Innere Medizin II, Hämatologie, Onkologie, Klinische Immunologie und Rheumatologie

Post ASH 2025 Orlando

Multiples Myelom

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Late breaking abstracts ASH 2025

PRESENTATION ID LBA-1
OCCC - West Hall D2
Minimal residual disease (MRD)-negative outcomes following a novel, *in vivo* gene therapy generating anti–B-cell maturation antigen (BCMA) chimeric antigen receptor (CAR)-T cells in patients with relapsed and refractory multiple myeloma (RRMM): Preliminary results from inMMyCAR, the first-in-human phase 1 study of KLN-1010
Phoebe Joy Ho, MBBS, DPhil, FRACP, FRCPA

PRESENTATION ID LBA-2
OCCC - West Hall D2
Primary results from VAYHIT2, a randomized, double-blind, phase 3 trial of ianalumab plus eltrombopag versus placebo plus eltrombopag in patients with primary immune thrombocytopenia (ITP) who failed first-line corticosteroid treatment
Hanny Al-Samkari, M.D.

PRESENTATION ID LBA-3
OCCC - West Hall D2
Pirtobrutinib vs bendamustine plus rituximab (BR) in patients with CLL/SLL: First results from a randomized phase III study Examining a non-covalent BTK inhibitor in untreated patients
Wojciech Jurczak, MD, PhD

PRESENTATION ID LBA-4
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Whole genome transcriptome sequencing in inherited bone marrow failure syndromes and related diseases – the ibmdx study
Lucy Fox, MBBS BCom/BSc DMedSci FRACP FRCPA

PRESENTATION ID LBA-5
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A hospital policy of tranexamic acid to reduce transfusion in major non-cardiac surgery: The traction trial
Brett Houston

PRESENTATION ID LBA-6
OCCC - West Hall D2
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 (Pts) with relapsed refractory multiple myeloma (RRMM): Results of majestec-3
María-Victoria Mateos, MD, PhD

Practice changing

Agenda

1. Preliminary results from inMMyCAR, a first-in-human phase 1 study of KLN-1010 *(in vivo CAR-T cells)*
   LBA

2. 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
   LBA

3. 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

Late breaking abstracts ASH 2025

LBA-1

MRD-negative outcomes following a novel, *in vivo* gene therapy generating anti-BCMA CAR-T cells in patients with RRMM: Preliminary results from inMMyCAR, the first-in-human Phase 1 study of KLN-1010

Simon Harrison[1], P. Joy Ho[2], Sueh-li Lim[3], Stephanie Talam[2], Hannah Pahl[1], Dharmesh Dingar[4], Scott Currence[4], Travis Quigley[4], Andrew Spencer[3]

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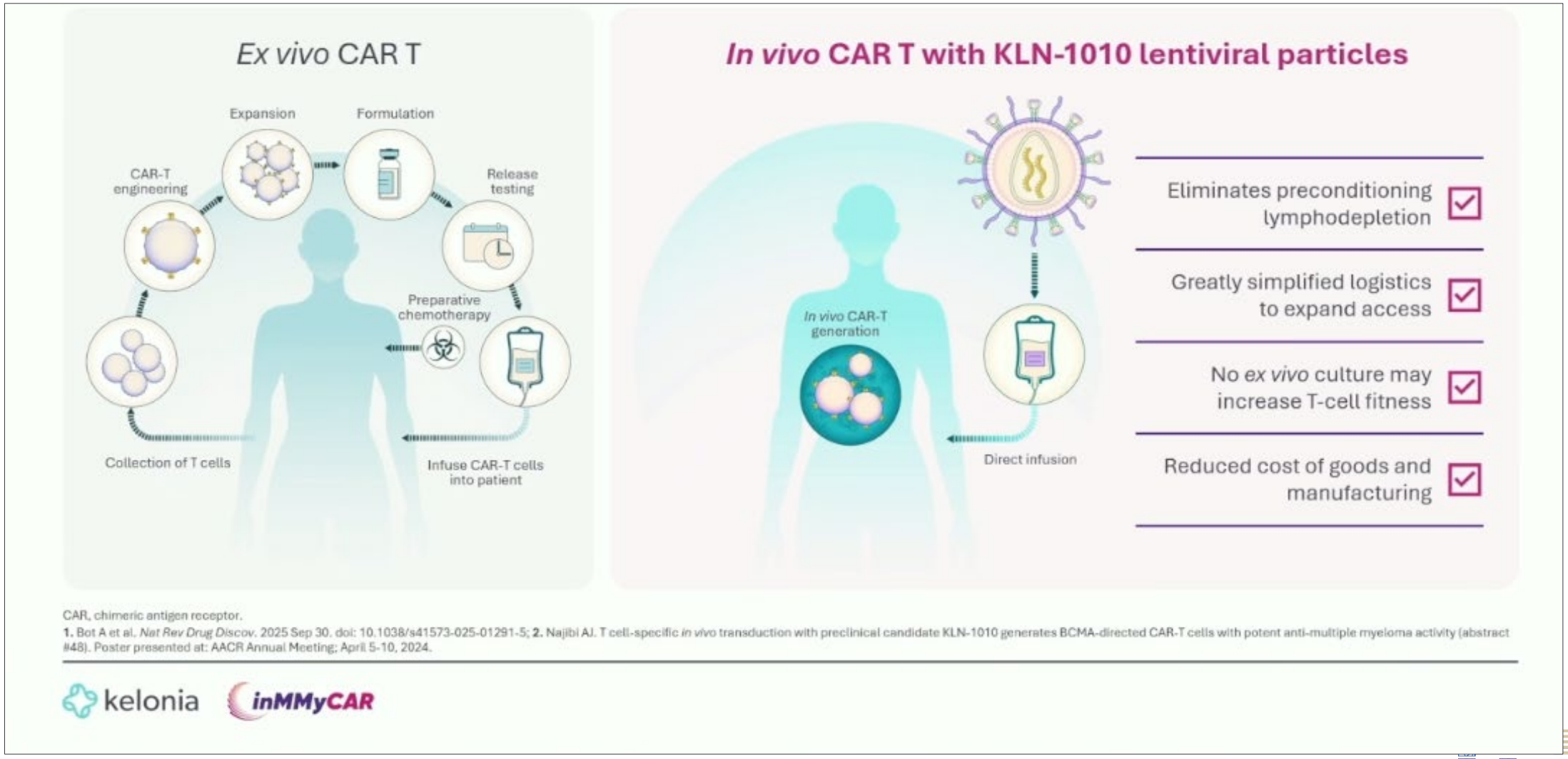
kelonia inMMyCAR

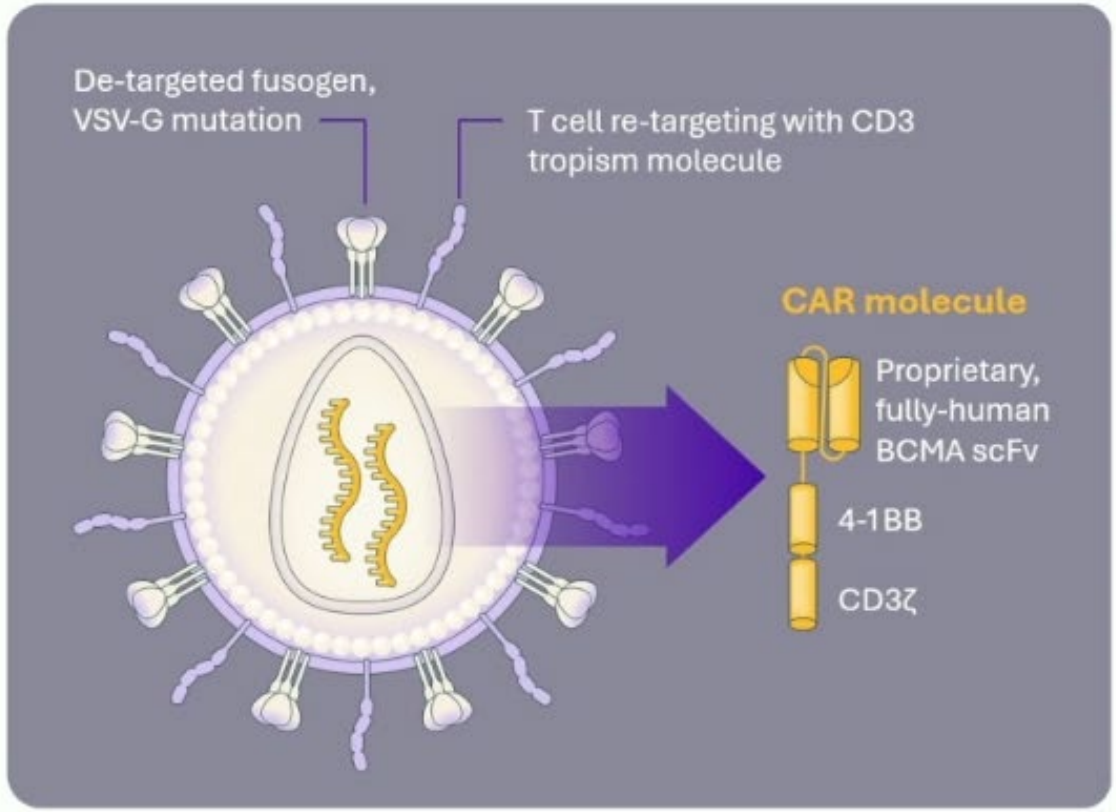
Presented at the 67th ASH Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

inMMyCAR (KLN-1010) – *in vivo* gene delivery



inMMyCAR – KLN-1010 (mod. LVV)

- **Envelope-modified, replication-incompetent, self-inactivating lentiviral vector**
- **De-targeted VSV-G fusogen** avoids delivery to LDL-expressing cells while maintaining high transduction efficiency
- **Precise re-targeting to T cells** with a CD3 scFv; avoids liver uptake and drug sinks
- Anti-BCMA CAR was **selected based on high levels of activity to BCMA-positive tumors**



BCMA, anti–B-cell maturation antigen; CAR, chimeric antigen receptor; CD3, cluster of differentiation 3; CD3ζ, cluster of differentiation 3 zeta chain; LDL, low-density lipoprotein; LVV, lentiviral vector; scFv, single-chain variable fragment; VSV-G, vesicular stomatitis virus glycoprotein.

Wood JT et al. Toward treatment with gene-modified B cells engineered *in vivo* using iGPS particles (abstract #1281). Poster presented at: ASGCT 28th Annual Meeting; May 13-17, 2025.

