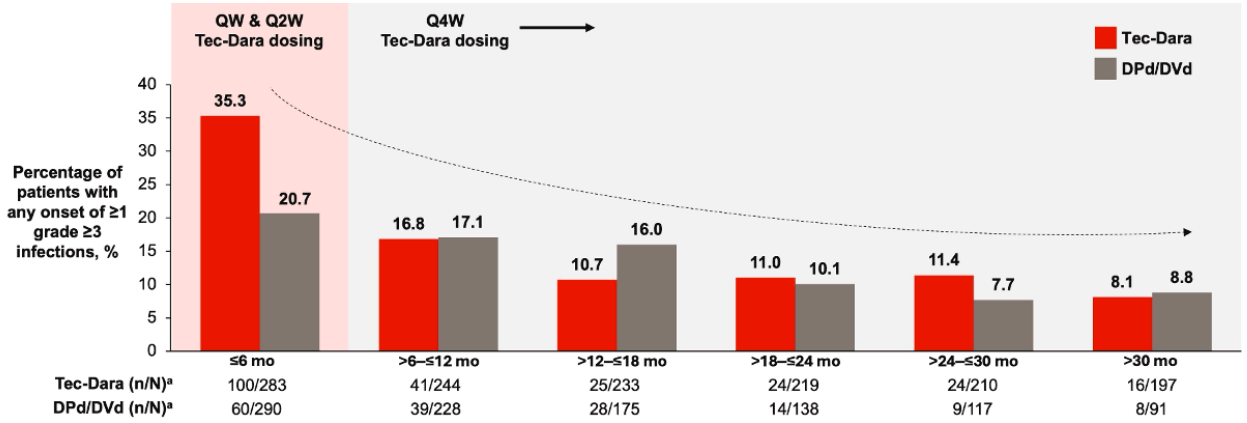


Mateos MV et al, ASH, 2025; Costa LJ. et al, NEJM, 2025

MAJESTEC-3: TEC-DARA

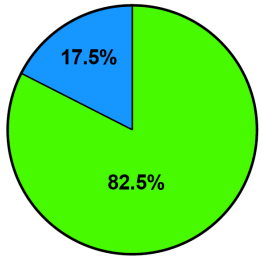
TEAE, n (%)[c]	Tec-Dara (n=283)		DPd/DVd (n=290)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Any TEAE	283 (100)	269 (95.1)	290 (100)	280 (96.6)
Hematologic				
Neutropenia	222 (78.4)	214 (75.6)	240 (82.8)	228 (78.6)
Anemia	111 (39.2)	58 (20.5)	103 (35.5)	50 (17.2)
Thrombocytopenia	103 (36.4)	55 (19.4)	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[d]				
CRS[e]	170 (60.1)	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)

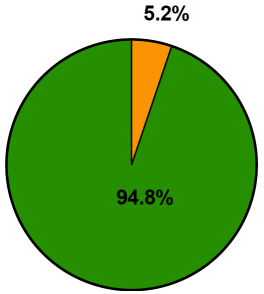
TEAE, n (%)	Tec-Dara (n=283)		DPd/DVd (n=290)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Any infection	273 (96.5)	153 (54.1)	244 (84.1)	126 (43.4)
Treatment-emergent infection or infestation[e]				
COVID-19	124 (43.8)	17 (6.0)	97 (33.4)	6 (2.1)
URTI	115 (40.6)	12 (4.2)	88 (30.3)	7 (2.4)
Pneumonia	65 (23.0)	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)
UTI	29 (10.2)	4 (1.4)	27 (9.3)	1 (0.3)

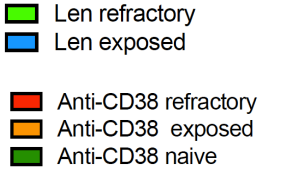


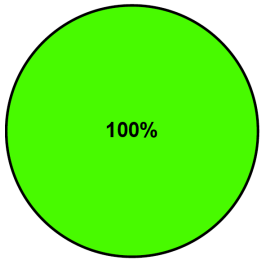
Mateos MV et al, ASH, 2025; Costa LJ. et al, NEJM, 2025

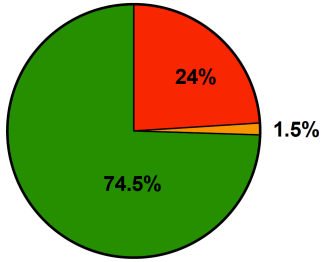
MAJESTEC-3 vs CARTITUDE 4

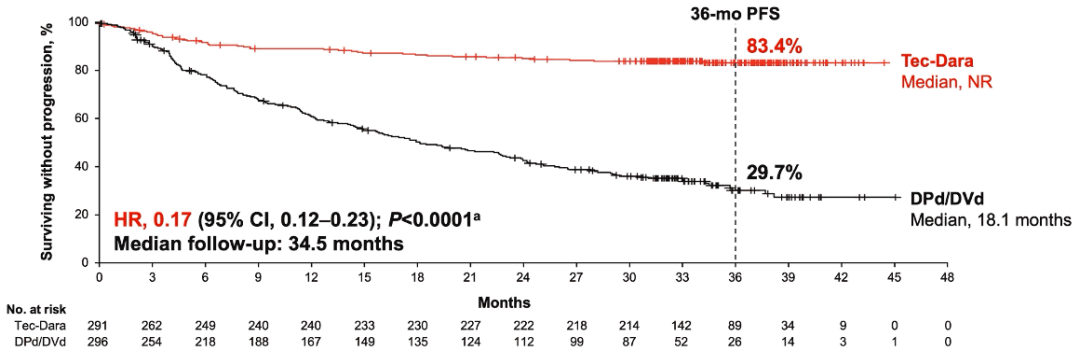


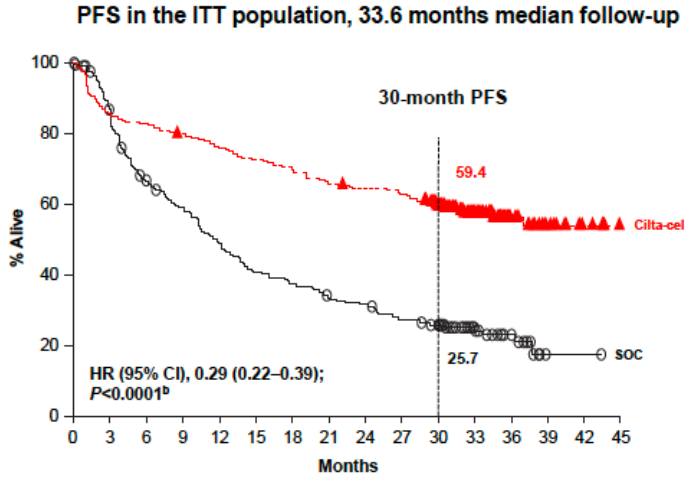












Mateos MV et al, ASH, 2025; Costa LJ. et al, NEJM, 2025; Mateos MV et al, IMS, 2024

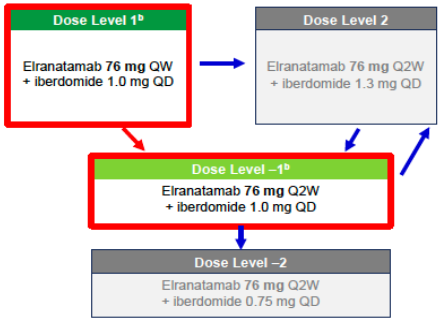
Safety and Efficacy of Elranatamab in Combination With Iberdomide in Patients With Relapsed or Refractory Multiple Myeloma: Results from the Phase 1b MagnetisMM-30 Trial

Attaya Suvannasankha,[1] Jonathan L. Kaufman,[2] Ashraf Badros,[3] Michel Pavic,[4] Hock-Choong Lai,[5] Muhammad S Raza,[6] Parth S Shah,[7] Patrick Y. Muller,[8] Jorge Acosta,[8] Margaret Hoyle,[9] Erik R Vandendries,[10] Jay Cheng,[11] Alexander Lesokhin[12]

Patients with RRMM

Key inclusion criteria
- Age ≥18 years with MM per IMWG criteria
- ECOG PS 0-1
- 2-4 prior LOTs, including ≥1 IMiD and ≥1 PI[a]
- Relapsed or refractory to last LOT

Key exclusion criterion
- Stem cell transplant ≤12 weeks prior to enrollment or active GVHD
- Ongoing grade ≥2 peripheral sensory or motor neuropathy; history of grade ≥3 peripheral motor polyneuropathy



