4th edition

Unmet challenges in high risk hematological malignancies: from benchside to clinical practice

Turin, March 26-27, 2026

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Bispecific antibodies: roles in real life

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Disclosures of Karthik Ramasamy

Research support from: Celgene(BMS), Takeda, Janssen, Amgen, GSK, Pfizer

Speaker fees from: Celgene (BMS), Takeda, Sanofi, Recordati Rare Diseases, Menarini Stemline, Janssen, Pfizer, GSK, Adaptive Biotech

Advisory board support from: Astra Zeneca, Celgene (BMS), Takeda, Janssen, Amgen, AbbVie, Sanofi, Oncopeptides, Karyopharm, GSK, Recordati Rare Diseases, Pfizer, Thermofisher (The Binding site), Kite Pharma

Travel fees from: Takeda, Amgen, Menarini Stemline

Overview

- Clinically Accessible
- Clinical efficacy in routine care
- Interventions to Manage toxicity with Bispecifics
- Bispecifics as platform to augment outcomes
- Novel methodologies to overcome resistance challenges and tumour heterogeneity

Access to Bispecific antibody therapy in MM

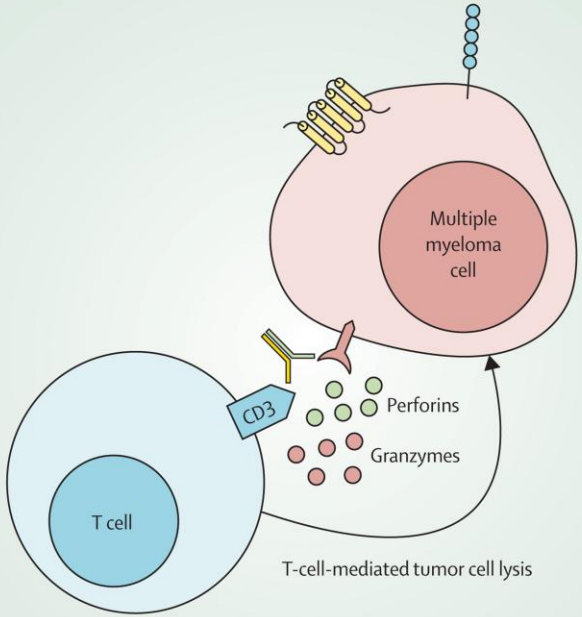
Country	Teclistamab	Elranatamab	Talquetamab	Linvoseltamab
US	Routine	Routine	Routine	Routine
UK	Routine	Managed	Routine	Not routine / pending
Germany	Routine	Routine	Routine	EMA Approved / variable
France	Routine	Routine	Routine	EMA Approved / variable
Italy	EMA Approved / variable	EMA Approved / variable	EMA Approved / variable	EMA Approved / variable
Spain	EMA Approved / variable	EMA Approved / variable	EMA Approved / variable	EMA Approved / variable
Canada	Approved / variable	Approved / variable	Approved / variable	Not routine / not identified
Australia	Approved / variable	Approved / variable	Approved / variable	Not routine / not identified
Japan	Not routine / pending	Routine	Routine	Not routine / not identified

Targets and off the shelf sequencing

BCMA-targeting bispecific antibodies
- Teclistamab*
  RP2D: ≥PR 63%; CR 46%; median PFS 11 months
- Elranatamab*
  RP2D: ≥PR 61%; CR 35%; median PFS not reached
  (PFS at 15 months: 50·9%)
- Linvoseltamab
  RP2D: ≥PR 71%; CR 30%
- ABBV-383
  RP2D: ≥PR 65%; CR 5%; median PFS not reached
- Alnuctamab
  30 mg SC: ≥PR 67%; CR 44%; median PFS 11·4 months
- HPN217
  RP2D: ≥PR 63%; CR 21%

FcRH5-targeting bispecific antibodies
- Cevostamab
  132–198 mg: ≥PR 56·7%; CR 8·4%

GPRC5D-targeting bispecific antibodies
- Talquetamab*
  Two RP2Ds
  400 µg/kg Q1W: ≥PR 74%; CR 34%; median PFS 7·5 months
  800 µg/kg Q2W: ≥PR 72%; CR 39%; median PFS 14·2 months
- Forimtamig
  Intravenous group: ≥PR 71%; CR 35%
  Subcutaneous group: ≥PR 64%; CR 26%



BCMA
- Member of the TNF receptor superfamily; critical role in differentiation of normal B cells to plasma cells
- Highly expressed on multiple myeloma cells
- Normal tissue expression: mature B cells, normal plasma cells, and plasmacytoid dendritic cells

FcRH5
- Biological function unknown; member of the immunoglobulin receptor superfamily
- Highly expressed on multiple myeloma cells
- Normal tissue expression: B-cell lineage, including normal plasma cells

GPRC5D
- Orphan G-protein-coupled receptor with unknown function
- Expression levels significantly higher on multiple myeloma cells than on normal plasma cells
- Normal tissue expression: normal plasma cells, and cells that produce hard keratin, such as in hair follicles

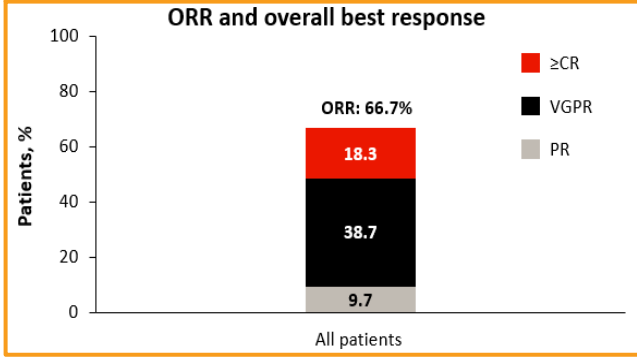
Van de Donk Lancet Haem 2024

The REALiTAL study

REALiTAL study key facts

- Retrospective, non-interventional study in 7 countries to describe the management and outcomes of patients treated with talquetamab in R/R MM outside of clinical trials
- N=93, heavily pre-treated; 86.0% penta-class exposed (97.8% triple-class exposed), 61.3% previously received anti-BCMA treatments. 72.9% of patients had high-risk cytogenetics at baseline*
- Median follow-up 15.0 (range, 0.4–25.3) months

REALiTAL study results



Results by VGPR status	Overall	≥VGPR	<VGPR
Median DoR months	12.3 (95% CI, 7.9–NE)	13.4 (95% CI, 8.3–NE)	6.8 (95% CI, 1.45–NE)
Median PFS months	8.2 (95% CI, 6.1–10.7)	18.2 (95% CI, 10.6–NE)	2.9 (95% CI, 2.2–4.1)
Median OS months	25.3 (95% CI, 17.3–NE)	25.3 (95% CI, NE–NE)	11.5 (95% CI, 6.3–NE)

REALiTAL safety data

- No new safety signals were identified; the safety profile was consistent with that previously reported
  - Most common TEAEs were skin/nail toxicity, oral toxicity, CRS and infections
  - Discontinuation of treatment due to AEs was n=5
  - All but 1 CRS events resolved/were resolving at the time of data collection

Results aligned with previous studies, deep response to talquetamab was associated with prolonged PFS and OS in hard-to-treat, heavily pre-treated patients with R/R MM

*Presence of t(4;14), t(14;16), del17o13 and amp1q21.

AE, adverse event; BCMA, B-cell maturation antigen; CI, confidence interval; CR, complete response; CRS, cytokine release syndrome; DoR, duration of response; NE, not estimable; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; R/R MM, relapsed/refractory multiple myeloma; TEAE, treatment-emergent adverse event; VGPR, very good partial response.