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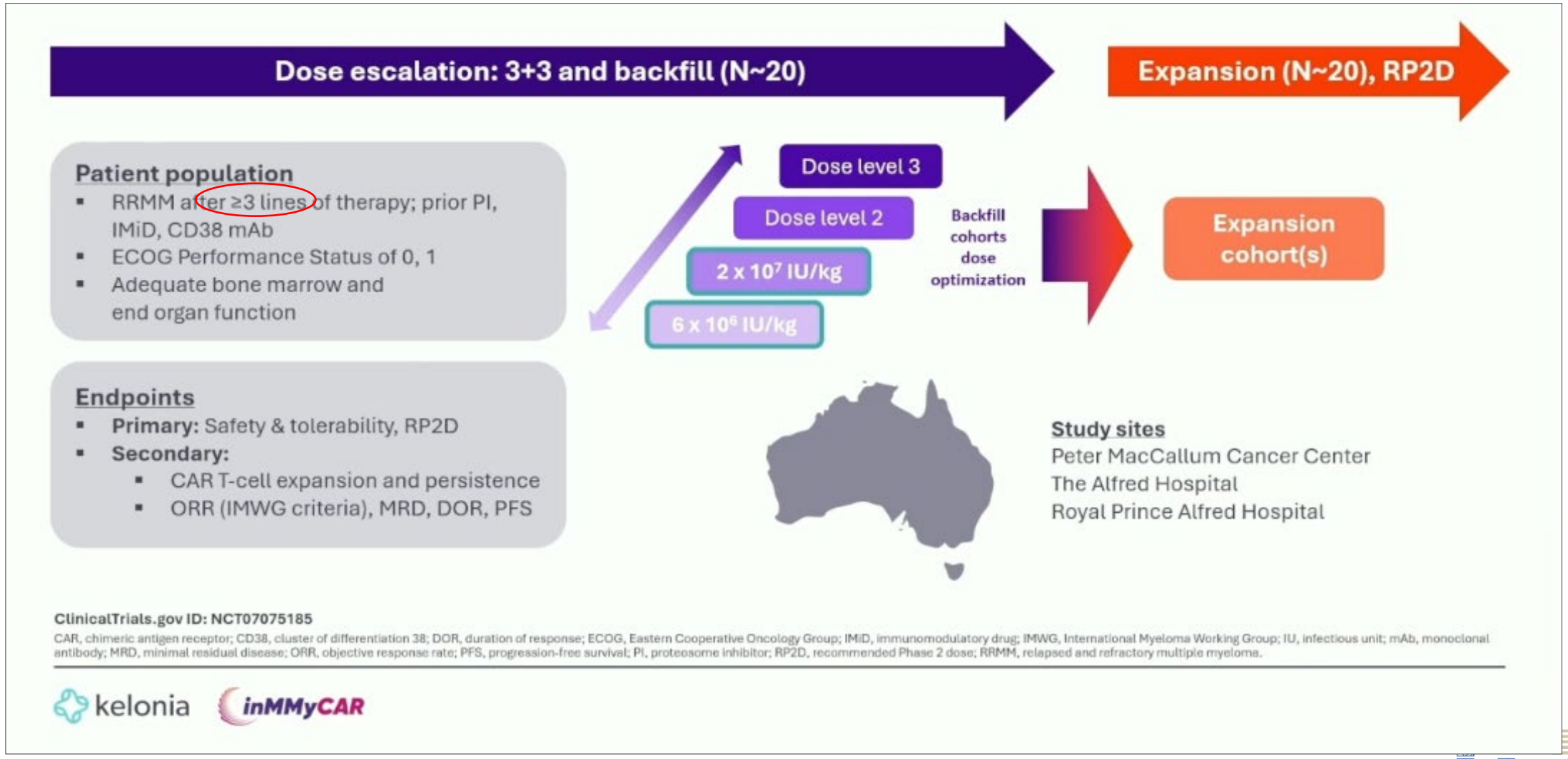
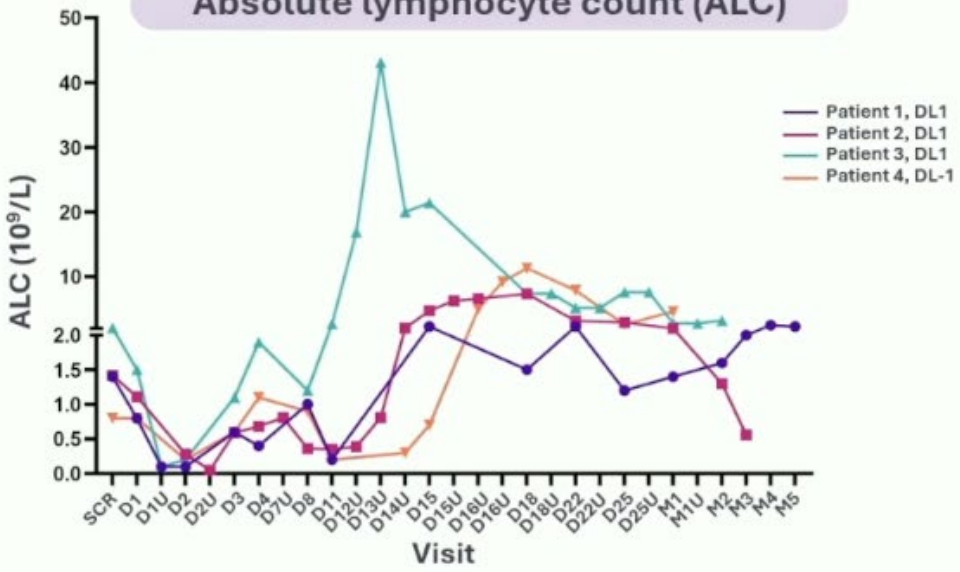
inMMyCAR (KLN-1010) – *study design*



inMMyCAR – CAR-T expansion

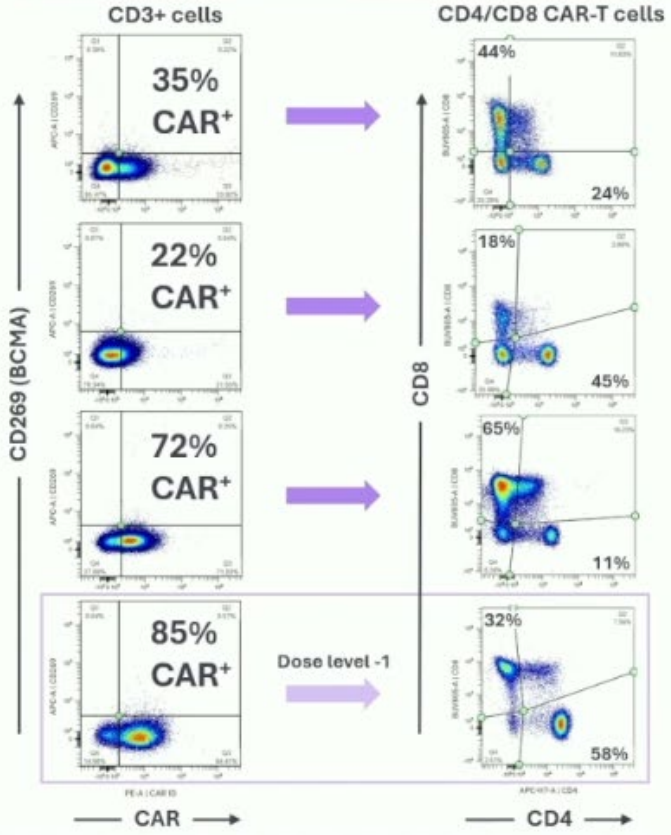
CAR-T expansion without lymphodepleting chemotherapy

Absolute lymphocyte count (ALC)



- **Dexamethasone** administered to patients 3 and 4
- **No clinical sequalae** related to lymphocytosis

Blood CAR-T cells (day 15)



BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; CD, cluster of differentiation; D, study day; DL, dose level; IU, infectious unit; M, month; SCR, screening; U, unscheduled measurements outside study specified schedule.

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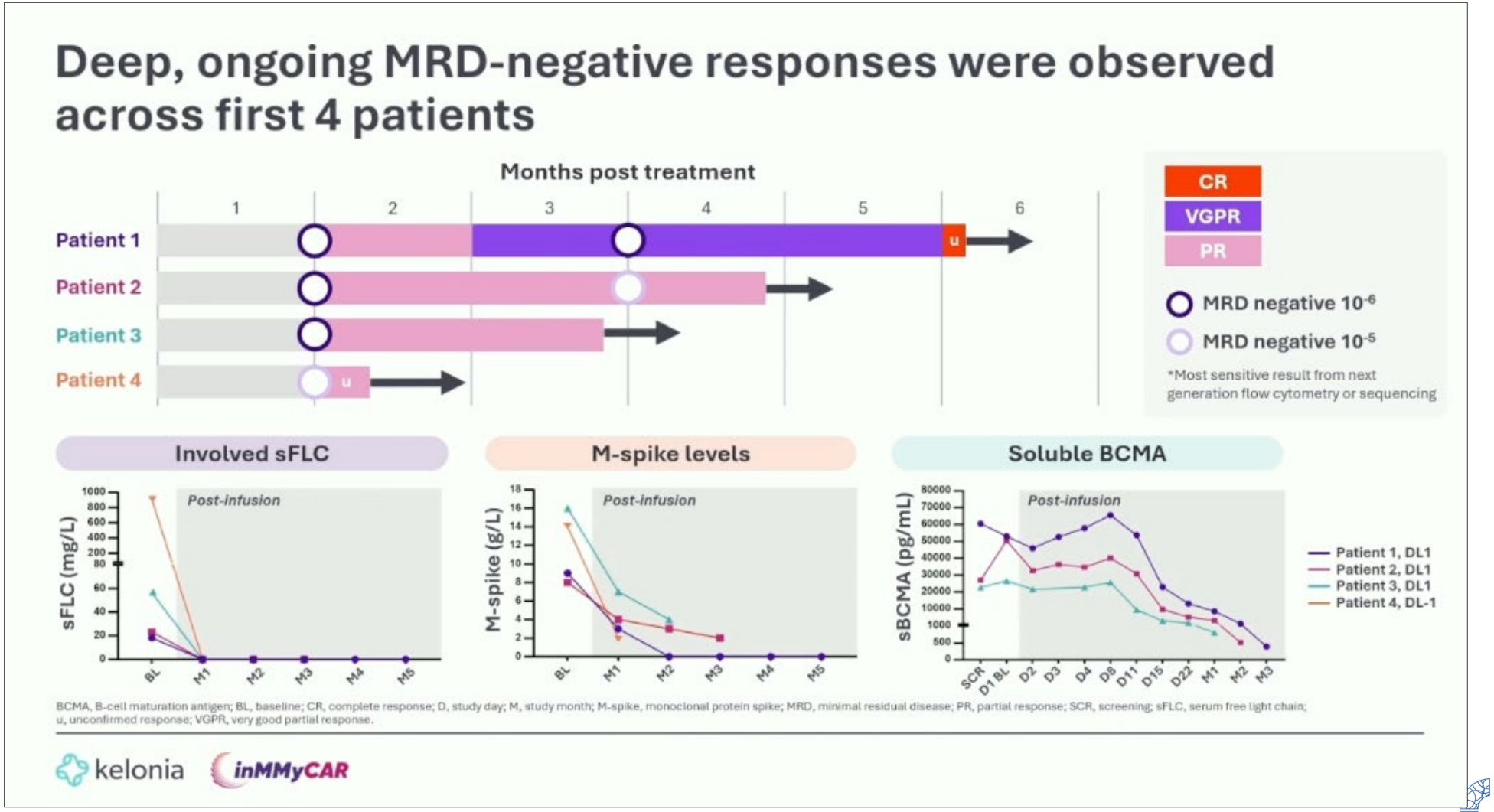
C_{max} of vector copies/µg genomic DNA	
Patient 1	51,647
Patient 2	65,873
Patient 3	108,730

C_{max} of vector copies/µg genomic DNA from approved *ex vivo* CAR-T product[1]		
Summary statistic	**CARTITUDE-1**	**CARTITUDE-4**
Median	47,806	34,891
Range	7189-115,234	935-104,861

inMMyCAR – Response



inMMyCAR – Safety

CRS (patient population, N=4)		
Onset, study day (range)		
Median onset	10 (10-12)	
Duration, days (range)		
Median duration	5.5 (2-8)	
Event, n	**Grade 1-2**	**Grade ≥3**
Dose level 1	2	0
Dose level -1	1	0
Supportive care, n		
Dexamethasone	3	
Tocilizumab	3	

ICANS, delayed neurotoxicity (patient population, N=4)		
Event, n	**Grade 1-2**	**Grade ≥3**
ICANS	0	0
Delayed neurotoxicity *(parkinsonism, cranial nerve palsy, peripheral neuropathy)*	0	0

CRS, cytokine release syndrome; ICANS, Immune Effector Cell-Associated Neurotoxicity Syndrome.

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inMMyCAR – Safety

- Minimal events of cytopenia; only 1 case of Grade 4 (transient neutropenia related to margination)
- Markedly lower number of events compared to *ex vivo* CAR-T therapies

TEAEs in >1 patient	Grade 1-2, n	Grade ≥3, n
IRR	2	1 (DLT)
Lymphocytosis	1	1
Hypomagnesemia	2	0
Hypokalemia	2	0

TEAEs Grade ≥3	Patients, n	Study day	Duration, days
Febrile neutropenia	1	1	2
IRR	1	1	3
Lymphopenia	1	2, 8	2, 5
Lymphocytosis	1	13	3
Anemia	1	15	2
Vasovagal syncope	1	27	1
Pneumonia	1	86	8

Cytopenia			
	Grade ≥3, n	Study day	Duration, days
Anemia	1	15	2
Thrombocytopenia	1	16	2
Neutropenia	2	1, 15	2, 2
		14	3

Infusion-related reactions			
	Grade 1-2, n	Grade ≥3, n	Supportive care
Dose level 1	1	1	Tocilizumab, steroid
Dose level -1	1	0	Paracetamol

CAR, chimeric antigen receptor; DLT, dose-limiting toxicity; IRR, infusion-related reaction; TEAE, treatment-emergent adverse event.

