Updates in BCMA-directed therapies in multiple myeloma from ASH 2024

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Recorded following the **66th ASH Annual Meeting and Exposition**
(7–10 December 2024, San Diego, CA, USA)

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Approved indications for BCMA-targeting agents

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4738: MagnetisMM-3: Long-term update and efficacy and safety of less frequent dosing of elranatamab in patients with RRMM

Miles Prince H, et al.

Baseline characteristics

Refractory to ≥1 PI, ≥1 IMiD, and ≥1 anti-CD38 antibody	BCMA-naive (N=123)
Median age, years (range)	68 (36–89)
Median prior lines of therapy, n (range)	5 (2–22)
Prior stem cell transplant, %	71
Triple-class exposed/refractory, %	100/97
Penta-class exposed/refractory, %	71/42
Extramedullary disease, %	32
R-ISS III, %	15
High-risk cytogenetics, %	25
Refractory to last line of therapy, %	96

Treatment schedule

Subcutaneous elranatamab as step-up priming doses followed by 76 mg QW

Patients with ≥6 cycles of QW dosing achieving PR or better for ≥2 months were transitioned to:

Q2W dosing

Patients with ≥6 cycles of Q2W dosing were transitioned to:

Q4W dosing

BCMA, B-cell maturation antigen; IMiD, immunomodulatory drug; PI, proteasome inhibitor; PR, partial response; QW, once weekly; Q2W, every 2 weeks; Q4W, every 4 weeks; R-ISS, Revised International Staging System; RRMM, relapsed/refractory multiple myeloma.

Miles Prince H, et al. Presented at ASH 2024, San Diego, CA, USA, 7–10 December 2024. Abstr. 4738.

4738: MagnetisMM-3: Long-term update and efficacy and safety of less frequent dosing of elranatamab in patients with RRMM

Miles Prince H, et al.

Efficacy after dosing switch (N=123)

58 switched to **Q2W**

28 switched to **Q4W**

Of **27 responders*** to the **Q4W switch:**

93% **Maintained response** for **≥6 months** post-switch

88% **Maintained** a **complete response or better**

4% Had **progressive disease**

mPFS **17.2** months

mOS **24.6** months

MRD rate **90%**

Safety

Most frequent TEAEs (≥20% before/after switch) in Q4W group (n=27)

Grade 3/4 TEAE by system organ class, %	Before switch to Q4W	After switch to Q4W
Any	46	46
Blood, lymphatic	32	32
Infections, infestations	18	11
Gastrointestinal	4	4
Musculoskeletal, CTD	7	-
Respiratory, mediastinal, thoracic	4	-
Metabolism, nutrition	-	4

Reducing elranatamab dosing frequency to Q4W may improve safety without compromising efficacy.

*Responders per blinded independent central review who switched to Q4W dosing ≥6 months before the data cutoff.
CTD, connective tissue disorders; m, median; MRD, minimal residual disease; OS, overall survival; PFS, progression-free survival; Q2W, every 2 weeks; Q4W, every 4 weeks; RRMM, relapsed/refractory multiple myeloma; TEAE, treatment-emergent adverse event.
Miles Prince H, et al. Presented at ASH 2024, San Diego, CA, USA, 7–10 December 2024. Abstr. 4738.

934: Outcomes of elderly patients with RRMM treated with teclistamab: A multicenter study from the US Multiple Myeloma Immunotherapy Consortium

Paslovsky O, et al.

Baseline characteristics by age group

• RRMM, receiving SOC teclistamab

	≥75 years (n=83)	<75 years (n=302)	P value
Median prior lines of therapy, n	6	6	--
ECOG PS ≥2, %	29	24	0.37
Triple-class refractory, %	77	85	0.06
Penta-class refractory, %	30	39	0.15
High-risk cytogenetic abnormalities, %	45	58	0.03
Double-hit myeloma, %	12	24	0.02
Extramedullary disease at baseline, %	22	40	0.002
Prior ASCT, %	43	72	<0.0001
Prior BCMA-directed therapy, %	33	55	0.0003

ASCT, autologous stem cell transplant; BCMA, B-cell maturation antigen; ECOG PS, Eastern Cooperative Oncology Group performance status; RRMM, relapsed/refractory multiple myeloma; SOC, standard of care.

Paslovsky O, et al. Presented at ASH 2024, San Diego, CA, USA, 7–10 December 2024. Abstr. 934.

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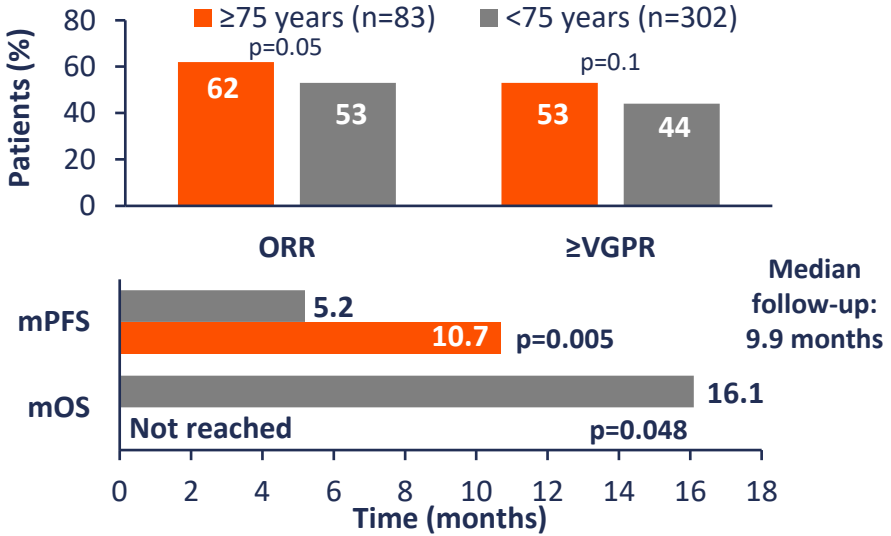
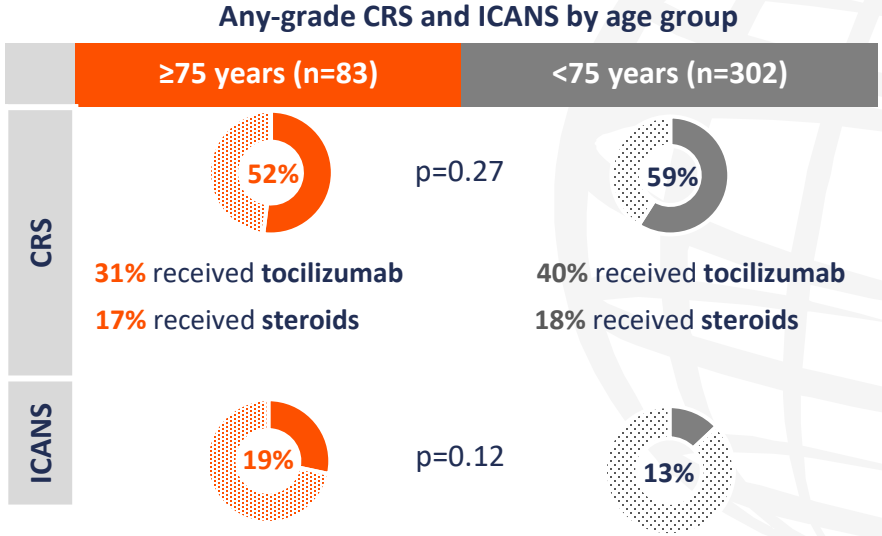
Efficacy



Safety



Teclistamab in the real-world setting demonstrates comparable efficacy and safety in patients aged ≥75 years to that in MajesTEC-1 overall. Multivariate analysis showed aged ≥75 years had no significant impact on survival outcomes. Authors concluded age should not preclude the use of teclistamab.

CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; m, median; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; VGPR, very good partial response. Paslovsky O, et al. Presented at ASH 2024, San Diego, CA, USA, 7–10 December 2024. Abstr. 934.

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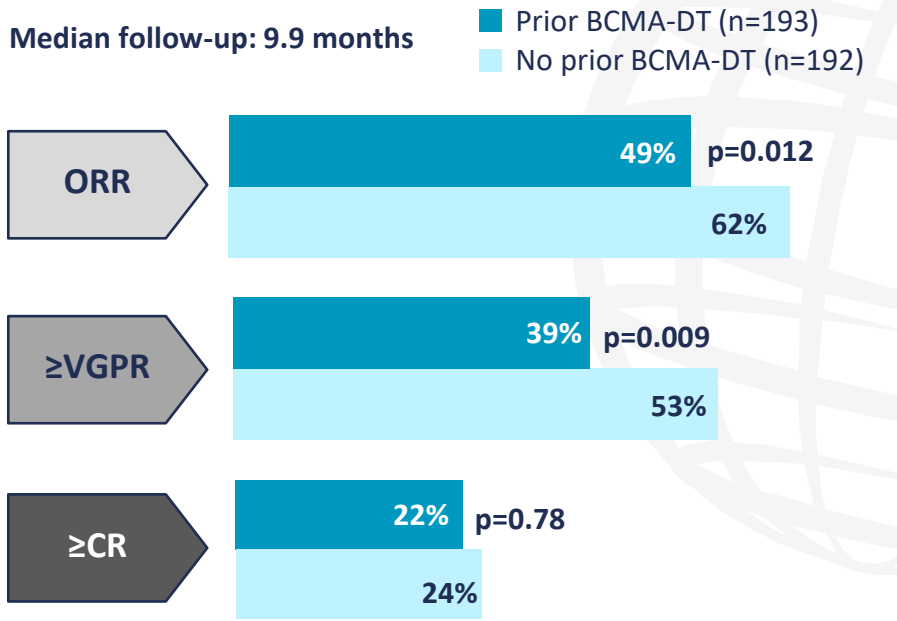
897: Outcomes of teclistamab in patients with RRMM with prior exposure to BCMA-DT: A multicenter study from the US Multiple Myeloma Immunotherapy Consortium

Dima D, et al.

Baseline characteristics in the prior BCMA-DT group

RRMM, prior BCMA-DT, on SOC teclistamab across 14 US centers	n=193
No. of prior BCMA-DTs, %	
1	77
2	22
3	1
ECOG PS ≥2, %	24
High-risk cytogenetics (any), %	61
Extramedullary disease, %	22
Penta-refractory, %	42
ORR to most recent prior BCMA-DT, %	
Overall (n=193)	69
ADC (n=56)	48
CAR T-cell therapy (n=129)	78
Bispecific antibody (n=8)	75

Response rates by prior BCMA-DT status



ADC, antibody–drug conjugate; BCMA-DT, B-cell maturation antigen-directed therapy; CAR, chimeric antigen receptor; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; ORR, overall response rate; RRMM, relapsed/refractory multiple myeloma; SOC, standard of care; VGPR, very good partial response.

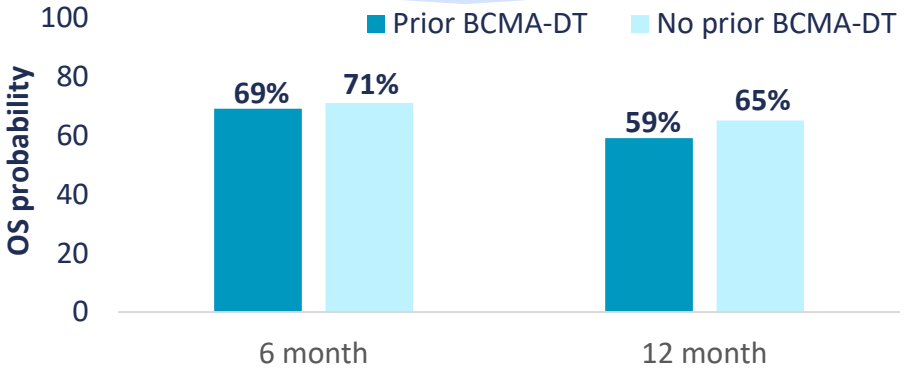
Dima D, et al. Presented at ASH 2024, San Diego, CA, USA, 7–10 December 2024. Abstr. 897.

897: Outcomes of teclistamab in patients with RRMM with prior exposure to BCMA-DT: A multicenter study from the US Multiple Myeloma Immunotherapy Consortium

Dima D, et al.

Outcomes by prior BCMA-DT status and type

6- and 12-month OS rates



ORR

48% ADC

51% CAR T-cell therapy

13% Bispecific antibody

PFS by number and most recent prior BCMA-DT type

PFS (months) by number of prior BCMA-DT

PFS (months) by prior BCMA-DT type

ADC, antibody–drug conjugate; BCMA-DT, B-cell maturation antigen-directed therapy; CAR, chimeric antigen receptor; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; RRMM, relapsed/refractory multiple myeloma.

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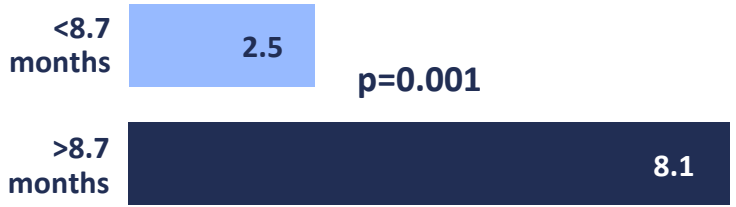
897: Outcomes of teclistamab in patients with RRMM with prior exposure to BCMA-DT: A multicenter study from the US Multiple Myeloma Immunotherapy Consortium

Dima D, et al.

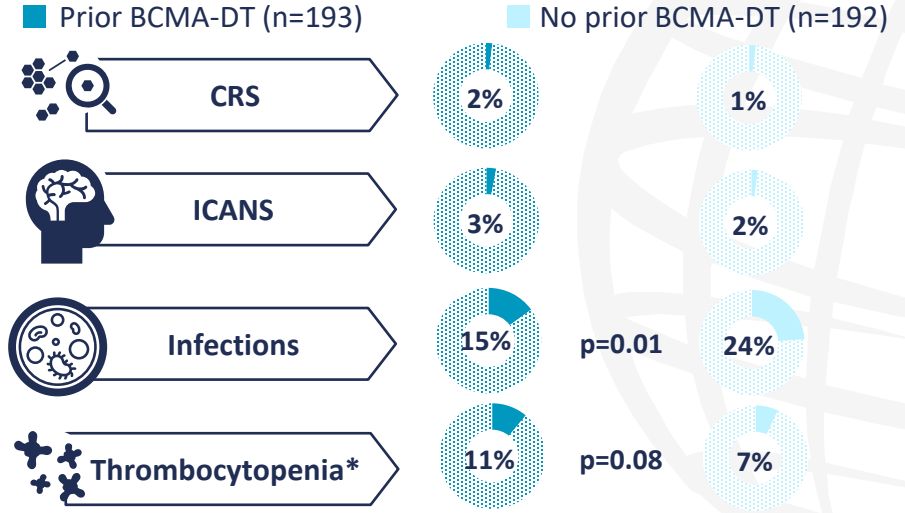
Optimal cut-off for time from last BCMA-DT exposure to teclistamab initiation

PFS (months) by time gap between last exposure to prior BCMA-DT and teclistamab initiation



Maximally selected rank statistics analysis identified **8.7 months** as the optimal cut-off time from last BCMA-DT exposure to teclistamab initiation

Major (grade ≥3) AEs by prior BCMA-DT status



Receipt of BCMA-DT prior to teclistamab showed a trend towards worse PFS and lower likelihood of obtaining overall response. Waiting >9 months between sequencing BCMA therapies may be associated with improved PFS.