Uttervall K, et al. EHA 2025. Poster presentation PF742.

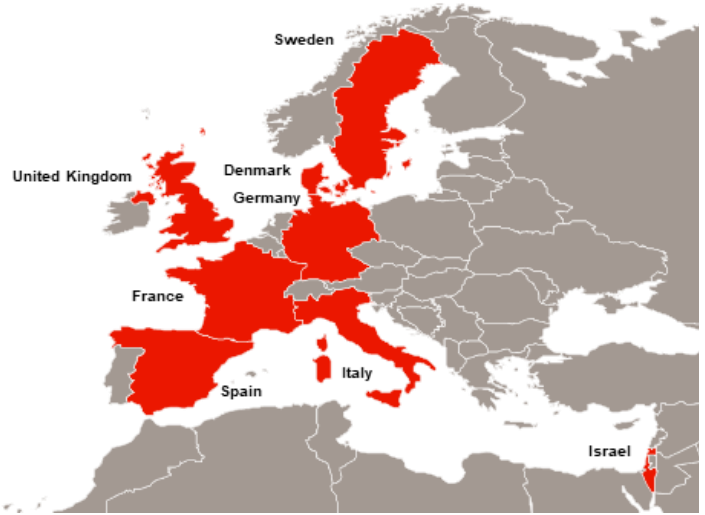
REALiTEC: Study Overview[1]

- REALiTEC aims to describe the use of teclistamab for the treatment of patients with R/R MM outside clinical trials

Data collected from patient medical records	Treatment outcomes measured
• Demographics • Disease characteristics • Prior therapies • Effectiveness and safety	• Response rates* • Time to first and best response • DoR, PFS, OS • AEs (CRS†, ICANS, infections and other AEs) • Subsequent treatments

Informed consent was collected from all patients prior to data collection

113 patients were included
(100 pre-approval access, 13 commercial)
from 23 sites across 8 countries



*Responses were evaluated according to IMWG criteria. †Due to the risk of CRS, patients should be instructed to remain within proximity of a healthcare facility and monitored for signs and symptoms daily for 48 hours after administration of all doses within the TECVAYLI® step-up dosing schedule.[2,3]

AE, adverse event; CRS, cytokine release syndrome; DoR, duration of response; ICANS, immune effector cell-associated neurotoxicity syndrome; IMWG, International Myeloma Working Group; MM, multiple myeloma; OS, overall survival; PAA, preapproval access; PFS, progression-free survival; R/R, relapsed and refractory.

References: 1. Shragai T, *et al.* Oral presentation at IHTM Spring Meeting 2025. 2. TECVAYLI® 90 mg/mL solution for injection. Summary of Product Characteristics. Available from: https://www.medicines.org.uk/emc/product/14420/smpc (Accessed June 2025). 3. TECVAYLI® 10 mg/mL solution for injection. Summary of Product Characteristics. Available from: https://www.medicines.org.uk/emc/product/14390/smpc (Accessed June 2025).

REALiTEC: Patient Characteristics[1]

Characteristic	n=113*
Age, years, median (range)	66 (43–86)
<65 years, n (%)	47 (41.6)
≥65 to <75 years, n (%)	49 (43.4)
≥75 years, n (%)	17 (15.0)
Male, n (%)	57 (50.4)
ECOG PS ≥1, n (%)	27/49 (55.1)
ISS stage, n (%)	
I	32/94 (34.0)
II	41/94 (43.6)
III	21/94 (22.3)
High-risk cytogenetics,† n (%)	32/62 (51.6)
Extramedullary plasmacytoma, n (%)	9/59 (15.3)
LDH >245 U/L, n (%)	28/86 (32.6)

Characteristic	n=113*
Patients ineligible for MajesTEC-1, n (%)	78 (69.0)
Years since diagnosis, median (range)	6.88 (0.7–24.2)
Previous lines of therapy, median (range)	6 (2–12)
Triple-class exposed, n (%)	112 (99.1)
Penta-class exposed, n (%)	100 (88.5)
Triple refractory, n (%)	89 (78.8)
Penta refractory, n (%)	50 (44.2)
Refractory to the last line of therapy, n (%)	86 (76.1)
Autologous SCT, n (%)	86 (76.1)
Patients receiving prior BCMA, n (%)‡	38 (33.6)
No. of therapies	43
CAR-T	10
ADC	32
BsAbs	1

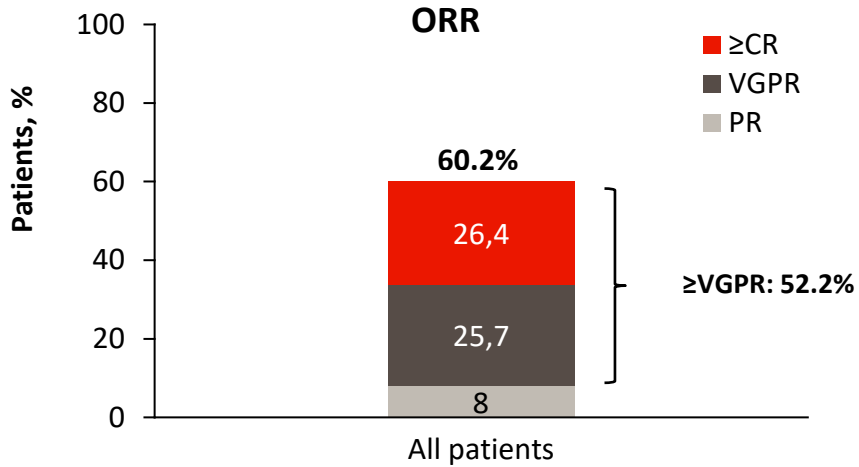
Adapted from Shragai T, *et al.* 2025.[1]

The patient population was heavily pretreated, with a median of 6 prior lines of therapy

*Data available added as denominators if some were missing and not available in the clinical chart for the whole cohort. †High risk defined as having presence of t(4;14), t(14;16), del17p13 and amp1q21. ‡38 patients received 43 prior BCMA-directed therapies.
ADC, antibody–drug conjugate; BCMA, B-cell maturation antigen; BsAb, bispecific antibody; CAR, chimeric antigen receptor; ECOG PS, Eastern Cooperative Oncology Group performance status; ISS, International Staging System; LDH, lactate dehydrogenase; SCT, stem cell transplant.
Reference: 1. Shragai T, *et al.* Oral presentation at IHTM Spring Meeting 2025.

REALiTEC: Response Rates[1]

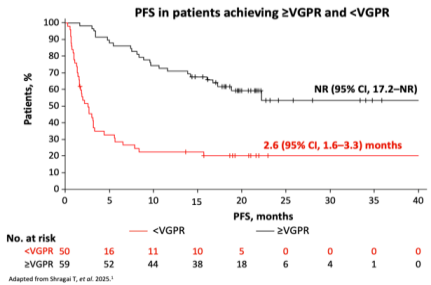
- With a **median follow-up of 20.7 months** (0.7–35.8),
- the median duration of treatment was 9.4 months (0.26–35.8)



Adapted from Shragai T, *et al.* 2025.[1]

CI, confidence interval; CR, complete response; ORR, overall response rates; PR, partial response; VGPR, very good partial response.
Reference: 1. Shragai T, *et al.* Oral presentation at IHTM Spring Meeting 2025.

REALiTEC: PFS[1]



Median follow-up: 20.7 months (range, 0.7–35.8)

- Median PFS in all patients was 9.7 months (95% CI, 5.5–18.8)
- Median PFS in patients achieving ≥VGPR was NR, with a 12-month estimate of 71.2% (95% CI, 57.8–81)

Median PFS was improved in patients achieving deep responses (≥VGPR)

CI, confidence interval; NR, not reached; PFS, progression-free survival; VGPR, very good partial response.
References: 1. Shragai T, *et al.* Oral presentation at IHTM Spring Meeting 2025.