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inMMyCAR – Conclusion

- **Lymphodepletion not required** for *in vivo* CAR-T cell generation and expansion in the peripheral blood
  - CAR-T cell expansion peaked around day 15; memory-phenotype T cells persisted in the bone marrow and blood through month 3
  - Similar outcomes have been associated with durable remissions with *ex* vivo CAR-T cells in MM
- **Favorable safety and tolerability profiles** using **off-the-shelf** product make outpatient therapy feasible
  - CRS was consistent with those seen with *ex vivo* CAR-T therapies, while cytopenias were notably limited
- **100% early MRD-negative responses** with deepening of IMWG response over time; MRD-negative BM response is **sustained through 3 months** in the first 2 patients with longest follow-up
- **Initial MRD-negative response and persistent CAR-T cells prognostic of ongoing clinical responses**
  - Establishing durability of response remains a priority in continued follow-up; updated results will be presented at future meetings

BM, bone marrow; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; IMWG, International Myeloma Working Group; MM, multiple myeloma; MRD, minimal residual disease.

kelonia inMMyCAR

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

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Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

https://www.congresshub.com/ASH2025/Oncology/Teclistamab/Mateos-LBA

MajesTEC-3: Phase 3 Study Design

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

- **Tec-Dara**
- **DPd/DVd per investigator's choice[b]**

Primary endpoint

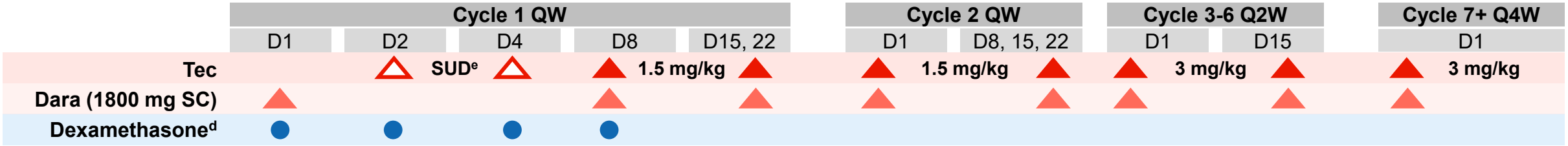
- PFS per IRC

Key secondary endpoints

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

Other secondary endpoints

- Safety
- PK and immunogenicity



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

[a]Prior exposure to anti-CD38 mAbs was permitted. [b]DPd/DVd were administered per the approved schedules. [c]Response and disease progression were assessed by a blinded IRC per IMWG criteria. [d]Dexamethasone, acetaminophen, and diphenhydramine premedication was required for the first 2 weeks; subsequent dexamethasone was not required thereafter. [e]Patients received SUD of 0.06 mg/kg and 0.3 mg/kg on Days 2 and 4, respectively.
BCMA, B-cell maturation antigen; CR, complete response; Dara, daratumumab; DPd, daratumumab, pomalidomide, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; IMWG, International Myeloma Working Group; IRC, independent review committee; LOT, line of therapy; mAb, monoclonal antibody; MRD, minimal residual disease; MySIm-Q, Multiple Myeloma Symptom and Impact Questionnaire; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; PK, pharmacokinetics; QW, weekly; Q2W, every 2 weeks; Q4W, every 4 weeks; RRMM, relapsed refractory multiple myeloma; SC, subcutaneous; SUD, step-up dosing; Tec, teclistamab.

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MajesTEC-3: Baseline Demographic and Disease Characteristics

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)
Other[a]	20 (6.9)	19 (6.4)

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/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	14 (4.8)	17 (5.7)
High-risk cytogenetics,[c] n/N (%)	104/285 (36.5)	104/294 (35.4)

Baseline demographic and disease characteristics were well balanced and reflective of patients seen in real-world practice

[a]"Other" includes Native Hawaiian or Pacific Islander (Tec-Dara, n=1 [0.3%]; DPd/DVd, n=0; total, n=1 [0.2%]), American Indian or Alaska Native (Tec-Dara, n=0; DPd/DVd, n=1 [0.3%]; total, n=1 [0.2%]), not reported (Tec-Dara, n=14 [4.8%]; DPd/DVd, n=16 [5.4%]; total, n=30 [5.1%]), and unknown (Tec-Dara, n=5 [1.7%]; DPd/DVd, n=2 [0.7%]; total, n=7 [1.2%]). [b]Maximum value from bone marrow biopsy or bone marrow aspirate was selected if both results were available. [c]Presence of ≥1 of del(17p), t(4;14), or t(14;16).
BMPC, bone marrow plasma cell; Dara, daratumumab; DPd/DVd, daratumumab and dexamethasone with either pomalidomide or bortezomib; ECOG PS, Eastern Cooperative Oncology Group performance status; ISS, International Staging System; Tec, teclistamab.

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MajesTEC-3: Prior Lines of Therapy

Characteristic	Tec-Dara (n=291)	DPd/DVd (n=296)
Prior LOTs		
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)

- The number of patients with prior anti-CD38 exposure was low
- >80% of patients were refractory to lenalidomide

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, n (%)	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)

Patients had a median of 2 prior LOTs, and >85% of patients were refractory to a PI or IMiD

Dara, daratumumab; DPd/DVd, daratumumab and dexamethasone with either pomalidomide or bortezomib; IMiD, immunomodulatory drug; LOT, line of therapy; PI, proteasome inhibitor; Tec, teclistamab.

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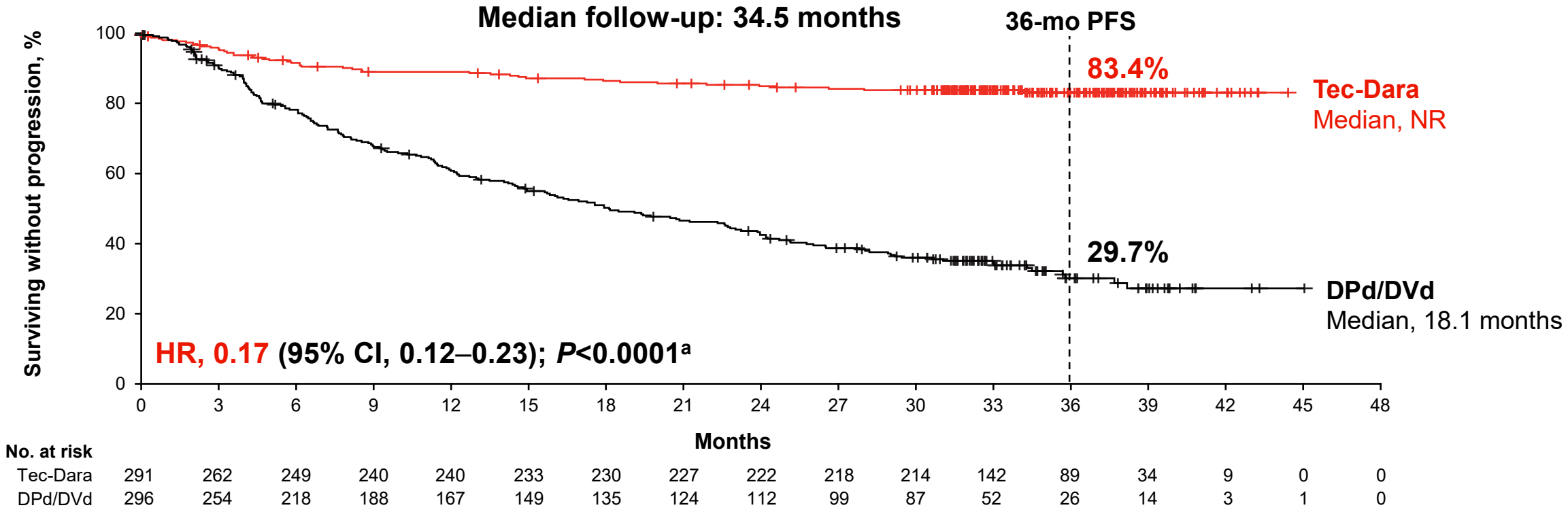
MajesTEC-3: PFS (Primary Endpoint)



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

[a]The *P* value crossed the prespecified stopping boundary for superiority for the first interim analysis (*P*=0.0139).
CI, confidence interval; Dara, daratumumab; DPd/DVd, daratumumab and dexamethasone with either pomalidomide or bortezomib; HR, hazard ratio; NR, not reached; PFS, progression-free survival; Tec, teclistamab.

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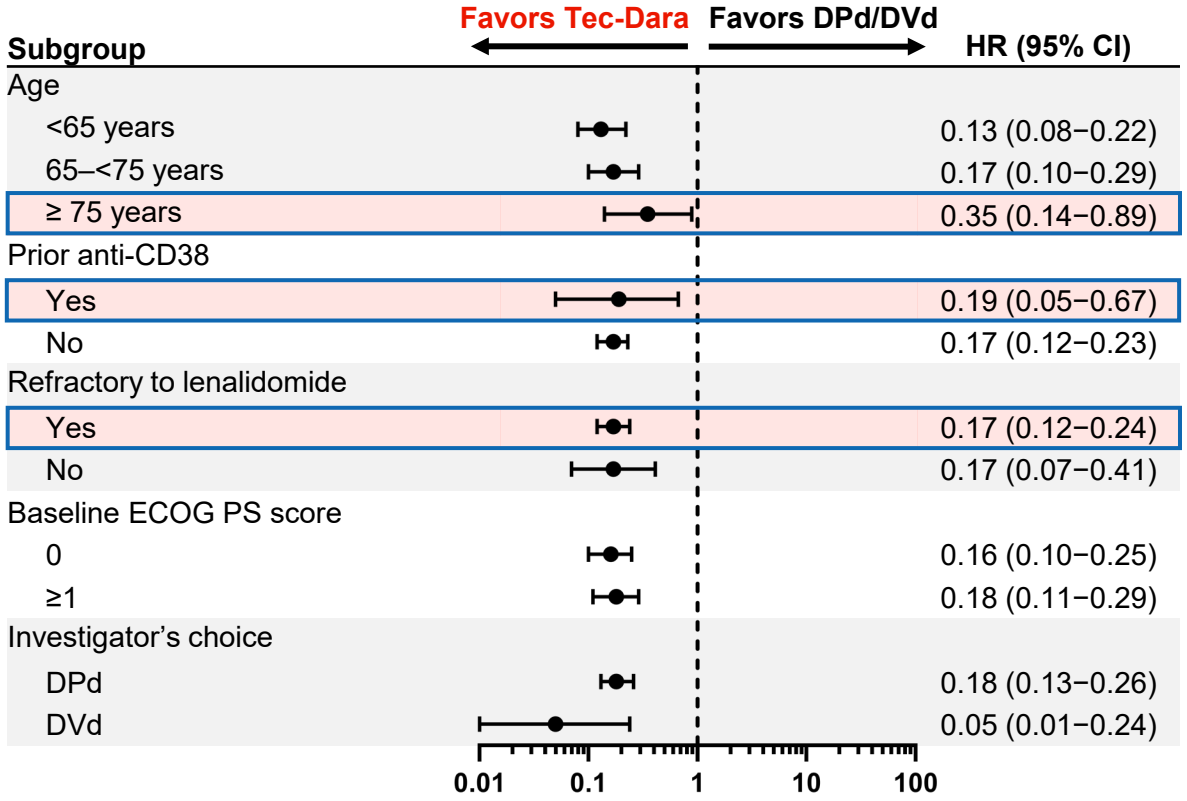
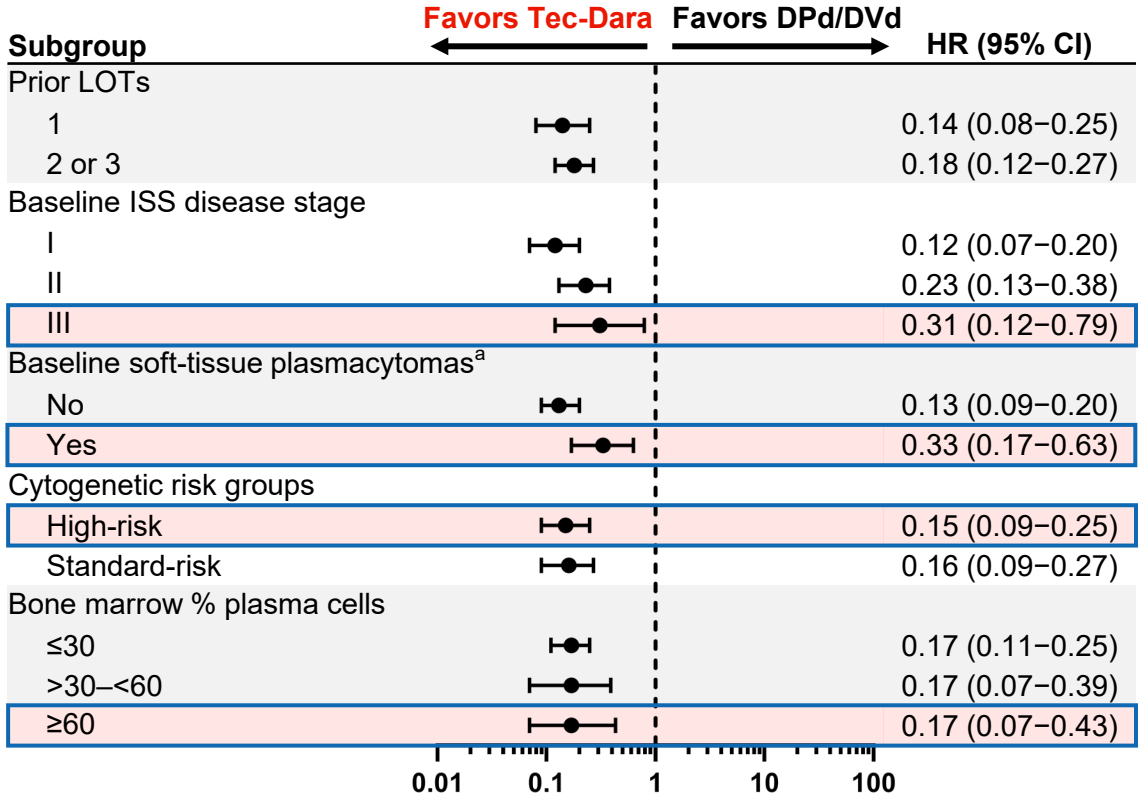
MajesTEC-3: PFS Subgroup Analysis





Superior PFS benefit with Tec-Dara was consistent across all subgroups[b]

[a]Baseline soft-tissue plasmacytomas contain both extramedullary and paraskeletal plasmacytomas. [b]Not all clinically meaningful and prespecified subgroups that were assessed are shown; however, PFS was improved versus DPd/DVd across all subgroups.
CI, confidence interval; Dara, daratumumab; DPd/DVd, daratumumab and dexamethasone with either pomalidomide or bortezomib; DPd, daratumumab, pomalidomide, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; ISS, International Staging System; LOT, line of therapy; PFS, progression-free survival; Tec, teclistamab.