*At Day 30. AE, adverse event; BCMA, B-cell maturation antigen; BCMA-DT, BCMA-directed therapy; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; PFS, progression-free survival; RRMM, relapsed/refractory multiple myeloma.

Dima D, et al. Presented at ASH 2024, San Diego, CA, USA, 7–10 December 2024. Abstr. 897.

936: Comparative safety and efficacy of ciltacabtagene autoleucel (cilta-cel) and idecabtagene vicleucel (ide-cel) CAR T-cell therapies in RRMM

Hansen DK, et al.

Baseline characteristics were well balanced after inverse probability of treatment weighting

RRMM, infused with ide-cel or cilta-cel

	Ide-cel (n=350)	Cilta-cel (n=236)	P-value
Age, years	65	64	0.2
Median follow up, months	13.0	12.6	
Extramedullary disease, %	24	26	0.7
High-risk cytogenetics, %	33	38	0.2
Prior BCMA therapy, %	18	14	0.2
Penta-class refractory, %	35	30	0.15
Fludarabine/cyclophosphamide lymphodepletion, %	91	81	<0.001
No bridging therapy, %	28	24	
≥PR to bridging therapy, %	10	21	
SD/PD response to bridging therapy, %	62	55	

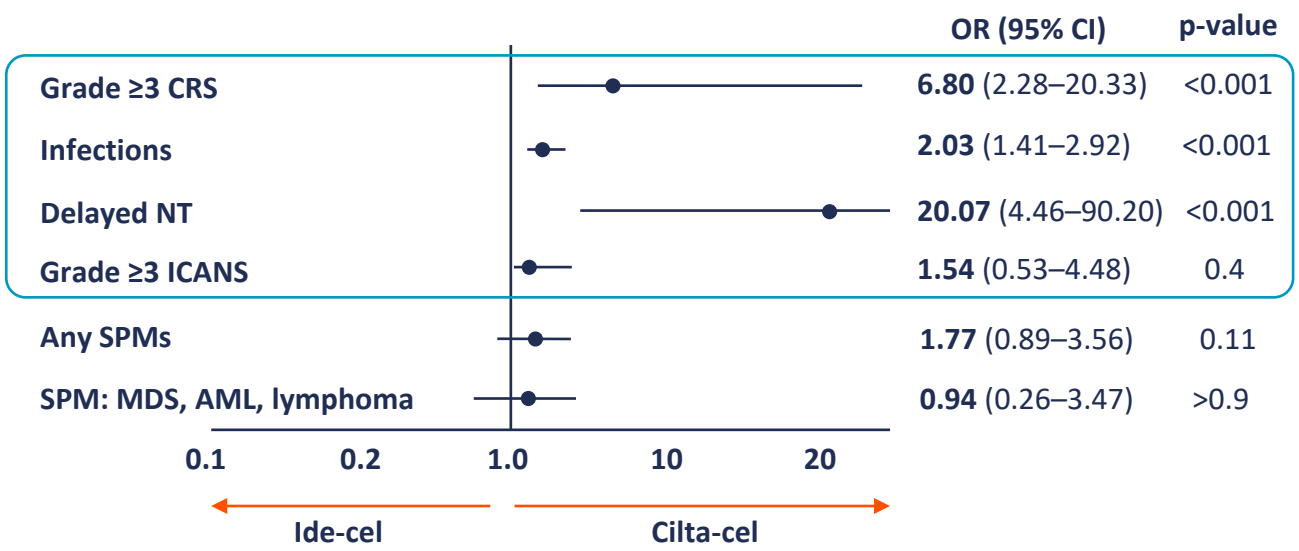
BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; PD, progressive disease; PR, partial response; RRMM, relapsed/refractory multiple myeloma; SD, stable disease.

Hansen DK, et al. Presented at ASH 2024, San Diego, CA, USA, 7–10 December 2024. Abstr. 936.

936: Comparative safety and efficacy of ciltacabtagene autoleucel (cilta-cel) and idecabtagene vicleucel (ide-cel) CAR T-cell therapies in RRMM

Hansen DK, et al.

Incidence of key toxicities with cilta-cel compared with ide-cel therapy



Non-relapse mortality

Higher in **cilta-cel-treated patients** but this was **not** statistically significant

HR 1.24

(95% CI 0.67–2.30)
p=0.49

AML, acute myeloid leukaemia; CAR, chimeric antigen receptor; CI, confidence interval; cilta-cel, ciltacabtagene autoleucel; CRS, cytokine release syndrome; HR, hazard ratio; ICANS, immune effector cell-associated neurotoxicity syndrome; ide-cel, idecabtagene vicleucel; MDS, myelodysplastic syndromes ;NT, neurotoxicity; OR, odds ratio; RRMM, relapsed/refractory multiple myeloma; SPM, second primary malignancy.

Hansen DK, et al. Presented at ASH 2024, San Diego, CA, USA, 7–10 December 2024. Abstr. 936.

936: Comparative safety and efficacy of ciltacabtagene autoleucel (cilta-cel) and idecabtagene vicleucel (ide-cel) CAR T-cell therapies in RRMM

Hansen DK, et al.

Treatment responses and survival outcomes with cilta-cel compared with ide-cel therapy

		OR (95% CI)	P value
Best CR or better		2.42 (1.63–3.60)	<0.001
Best ORR (≥PR)		1.60 (0.90–2.83)	0.11

		HR (95% CI)	P value
ITT	PFS	0.43 (0.34–0.55)	<0.001
	OS	0.53 (0.40–0.73)	<0.001

		HR (95% CI)	P value
Infused	PFS	0.48 (0.36–0.63)	<0.001
	OS	0.67 (0.46–0.97)	0.03

Comparing cilta-cel vs ide-cel in SOC setting for RRMM showed:

- **Higher efficacy** (responses and survival)
- **Higher toxicities**: severe CRS, delayed NT, infections, trend for SPMs
- **No difference** in other toxicities and non-relapse mortality

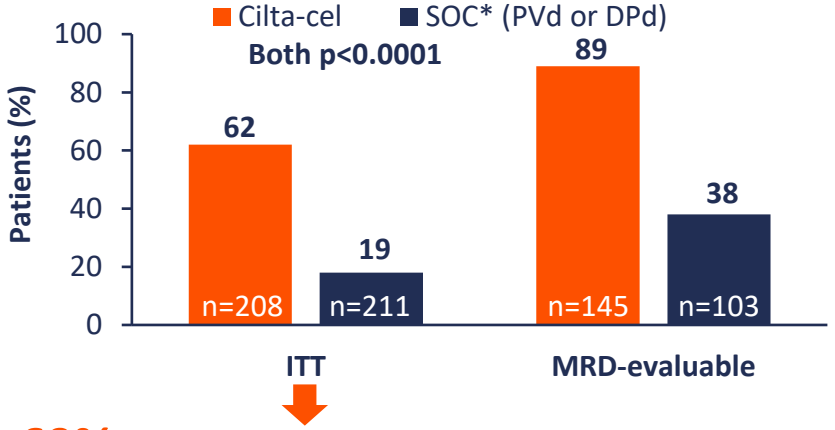
- Results remained consistent in sensitivity analyses
- Limitations include a retrospective study design and inherent biases in real-world data

CAR, chimeric antigen receptor; CI, confidence interval; CR, complete response; CRS, cytokine release syndrome; HR, hazard ratio; ITT, intention-to-treat; NT, neurotoxicities; OR, odds ratio; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; RRMM, relapsed/refractory multiple myeloma; SOC, standard-of-care; SPM, second primary malignancies. Hansen DK, et al. Presented at ASH 2024, San Diego, CA, USA, 7–10 December 2024. Abstr. 936.