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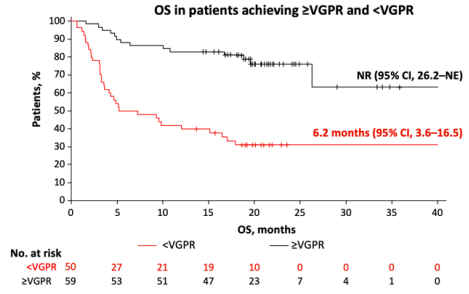
REALiTEC: OS[1]



Median follow-up 20.7 months (range, 0.7–35.8)

- Median OS in all patients was 26.3 months (95% CI, 16.5–NE)
- Median OS in patients achieving ≥VGPR was NR, with a 12-month estimate of 83.1% (70.8–90.5%)

Median OS was improved in patients achieving deep responses (≥VGPR)

CI, confidence interval; NE, not estimable; NR, not reached; OS, overall survival; VGPR, very good partial response.
Reference: 1. Shragai T, *et al.* Oral presentation at IHTM Spring Meeting 2025.

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Baseline Demographics

Characteristic	Overall dataset N=79
Age	
Median/ yrs	67
>75yrs	16 (20%)
Gender	
Female	39 (49%)
Male	40 (51%)
Race	
White	55 (75%)
Black	12 (16%)
Asian/ Pacific	6 (8%)
Creatinine Clearance	
>30ml/min	20 (33%)
≤30ml/min	40 (67%)
ECOG Performance status	
0-2	24 (30%)
3-4	9 (11%)
Eligible for MagnetisMM3 trial	
No	40 (53%)
Yes	35 (47%)

Real World Efficacy and Safety of Elranatamab, a BCMA Bispecific Antibody for Patients with Relapsed and Refractory Multiple Myeloma: An International Myeloma Working Group Immunotherapy Database Analysis

Rakesh Popat[1], Oliver Morjaria[1], Carlyn Rose Tan[2], Saad Usmani[3], Alissa Visram[3], Susan Bal[4], Luciano Costa[4], Roman Hajek[5], Jana Mihalyova[5], Joaquin Martinez-Lopez[6], Alberto Blanco[6], Meletios A Dimopoulos[7], Efstathios Kastritis[7], Chandramouli Nagarajan[8], Shimin Jasmine Chung[9,10], Myo Htut[10], Wee Joo Chng[11], Allison Tso[12], Thomas Martin[13], Mrugakshi Dave[14], Chiung-Yu Huang[15, 16], Andrew Cowan[16], Hermann Einsele[17], Yi Lin[18], Hira Mian[3]

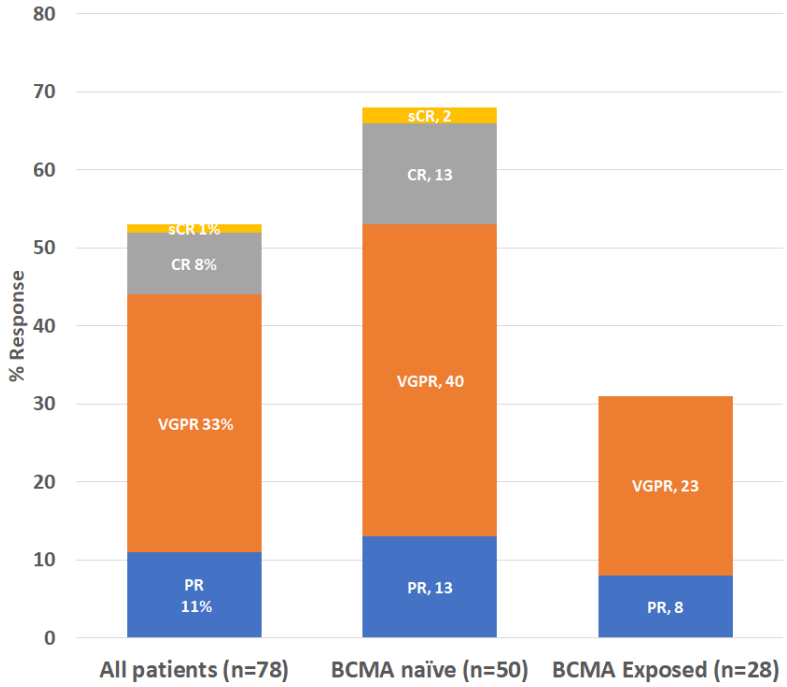
[1]University College London Hospital, London, United Kingdom, [2]Memorial Sloan Kettering Cancer Center, New York, NY, [3]McMaster University, Hamilton, ON, Canada, [4]University of Alabama at Birmingham, Birmingham, Alabama, USA, [5]University of Ostrava, Ostrava, Czech Republic, [6]Complutense University, CNIO, Madrid, Spain, Spain, [7]National and Kapodistrian University of Athens, Athens, Greece, [8]Singapore General Hospital and National Cancer Centre Singapore, [9]Singapore General Hospital, [10]City of Hope, Duarte, CA, USA, [11]National University Cancer Institute, Singapore, Singapore, [12]Tan Tock Seng Hospital, Singapore, [13]University of California San Francisco, San Francisco, California, USA, [14]International Myeloma Foundation, [15]University of California San Francisco, San Francisco, California, USA, [16]Fred Hutch Cancer Center, University of Washington, Seattle, WA, [17]University Hospital Wurzburg, Wurzburg, Germany, [18]Mayo Clinic, Rochester, Minnesota.

Presented by R Popat at the American Society of Hematology Annual Congress 2025 Publication Number: 4588

Characteristic	N=79
Prior lines, median (range)	5 (1-11)
Prior BCMA exposure, n (%)	
Any	26 (35%)
CAR-T alone	7 (9%)
ADC alone	4 (5%)
BsAb alone	5 (7%)
BsAb plus CAR-T	6 (8%)
ADC plus BsAb	3 (4%)
High risk cytogenetics, n(%)	34 (45%)
Extramedullary disease, n(%)	7 (13%)
Penta-refractory	24 (32%)

Efficacy

ORR	54%	67%	31%	p=0.004



	6 month	12 month
PFS, % (95% CI)	64% (54-77%)	52% (40-67%)
OS, % (95% CI)	74% (64-85%)	58% (45-74%)

Median follow up 6.3m (range 0.5-35.0)

Presented by R Popat at the American Society of Hematology Annual Congress 2025 Publication Number: 4588

Tools to reduce adverse events with Bispecific antibody therapy in MM

1. Optimal anti-infection prophylaxis
2. Reducing treatment frequency – Weekly to fortnightly to monthly
3. Fixed duration treatment approach

REALITEC Results: CRS* and ICANS

- CRS* and ICANS were mostly low grade, with only 2 (1.8%) patients experiencing a grade 3 CRS* event and none with a grade 4 event[1]
  - All events resolved, and no patients discontinued due to CRS* or ICANS[1]
  - 15% received tocilizumab as treatment for CRS*; none received prophylactic tocilizumab[1]
- ICANS was observed in 4 (3.5%) patients with no grade ≥3 events[1]

Summary of TEAEs of interest[1]