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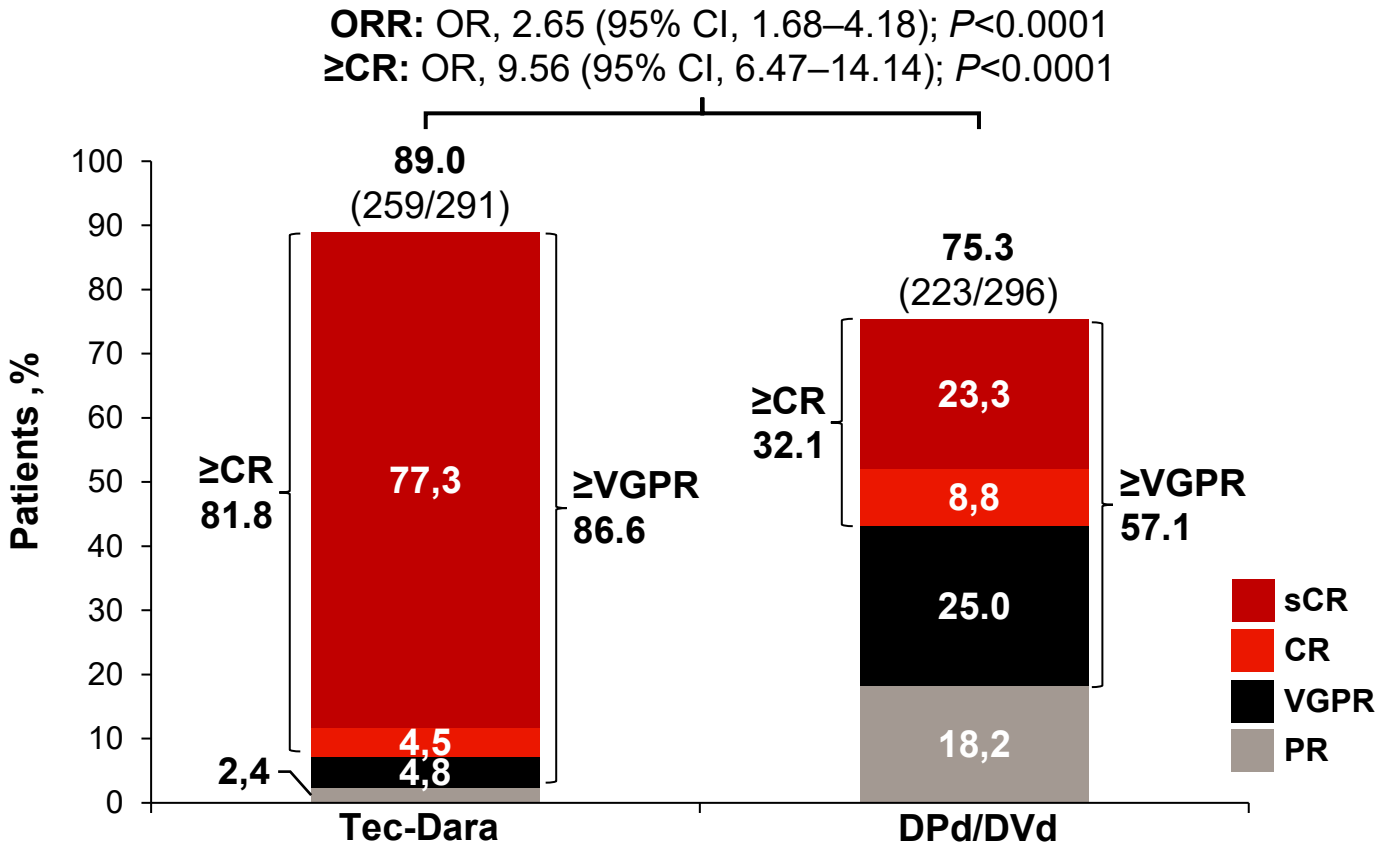
MajesTEC-3: Treatment Response[a] and Response Duration



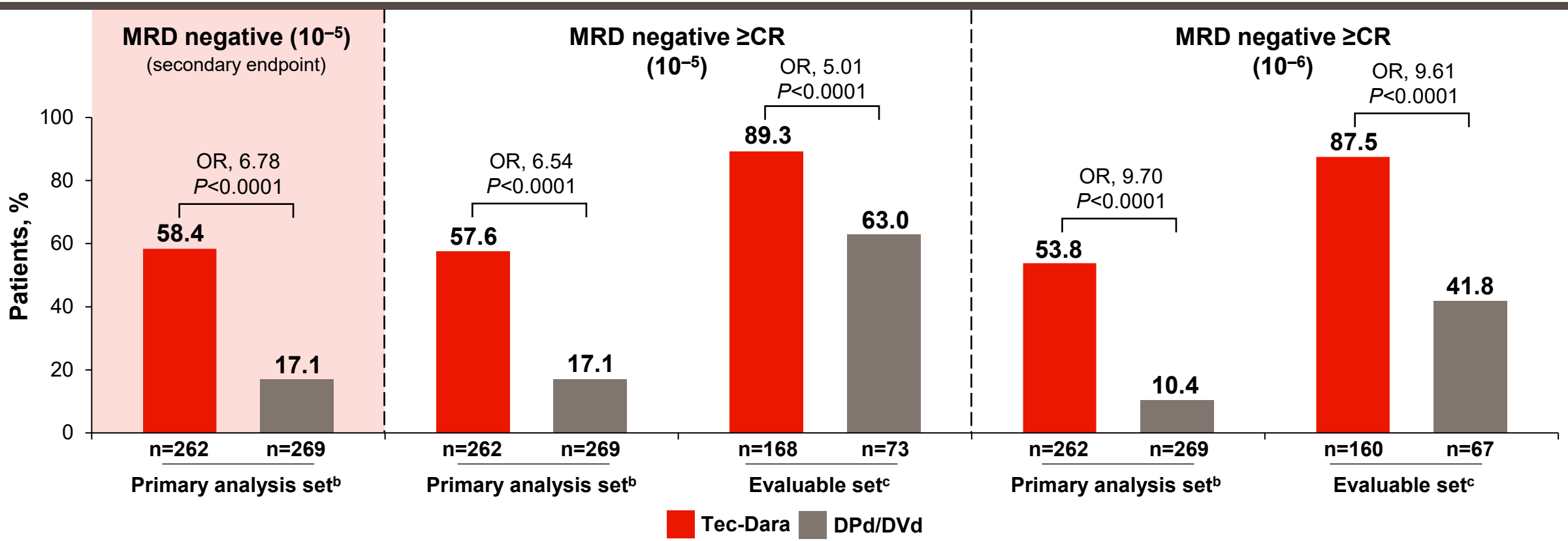
	Tec-Dara (n=259)	DPd/DVd (n=223)
Median (range) time to first response, months	1.2 (0.9–25.0)	1.2 (0.7–6.3)
Median (range) time to first ≥CR, months	6.9 (1.0–34.5)	6.9 (1.5–18.8)
Median (95% CI) DOR	NE (NE–NE)	23.5 (19.8–29.9)
36-month DOR, % (95% CI)	88.5 (83.7–92.0)	36.4 (28.9–43.9)

Tec-Dara demonstrated significantly higher ORR, ≥CR rate, and DOR versus DPd/DVd

Median follow-up, 34.5 months.
[a]Response and disease progression were assessed by an independent review committee in accordance with the International Myeloma Working Group response criteria.
CI, confidence interval; CR, complete response; Dara, daratumumab; DOR, duration of response; DPd/DVd, daratumumab and dexamethasone with either pomalidomide or bortezomib; NE, not estimable; OR, odds ratio; ORR, overall response rate; PR, partial response; sCR, stringent complete response; Tec, teclistamab; VGPR, very good partial response.

Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

MajesTEC-3: MRD Negativity[a]



Tec-Dara delivered significantly higher MRD-negative ≥CR rates versus DPd/DVd

Median follow-up: 34.5 months.

[a]MRD was assessed in the bone marrow by NGS in accordance with International Myeloma Working Group guidelines. [b]The MRD NGS primary analysis set was defined as all randomized patients in the study except those recruited in China (due to China instead utilizing NGF for MRD assessment). [c]The MRD NGS evaluable set was defined as patients who achieved ≥CR, had a successful baseline calibration, and had ≥1 post-baseline MRD sample with a positive or negative result (per NGS) at the indicated threshold.

CR, complete response; Dara, daratumumab; DPd/DVd, daratumumab and dexamethasone with either pomalidomide or bortezomib; MRD, minimal residual disease; NGF, next-generation flow; NGS, next-generation sequencing; OR, odds ratio; Tec, teclistamab.

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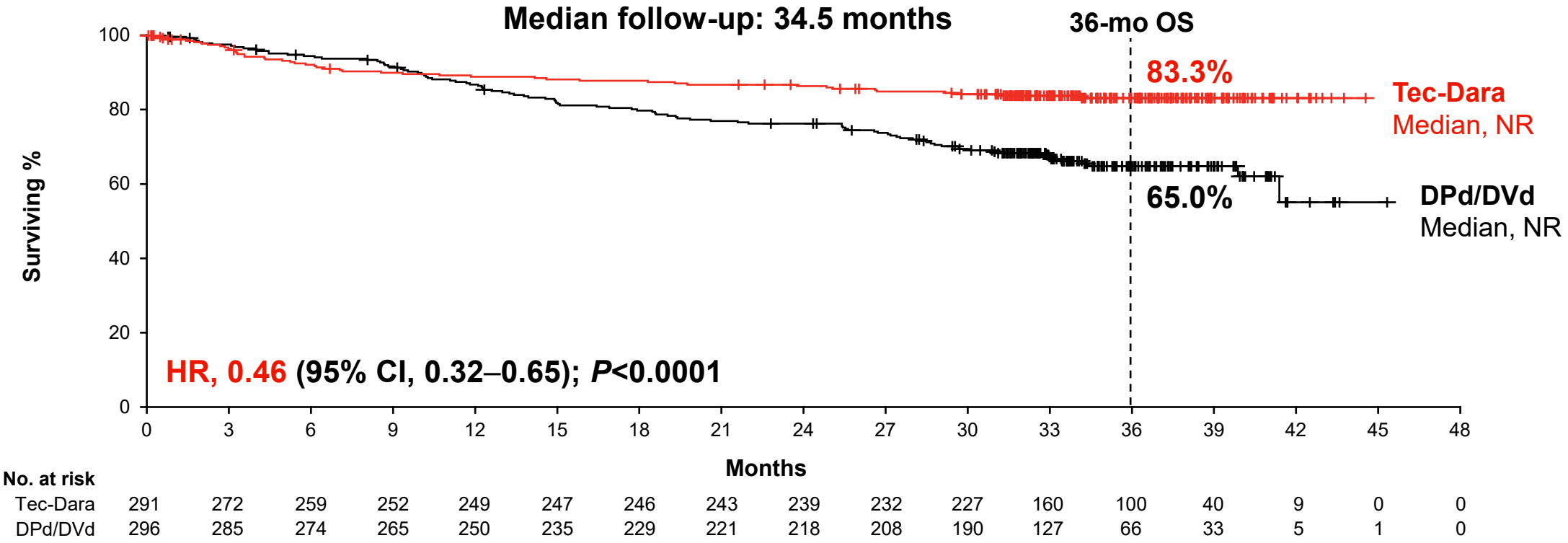
MajesTEC-3: OS



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

Anlaysis of RMST demonstrated an OS benefit for Tec-Dara versus DPd/DVd (RMST difference, 2.15 months; *P*=0.0088).
CI, confidence interval; Dara, daratumumab; DPd/DVd, daratumumab and dexamethasone with either pomalidomide or bortezomib; HR, hazard ratio; NR, not reached; OS, overall survival; RMST, restricted mean survival time; Tec, teclistamab.