Primary endpoint
- DLTs during DLT observation period

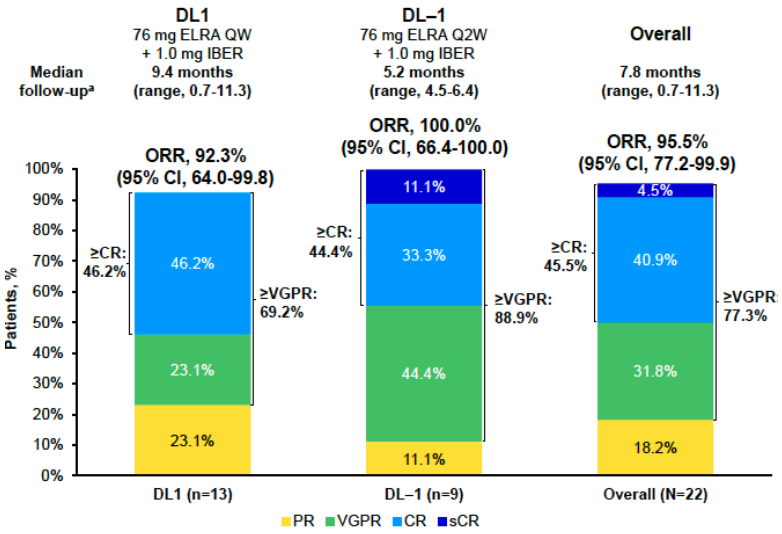
Secondary endpoints
- AEs and laboratory abnormalities
- ORR[c]
- CR rate[c]
- Time-to-event endpoints[c]
- PK
- MRD negativity rate[c]
- Immunogenicity

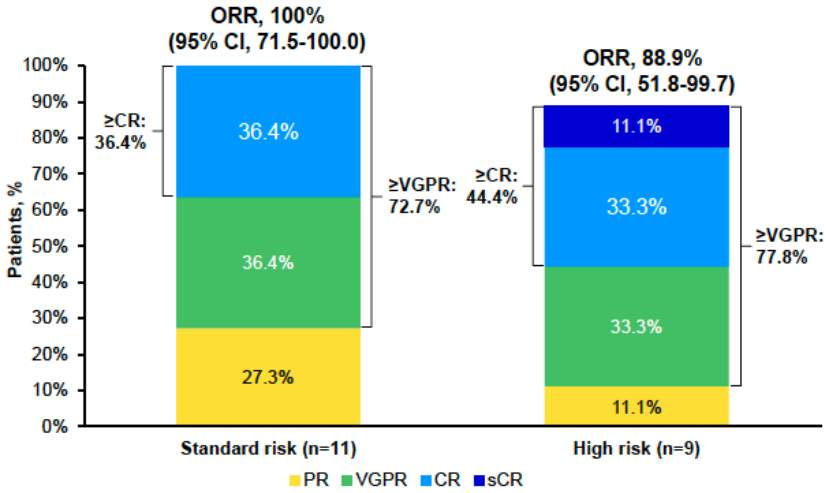
	DL1 76 mg ELRA QW + 1.0 mg IBER (n=13)	DL–1 76 mg ELRA Q2W + 1.0 mg IBER (n=9)	Overall (N=22)
Age, median (range), years	65.0 (55-83)	69.0 (46-79)	68.0 (46-83)
Male, n (%)	6 (46.2)	4 (44.4)	10 (45.5)
Race, n (%)			
Asian	1 (7.7)	0	1 (4.5)
Black or African American	5 (38.5)	1 (11.1)	6 (27.3)
White	7 (53.8)	8 (88.9)	15 (68.2)
ECOG PS, n (%)			
0	5 (38.5)	5 (55.6)	10 (45.5)
1	8 (61.5)	4 (44.4)	12 (54.5)
R-ISS disease stage, n (%)			
I	4 (30.8)	1 (11.1)	5 (22.7)
II	6 (46.2)	8 (88.9)	14 (63.6)
III	1 (7.7)	0	1 (4.5)
Cytogenetic risk, n (%)			
Standard	9 (69.2)	2 (22.2)	11 (50.0)
High[a]	4 (30.8)	5 (55.6)	9 (40.9)
Extramedullary disease by investigator, n (%)[b]	2 (15.4)	2 (22.2)	4 (18.2)
No. of prior lines of therapy, median (range)	2.0 (2.0-4.0)	3.0 (1.0-4.0)	2.5 (1.0-4.0)
Prior stem cell transplant, n (%)	10 (76.9)	7 (77.8)	17 (77.3)
Triple-class refractory status, n (%)[c]	7 (53.8)	4 (44.4)	11 (50.0)
Refractory to last line of therapy, n (%)	12 (92.3)	7 (77.8)	19 (86.4)

	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)

Suvannasankha A. et al, ASH, 2025

MAGNETISM 30: ELRA-IBER





Early and encouraging efficacy

- With a median follow-up of 7.8 months the ORR was 95.5% and ≥CR rate was 45.5%
- Responses occurred early and are expected to deepen further with longer follow-up

Safety profile was consistent with known toxicities of individual components

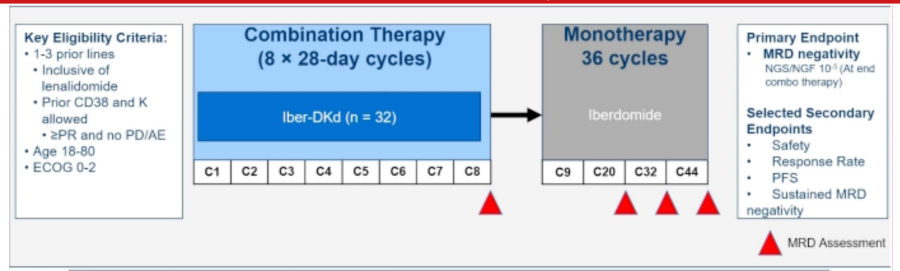
- The most frequent TEAEs were hematologic adverse events, infections, and CRS
- The majority of infections were grade ≤2 and there were no infections grade >3
- All CRS and ICANS events were grade ≤2

Suvannasankha A. et al, ASH, 2025

A phase 2 trial of iberdomide, carfilzomib, daratumumab and dexamethasone quadruplet therapy for relapsed/refractory multiple myeloma: The **ReKInDLE** study

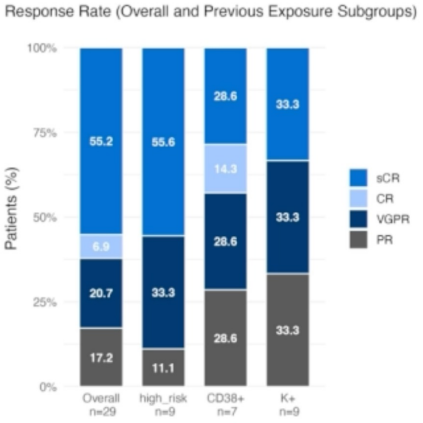
Ola Landgren, James Hoffman, Abhishek Pandey, Andrew Kowalski, Michael Durante, David Coffey, Marcella Kaddoura, Brian Walker, Leslie Gallardo, Elizabeth Lyubchenko, Massiel Lopez, Fiorela Flores, Liettel Ortega, Rabia Bukhari, Kellye Koubek, Caterine Diaz, Stephanie Mompoint, Sindy Gutierrez, Faika Shah, Stephanie Fernandes, Michelle Armogan, Dickran Kazandjian, **Benjamin Diamond**

	N = 32
Lytic Bone Disease, n (%)	27 (84)
Extramedullary Disease, n (%)	6 (19)
High Risk Cytogenetics (IMS-IMWG 2025)	10 (31)
Prior lines of therapy, n (%)	
1	24 (75)
2-3	8 (25)
IMiD refractory, n (%)	30 (94)
1 IMiD	27 (84)
2 IMiDs	3 (9)
Prior Carfilzomib	11 (34)
Prior anti-CD38	9 (28)
Prior ASCT	15 (47)



Iberdomide (Iber): 1mg 21/28 days (C1-C44)
Daratumumab (D): 1800mg SC (C1-C2 QW; C3-C6 Q2W; C7-C8 Q4W)
Carfilzomib (K): 20/56 mg/m² Days 1, 8, 15 (C1-C8)
Dexamethasone (d): 40mg C1-C4; 20mg C5-C8

1. MRD Assessment preferentially by NGS, flow cytometry otherwise. 2. MRD may be assessed at achievement of suspected CR and/or end of combination therapy. 3. Anticoagulation with an oral XA inhibitor or low molecular weight heparin were required unless at the discretion of investigator. 4. Must complete 4 cycles to be eligible for primary endpoint unless disease progression occurs prior; MRD may be assessed prior to end of combination therapy. AE; Adverse Event, C; Cycle, D; Day, ECOG; Easter Cooperative Oncology Group Performance Status, MRD; Minimal Residual Disease, NGS/F; Next Generation Sequencing/Flow, PD; Progressive Disease, PFS; Progression Free Survival, PR; Partial Response.