1032: Ciltacabtagene autoleucel vs SOC in patients with lenalidomide-refractory MM after 1–3 lines of therapy: MRD negativity in the phase III CARTITUDE-4 trial

Popat R, et al.

MRD-negativity rate (10^{-5})

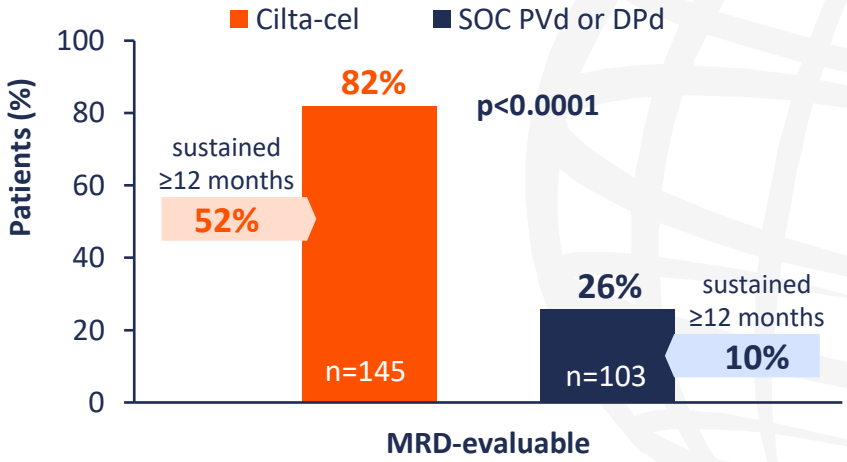


69% of evaluable patients achieved MRD negativity by day 56

rising to

86% by month 6 post-cilta-cel infusion

Overall and sustained† MRD-negativity ≥CR (10^{-5})



†Defined as confirmed MRD negativity ≥12 months apart and without MRD positivity in between‡

‡Patients were evaluable for sustained MRD negativity if they achieved MRD negativity and had ≥1 evaluable MRD sample ≥12 months after the first negative result or progressed/died/started subsequent treatment <12 months after the first negative result.

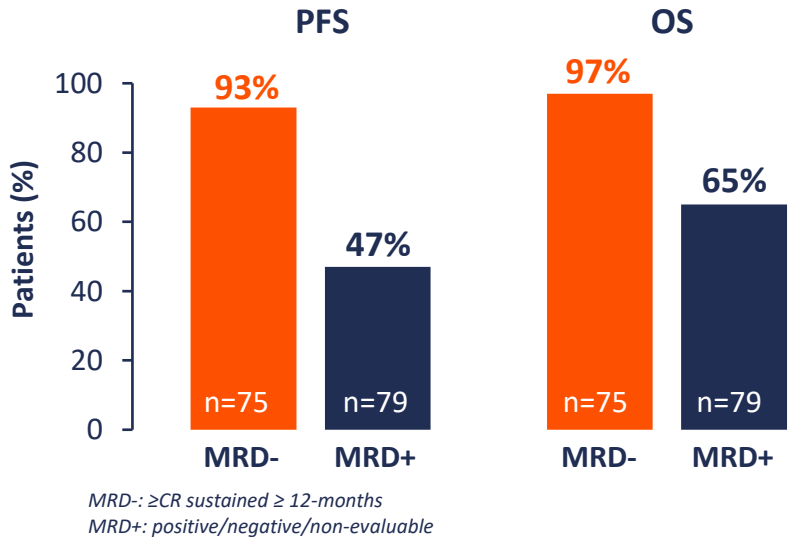
Cilta-cel, ciltacabtagene autoleucel; CR, complete response; d, dexamethasone; D, daratumumab; ITT, intent-to-treat; MM, multiple myeloma; MRD, minimal residual disease; P, pomalidomide; SOC, standard of care; V, bortezomib.

Popat R, et al. Presented at ASH 2024, San Diego, CA, USA, 7–10 December 2024. Abstr. 1032.

1032: Ciltacabtagene autoleucel vs SOC in patients with lenalidomide-refractory MM after 1–3 lines of therapy: MRD negativity in the phase III CARTITUDE-4 trial

Popat R, et al.

30-month survival rates in patients with sustained MRD-negative (10^{-5}) ≥CR post-cilta-cel



MRD-: ≥CR sustained ≥ 12-months
MRD+: positive/negative/non-evaluable

30-month survival rates in patients who received cilta-cel as study treatment in CARTITUDE-1 and -4

	CARTITUDE-1 (n=97)	CARTITUDE-4 (n=176)
30-month PFS rate, %	54	68
30-month OS rate, %	68	84

Patients treated with cilta-cel achieved rapid and deep MRD-negativity; sustained MRD-negative ≥CR corresponded to high rates of PFS and OS, supporting its prognostic value in patients treated with CAR T-cell therapy.

CAR, chimeric antigen receptor; cilta-cel, ciltacabtagene autoleucel; CR, complete response; MM, multiple myeloma; MRD, minimal residual disease; OS, overall survival; PFS, progression-free survival; SOC, standard of care.

Popat R, et al. Presented at ASH 2024, San Diego, CA, USA, 7–10 December 2024. Abstr. 1032.

New approaches to the use of existing BCMA-targeting agents

Prof. Katja Weisel
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772: BVd vs DVd in RRMM: Overall survival analysis and updated efficacy outcomes of the phase III DREAMM-7 trial

Hungria V, et al.

Baseline characteristics

- Anti-BCMA-naïve adults with MM
- ≥1 prior line of therapy
- PD on/after latest therapy
- Not refractory/intolerant to bortezomib or daratumumab