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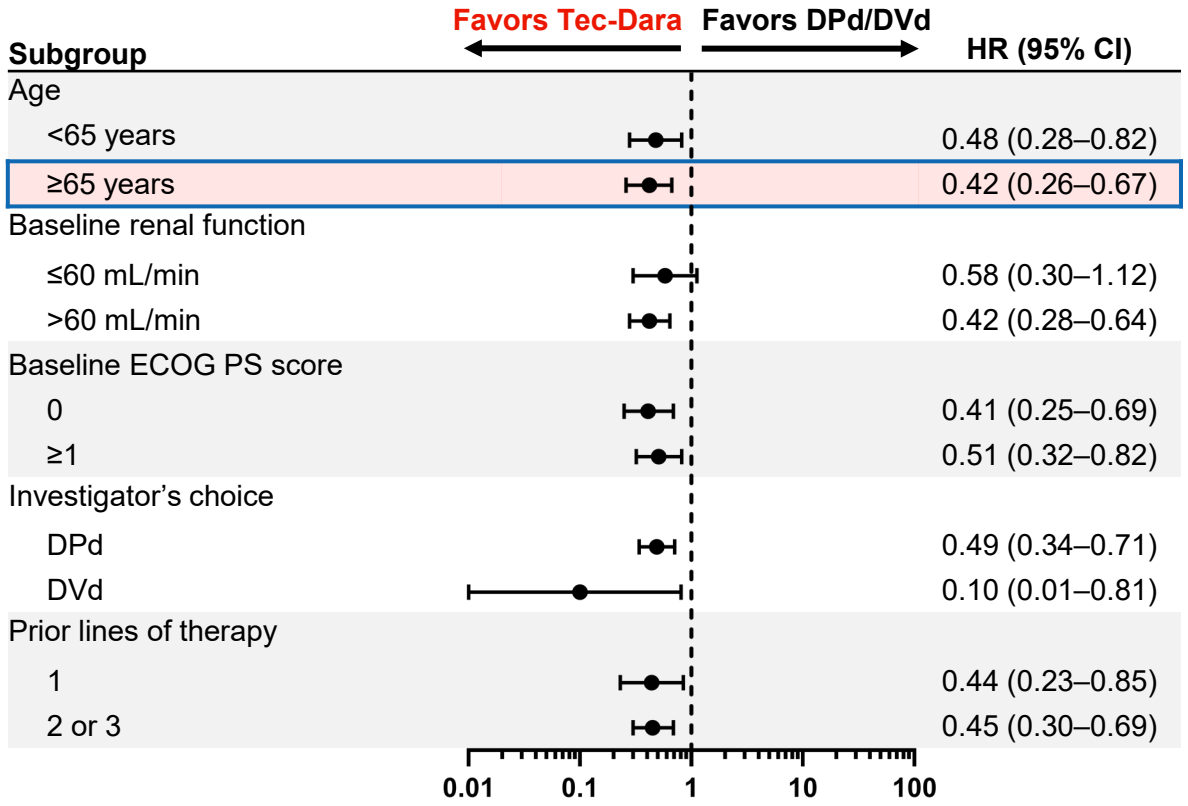
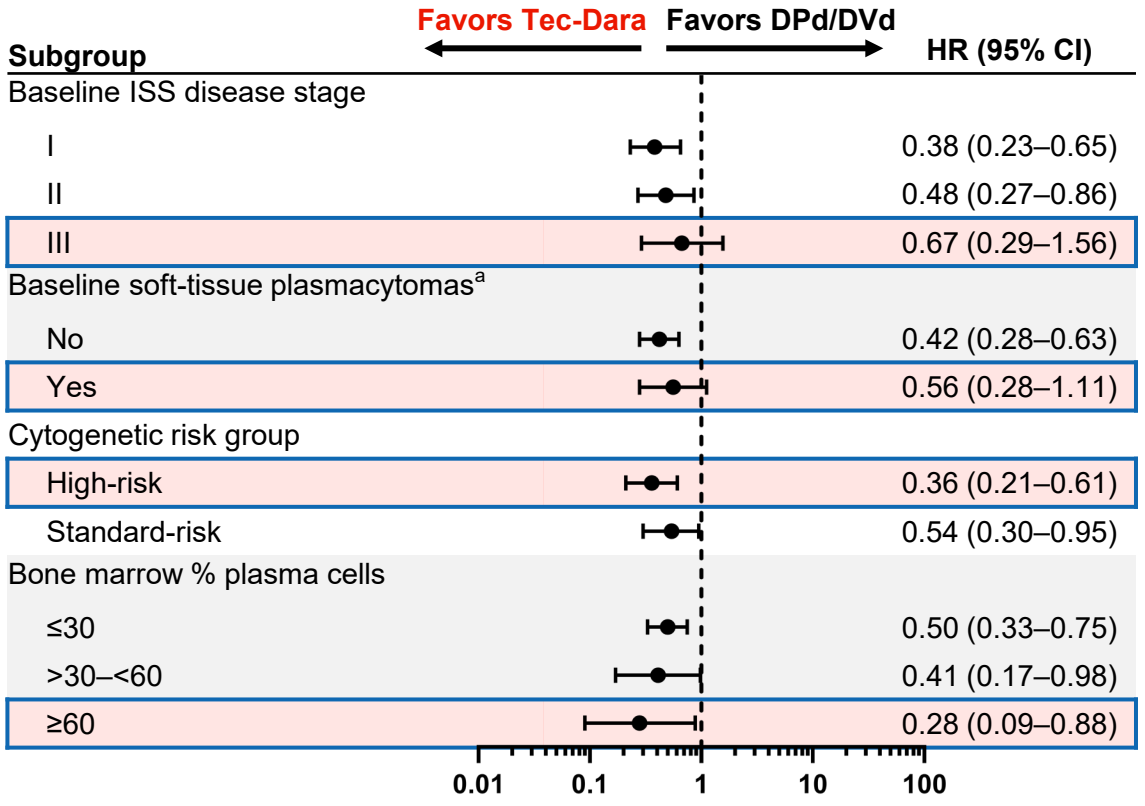
MajesTEC-3: OS Subgroup Analysis





OS was improved with Tec-Dara versus DPd/DVd across all prespecified subgroups[b]

[a]Baseline soft-tissue plasmacytomas contain both extramedullary and paraskeletal plasmacytomas. [b]Not all prespecified subgroups that were assessed are shown; however, OS was improved versus DPd/DVd across all subgroups. CI, confidence interval; Dara, daratumumab; DPd/DVd, daratumumab and dexamethasone with either pomalidomide or bortezomib; DPd, daratumumab, pomalidomide, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; ISS, International Staging System; OS, overall survival; Tec, teclistamab.

Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

MajesTEC-3: Overall Safety Profile

- Of CRS events, most were grade 1 (44.2%) and grade 2 events were low (15.9%)
  - All resolved, with no grade 2 events post–Cycle 1
- ICANS was low (1.1%)[a]; all resolved
- TEAE profile was generally comparable between Tec-Dara and DPd/DVd

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)

[a]Grade 2, n=2; Grade 4, n=1 (led to discontinuation of teclistamab). [b]Includes the most common TEAEs of any grade occurring in ≥30% of patients in either treatment group and the most common grade 3/4 TEAEs occurring in ≥10% of patients in either treatment group. [c]Hypogammaglobulinemia, COVID-19, COVID-19 pneumonia, URTI, and pneumonia were also reported but are discussed on the following summary of infections slide.
AE, adverse event; CRS, cytokine release syndrome; Dara, daratumumab; DPd/DVd, daratumumab and dexamethasone with either pomalidomide or bortezomib; ICANS, immune effector cell–associated neurotoxicity syndrome; OS, overall survival; Tec, teclistamab; TEAE, treatment-emergent adverse event; URTI, upper respiratory tract infection.

Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

MajesTEC-3: Summary of Infections

- Any grade infections were common and comparable; most common were COVID-19 and URTI
  - Grade 3/4 COVID-19–related infections were higher in the Tec-Dara group
- 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[b]
  - 12 occurred <6 months prior to implementation of reinforced IgRT and prophylaxis guidance per protocol amendment (Feb 2023)
  - 9 patients did not receive any IgRT

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)

After implementation of reinforced guidance on IgRT, 1 fatal infection occurred with Tec-Dara

[a]Hypogammaglobulinemia was defined as patients with ≥1 TEAE of hypogammaglobulinemia or a post-baseline IgG value <400 mg/dL. Rate of hypogammaglobulinemia in the DPd/DVd arm was 60.3% (n=175). [b]In the DPd/DVd group, 4 patients had a fatal infection, 2 of which occurred after the implementation of protocol amendment #6. [c]Protocol amendment #6 affirmed the importance of medical monitoring of IgG levels and adherence to protocol-specified Ig supplementation guidance. [d]Most common defined as occurring in ≥10% of patients in either treatment group; shown with percent occurrence of respective grade 3/4 infection.
Dara, daratumumab; DPd/DVd, daratumumab and dexamethasone with either pomalidomide or bortezomib; Ig, immunoglobulin; IgG, immunoglobulin G; IgRT, immunoglobulin replacement therapy; Tec, teclistamab; TEAE, treatment-emergent adverse event; URTI, upper respiratory tract infection.

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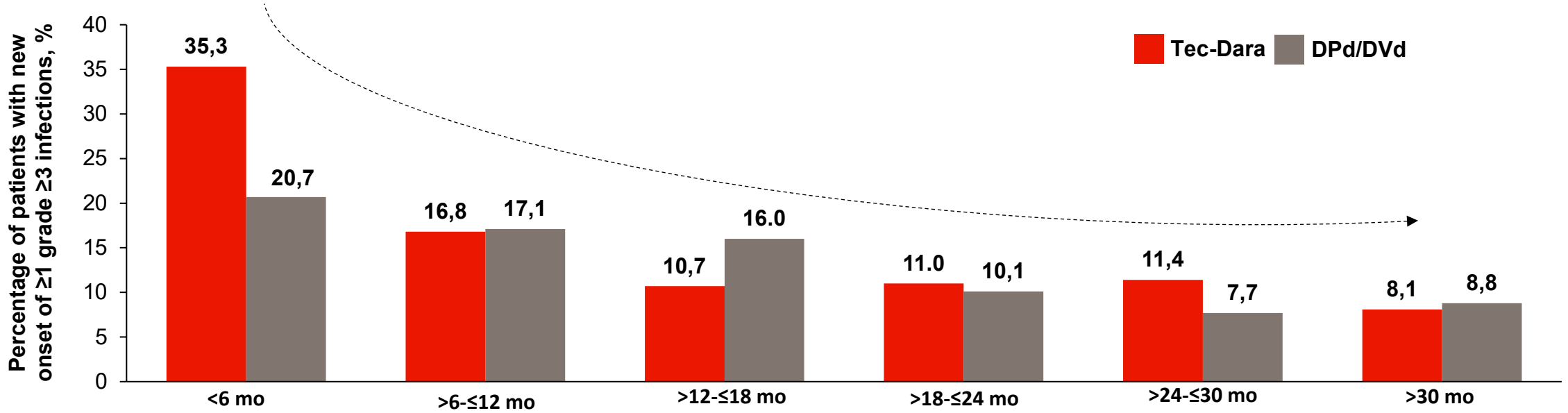
MajesTEC-3: Grade ≥3 Infections Over Time

- New-onset grade ≥3 infections decreased after 6 months of treatment



	<6 mo	>6-≤12 mo	>12-≤18 mo	>18-≤24 mo	>24-≤30 mo	>30 mo
Tec-Dara (n/N)[a]	100/283	41/244	25/233	24/219	24/210	16/197
DPd/DVd (n/N)[a]	60/290	39/228	28/175	14/138	9/117	8/91

Infection rates were comparable across groups from 6 months and substantially decreased over time

[a]Includes patients who are in the TEAE-reporting period for the specific window. Noting that patients are counted only once in a window for any given event, regardless of the number of times they actually experienced the event within the specific time window.
Dara, daratumumab; DPd/DVd, daratumumab and dexamethasone with either pomalidomide or bortezomib; TEAE, treatment-emergent adverse event; Tec, teclistamab.