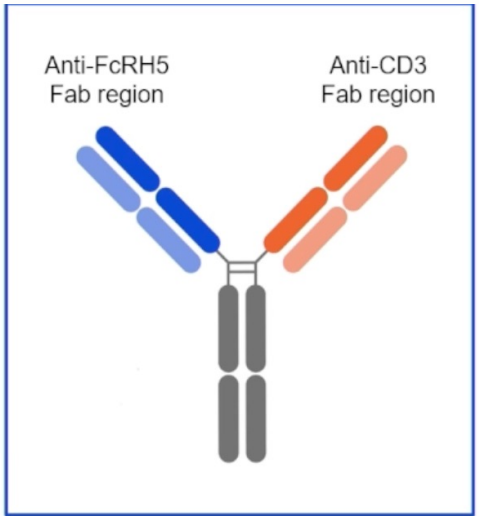


Overall Response Rate was 100%
Primary Endpoint: MRD-negativity (10^{-5}) as best response: 70.8%

Landgren O at al ASH 2025

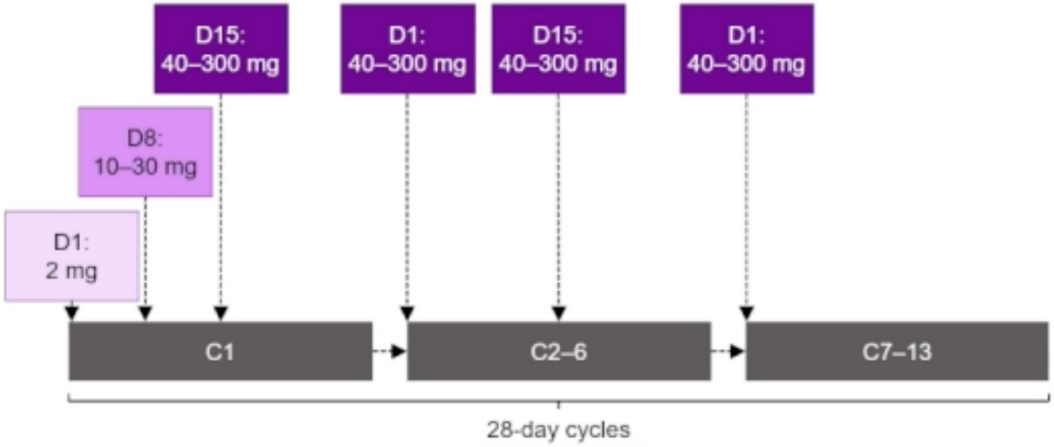
Subcutaneous cevostamab demonstrates manageable safety and clinically meaningful activity in relapsed/refractory multiple myeloma (RRMM): First results from the Phase Ib CAMMA 3 study

P Joy Ho,[1] Hang Quach,[2] Sosanna Delimpasi,[3] Armando Santoro,[4,5] Cindy H-S Lee,[6] Nicolas Kint,[7] Sylvia Faict,[8] Yanke Yu,[9] Olivier Catalani,[10] Ameet Mishra,[9] Tulika Tyagi,[9] Clare Devlin,[11] Semira Sheikh,[10] Meletios A Dimopoulos[12]



SC dosing schedule in the dose-escalation stage

- Fixed-duration treatment (13 cycles, ~12 months)*
- C1 step-up dosing
- C1–2 IV corticosteroid premedication; C1–13 acetaminophen and diphenhydramine
- Hospitalization after each C1 injection



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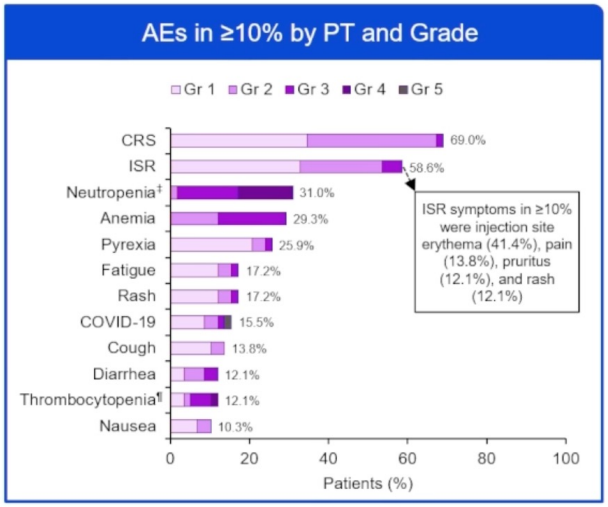
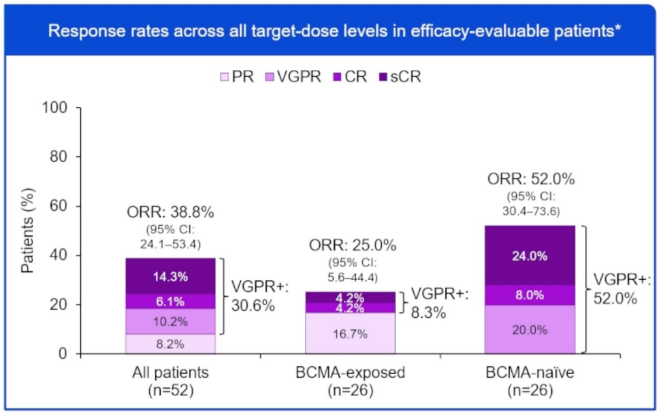
CAMMA-3: CEVOSTAMAB

n (%) unless stated		N=58
Median age, years (range)		63.5 (33–81)
Male		41 (70.7)
ECOG PS	0	27 (46.6)
	1	31 (53.4)
ISS stage	I	27 (46.6)
	II	25 (43.1)
	III	6 (10.3)
High-risk cytogenetics*		10 (17.2)
del(17p)		5 (8.6)
t(4,14)		5 (8.6)
t(14,16)		2 (3.4)
Extramedullary disease		18 (31.0)
Median time from diagnosis, years (range)		7.0 (0.8–16.4)

n (%) unless stated	N=58
Median number of prior lines of therapy, n (range)	5 (2–11)
Any prior BCMA-targeted therapy	28 (48.3)
CAR-T	6 (10.3)
ADC	19 (32.8)
Bispecific antibody	5 (8.6)
Triple-class refractory†	37 (63.8)
Penta-drug refractory‡	19 (32.8)



n (%)	N=58
AE of infection of any Gr	26 (44.8)
Gr 3–5 AE of infection	9 (15.5)
Gr 3	6 (10.3)
Gr 4	1 (1.7)
Gr 5 (fatal)	2 (3.4)†
	†COVID-19 (n=1) and staphylococcal infection (n=1); both events considered unrelated to treatment
SAE of infection	11 (19.0)
AE of infection leading to discontinuation	1 (1.7)‡
	‡COVID-19 (n=1); event considered unrelated to treatment
IVIg administration	24 (41.4)



- SC cevostamab induced clinically meaningful responses at target doses ≥120 mg, with more pronounced activity in BCMA-naïve patients
- ORR and VGPR+ rates were 38.8% and 30.6% in all patients, 25.0% and 8.3% in BCMA-exposed, and 52.0% and 52.0% in BCMA-naïve
- 80% of MRD-evaluable CR+ patients were MRD negative at the 10^{-5} level
- Median DOR among responders was 12.3 months in all patients, 8.3 months in BCMA-exposed, and NR in BCMA-naïve