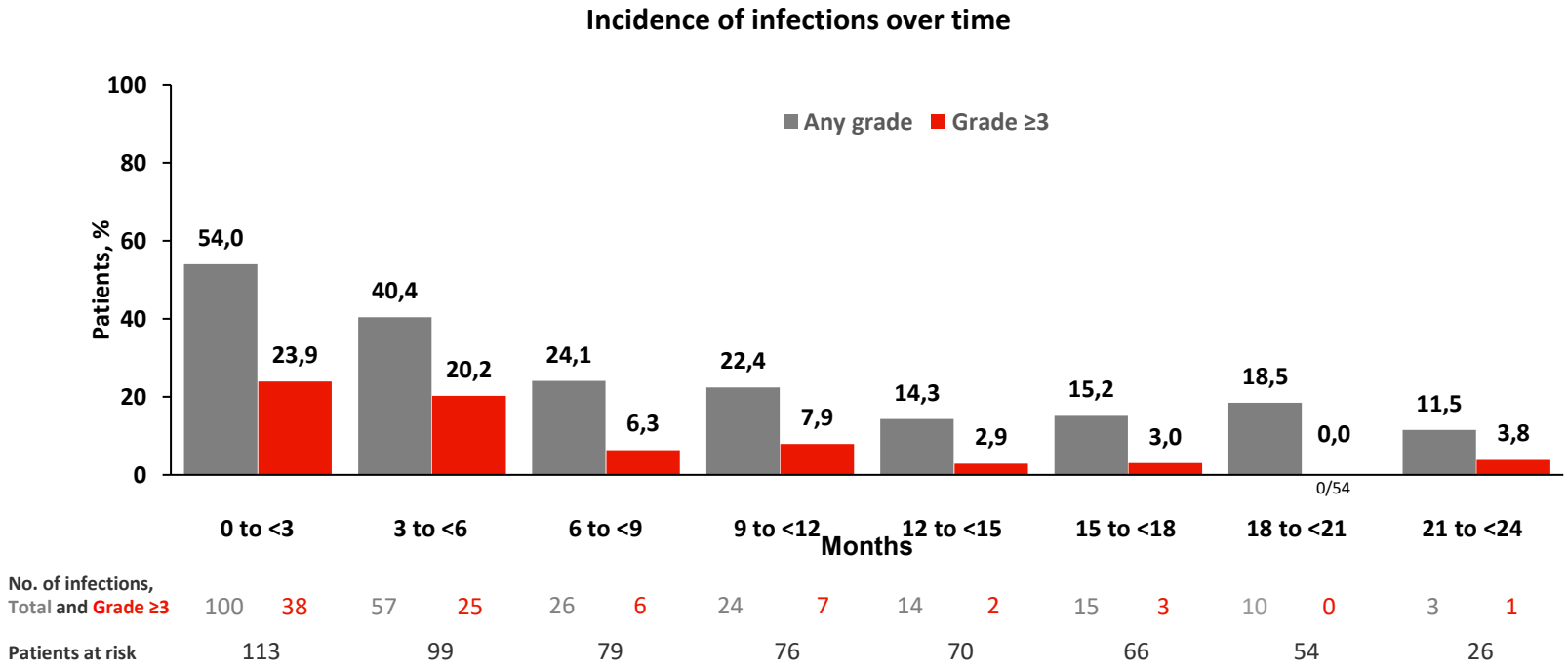
TEAE, n (%)	N=113	
	Any grade, n (%)	Grade 3/4, n (%)
Patients with any TEAE, n (%)	108 (95.6)	85 (75.2)
Infections	80 (70.8)	44 (38.9)
Pneumonia	24 (21.2)	16 (14.2)
COVID-19	17 (15.0)	8 (7.1)
Infection (unknown)	12 (10.6)	2 (1.8)
Upper respiratory tract infection	11 (9.7)	0
CMV reactivation	3 (2.7)	1 (0.9)
Hematological TEAEs		
Neutropenia	40 (35.4)	37 (32.7)
Anaemia	29 (25.7)	19 (16.8)
Thrombocytopenia	21 (18.6)	17 (15.0)
Non-haematological TEAEs		
CRS*	63 (55.8)	2 (1.8)
Diarrhoea	17 (15.0)	0
Neurological TEAEs of interest		
Peripheral sensory neuropathy	5 (4.4)	0
ICANS	4 (3.5)	0
Motor dysfunction	1 (0.9)	0
Encephalopathy†	3 (2.7)	1 (0.9)

Table adapted from Perrot A, *et al.* 2025.[1]

*Due to the risk of CRS, patients should be instructed to remain within proximity of a healthcare facility and monitored for signs and symptoms daily for 48 hours after administration of all doses within the teclistamab step-up dosing schedule.[2,3]
†Includes toxic encephalopathy and encephalopathy.
AE, adverse event; COVID-19, coronavirus disease 2019; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome.

References: 1. Perrot A, *et al.* Presentation at COMy 2025. Poster 55. 2. TECVAYLI® 90 mg/mL solution for injection. Summary of Product Characteristics. Available from: https://www.medicines.org.uk/emc/product/14420/smpc. 3. TECVAYLI® 10 mg/mL solution for injection. Summary of Product Characteristics. Available from: https://www.medicines.org.uk/emc/product/14390/smpc.

Results: Infections[1]



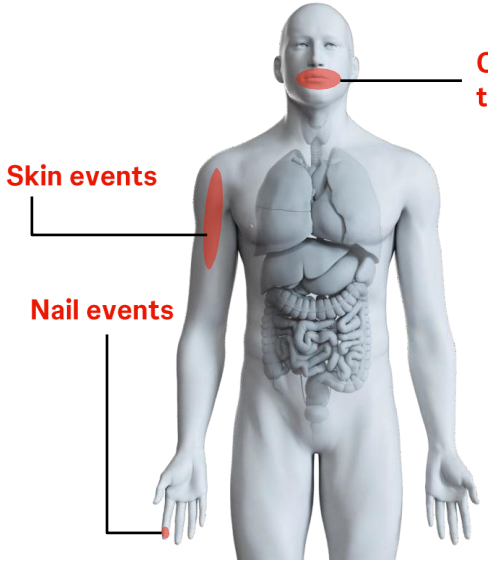
Please refer to the SmPC for full safety information.

Reference: 1. Perrot A, *et al.* Presentation at COMy 2025. Poster 55.

MonumenTAL-1: AEs associated with GPRC5D-targeting therapy are distinct but manageable[1–3]

AE, any grade, n (%)[1]	0.4 mg/kg QW (n=143)	0.8 mg/kg Q2W (n=154)	Prior TCR therapy (n=78)
Taste changes*			
Total	103 (72.0)	110 (71.4)	59 (75.6)
Leading to dose reduction	10 (7.0)	6 (3.9)	4 (5.1)
Leading to discontinuation	0	3 (1.9)	0
Nail-related AE†			
Total	79 (55.2)	82 (53.2)	46 (59.0)
Leading to dose reduction	1 (0.7)	1 (0.6)	1 (1.3)
Leading to discontinuation	0	0	0
Skin-related AE‡			
Total	81 (56.6)	113§(73.4)	50 (64.1)
Leading to dose reduction	5 (3.5)	1 (0.6)	2 (2.6)
Leading to discontinuation	2 (1.4)	1 (0.6)	0
Rash-related AE¶			
Total	57 (39.9) ‖	46 (29.9)**	25 (32.1)‡‡
Leading to dose reduction	1 (0.7)	1 (0.6)	0
Leading to discontinuation	0	0	0

Events associated with GPRC5D-targeting therapy



AEs associated with talquetamab are distinct but clinically manageable with appropriate education and support[2]

With extended follow-up, discontinuation rates due to AEs remained low, and no new discontinuations occurred due to talquetamab-related AEs[3]

*Including ageusia, dysgeusia, hypogeusia and taste disorder; †Including nail discoloration, nail disorder, onycholysis, onychomadesis, onychoclasis, nail dystrophy, nail toxicity and nail ridging; ‡Including skin exfoliation, dry skin, pruritus and palmar–plantar erythrodysesthesia syndrome; §Including 1 (0.6%) Grade 3/4 event; ¶Including rash, maculopapular rash, erythematous rash and erythema; ‖Including two (1.4%) Grade 3/4 events; **Including 8 (5.2%) Grade 3/4 events; ‡‡Including two (2.6%) Grade 3/4 events.
AE, adverse event; GPRC5D, G-protein-coupled receptor family C group 5 member D; Q2W, every 2 weeks; QW, once weekly; TCR, T-cell redirection.
1. Rasche L, et al. EHA 2024. Poster presentation P915; 2. Chari A, et al. Clin Lymphoma Myeloma Leuk. 2024;24:665–93.e14; 3. Rasche L, et al. ASCO 2025. Poster presentation P96.