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MajesTEC-3: Conclusions

Tec-Dara versus DPd/DVd in 1–3 prior LOTs in RRMM demonstrated:

- Significant improvement in PFS with lowest HR to date, 0.17[1-5] and 36-mo PFS of 83.4%; consistent benefit observed across subgroups
- Significant improvement in OS (HR, 0.46); plateau at ~6 mo suggesting potential for functional cure in sustained responders
- More than double the rates of ≥CR, MRD-negative ≥CR at 10^{-6}, and 36-mo DOR
- Significant improvement in HRQoL (HR, 0.50), with patients living longer without MM symptoms getting worse
- A well-characterized safety profile in which infections were common; serious infections were controlled with robust Ig replacement and prophylaxis
- A low rate of grade 2 CRS that was manageable with tocilizumab
- Convenience of administration per Dara-approved dosing schedule that is familiar for health care providers, making Tec-Dara a synergistic immunotherapy amenable to medical adoption in the community

Unprecedented PFS and OS support Tec-Dara as a new 2L+ immunotherapy-based SOC across academic/community settings

2L+, second-line and beyond; CR, complete response; CRS, cytokine release syndrome; Dara, daratumumab; DOR, duration of response; DPd/DVd, daratumumab and dexamethasone with either pomalidomide or bortezomib; HR, hazard ratio; HRQoL, health-related quality of life; Ig, immunoglobulin; LOT, line of therapy; MM, multiple myeloma; MRD, minimal residual disease; OS, overall survival; PFS, progression-free survival; RRMM, relapsed refractory multiple myeloma; SOC, standard of care; Tec, teclistamab.

1. San-Miguel J, et al. *N Engl J Med*. 2023;389:335-347. 2. Usmani SZ, et al. *Blood Adv*. 2023;7:3737-3748. 3. Hungria V, et al. *N Engl J Med*. 2024;391:393-407. 4. Dimopoulos MA, et al. *N Engl J Med*. 2024;391:408-421. 5. Martin T, et al. *Blood Cancer J*. 2023;13:72.

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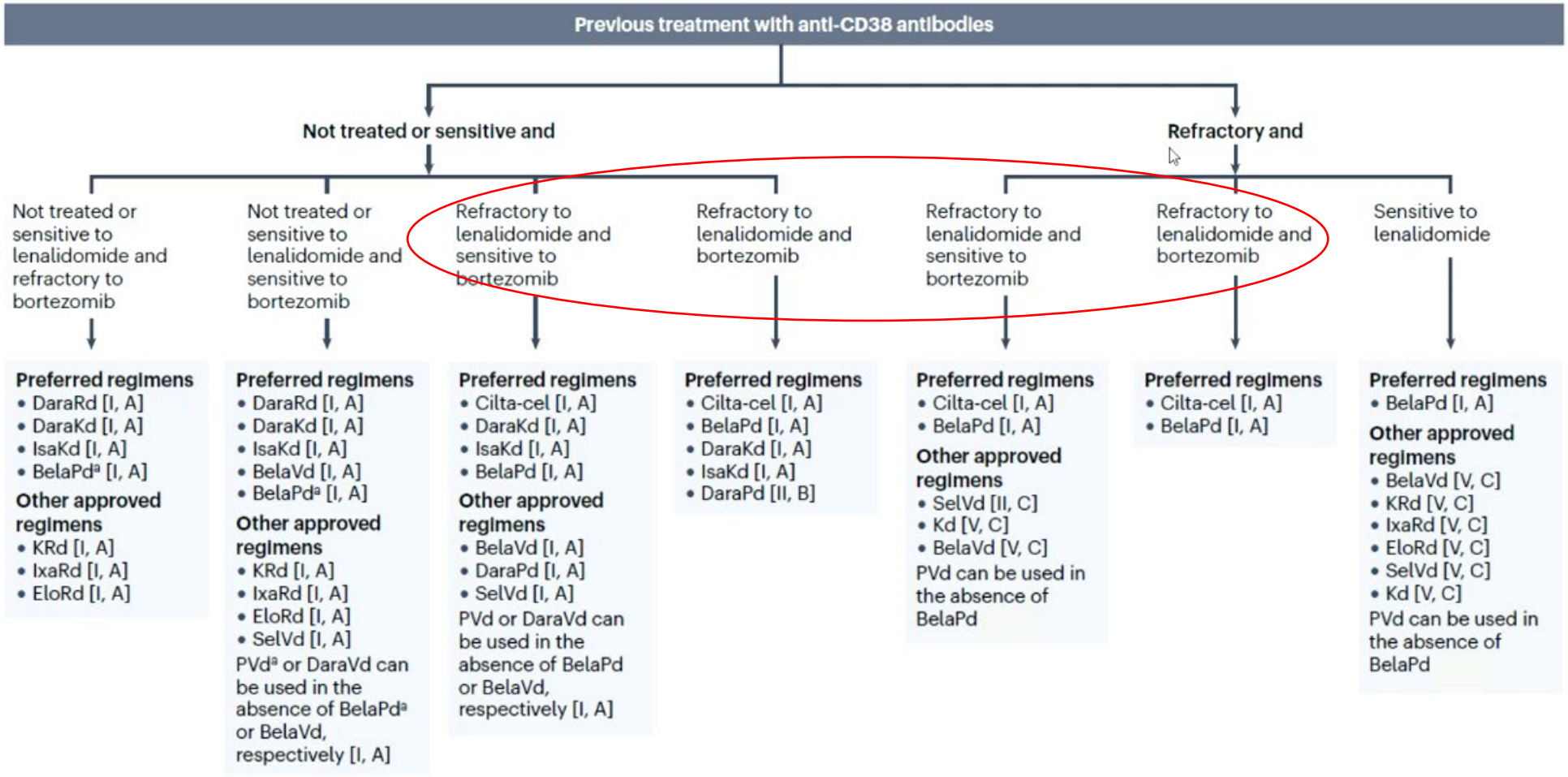
EHA/EMN Guidelines 2025 – Secondline therapy

Tec-Dara



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]*, María-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]

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*Contributed equally

Presented by S Usmani at the 67th American Society of Hematology (ASH) Annual Meeting; December 6–9, 2025; Orlando, Florida, USA

EMD is associated with poor survival in myeloma

BONE DEPENDENT

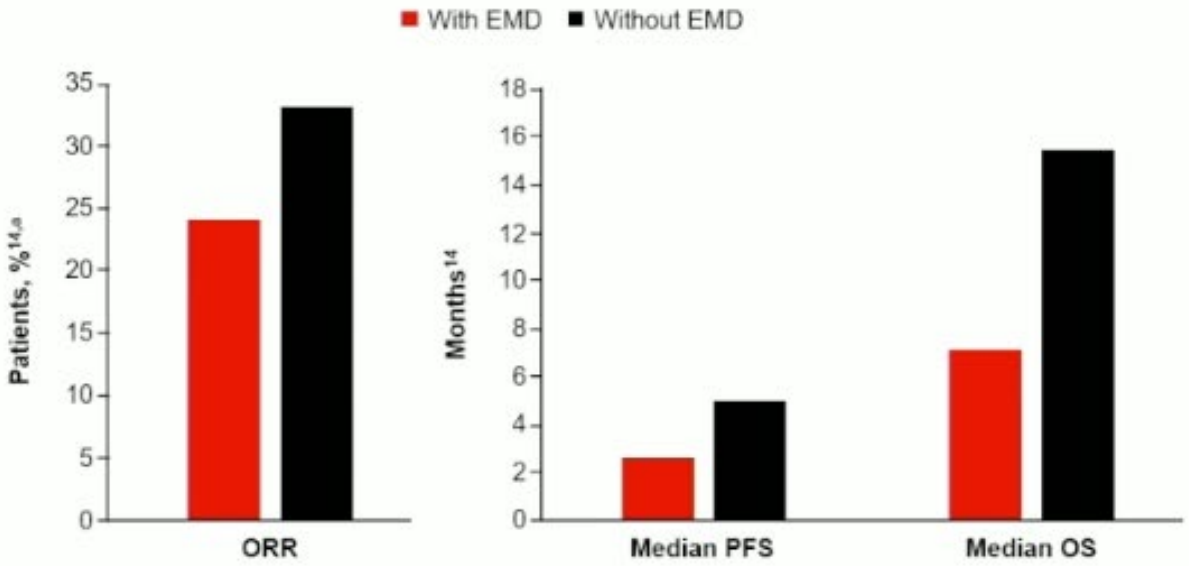
Paramedullary disease[1,2]
Plasmacytomas growing contiguously with bone and extending into soft tissue after cortical disruption

BONE INDEPENDENT

True EMD[1,2]
Soft tissue/organ-associated plasmacytomas noncontiguous with bony structures

Inferior outcomes vs patients with paramedullary plasmacytomas and patients with myeloma without EMD[3-14]

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]

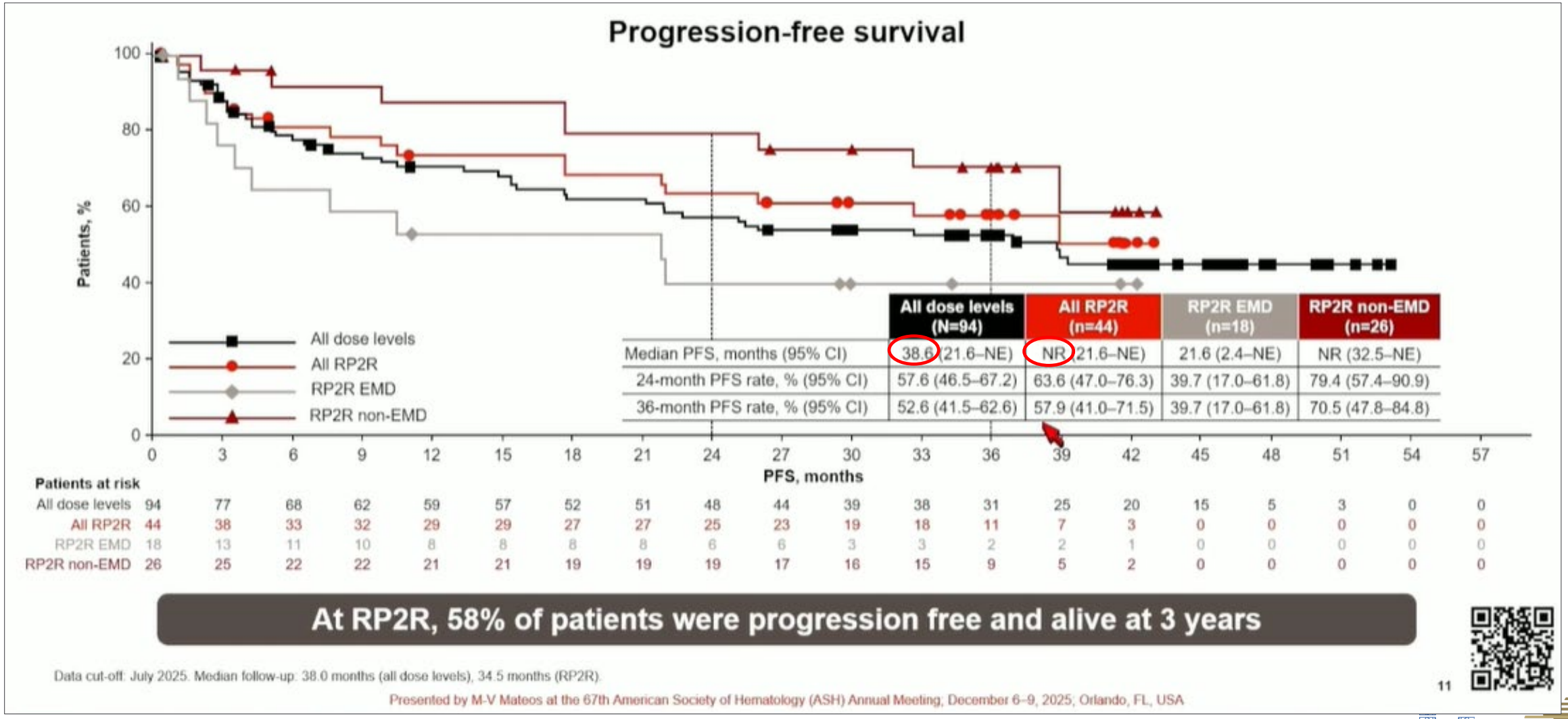


[a]Defined as the proportion of patients who achieved a PR or better. ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; SOC, standard-of-care.