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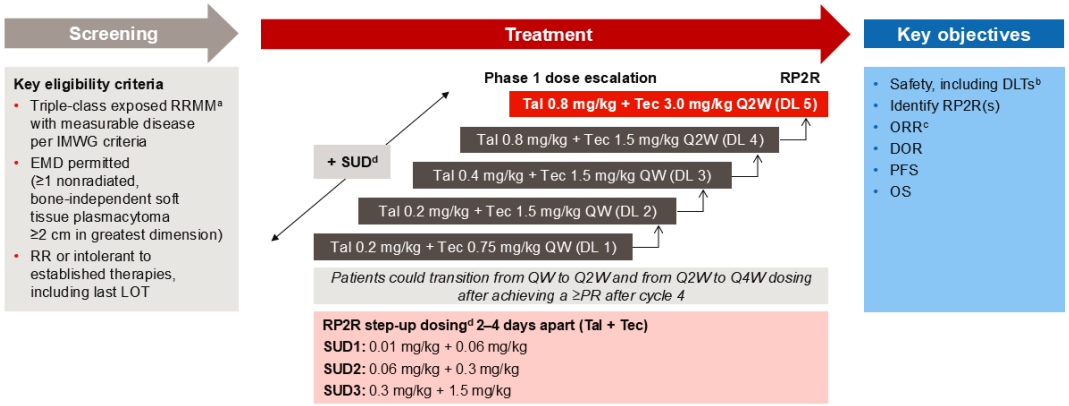
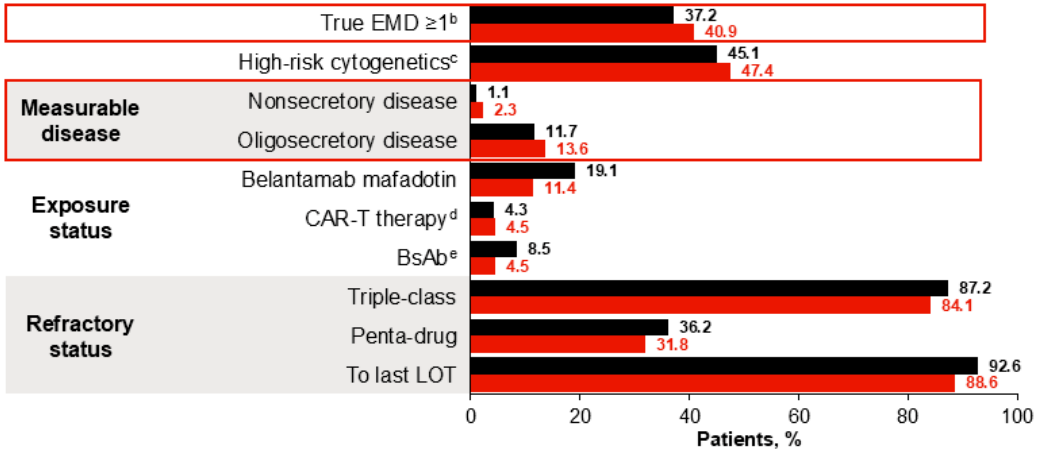
Safety and Efficacy of Talquetamab + Teclistamab in Patients With Relapsed/Refractory Multiple Myeloma From Phase 1b of RedirecTT-1: Results With an Extended Median Follow-Up of 3 Years

María-Victoria Mateos[1*], Hila Magen[2], Moshe Gatt[3], Michael Sebag[4], Kihyun Kim[5], Chang-Ki Min[6], Enrique M Ocio[7], Sung-Soo Yoon[8], Michael P Chu[9], Paula Rodríguez-Otero[10], Irit Avivi[11], Natalia A Quijano Cardé[12], Maria Krevvata[12], Todd Henninger[13], Payal Thakkar[13], Mariacristina Festa[14], Guoqiang Zhang,[12] Sheetal Khedkar,[15] Lin Huang[12], Jiangxiu Zhou[12], Mikihiro Takamoto[16], Lixia Pei[13], Jiashen Lu[17], Carmela Maffucci[13], Emma Scott[12], Albert Oriol[18], Daniel Morillo[19], Yael C Cohen[11]

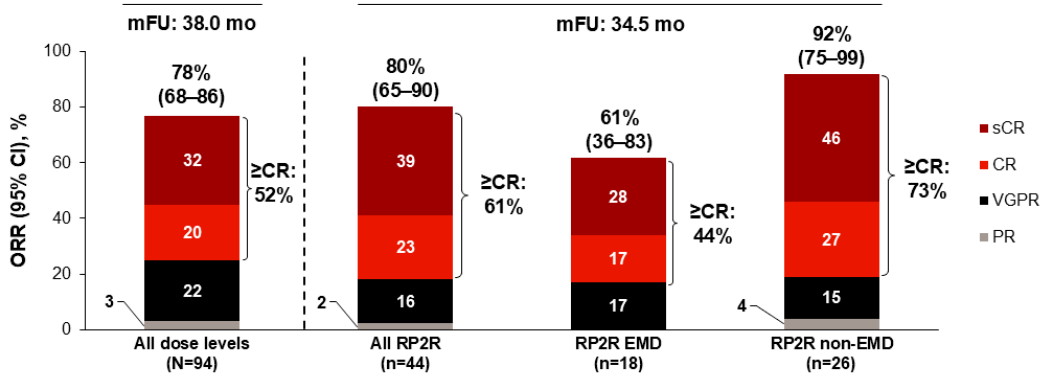


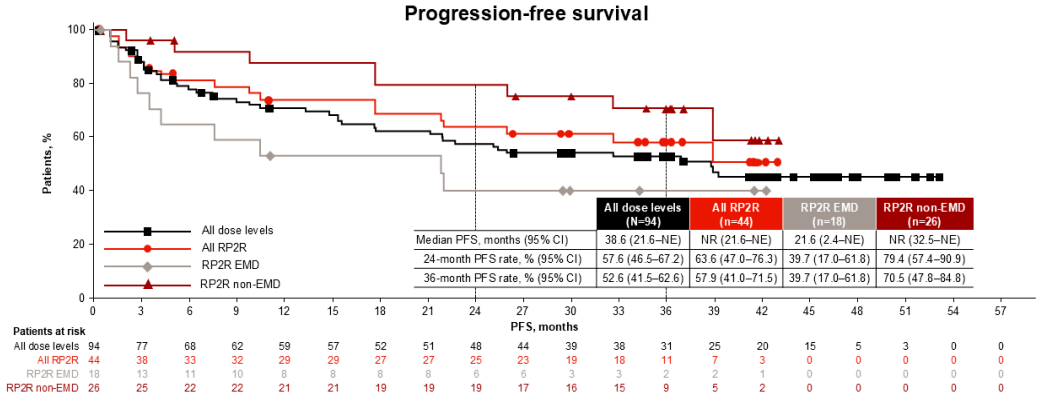
Patients treated with Tal + Tec	N=94 n=44
Age[a] (years)	64.5 (39–81) 63.0 (41–80)
Male	52.1% 52.3%
Years since diagnosis[a]	6.0 (0.3–14.6) 5.5 (0.3–12.8)
Prior LOT[a]	4 (1–11) 4 (2–10)

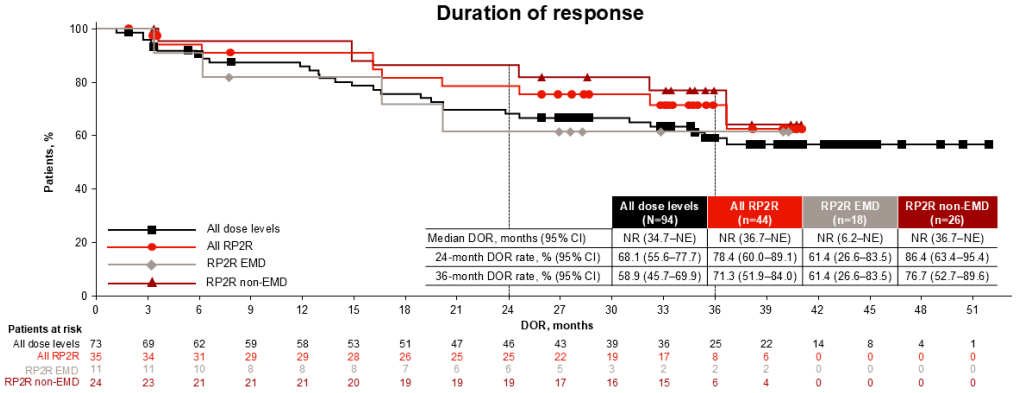


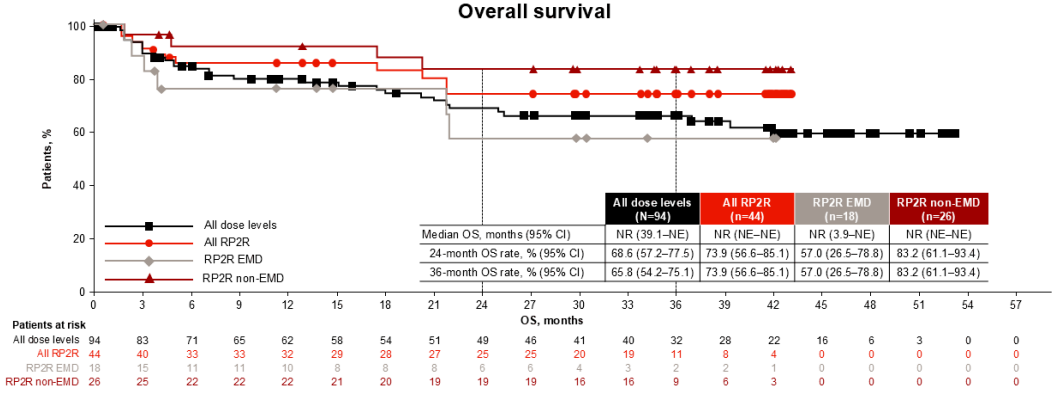
Mateos MV et al, ASH, 2025, Kumar S et al NEJM 2026