MonumenTAL-1: low rates of severe infections were observed with talquetamab, which decreased over time

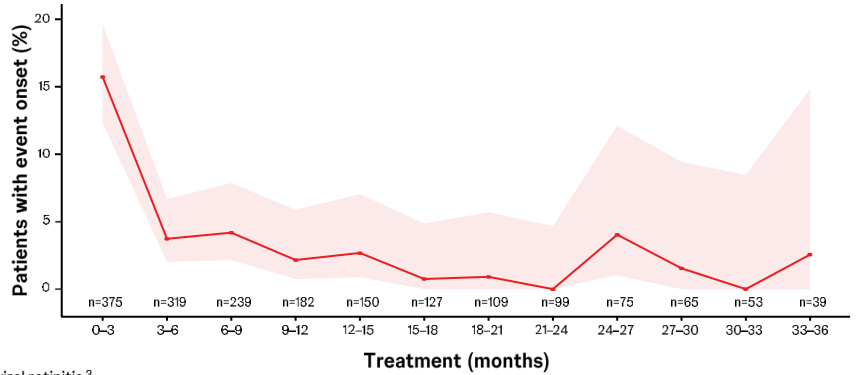
In MonumenTAL-1, most infections were low-grade, and new-onset grade 3/4 infections were most prevalent during the first 100 days.[1] Findings have remained consistent with longer follow-up[2–4]

Median follow-up was 25.6, 19.4 and 16.8 months in the QW, Q2W and prior TCR therapy cohorts, respectively[3]

Data cut-off: 11 October 2023[3]

Infections, n (%)	0.4 mg/kg QW (n=143)	0.8 mg/kg Q2W (n=145)	Prior TCR therapy (n=78)
Any grade	85 (59.4)	105 (68.2)	59 (75.6)
Grade 3/4	29 (20.3)	28 (18.2)	20 (25.6)
Led to death	3 (2.1)*	2 (1.4)†	0
Led to discontinuation	2 (1.4)	0	1 (2.0)
Opportunistic infections‡	5 (3.5)	9 (6.2)	3 (3.8)

New-onset grade ≥3 infections over time across combined cohorts (data cut-off: September 2024)[4]



*Deaths were due to COVID-19 pneumonia, fungal sepsis and septic shock.[1] †Deaths were due to COVID-19 pneumonia and infection.[1]
‡Defined as either oesophageal candidiasis, adenovirus, herpesvirus 6, ophthalmic herpes, varicella zoster, cytomegalovirus, fungal sepsis or viral retinitis.[3]
COVID-19, coronavirus disease 2019; Q2W, every 2 weeks; QW, once weekly; TCR, T-cell redirection.

1. Rodriguez-Otero P, et al. ASCO 2023. Poster presentation 8020; 2. Rasche L, et al. EHA 2024. Poster presentation P915; 3. Chari A, et al. Lancet Haematol. 2025;12:e269–81 (and supplementary appendix);
4. Rasche L, et al. ASCO 2025. Poster presentation P96.

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Volume 146, Supplement 1, 3 November 2025, Page 5814

Poster

654. Multiple Myeloma: Pharmacologic Therapies

Interim analysis of LimiTec, a prospective trial of limited-duration teclistamab for relapsed/refractory multiple myeloma

Beatrice Razzo [1], Rajshekhar Chakraborty [2], Hira Shaikh [3], Leonard Fiannaca [4], Sarah Girgis [4], Samantha Le [4], Sara Whittington [4], George Mellgard [2 5], David Lieberman [4], Ashkan Bigdeli [4], Jacquelyn Roth [4], Connnor Grady [4 6], Elizabeth Waugh [1], Francesca Nugent [3], Zachary Wolfe [7], Samer Al Hadidi [8], Carolina Schinke [8], Adam Binder [1], Christopher Strouse [3], Shivani Kapur [4]... Alfred Garfall [4]

Show more

https://doi.org/10.1182/blood-2025-5814

43 patients
Treated with Teclistamab
23% prior BCMA exposed
6-9 months VGPR : STOP
Failure free survival 73% @ 12 months

Bispecific antibody therapy in MM as a platform for combination approaches

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

22 Oct 2021 to 29 Sept 2023[b]

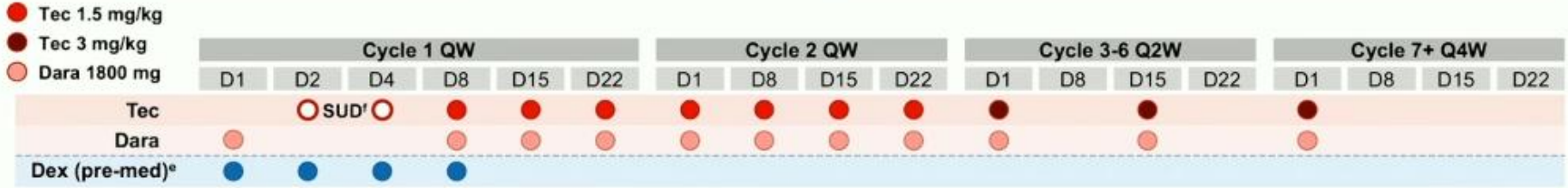
Tec-Dara
N=291
SC dosing following Dara schedule

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



SC dosing aligned with Dara schedule, with monthly dosing after 6 cycles; steroid sparing after Cycle 1 Day 8

[a]Prior exposure to anti-CD38 mAbs was permitted. [b]During the COVID-19 pandemic. [c]DPd/DVd were administered per the approved schedules. [d]Response and disease progression were assessed by a blinded IRC per IMWG criteria. [e]Dexamethasone, acetaminophen, and diphenhydramine pre-medication was required for the first 2 weeks; subsequent dexamethasone was not required thereafter. [f]Patients received SUD of 0.06 mg/kg and 0.3 mg/kg on Days 2 and 4, respectively.

CR, complete response; D, day; Dex, dexamethasone; 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; MRD, minimal residual disease; MySIm-Q, Multiple Myeloma Symptom and Impact Questionnaire; ORR, overall response rate; PFS, progression-free survival; PI, proteasome inhibitor; PK, pharmacokinetics; pre-med, pre-medication; QW, weekly; Q2W, every 2 weeks; Q4W, every 4 weeks; SC, subcutaneous; SUD, step-up dosing.

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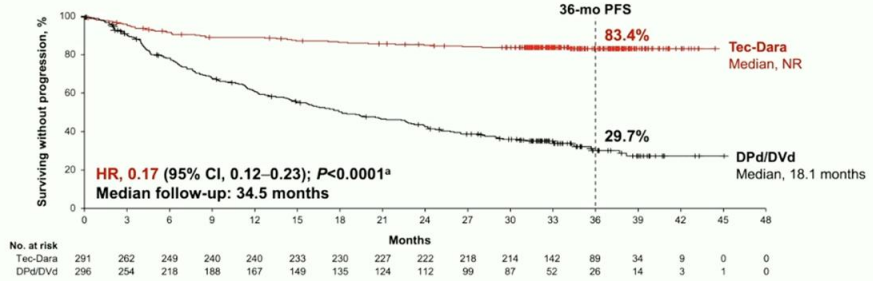
Dramatic Time to event outcomes !