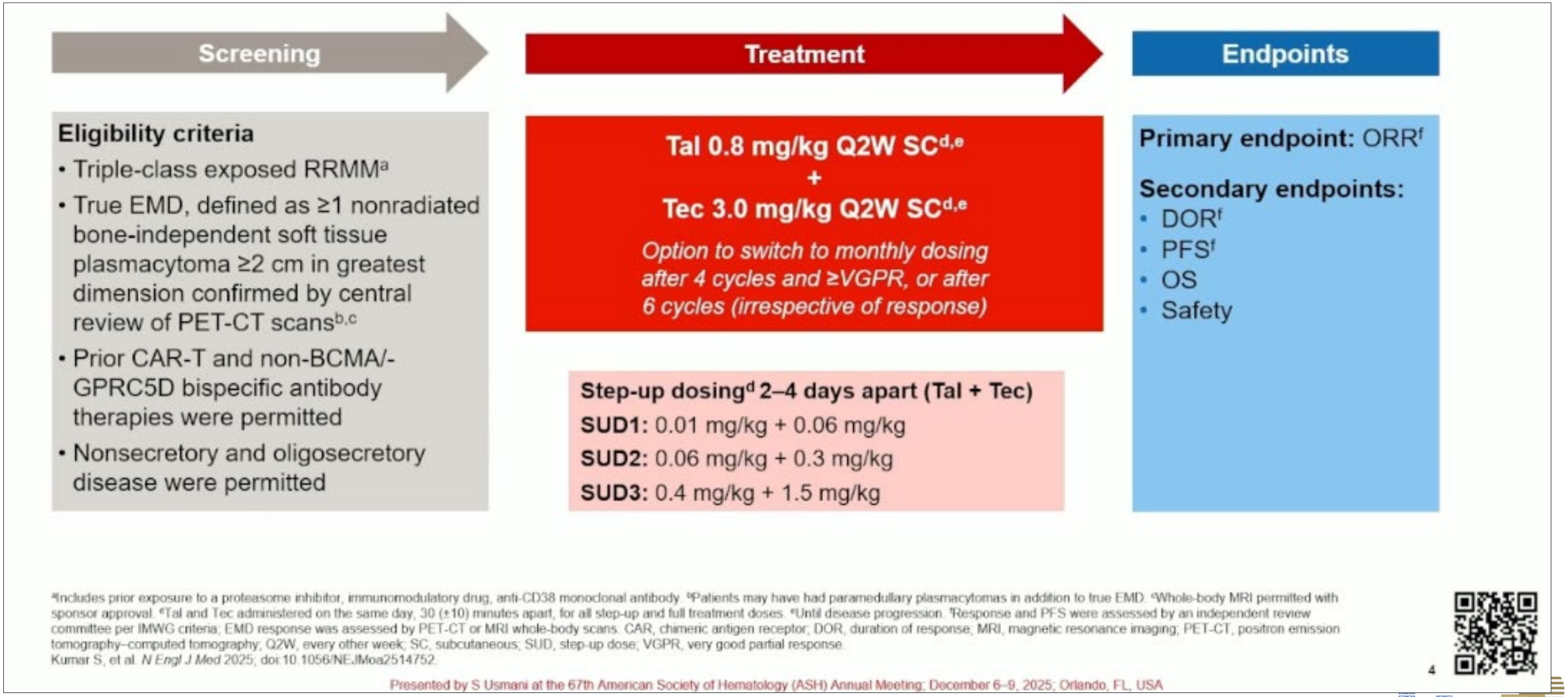
1. Ho M, et al. *Curr Oncol* 2025;32:182. 2. Bladé J, et al. *Blood Cancer J* 2022;12:45. 3. Rosiñol L, et al. *Br J Haematol* 2021;194:496-507. 4. Pour L, et al. *Haematologica* 2014;99:360-4. 5. Mangiacavalli S, et al. *Ann Hematol* 2017;96:73–80. 6. Rasche L, et al. *Ann Hematol* 2012;91:1031-7. 7. Richard S, et al. *Blood* 2022;140(Suppl 1):4301-2. 8. Pan D, et al. *Blood* 2023;142(Suppl 1):1006. 9. Dima D, et al. *Blood Cancer J* 2024;14:90. 10. Zanwar S, et al. *J Hematol Oncol* 2024;17:42. 11. Usmani SZ, et al. *Haematologica* 2012;97:1761-7. 12. Beksac M, et al. *Haematologica* 2020;105:201-8. 13. Voorhees PM, et al. *Ann Hematol* 2025; doi: 10.1007/s00277-025-06705-3. 14. Moreau P, et al. *Clin Lymphoma Myeloma Leuk* 2025:S2152-2650(25)00106-5.

Presented by S Usmani at the 67th American Society of Hematology (ASH) Annual Meeting; December 6–9, 2025; Orlando, FL, USA

RedirecTT-1 Phase 1b – mPFS at 38 mo follow up



RedirecTT-1 Phase 2 EMD: largest dedicated study in patients with true EMD



[a]Includes prior exposure to a proteasome inhibitor, immunomodulatory drug, anti-CD38 monoclonal antibody. [b]Patients may have had paramedullary plasmacytomas in addition to true EMD. [c]Whole-body MRI permitted with sponsor approval. [d]Tal and Tec administered on the same day, 30 (±10) minutes apart, for all step-up and full treatment doses. [e]Until disease progression. [f]Response and PFS were assessed by an independent review committee per IMWG criteria; EMD response was assessed by PET-CT or MRI whole-body scans. CAR, chimeric antigen receptor; DOR, duration of response; MRI, magnetic resonance imaging; PET-CT, positron emission tomography–computed tomography; Q2W, every other week; SC, subcutaneous; SUD, step-up dose; VGPR, very good partial response.

Kumar S, et al. *N Engl J Med* 2025; doi:10.1056/NEJMoa2514752.

Presented by S Usmani at the 67th American Society of Hematology (ASH) Annual Meeting; December 6–9, 2025; Orlando, FL, USA

RedirecTT-1: Baseline characteristics

Characteristic	All Patients (N = 90)
Median age, yr (range)	64.5 (42-84)
Male, %	63.3
Median years since diagnosis, yr (range)	4.7 (0.7-21.4)
Median number prior LOT, n (range)	4 (1-10)
EMD location, n of tumors (%)	
▪ Lymph node	95 (42.2)
▪ Organ	63 (35.6)
▪ Soft tissue	78 (56.7)
▪ Paramedullary	32 (23.3)
EMD tumor volume (%)	
▪ <25 cm^2	47.8
▪ 25-50 cm^2	23.3
▪ >50 cm^2	28.9

Characteristic, %	All Patients (N = 90)
Measurable disease	
▪ Nonsecretory disease	4.4
▪ Oligosecretory disease	34.4
Prior treatment	
▪ Belantamab mafodotin	12.2
▪ Anti-BCMA CAR T-cell therapy	20.0
▪ Anti-FcRH5 BsAb	8.9
Refractory status	
▪ Triple class	84.4
▪ Penta drug	35.6
▪ Refractory to last LOT	83.3

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Usmani. ASH 2025. Abstr 698. Kumar. NEJM. 2025; 2514752.

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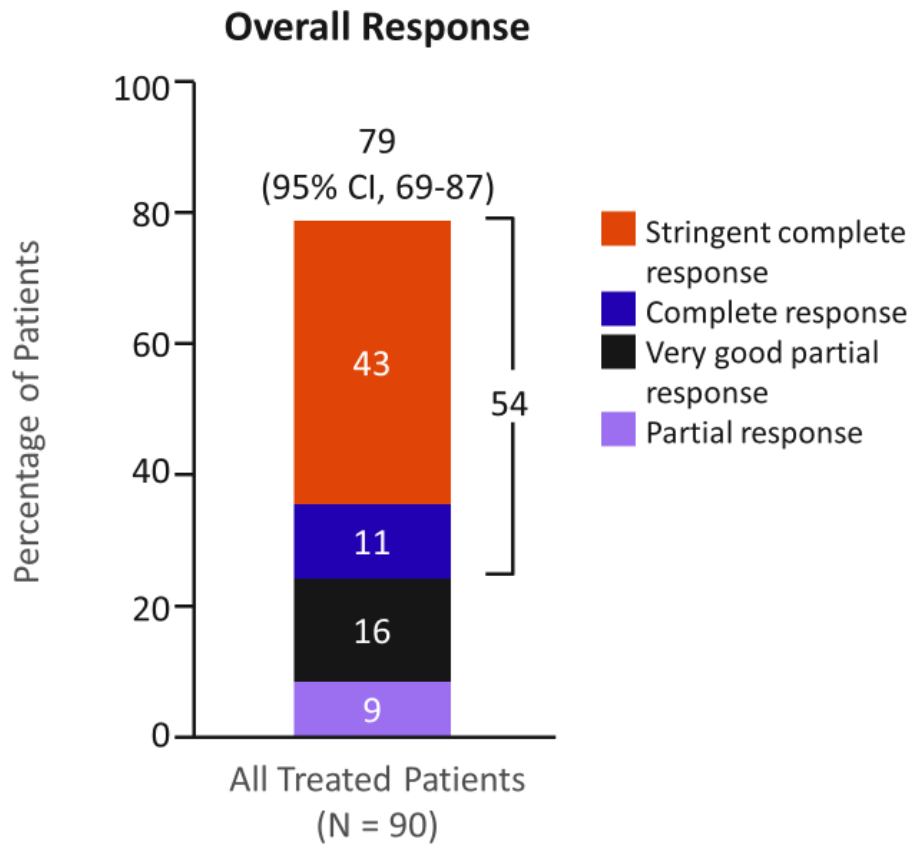
RedirecTT-1: Efficacy (after 16,8 mo med follow up)



Parameter	All Patients (N = 90)
Median DoR, mos (95% CI)	NR (11.5-NE)
12-mo DoR, % (95% CI)	62.1 (49.0-72.7)
Median time to first response, mo (range)	2.6 (1.0-5.8)
Median time to best response, mo (range)	5.1 (1.0-16.6)
Median PFS, mo (95% CI)	15.0 (10.3-NE)
12-mo PFS, % (95% CI)	57.5 (46.4-67.1)
Median OS, mo (95% CI)	NR (19.7-NE)
12-mo OS, % (95% CI)	73.8 (63.3-81.8)

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RedirecTT-1: Responses by subgroups

Parameter, % (95% CI)	All Patients (N = 90)	Organ EMD* (n = 32)	Nonorgan EMD† (n = 58)	Baseline EMD Tumor Volume		
				< 25 cm^2 (n = 43)	25-50 cm^2 (n = 21)	>50 cm^2 (n = 26)
ORR	79 (69-87)	78 (60-91)	79 (67-89)	93 (81-99)	67 (43-85)	65(44-83)
sCR	44	47	43	51	43	35
CR	9	9	9	7	14	8
VGPR	17	16	17	21	10	15
PR	9	6	10	14	0	8
≥CR	53	56	52	58	57	42

*Organ EMD: kidney, liver, lung, and others.
†Nonorgan EMD: lymph node and soft tissue.

- mDoR for patients with organ EMD was not reached
- mDoR for patients with nonorgan EMD was 15.4 mo

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Usmani. ASH 2025. Abstr 698. Kumar. NEJM. 2025; 2514752.