REDIRECTT-1: TEC-TAL



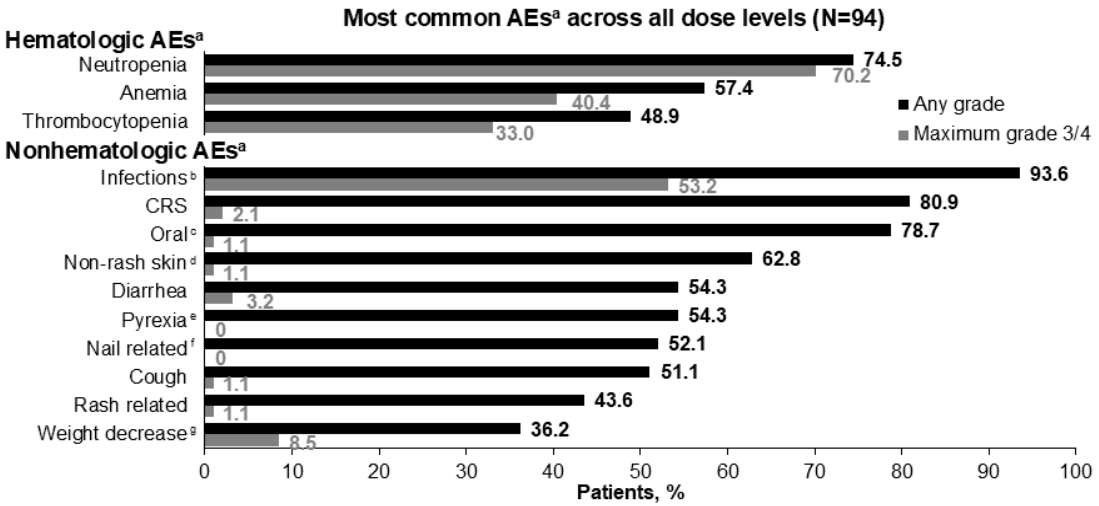


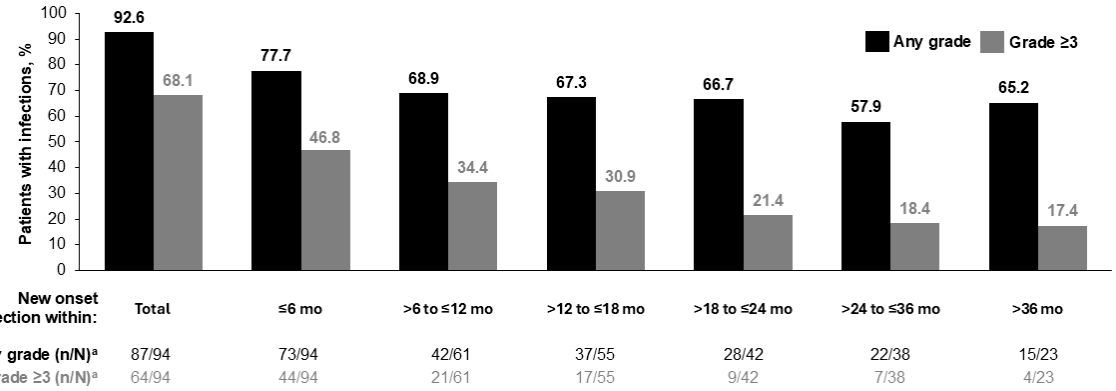




Mateos MV et al, ASH, 2025, Kumar S et al NEJM 2026

REDIRECTT-1: TEC-TAL





New onset infection within:	Total	≤6 mo	>6 to ≤12 mo	>12 to ≤18 mo	>18 to ≤24 mo	>24 to ≤36 mo	>36 mo
Any grade (n/N)[a]	87/94	73/94	42/61	37/55	28/42	22/38	15/23
Grade ≥3 (n/N)[a]	64/94	44/94	21/61	17/55	9/42	7/38	4/23

Most common AEs (≥15% overall), n (%)	All dose levels (N=94)		RP2R (n=44)	
	Any Grade	Maximum Grade 3/4	Any Grade	Maximum Grade 3/4
Median follow-up	38.0 months		34.5 months	
Infections	88 (93.6)	50 (53.2)	41 (93.2)	19 (43.2)
COVID-19[a]	38 (40.4)	15 (16.0)	20 (45.5)	7 (15.9)
URTI	29 (30.9)	4 (4.3)	15 (34.1)	1 (2.3)
Pneumonia	25 (26.6)	10 (10.6)	11 (25.0)	4 (9.1)
Nasopharyngitis	16 (17.0)	0	4 (9.1)	0
Rhinovirus infection	16 (17.0)	3 (3.2)	6 (13.6)	0
UTI	12 (12.8)	2 (2.1)	8 (18.2)	1 (2.3)

At ~3 years of follow-up, the dual BsAb combination of Tal + Tec at RP2R of Tal 0.8 mg/kg + Tec 3.0 mg/kg Q2W demonstrated:

- 80% ORR and 61% ≥CR rate, with responses deepening over time'
- At 3 years, 58% PFS rate and 71% DOR rate
- Combinability, with safety profile of the RP2R consistent with each of the monotherapies

Mateos MV et a, ASH, 2025, Kumar S et al NEJM 2026

MonumenTAL-6 study design

Key eligibility criteria

- 1–4 prior LOT, including anti-CD38 mAb and Len
- ECOG PS ≤2
- Naive to Tec, Pom, GPRC5D-directed therapy
- Naive to Elo (EPd arm)

1:1:1 randomization

- **Tal + Tec**
- **Tal + Pom**
- **Investigator's choice: EPd or PVd**

Primary endpoint

- PFS

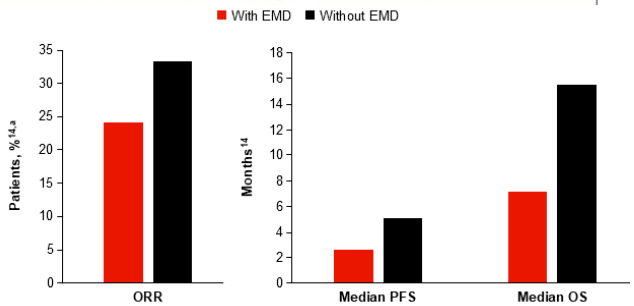
Key secondary endpoints

- ORR
- ≥CR
- MRD-negative CR
- OS

Efficacy and Safety of Talquetamab + Teclistamab in Patients With Relapsed/Refractory Multiple Myeloma and Extramedullary Disease: Updated Phase 2 Results From the RedirecTT-1 Study With Extended Follow-Up

Saad Z Usmani[1*], Shaji Kumar[2*], Maria-Victoria Mateos[3], Jing Christine Ye[4], Shebli Atrash[5], Hila Magen[6], Hang Quach[7], Michael P Chu[8], Suzanne Trudel[9], Joshua Richter[10], Paula Rodríguez-Otero[11], Hun Chuah[12], Moshe Gatt[13], Eva Medvedova[14], Shahzad Raza[15], Dok Hyun Yoon[16], Tadao Ishida[17], Jeffrey V Matous[18], Laura Rosiñol[19], Koichi Onodera[20], Carmela Maffucci[21], Emma Scott[22], Christoph Heuck[22], Jenny Zhang[22], Todd Henninger[21], Lisa O'Rourke[22], Payal Thakkar[21], Mariacristina Festa[23], Guoqiang Zhang[22], Sheetal Khedkar[24], Lin Huang[22], Jiangxiu Zhou[22], Mikihiro Takamoto[25], Lixia Pei[21], Jiashen Lu[26], Nicholas Au[22], Maria Krevvata[22], Yael C Cohen[27]

Patients with true EMD are 87% less likely to respond to real-world SOC treatments[13] and have worse outcomes vs patients without EMD[14]



Screening

Eligibility criteria

- Triple-class exposed RRMM[a]
- True EMD, defined as ≥1 nonradiated bone-independent soft tissue plasmacytoma ≥2 cm in greatest dimension confirmed by central review of PET-CT scans[b,c]
- Prior CAR-T and non-BCMA/-GPRC5D bispecific antibody therapies were permitted
- Nonsecretory and oligosecretory disease were permitted

Treatment

Tal 0.8 mg/kg Q2W SC[d,e]
+
Tec 3.0 mg/kg Q2W SC[d,e]

Option to switch to monthly dosing after 4 cycles and ≥VGPR, or after 6 cycles (irrespective of response)

Step-up dosing[d] 2–4 days apart (Tal + Tec)
SUD1: 0.01 mg/kg + 0.06 mg/kg
SUD2: 0.06 mg/kg + 0.3 mg/kg
SUD3: 0.4 mg/kg + 1.5 mg/kg