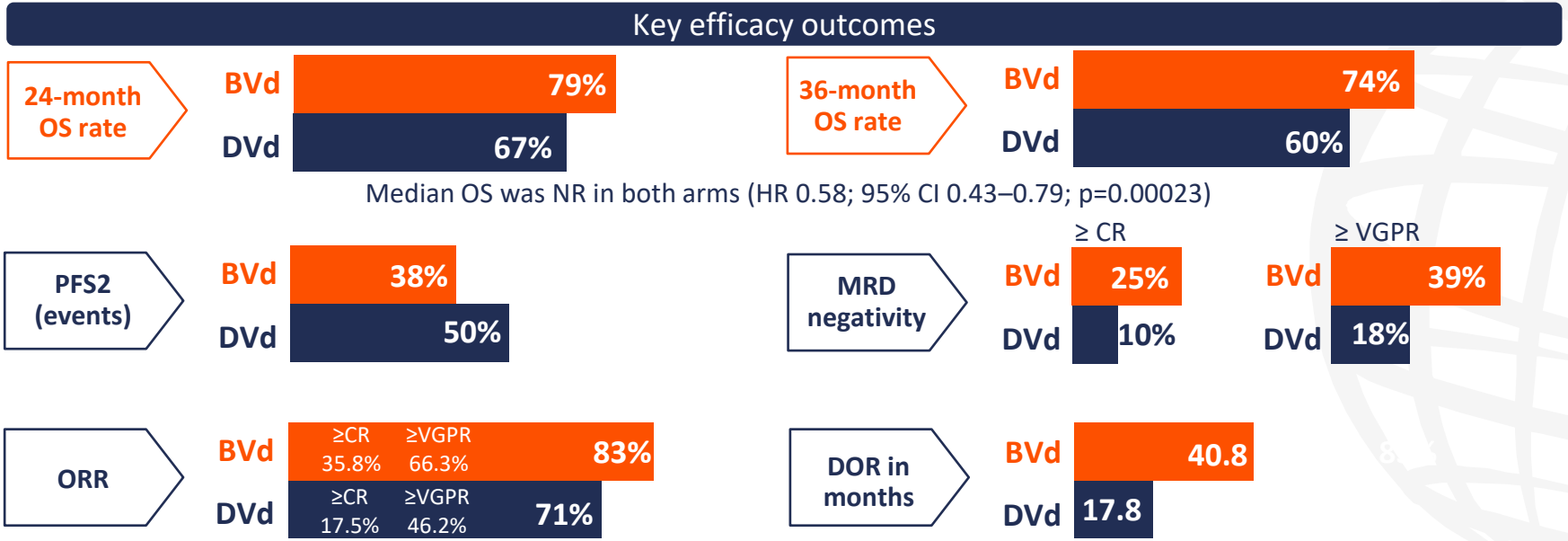
	Randomized (N=494)	
	BVd ITT n=243 (treated, n=242)	**DVd ITT n=251** (treated, n=246)
Age, years (range)	65 (34–86)	64 (32–89)
1 prior line of therapy, %	51	50
High-risk cytogenetic abnormality, %	28	27
Prior bortezomib, %	86	84
Prior lenalidomide, %	52	52
Lenalidomide refractory, %	33	35
Prior daratumumab, %	1	2
39.4 months median follow-up (0.1–52.3) **Ongoing treatment**	**25%**	**15%**

B, belantamab mafodotin; BCMA, B-cell maturation antigen; D, daratumumab; d, dexamethasone; ITT, intent-to-treat; PD, progressive disease; RRMM, relapsed/refractory multiple myeloma; V, bortezomib. Hungria V, et al. Presented at ASH 2024, San Diego, CA, USA, 7–10 December 2024. Abstr. 772.

772: BVd vs DVd in RRMM: Overall survival analysis and updated efficacy outcomes of the phase III DREAMM-7 trial

Hungria V, et al.

Key efficacy outcomes



Significant PFS, OS, DOR and MRD-negativity benefits were observed with BVd vs DVd, suggesting that BVd could become a new standard-of-care treatment option for patients with RRMM.

B, belantamab mafodotin; CI, confidence interval; CR, complete response; D, daratumumab; d, dexamethasone; DOR, duration of response; HR, hazard ratio; MRD, minimal residual disease; NR, not reached; ORR, overall response rate; OS, overall survival; PFS2, progression-free survival on second line of therapy; RRMM, relapsed/refractory multiple myeloma; V, bortezomib; VGPR, very good partial response. Hungria V, et al. Presented at ASH 2024, San Diego, CA, USA, 7–10 December 2024. Abstr. 772.

772: BVd vs DVd in RRMM: Overall survival analysis and updated efficacy outcomes of the phase III DREAMM-7 trial

Hungria V, et al.

Key safety outcomes

Safety summary, n (%)	BVd (N=242)	DVd (N=246)
Any AE	242 (100)	246 (100)
Grade 3/4 AE	230 (95)	191 (78)
AEs leading to permanent discontinuation of study drug	77 (32)	47 (19)
Any SAE	129 (53)	94 (38)
Fatal SAE	26 (11)	20 (8)
Deaths	69 (29)	101 (41)
Cancer	23 (10)	53 (22)
CV condition	8 (3)	4 (2)
Sepsis	8 (3)	4 (2)
Stroke	0	1 (<1)
Trauma	0	1 (<1)
Other non-CV condition	24 (10)	25 (10)

Non-ocular AEs of clinical interest included:

Blood and lymphatic system disorders
Thrombocytopenia, anaemia and neutropenia

Infections and infestations
Pneumonia

BCVA outcomes

Changes at follow-up in patients with bilateral worsening of BCVA from normal or >20/25 baseline:

- **93%** had first event **resolved to ≤20/50**
- **80%** had first event **resolved to ≤20/200**
- **96%** had first event **improved to ≤20/50**
- **100%** had first event **improved to ≤20/200**

Blurred vision was the most common AE in BVd arm with 68% (any grade) and 24% (3/4 grade) experiencing it

Safety and tolerability of BVd was consistent with the primary analysis.

AE, adverse event; B, belantamab mafodotin; BCVA, bestcorrected visual acuity; CV, cardiovascular; D, daratumumab; d, dexamethasone; SAE, serious adverse event; V, bortezomib.

Hungria V, et al. Presented at ASH 2024, San Diego, CA, USA, 7–10 December 2024. Abstr. 772.

497: Phase I study of belantamab mafodotin in combination with standard of care in transplant-ineligible newly diagnosed MM: DREAMM-9 updated interim analysis

Usmani SZ, et al.

Safety endpoints

- 108 patients recruited across 8 cohorts*
- Median age (range): 74.0 (51–88) years
- Median follow-up: 7.8–37.6 months

Patients who received ≥1 dose of B (n=105)

100% experienced AEs

Across cohorts (n=105)

55% experienced Gr ≥3 ocular events†

95% experienced dose interruptions/delays

33% dose reductions in affected patients

Cohorts 1–3 had the highest proportion of Gr ≥3 KVA events

C1	C2	C3
83%	92%	85%
B 1.9 mg/kg Q3/4W* (N=12)	B 1.9 mg/kg Q6/8W* (N=12)	B 1.4 mg/kg Q3/4W* (N=13)

Most common non-ocular Gr ≥3 AEs across all cohorts

Thrombocytopenia	Neutropenia	COVID-19 pneumonia
30%	26%	14%

*All cohorts received B with standard VRd for Cycles 1–8 (21-day cycle), followed by Rd for Cycles 9+ (28-day cycle). †Based on KVA.
AE, adverse event; B, belantamab mafodotin; C, cohort; d, dexamethasone; Gr, grade; KVA, keratopathy and visual acuity scale; MM, multiple myeloma; Q3/4W, every 3/4 weeks; Q6/8W, every 6/8 weeks; R, lenalidomide; V, bortezomib.
Usmani SZ, et al. Presented at ASH 2024, San Diego, CA, USA, 7–10 December 2024. Abstr. 497.

497: Phase I study of belantamab mafodotin in combination with standard of care in transplant-ineligible newly diagnosed MM: DREAMM-9 updated interim analysis

Usmani SZ, et al.

Safety and efficacy outcomes

BCVA analyses

had a decrease in BCVA score†

- Median **time to onset 194 days** (range: 42–713)
- **Resolved in 89%** of patients in a median of **85 days** (range: 22–421)

- Longest median time to onset reported with longer dosing intervals
- Shortest median time to onset (76 days) with C1 (Q3/4W)

Across cohorts*

ORR 71–100%

≥CR 30–92%

Time to ≥VGPR

ranged from: 2.1–3.2 months

MRD-negativity rates in patients

		with ≥VGPR	with ≥CR
B 1.0 mg/kg Q12W* (N=10)	C8	10%	0%
B 1.9 mg/kg Q3/4W* (N=12)	C1	83%	75%

Higher starting doses and shorter intervals of belantamab mafodotin were associated with higher and faster MRD-negativity rates. Lower and longer dosing intervals were associated with fewer ocular events and increased time to onset of clinically meaningful BCVA changes.