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RedirecTT-1: Safety

AEs in ≥30% of Patients, %	All Patients (N = 90)	
	Any Grade	Grade 3/4
Neutropenia	72.2	63.3
Anemia	53.3	33.3
Thrombocytopenia	37.8	25.6
Oral AEs	86.7	4.4
Infections	80.0	33.3
CRS	77.8	0
Non-rash skin	68.9	0
Nail-related	55.6	0
Weight decrease	53.3	12.2
Cough	40.0	0
Diarrhea	37.8	4.4
Nausea	32.2	0
Hypokalemia	31.1	7.8
Pyrexia	31.1	1.1
Rash related	31.1	1.1
Fatigue	30.0	3.3

Outcome, n (%)	Initial Q2W Dosing (N = 90)	After Adjustment to Q4W Dosing (n = 56)
All infections	65 (72.2)	34 (60.7)
▪ Grade ≥3 infections	29 (32.2)	14 (25.0)
Weight decrease	46 (51.1)	15 (26.8)
▪ Grade 3/4 weight decrease	8 (8.9)	5 (8.9)
Oral Aes	77 (85.6)	12 (21.4)
▪ Grade 3/4 oral AEs	3 (3.3)	2 (3.6)

- 11 patients had grade 5 AEs; 6 were drug related; 7 were nonresponders with poor prognosis
- 8.9% of patients discontinued either drug due to AEs

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RedirecTT-1: Infections

Infections, n (%)	All Patients (N = 90)[1]	
	Any Grade	Grade 3/4
Any	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 URTI	9 (10.0)	2 (2.2)

- Grade 3/4 infections primarily occurred in the first 6 mo
  - Grade 3/4 infection rate was consistent with teclistamab monotherapy[2]
- Median duration of infection: 13.0 days
- Immunoglobulin <400 mg/dL in 22.2% of patients at baseline
- Posttreatment hypogammaglobulinemia reported in 71.1% of patients
- 75.6% of patients received immunoglobulin replacement, which was recommended for infection prophylaxis

Grade 5 Opportunistic Infections, n (%)	Study Day of Death	IgG Level Prior to Death, mg/dL	Received ≥1 Dose of Ig Replacement	Response at Time of Death
Klebsiella sepsis	38	70	No	PR
COVID-19 Pneumonia	63	2455	No	SD
Klebsiella pneumonia	86	892	Yes	PR
Pseudomonal sepsis	190	246	No	PR
Escherichia sepsis	240	449	Yes	VGPR
Pneumonia	254	346	Yes	PD

1. Usmani. ASH 2025. Abstr 698. 2. Moreau. NEJM. 2022;387:495. Kumar. NEJM. 2025; 2514752.

RedirecTT-1: Conclusions

TCE-RRMM mit EMD:

- ORR: 79%; 12-mo DoR rate 62.1%; mPFS 15.0 mo; 12-mo OS rate 73.8%

- Lower EMD tumor volume correlated with a higher ORR

- Safety profile was consistent with individual agents, including infections that required prophylaxis and management

- Investigators conclude that this combination may be a new standard of care for patients with triple class–exposed R/R MM with true EMD

Zusammenfassung

1. inMMyCAR (KLN-1010):

   in-vivo generierte CAR-T-Zellen, keine Lymphodepletion notwendig, off-the-shelf, vergleichbares Safety-Profil zu ex-vivo CAR-T Zellen, weniger Zytopenien. 100% MRD Negativität nach 3 Monaten

2. MajesTEC-3:

   36-mo PFS von 83.4% (Tec-Dara), verbessertes OS mit Plateaubildung nach ~6 mo, konsequente Ig-Substitution zur Vermeidung schwerer Infektionen

   → *Zulassung in der Secondline Therapie zu erwarten*

   → *Breakthrough therapy designation granted by FDA*

3. RedirecTT-1 (TEC-TAL, EMD-Kohorte):

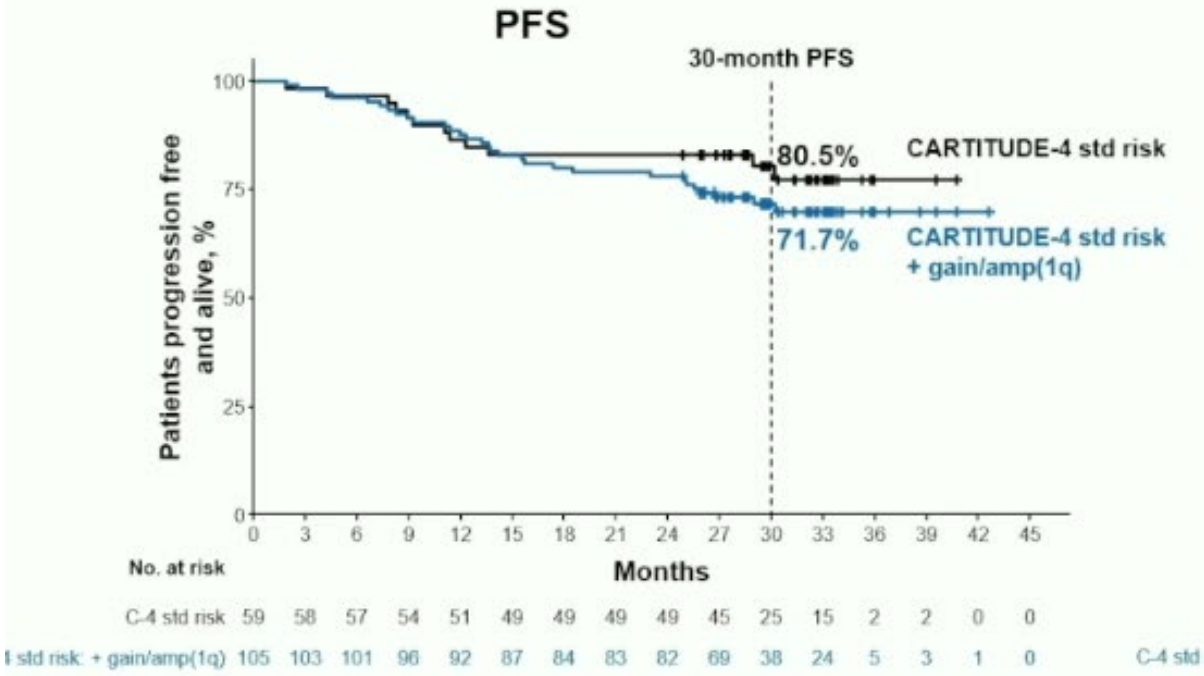
   ORR: 79%; 12-mo DoR bei 62.1%; mPFS 15.0 mo; 12-mo OS rate 73.8%

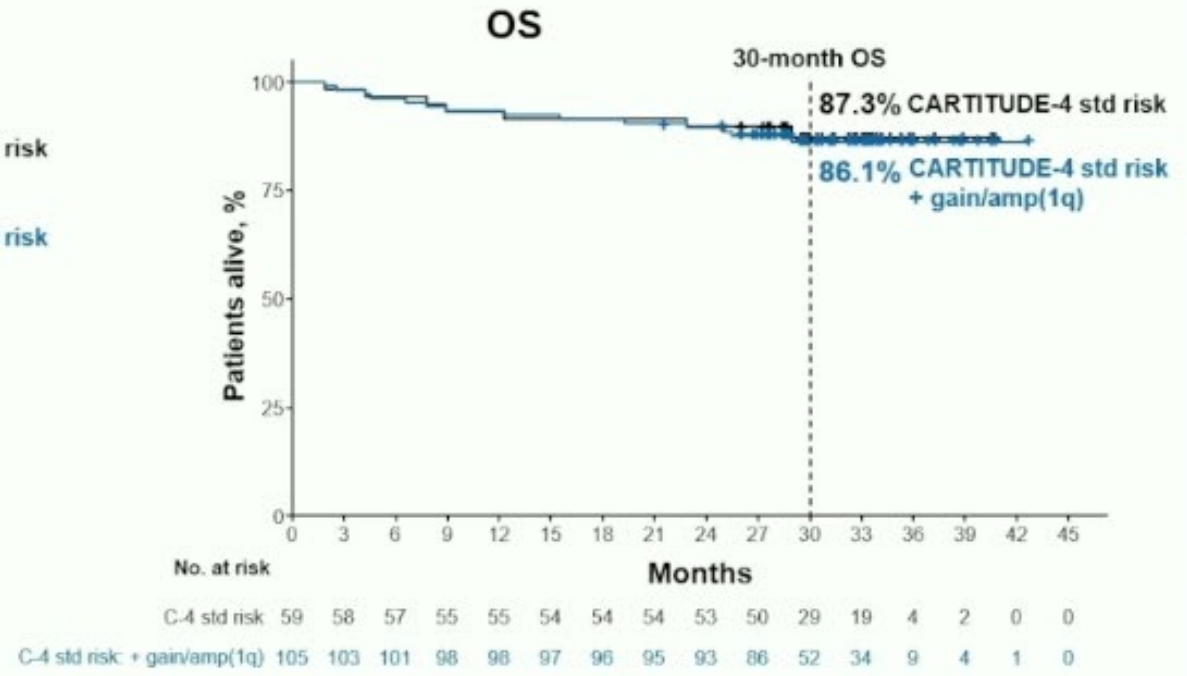
   Tumorvolumen korreliert mit ORR

   wird als neuer Standard für triple class–exposed R/R MM mit EMD diskutiert

Vielen Dank für ihre Aufmerksamkeit

CARTITUDE-4: PFS and OS in Patients With Standard-Risk Cytogenetics (As-Treated)





Summary of Cilta-cel Outcomes in Standard-Risk Myeloma (As-Treated Population)

	30-month PFS rate, %	30-month OS rate, %
CARTITUDE-4 (median 2 prior lines)		
Cilta-cel *Standard-risk cytogenetics per protocol*	80.5	87.3
Cilta-cel *Standard-risk cytogenetics per protocol + gain/amp(1q)*	71.7	86.1
CARTITUDE-1 (median 6 prior lines)		
Cilta-cel *Standard-risk cytogenetics per protocol including gain/amp(1q)*	59.9	70.6

Earlier use of cilta-cel in standard-risk RRMM led to higher survival rates

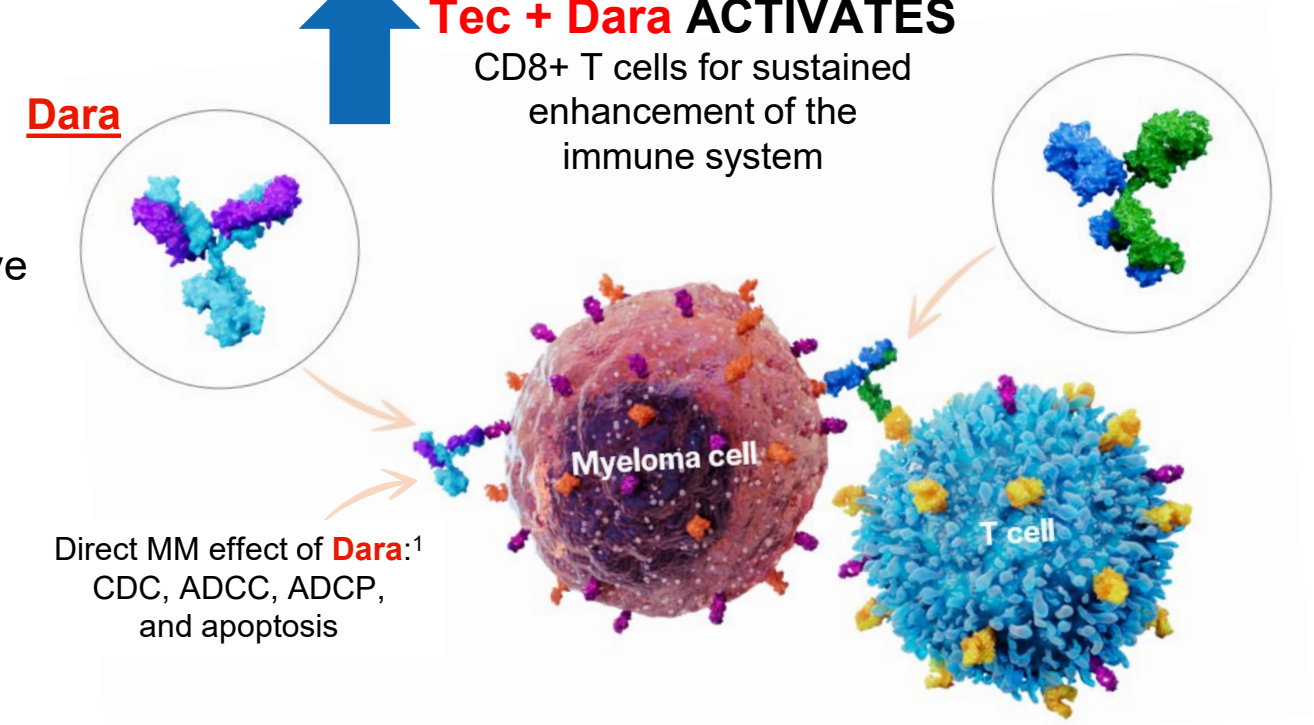
Presented by L Costa at the 67th American Society of Hematology (ASH) Annual Meeting; December 6–9, 2025; Orlando, FL, USA

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.

Presented by M-V Mateos at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL, USA.

RediredTT-1

- True extramedullary disease, characterized by soft tissue or organ-associated plasmacytomas noncontiguous with bony structures, is associated with poor prognosis in patients with R/R MM[1,2]

- GPRC5D and BCMA are heterogeneously expressed on EMD lesions, suggesting a rationale for a dual targeting approach[3]

- Phase II RedirecTT-1 trial is evaluating the combination of the anti-GPRC5D bispecific antibody talquetamab (tal) and the anti-BCMA bispecific antibody teclistamab (tec) in patients with R/R MM

  In primary analysis of phase II EMD cohort from RedirecTT-1 trial, tal + tec showed ORR (IRC) of 79% and 12-mo PFS of 61% after a median follow-up of 12.6 mo[4]

- Current analysis reports outcomes in the EMD cohort after a longer median follow-up of 16.8 mo, by EMD location, and the value of new tumor burden assessment as a prognostic indicator of response[5]

1. Moreau. Clin Lymphoma Myeloma Leuk. 2025;25:646. 2. Ho. Curr Oncol. 2025; 32:182. 3. John. Blood. 2024;144:2121-2135. 4. Kumar. NEJM. 2025; 2514752. 5. Usmani. ASH 2025. Abstr 698.