MajesTEC-3: PFS (Primary Endpoint)



Tec-Dara significantly improved PFS, with a plateauing curve after ~6 months and >90% of patients progression-free at 6 months sustaining such a benefit at 3 years

aThe *P* value crossed the prespecified stopping boundary for superiority for the first interim analysis (*P*=0.0139).
CI, confidence interval; HR, hazard ratio; NR, not reached.
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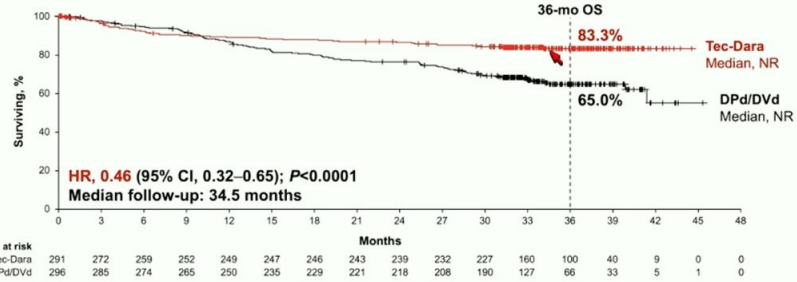
MajesTEC-3: OS



Tec-Dara significantly improved OS versus DPd/DVd, with 83% of patients alive at 3 years

Analysis of RMST demonstrated an OS benefit for Tec-Dara versus DPd/DVd (RMST difference, 2.15 months; *P*=0.0088).
RMST, restricted mean survival time.
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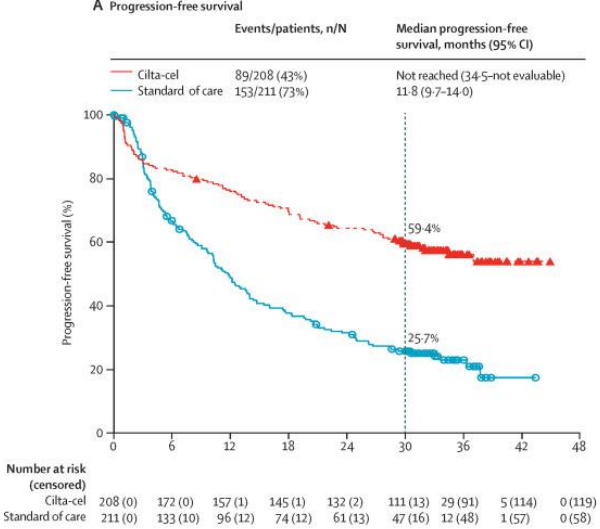
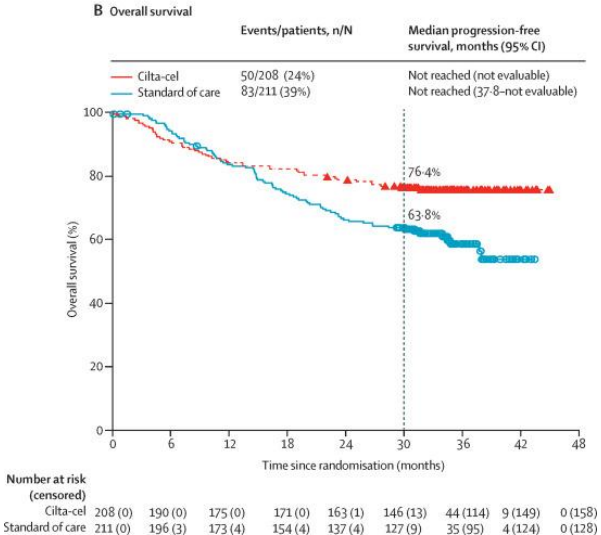
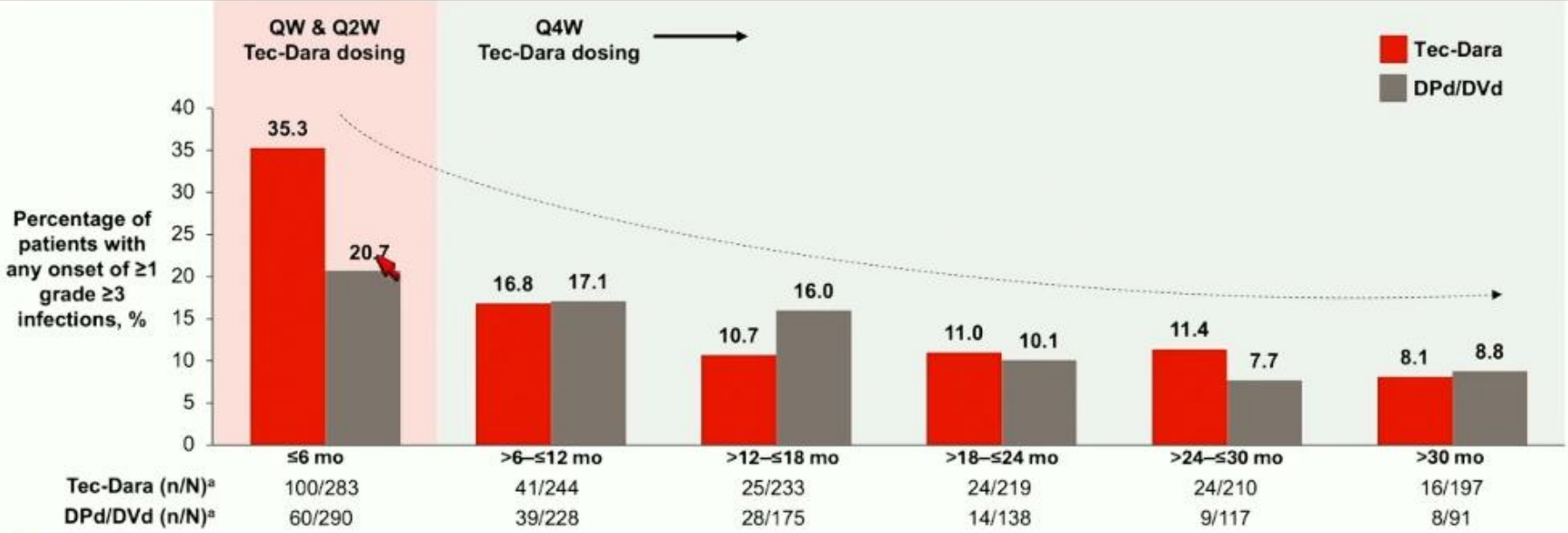
Long term follow up of CARTITUDE-4





Einsele H The Lancet Oncology, 2026; 27, 254-268

MajesTEC-3: Grade ≥3 Infections Over Time



	≤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

Any onset grade ≥3 infections were comparable across arms after 6 months and 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.