*All cohorts received B with standard VRd for Cycles 1–8 (21-day cycle), followed by Rd for Cycles 9+ (28-day cycle). † From baseline (20/25 or better) to 20/50 or worse.
B, belantamab mafodotin; BCVA, best-corrected visual acuity; C, cohort; CR, complete response; d, dexamethasone; MM, multiple myeloma; MRD, minimal residual disease; ORR, overall response rate; Q3/4W, every 3/4 weeks; Q12W, every 12 weeks; R, lenalidomide; V, bortezomib; VGPR, very good partial response.

Usmani SZ, et al. Presented at ASH 2024, San Diego, CA, USA, 7–10 December 2024. Abstr. 497.

493: Phase II study of teclistamab-based induction regimens in patients with TE NDMM: Results from the GMMG-HD10/DSMM-XX (MajesTEC-5) trial

Raab MS, et al.

Baseline characteristics and key efficacy outcomes

49 patients enrolled across study arms to receive teclistamab-based induction regimens*:
A: TEC (QW)-DR (n=10); **A1: TEC (Q4W)-DR** (n=20);
B: TEC (Q4W)-DVR (n=19)
Maintenance TEC-D x 18 cycles

Median duration of induction of study treatment: **2.6 months** (range 0.03–7.66)

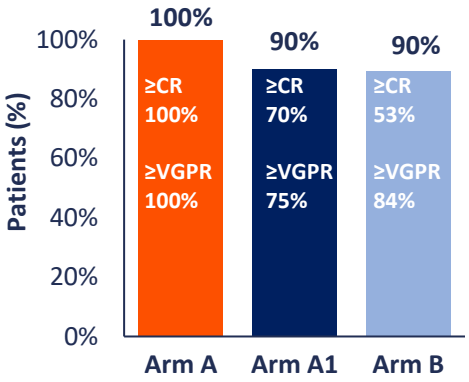
Median relative dose intensity:
- TEC: 99%
- D: 92%
- R: 87%
- V: 83%

Total cohort

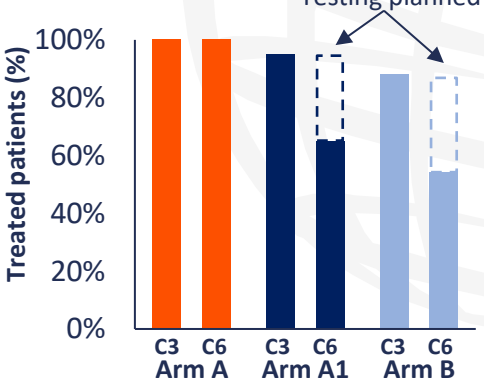
- **16%** aged ≥65 years
- **96%** ECOG-PS 0–1
- **12%** ISS stage III
- **20%** High cytogenic risk

- Two patients discontinued study treatment during induction (one in Arm A1 and one in Arm B)
- Induction ongoing in 24 patients

Response rate



MRD negativity (10^{-5})



*Each cycle was 28 days; dexamethasone also administered in cycles 1 and 2. C, cycle; CR, complete response; D, daratumumab; ECOG-PS, Eastern Cooperative Oncology Group Performance Status; ISS, International Staging System; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; QW, weekly; Q4W, every 4 weeks; R, lenalidomide; TE, transplant eligible; TEC, teclistamab; V, bortezomib; VGPR, very good partial response. Raab MS, et al. Presented at ASH 2024, San Diego, CA, USA, 7–10 December 2024. Abstr. 493.

493: Phase II study of teclistamab-based induction regimens in patients with TE NDMM: Results from the GMMG-HD10/DSMM-XX (MajesTEC-5) trial

Raab MS, et al.

Safety profile

Grade 3/4 TEAEs occurring in ≥10% of patients

Haematologic

- Neutropenia: 57%
- Lymphopenia: 43%
- Leukopenia: 18%

Non-haematologic

- ↑ GGT: 12%
- ↑ Lipase: 10%

Infections: 35%

CRS

- Occurred in **65%** of patients (all grade 1/2)
- All resolved; no discontinuations due to CRS

ICANS

- Not experienced in any patient

Infections

- No discontinuations due to infection
- Hypogammaglobulinaemia reported in 92% of patients
- Infection prophylaxis, including Ig replacement, was strongly recommended

TEC combined with DR and DVR as induction therapy was feasible with very high early clinical efficacy. Among patients with MRD assessment at data cut-off, all achieved MRD-negativity (10^{-5}) by the first MRD assessment. Stem cell mobilization was feasible with both regimens.

D, daratumumab; CRS, cytokine release syndrome; GGT, gamma-glutamyltransferase; ICANS, immune effector cell-associated neurotoxicity; Ig, immunoglobulin; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; R, lenalidomide; TE, transplant eligible; TEAE, treatment-emergent adverse event; TEC, teclistamab; V, bortezomib.

Raab MS, et al. Presented at ASH 2024, San Diego, CA, USA, 7–10 December 2024. Abstr. 493.

494: Phase III study of TEC-R vs TEC alone in NDMM as maintenance therapy following ASCT: Safety run-in results from the MajesTEC-4/EMN30 trial

Zamagni E, et al.

Safety outcomes

94 patients (median age ≈58 years) treated across 3 cohorts of different TEC dose frequencies:

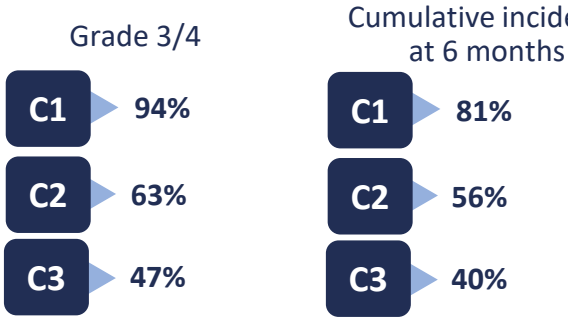
- **C1** (TEC-R; n=32): TEC QW → Q4W
- **C2** (TEC-R; n=32): TEC Q4W
- **C3** (TEC; n=30): TEC Q4W

- 86% patients remained on therapy (September 2024)
- Median follow-up: 21 months in C1; 9 months in C2 and C3

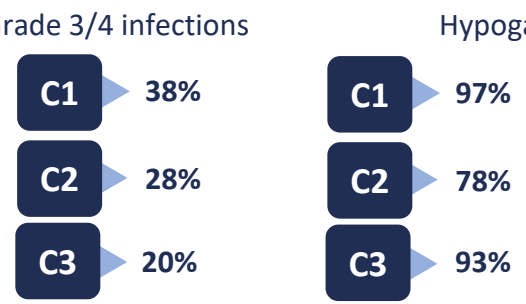
CRS: Occurred in **45%** of patients (all grade 1/2); most events occurred during TEC step-up dosing

ICANS: None reported

Neutropenia was the most common haematologic AE



Infections and hypogammaglobulinaemia



- **All patients** received ≥1 dose of IVIg or SCIg
- Infection prophylaxis, including Ig replacement, strongly recommended

There were low rates of treatment discontinuations due to TEAEs (5% overall)