Endpoints

Primary endpoint: ORR[f]

Secondary endpoints:

- DOR[f]
- PFS[f]
- OS
- Safety

90 patients received Tal + Tec

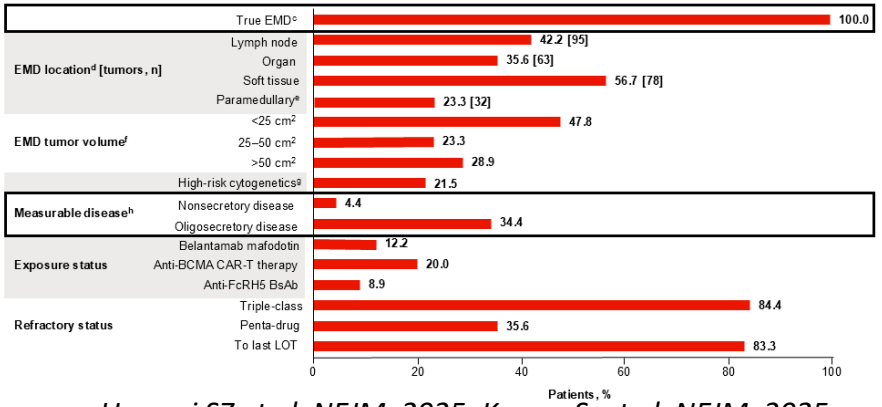
Age[a]
64.5 (42–84) years

Male
63.3%

Years since diagnosis[a,b]
4.7 (0.7–21.4)

Prior LOT[a]
4 (1–10)

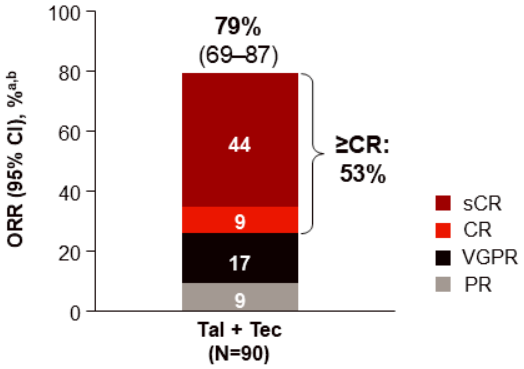
Baseline characteristics



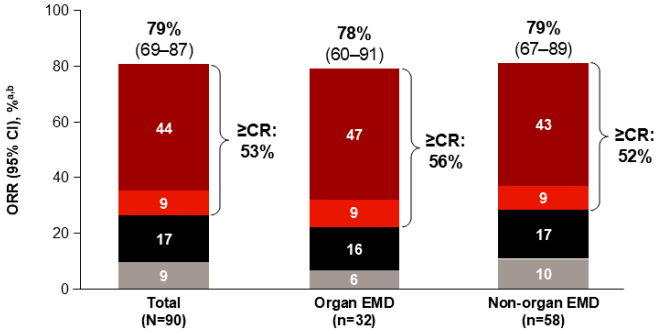
Usmani SZ et al, NEJM, 2025; Kumar S. et al, NEJM, 2025

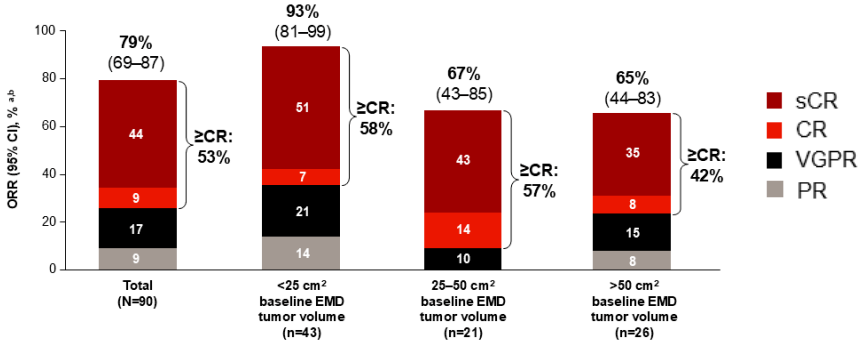
REDIRECTT-1: TEC-TAL

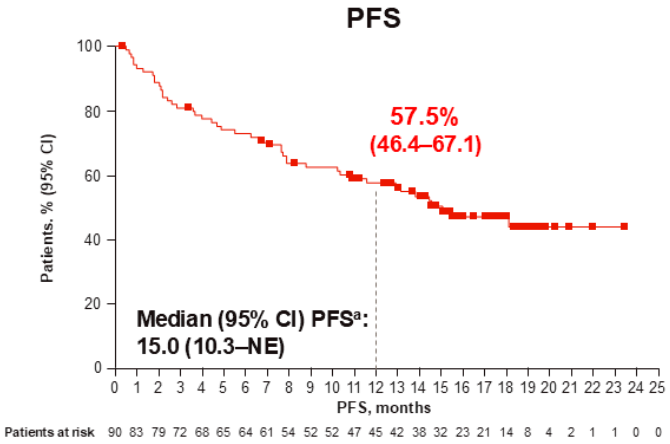
Organ EMD: kidney, liver, lung
Non organ EMD: soft tissue, lymph node

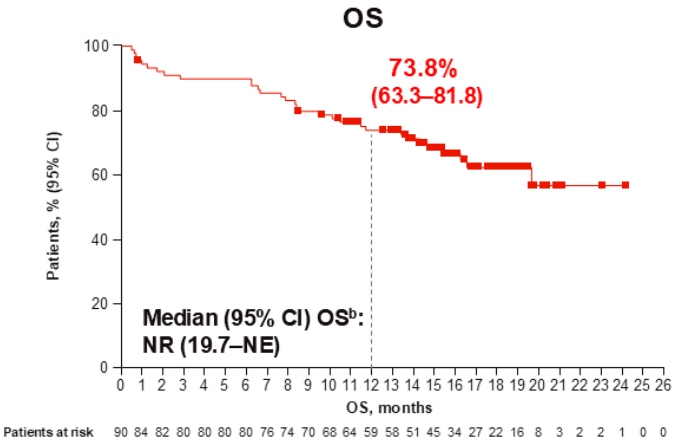


Median (range) time to:
- First response, 2.6 (1.0–5.8) months
- Best response, 5.1 (1.0–16.6) months





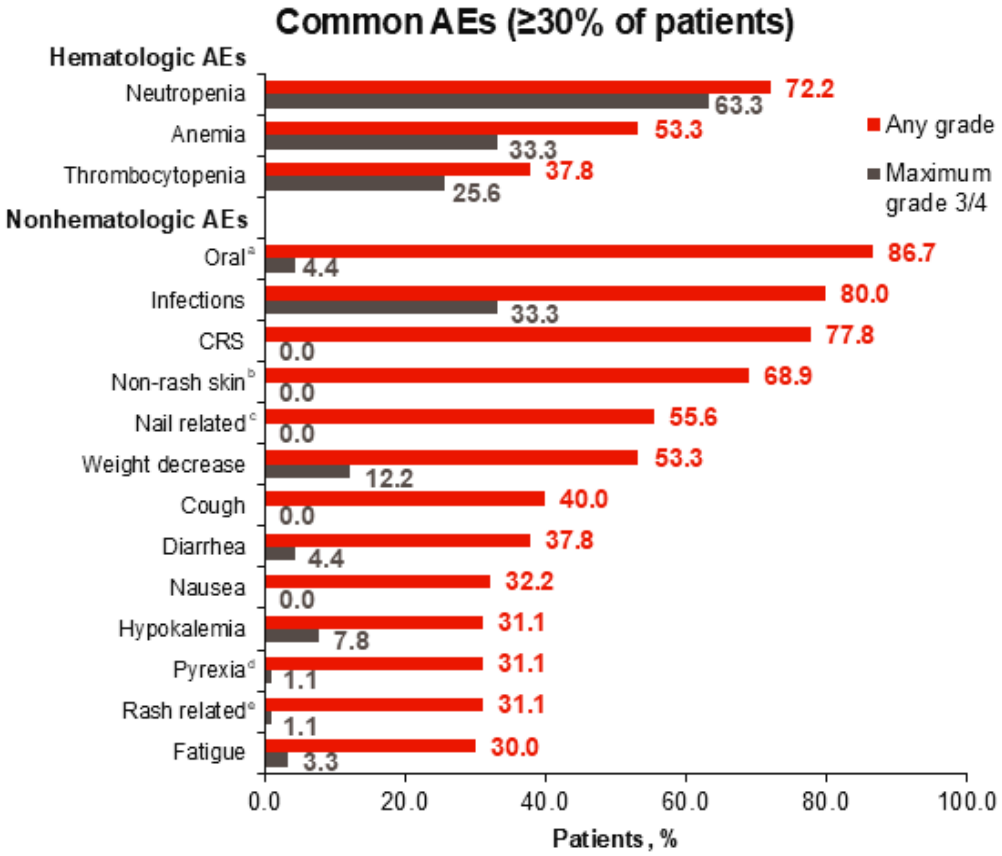




Usmani SZ et al, NEJM, 2025; Kumar S. et al, NEJM, 2025

RedirecTT study

REDIRECTT-1: TEC-TAL



Most common AEs (≥10% overall),[a] n (%)	Tal + Tec (N=90)	
	Any Grade	Maximum Grade 3/4
Infections	72 (80.0)	30 (33.3)
URTI	27 (30.0)	4 (4.4)
COVID-19	20 (22.2)	5 (5.6)
Pneumonia	19 (21.1)	8 (8.9)
UTI	12 (13.3)	4 (4.4)
Viral upper respiratory tract infection	9 (10.0)	2 (2.2)