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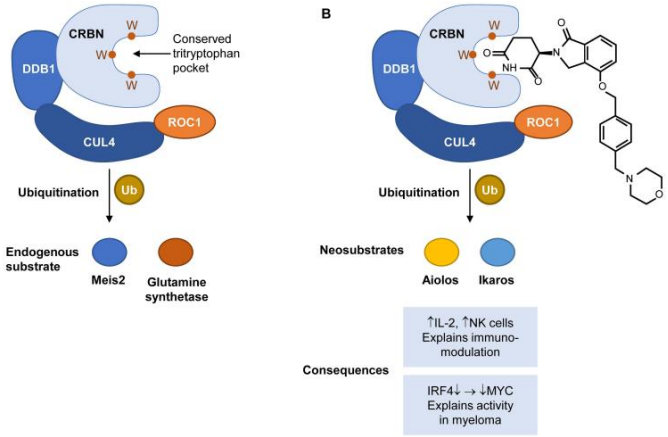
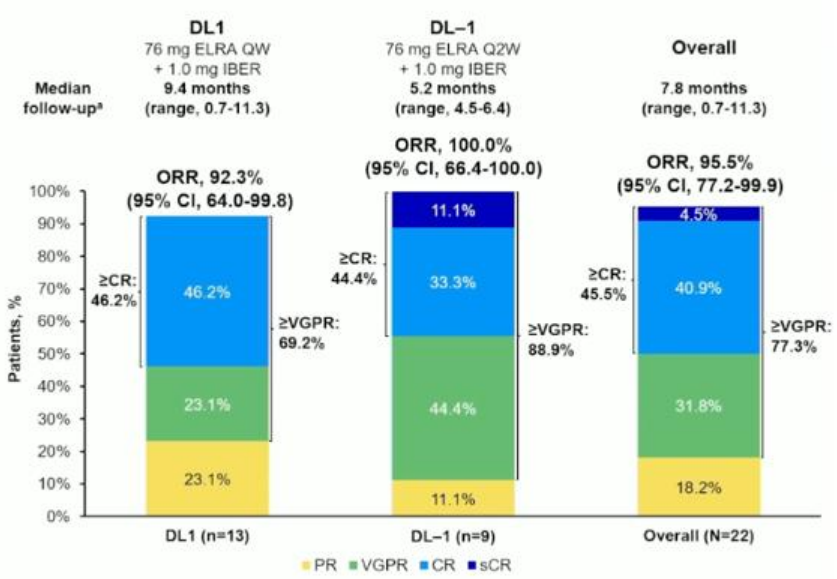
MagnetisMM-30: Elranatamab+ Iberdomide

22 patients
Prior lines: 2.5
Triple-class refractory: 50%
Median follow-up: 7.8 months

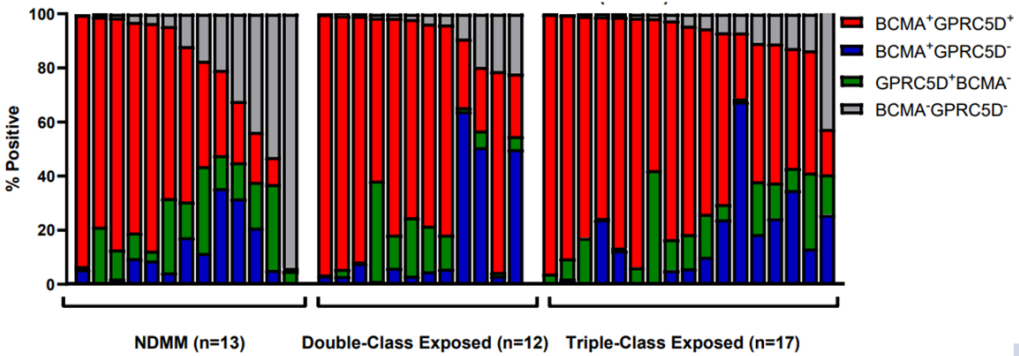
Mode of action of iberdomide



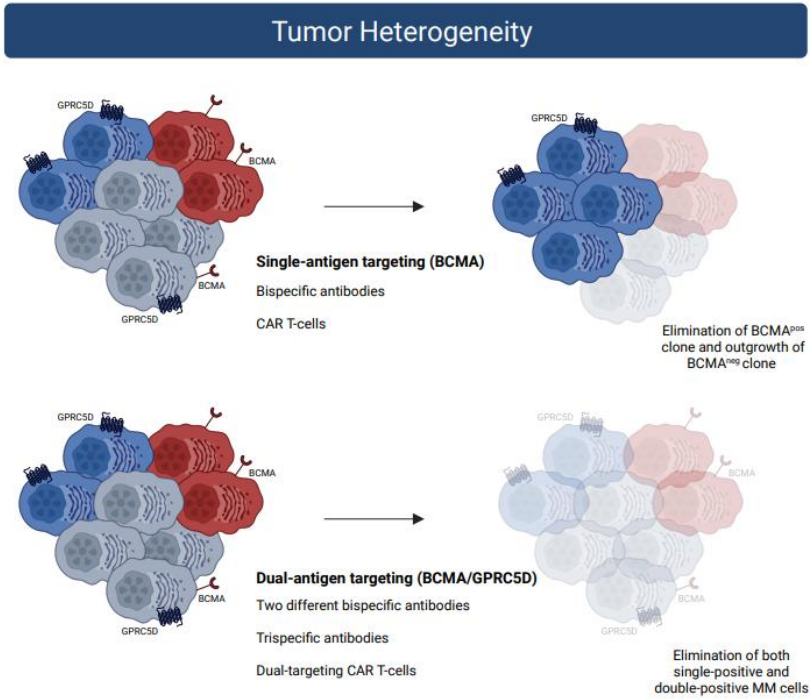


Dual targeting to address tumour heterogeneity and and prevent antigen escape

Substantial heterogeneity in BCMA and GPRC5D expression among patients and within the tumour