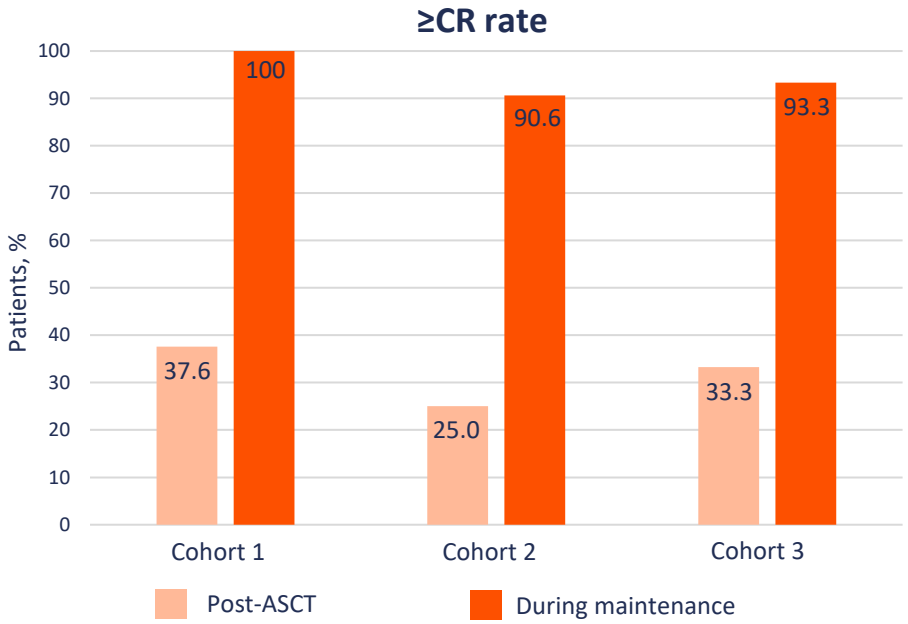
AE, adverse event; ASCT, autologous stem cell transplant; C, cohort; CRS, cytokine release syndrome; Cy, cycle; ICANS, immune effector cell-associated neurotoxicity; Ig, immunoglobulin; IV, intravenous; NDMM, newly diagnosed multiple myeloma; R, lenalidomide; SC, subcutaneous; TEAE, treatment-emergent AE; TEC, teclistamab.

Zamagni E, et al. Presented at ASH 2024, San Diego, CA, USA, 7–10 December 2024. Abstr. 494.

494: Phase III study of TEC-R vs TEC alone in NDMM as maintenance therapy following ASCT: Safety run-in results from the MajesTEC-4/EMN30 trial

Zamagni E, et al.

Efficacy data



100% of evaluable patients were MRD negative during maintenance across all three cohorts

TEC-R and TEC may be safely administered as maintenance therapy following ASCT in NDMM. These data informed the randomized part of MajesTEC-4/EMN30, which is actively enrolling.

ASCT, autologous stem cell transplant; CR, complete response; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; R, lenalidomide; TEC, teclistamab.

Zamagni E, et al. Presented at ASH 2024, San Diego, CA, USA, 7–10 December 2024. Abstr. 494.

495: TEC-DP in patients with RRMM: Results from the MajesTEC-2 Cohort A and TRIMM-2 studies

D'Souza A, et al.

Safety outcomes

- 27 patients (TRIMM-2 n=10; MajesTEC-2 n=17)
- Median age (range) across cohorts: 62 (35–79) years
- Median follow-up (range): 25.8 (0.5–39.6) months

CRS

- Occurred in **56%** of patients (all Gr 1/2)
- All events resolved

ICANS

- 1 case (Gr 2) that resolved

Gr 3/4 TEAEs occurring in ≥15% of patients

Neutropenia	78%
Lymphopenia	22%
Anaemia	19%
COVID-19 pneumonia	19%
Pneumonia	19%

Gr 3/4 infections occurred in 63% of patients, most commonly:

Pneumonia	19%
Sinusitis	4%
COVID-19 infection	7%

- 4 patients **discontinued due to nonfatal TEAEs**
- **7 deaths** due to: PD (1); respiratory infections (5); bacteraemia (1)
- 4 of the 6 patients with infection-related deaths also had hypogammaglobulinaemia and were not receiving IVIg prior to infection onset

No fatal infections occurred following the implementation of an intensified infection prophylaxis plan, including Ig replacement.

CRS, cytokine release syndrome; D, daratumumab; Gr, grade; ICANS, immune effector cell-associated neurotoxicity; Ig, immunoglobulin; IV, intravenous; P, pomalidomide; PD, progressive disease; RRMM, relapsed/refractory multiple myeloma; TEAE, treatment-emergent adverse event; TEC, teclistamab.

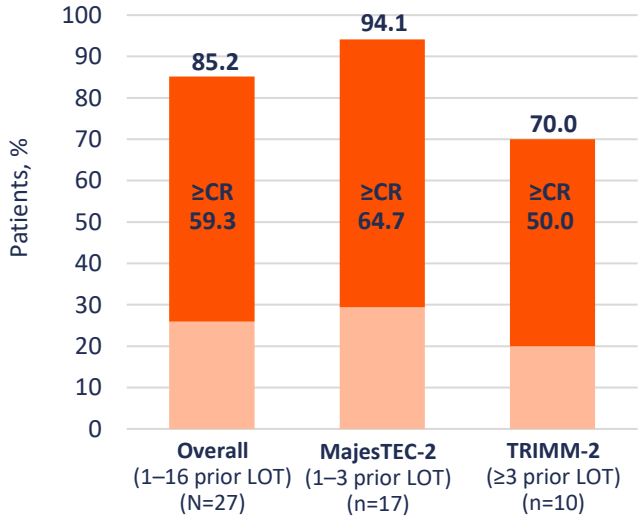
D'Souza A, et al. Presented at ASH 2024, San Diego, CA, USA, 7–10 December 2024. Abstr. 495.

495: TEC-DP in Patients with RRMM: Results from the MajesTEC-2 Cohort A and TRIMM-2 Studies

D'Souza A, et al.

Efficacy outcomes

Response rates



MajesTEC-2 (1–3 prior LOT)	**mDOR**	**NE** (range 9.7 months–NE)
	24-month PFS	**59.8%** (range 31.2–79.7)
TRIMM-2 (≥3 prior LOT)	**mDOR**	**25.6 months** (range 12.5–NE)
	24-month PFS	**46.7%** (range 15.0–73.7)

TEC-DP is feasible and shows promising efficacy, with a high rate of deep responses, in patients with RRMM, including D-exposed patients. Intensified recommendations may have improved the infection profile.

CR, complete response; D, daratumumab; LOT, line of therapy; mDOR, median duration of response; NE, not estimable; P, pomalidomide; PFS, progression-free survival; RRMM, relapsed/refractory multiple myeloma; TEC, teclistamab.

D'Souza A, et al. Presented at ASH 2024, San Diego, CA, USA, 7–10 December 2024. Abstr. 495.

Emerging BCMA-targeting agents

Prof. Katja Weisel
University Medical Center
Hamburg-Eppendorf,
Germany

Recorded following the **66th ASH Annual Meeting and Exposition**
(7–10 December 2024, San Diego, CA, USA)

1031: Phase II registrational study of anitocabtagene autoleucel (anito-cel) for the treatment of patients with RRMM: Preliminary results from the iMMagine-1 trial

Freeman CL, et al.

Baseline characteristics

- Triple-class–exposed (prior PI, IMiD, anti-CD38)
- Received ≥3 LOT and refractory to last line
- Evidence of measurable disease

	Safety evaluable (n=98)	Efficacy evaluable (n=86)
Age, years (range)	65 (38–78)	65 (38–78)
Extramedullary disease, %	16	15
High-risk cytogenetics, %	40	38
Refractory to last line of therapy, %	100	100
Penta-refractory, %	42	43
Median no. prior lines of therapy, n (range)	4 (3–8)	4 (3–8)
Prior ASCT, %	75	74
Bridging therapy, %	66	71

ASCT, autologous stem cell transplant; CD, cluster of differentiation; IMiD, immunomodulatory drug; LOT, line of therapy; PI, proteasome inhibitor; RRMM, relapsed/refractory multiple myeloma.