- 6.7% of patients had opportunistic infections,[b] 3.3% were grade 3/4

Deep and durable responses in true EMD with Tal + Tec; enhanced efficacy with an additional 4 months follow-up in a population with significant unmet clinical need

- ORR, 79% (≥CR, 53%)
- 12-month DOR rate, 62.1%
- Median PFS, 15.0 months
- 12-month OS rate, 73.8%

Usmani SZ et al, NEJM, 2025; Kumar S. et al, NEJM, 2025

Abstract: 823

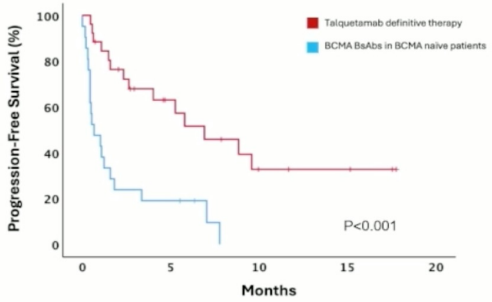
Real-World Outcomes of Bispecific T-Cell Engagers in Plasma Cell Leukemia

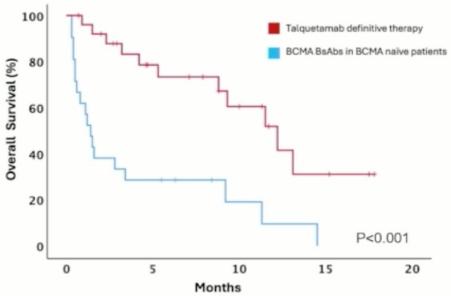
Mahmoud R. Gaballa[1], Kelley Julian[2], Aimaz Afrough[3], Doris K. Hansen[4], Utkarsh Goel[5], Andre De Menezes Silva Corraes[6], Danai Dima[7], Masooma Rana[8], Hitomi Hosoya[8], Lekha Mikkilineni[8], Lindsay Fogel[9], Shahzad Raza[5], Rahul Banerjee[7], Saurabh S. Zanwar[6], Oren Pasvolsky[1], Aishwarya Sannareddy[3], Azra Borogovac[10], James Davis[11], Kimberly Green[11], Noa Biran[9], Megan Herr[12], Leyla Shune[13], Evguenia Bhurtel[13], Shebli Atrash[14], Christopher Ferreri[14], Tiffany Richards[1], Muhammad Bilal Abid[1], Susan Bal[15], Hossam Ali[5], Christine Ye[1], Shambavi Richard[16], Gurbakhash Kaur[16], Kenneth Shain[4], Omar Castaneda-Puglianini[4], Adriana Rossi[16], Larry D. Anderson[3], Peter M. Voorhees[14], Jack Khouri[5], Surbhi Sidana[8], Andrew Portuguese[7], Murali Janakiram[10], Hans C. Lee[1], Yi Lin[6], Ariel Grajales-Cruz[4], Krina K. Patel[1], Douglas W. Sborov[2]

Characteristic	Overall (n=122), %	Teclistamab (n=45), %	Elranatamab (n=13), %	Talquetamab Definitive Treatment (n=51), %	Talquetamab Bridge to CAR-T (n=13), %	P value
Median Age (IQR)- year	65 (57-71)	66 (57-73)	66 (58-72)	64 (57-69)	65 (54-68)	0.85
Male	48	56	46	43	38	0.57
Race						0.68
White	77	76	85	76	77	
Black	15	18	0	16	15	
Others	8	6	15	8	8	
PCL status time of BsAb initiation						0.12
Active PCL	49	49	69	51	23	
Historical PCL only	48‡	42	31	49	77	
Unknown¶	3	9	0	0	0	
Prior PCL from diagnosis through last therapy pre-BsAb						0.23
Primary PCL	27	24	15	33	23	
Secondary PCL	65	69	85	53	77	
None	8	7	0	14	0	
High-Risk Cytogenetics						
Del17p	34	23	54	40	25	0.13
t(4:14)	20	16	31	15	42	0.12
t(14:16)	11	9	23	10	8	0.55
1q gain/amp	50	39	77	51	58	0.09
Del1p	14	14	31	12	0	0.16
High Bone Marrow Burden*	45	38	64	53	20	0.13
Extramedullary Disease (EMD)						0.97
Paraskeletal EMD	7	7	8	8	8	
True EMD	20	16	23	24	15	
CNS Myelomatosis	5	2	15	6	0	0.21
Prior Therapies						
Median Prior Lines of Therapy (IQR)	6 (4-8)	5 (4-7)	5 (4-7)	6 (5-9)	4 (4-5)	
Triple-Refractory	94	88	92	98	100	0.17
Penta-Refractory	57	53	54	68	25	0.05
Prior Transplant	73	73	62	80	54	0.20
Prior BCMA Treatment	57	42	38	82	23	<0.01
BsAb Usage						0.21
Monotherapy	94	100	92	90	92	
Combination with Other Agents	6	0	8	10	8	

¶ Four patients had historical PCL but unknown PCL status at the time of BsAb initiation. ‡ Within the historical PCL only cohort, 43% had primary PCL and 57% had secondary PCL. * High bone marrow burden defined as ≥50% plasma cells.

In Active PCL	mPFS (months)	mOS (months)
BCMA BsAbs in BCMA-naive patients	0.7 (95%CI 0-1.5)	1.4 (95%CI 0.8-2)
Talquetamab definitive therapy (regardless of BCMA exposure)	6.9 (95%CI 2.6-11.2)	12.2 (95%CI 8.1-16.3)





- Talquetamab was superior to BCMA bispecifics
  - mPFS 6.9 months, mOS 12.2 months (aligns with the broader cohort)
- Even in BCMA-naive patients, BCMA bispecifics had poor efficacy
  - mPFS 0.7 months, mOS 1.4 months

Gaballa MR et al ASH 2025

Take home

- BsAb in monoterapia →**BsAb+X** (Ab anti-CD38, IMIDs/Celmods..)

- BsAb in linee precoci (prima linea ?)
  -ottimizzazione della schedula per ridurre le tossicità
  - fixed duration

- Qual è il posizionamento del bispecifico?
  - Paziente fit vs intermediate fit/frail
  - Terapia di debulking vs terapia sequenziale

- Nuove target therapy/combinazioni per migliorare la risposta dei pazienti

Grazie per l'attenzione

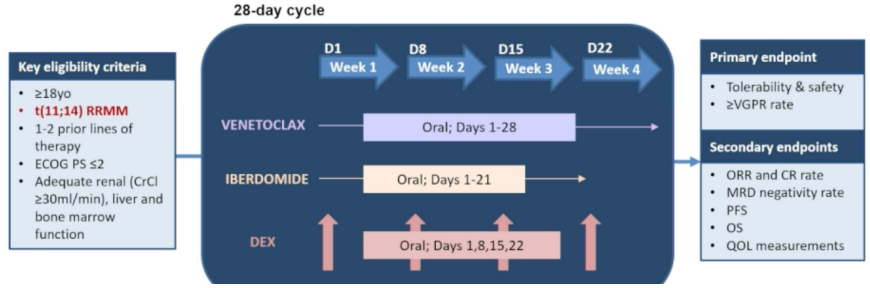
Interim analysis of efficacy and safety for Viber-M (ALLG MM25): A Phase Ib/II study of Venetoclax, Iberdomide and Dexamethasone for patients in first or second relapse of Multiple Myeloma with t(11;14)