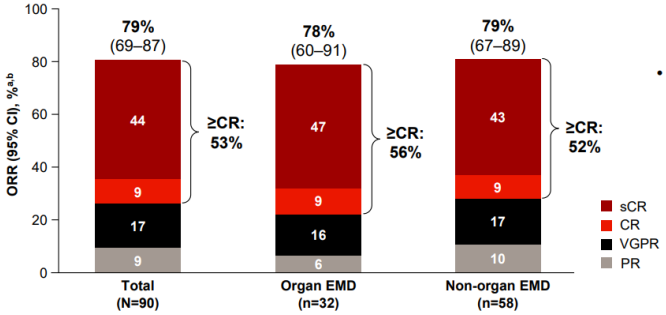


O'Neill et al. ASH 2025

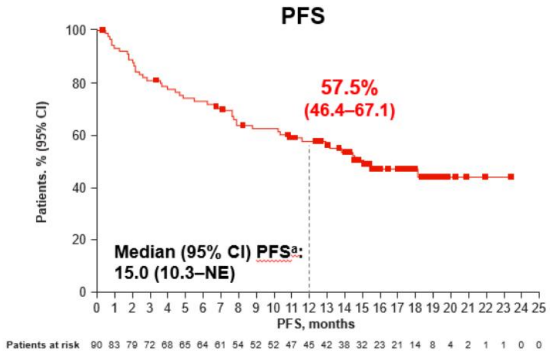


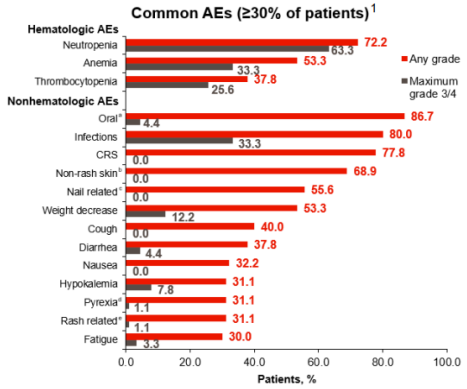
Van De Donk….Einsele. Blood 2026

TEC +TAL: RedirecTT-1 phase 2 for patients with extramedullary disease



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

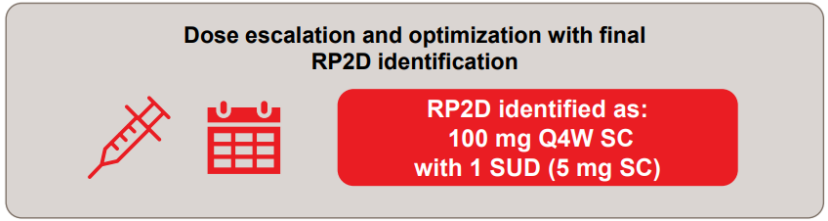


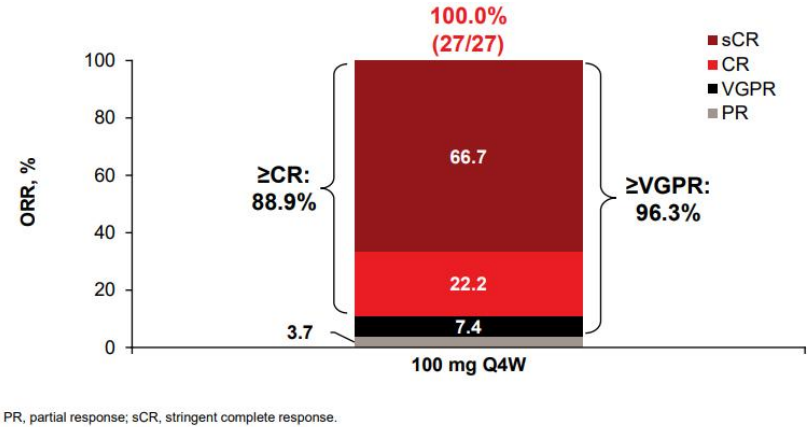


AEs were consistent with safety profiles of Tal and Tec

Ramantamig BCMA GPRc5D

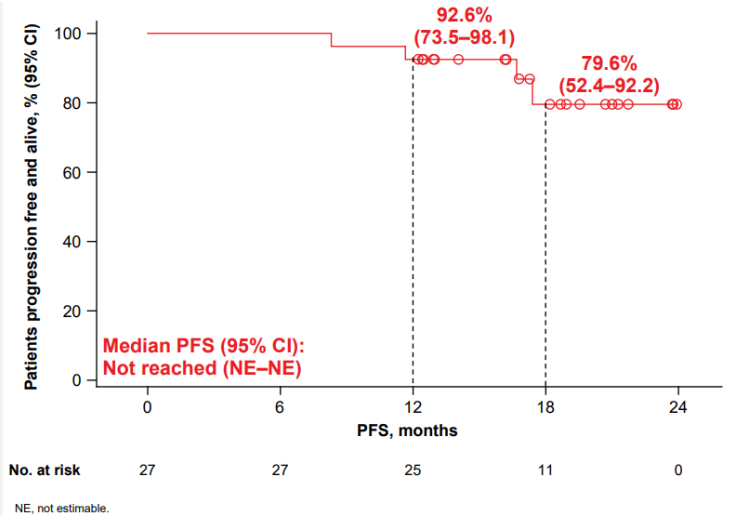
N=37
-Median 4 prior regimens,
-27 naive to BCMA/GPRC5D, 9 exposed
-Median follow-up: 17 months





PR, partial response; sCR, stringent complete response.

Across all RP2D patients (n=37): MRD-negativity rate of 100.0% at 10^{-5} (n=10/10) and 10^{-6} (n=7/7)

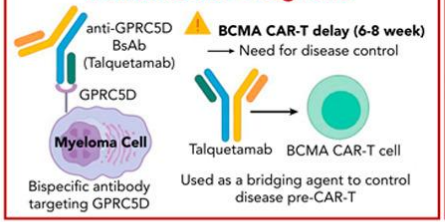


NE, not estimable.

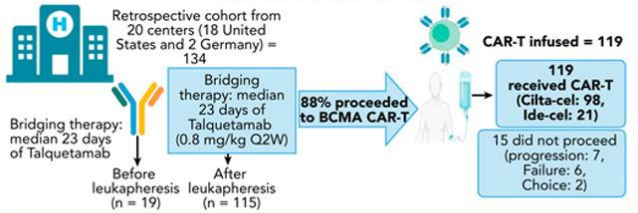
Van de Donk ASCO 2025; Krishnan ASH 2025

Sequential Targeting in Multiple Myeloma: Talquetamab, a GPRC5D Bispecific Antibody, as a Bridge to BCMA CAR-T Therapy

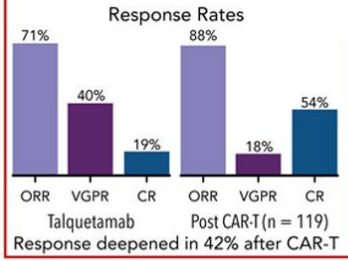
Rationale and Background



Patients and Methods



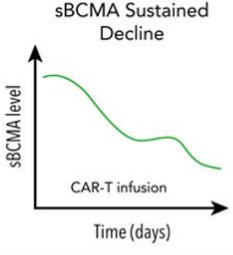
Results

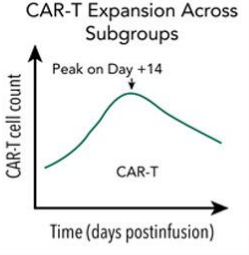


Toxicity

Talquetamab related
-CRS: 73% (mostly Grade 1-2)
-ICANS: 7% (Grade 3 in 2%)
-Skin (38%), Oral (70%), Nail (17%), Weight loss (15%)

CAR-T related
-CRS: 68% (Grade ≥3: 2%)
-ICANS: 6% (Grade 3 in 2%)
-Infections (5% Grade ≥3), Delayed neurotoxicity: 2 facial palsy (resolved)





Conclusions: **Talquetamab is a safe and effective bridging therapy that enabled most high-risk, heavily pretreated patients with myeloma to receive BCMA CAR-T, resulting in deep responses, sustained sBCMA decline, and consistent CAR-T expansion, supporting sequential targeting as a promising strategy in relapsed/refractory myeloma.**

*Dhakal et al. DOI: 10.1182/**blood**.2025029773*

blood Visual Abstract

Editorial > Blood. 2025 Oct 23;146(17):2012-2014. doi: 10.1182/blood.2025030525.

Designing a strong bridge to CAR-T cells with bispecifics

Francesca Gay [1 2], Mattia D'Agostino [1 2]

Affiliations + expand

PMID: 41129187 DOI: 10.1182/blood.2025030525

No abstract available

PubMed Disclaimer

Comment on

Sequential targeting in multiple myeloma: talquetamab, a GPRC5D bispecific antibody, as a bridge to BCMA CAR-T therapy.

Dhakal B, Akhtar OS, Fandrei D, Jensen A, Banerjee R, Pan D, Richard S, Friend R, Rees M, Costello P, Vazquez Martinez M, Pasvolsky O, Wagner C, Davis JA, Castaneda Puglianini O, Reshef R, Afrough A, Dima D, Bhutani M, Nadeem O, Parrondo R, Freeman C, Mikkilineni L, Raza S, Anderson LD Jr, Kapoor P, Hosoya H, Chhabra S, Grajales-Cruz A, Gaballa M, Midha S, Alsina M, Sborov D, Patel K, Lin Y, Ferreri C, Gagelmann N, Kumar A, Hansen D, Cowan A, Costa LJ, Merz M, Sidana S.

Blood. 2025 Oct 23;146(17):2063-2072. doi: 10.1182/blood.2025029773.

PMID: 40749169

Conclusions

1. Broad access to bispecific antibody therapy in MM, with off the Shelf availability for target sequencing

2. Real world optimisation is limiting some of the concerning infection Rates (dosing/ IVIG prophylaxis)

3. Bispecific platform combination approaches improves response rates and Tec Dara rivals BCMA CART in early relapse

4. Use of Trispecific approaches can limit emergence of resistance seen in a proportion of myeloma patients