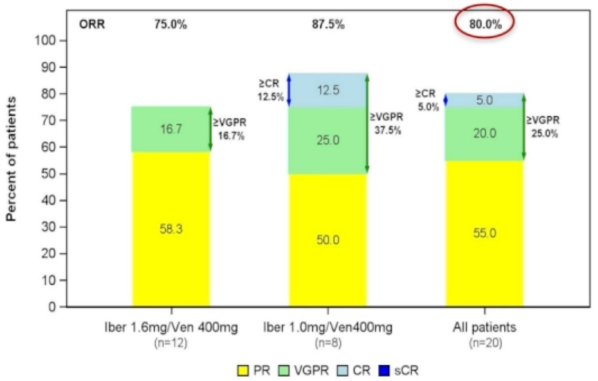
Shirlene Sim[1,2], Adam Bryant[3], Cecily Forsyth[4], Olga Motorna[5], Jennifer Brotchie[6], Jay Hocking[7], Angelina Yong[8], Nicole Chien[9], Ian Kerridge[10], Hock Choong Lai[11], Ann Solterbeck[12], Robert Traficante[12], Maritsa Jocic[13], Hang Quach[1,2]

Characteristic	N=20
Median age, range (years)	65 (41-83)
Gender	
Female, n (%)	8 (40)
ECOG performance status, n (%)	
0	15 (75)
1	5 (25)
Revised ISS (R-ISS), n (%)	
I	14/19 (73.7)
II	5/19 (26.3)
III	0/19 (0.0)
Standard risk	14 (70)
High risk*	6 (30)

Characteristic		N=20
Number of prior lines of therapy		
Median (range)		1 (1-2)
One n (%)		15 (75)
Two n (%)		5 (25)
Prior therapies, n (%)		
Bortezomib	Exposed	15 (75)
	Refractory	6 (30)
Lenalidomide	Exposed	15 (75)
	Refractory	13 (65)
Daratumumab	Exposed	4 (20)
	Refractory	4 (20)
Triple-class	Exposed	3 (15)

*High risk: Presence of del(17p), 1q gain/amp, t(4;14), t(14;16)





- ORR 80%
  - ≥VGPR 25%
  - ≥CR 5%
- Median time to first response: 41.5 days (range 28 – 62 days)

- Lenalidomide refractory patients (n=13):
  - ORR 85%
  - ≥VGPR 23%
- Daratumumab refractory (n=4):
  - ORR 75%
  - ≥VGPR 25%

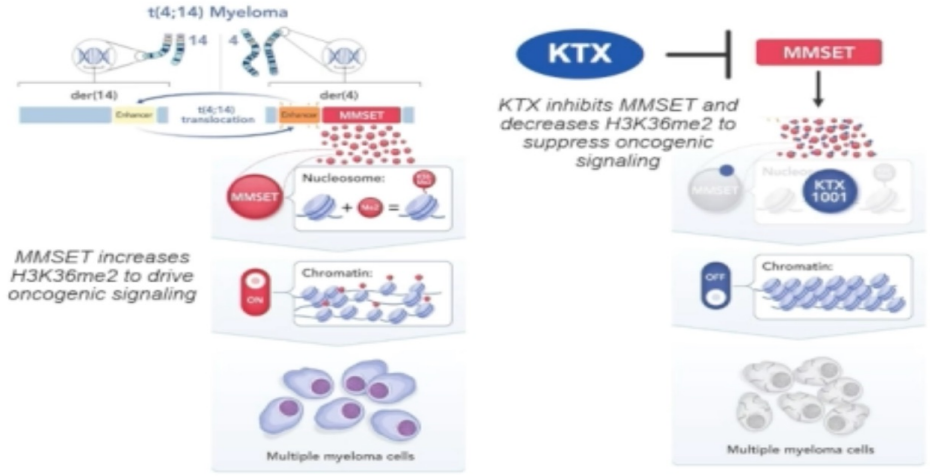
This triplet combination demonstrates encouraging early efficacy in t(11;14) MM patients who have had 1-2 prior lines of therapy, including in Len-refractory patients

- ORR of 80% and ≥VGPR rate of 25% at the end of cycle 3 of treatment, with similar responses demonstrated in Len- and Dara-refractory patients
- At median follow up of 12.2 months, 33/47 patients remain on treatment, with the longest duration on treatment of 26 months and ongoing

Sim S Ash 2025

Phase 1 Study of KTX-1001, a First-in-Class Oral MMSET/NSD2 Inhibitor, Demonstrates Clinical Activity in Relapsed/Refractory Multiple Myeloma

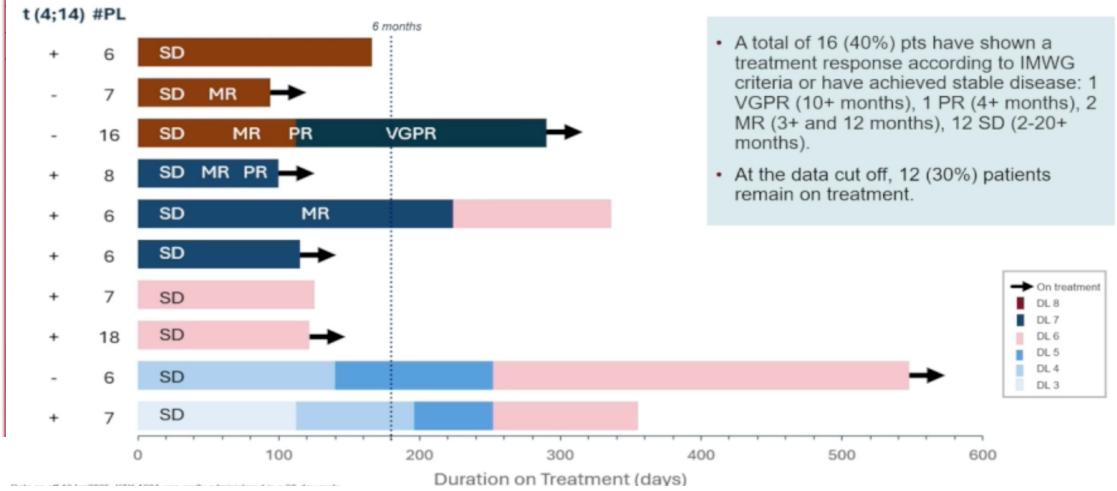
Saad Z. Usmani[1], Pierre Bories[2], Cristina Gasparetto[3], David Dingli[4], Sagar Lonial[5], David S. Siegel[6], Andrew J. Yee[7], Cindy Varga[8], Suzanne Trudel[9], Laura Rosiñol[10], Paula Rodriguez-Otero[11], Salomon Manier[12], Jesus G. Berdeja[13], Aimaz Afrough[14], Warren Baker[15], Seyed Alireza Hasheminasab[15], Anjan Thakurta[15], J. Erin Flynt[16], Vinidhra Sridharan[16], Miriam Barnett[16], Laura Versmée[16], Maria Victoria Mateos[17], Cyrille Touzeau[18], Alfred Chung[19], Vivek Roy[20], Edward A Stadtmauer[21]



Characteristic	Total Patients (n=40)
Median Age, years (range)	69 (50-83)
Sex, n (%)	
Male	19 (47.5)
Female	21 (52.5)
ECOG PS, n (%)	
0	9 (22.5)
1	31 (77.5)
Time since initial MM Diagnosis, median (range), years	8 (2-20)
EMD, n (%)	13 (32.5)
IMWG 2025 High-risk, n (%)*	12 (30)
Cytogenetic Abnormality, n (%)*	
t(4;14) translocation	19 (47.5)
t(4;14) with 1q+ or del(1p32)	8 (20)
t(4;14) alone**	11 (27.5)
t(14;20) translocation	1 (2.5)
1q21 amplification	5 (12.5)
del(17p)	4 (10)

Characteristic	Total Patients (n=40)
Prior Therapies, median (range)	6.5 (3-25)
3L, n(%)	4 (10)
4L, n(%)	5 (12.5)
≥ 5L, n(%)	31 (77.5)
Prior stem cell transplant	28 (70.0)
Prior therapy by Drug Class, n (%)	
IMiD™/PI	40 (100)
Anti-CD38	39 (98.0)
BCMA CAR-T	17 (42.5)
BCMA Targeted BsAb & ADC	23 (57.5)
Non-BCMA BsAb	16 (40.0)
• GPRC5D Targeted BsAb	13 (32.5)
• FcRH5 Targeted BsAb	3 (7.5)
Triple-drug exposed§	39 (98)
Penta-drug exposed§§	32 (80)

Exposure and Clinical Response in the Dose-Escalation Cohort on Treatment ≥ 3 Cycles



- A total of 16 (40%) pts have shown a treatment response according to IMWG criteria or have achieved stable disease: 1 VGPR (10+ months), 1 PR (4+ months), 2 MR (3+ and 12 months), 12 SD (2-20+ months).
- At the data cut off, 12 (30%) patients remain on treatment.

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