Freeman CL, et al. Presented at ASH 2024, San Diego, CA, USA, 7–10 December 2024. Abstr. 1031.

1031: Phase II registrational study of anitocabtagene autoleucel (anito-cel) for the treatment of patients with RRMM: Preliminary results from the iMMagine-1 trial

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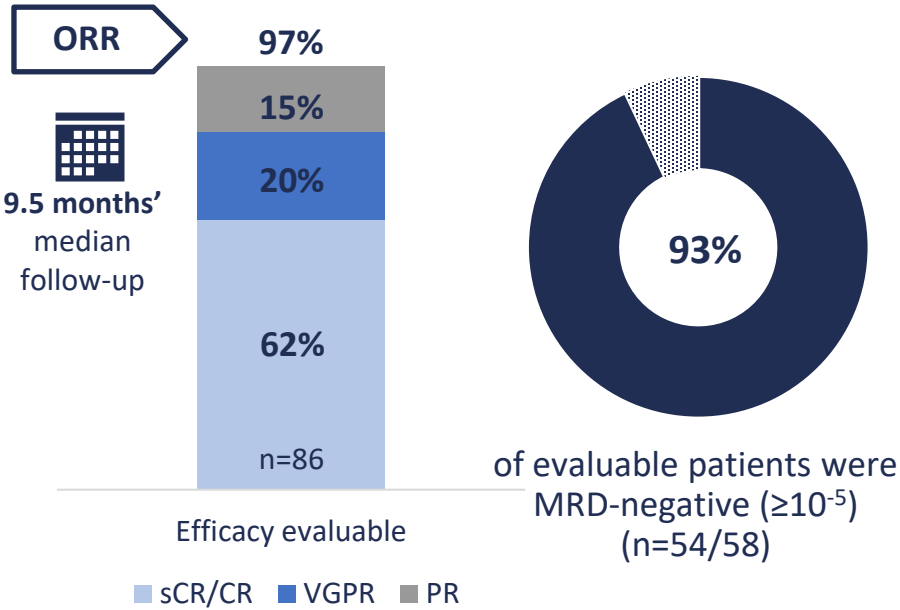
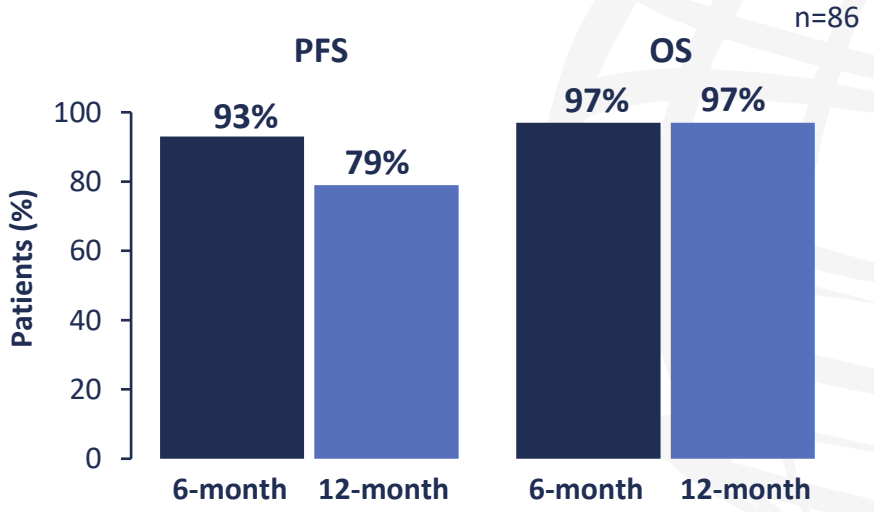
Response rates



of evaluable patients were MRD-negative ($\geq 10^{-5}$) (n=54/58)



CR, complete response; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; RRMM, relapsed/refractory multiple myeloma; sCR, stringent CR; VGPR, very good PR.

Freeman CL, et al. Presented at ASH 2024, San Diego, CA, USA, 7–10 December 2024. Abstr. 1031.

1031: Phase II registrational study of anitocabtagene autoleucel (anito-cel) for the treatment of patients with RRMM: Preliminary results from the iMMagine-1 trial

Freeman CL, et al.

Safety (n=98)

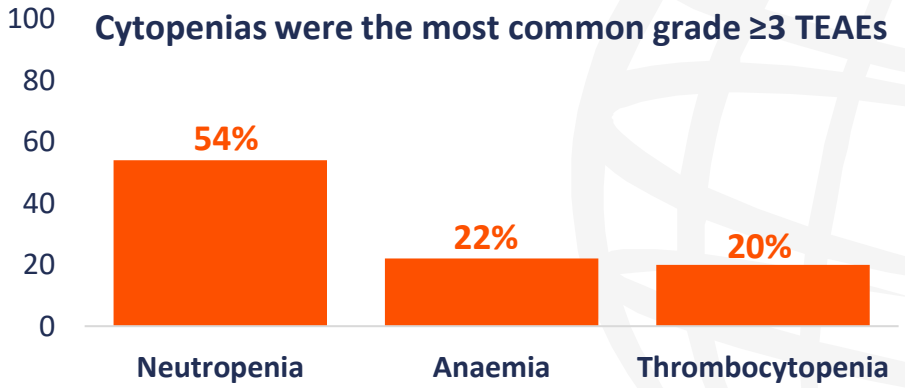
CRS

- Of any grade occurred in **83%** of patients with a **median onset of 4 days**
- **98%** instances resolved ≤14 days of anito-cel infusion

ICANS

- Of any grade occurred in **9%** of patients and **all cases resolved**
- **No delayed or non-ICANS NTs** observed, e.g. parkinsonism, cranial nerve palsies, Guillain–Barré syndrome

Cytopenias were the most common grade ≥3 TEAEs



- **No SPMs of T-cell origin or haematological malignancies reported**
- **No replication competent lentivirus detected**

Anito-cel demonstrated deep, durable responses in the fourth line RRMM setting and beyond, with a manageable safety profile, including no delayed or non-ICANS NTs.

CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; NT, neurotoxicity; RRMM, relapsed/refractory multiple myeloma; SPM, secondary primary malignancies; TEAE, treatment-emergent adverse event.

Freeman CL, et al. Presented at ASH 2024, San Diego, CA, USA, 7–10 December 2024. Abstr. 1031.

496: ABBV-383 plus daratumumab-dexamethasone in RRMM: A phase Ib dose-escalation and safety expansion study

Rodriguez C, et al.

Baseline characteristics (as of 12 September 2024)

- Adults with RRMM with ≥3 prior LOT
- Prior PI, IMiD, anti-CD38 permitted

	Daratumumab plus dexamethasone in combination with ABBV-383 dosed at:			
	20 mg (n=37)	40 mg (n=35)	60 mg (n=14)	Total (N=86)
Median age, years (range)	67 (46–89)	72 (39–87)	68 (47–84)	69 (39–89)
R-ISS III, %	24	24	21	24
High-risk cytogenetics, %	36	44	42	40
Median prior lines of therapy, n (range)	4 (3–10)	4 (3–9)	4 (3–7)	4 (3–10)
Prior anti-CD38 mAb exposure, %	68	77	57	70
Anti CD-38 mAb refractory, %	46	66	57	56
Triple-class exposed, %	68	77	57	70
Triple-class refractory, %	46	46	43	45

CD, cluster of differentiation; IMiD, immunomodulatory drug; LOT, line of therapy; mAb, monoclonal antibody; PI, proteasome inhibitor; R-ISS, Revised International Staging System; RRMM, relapsed/refractory multiple myeloma.

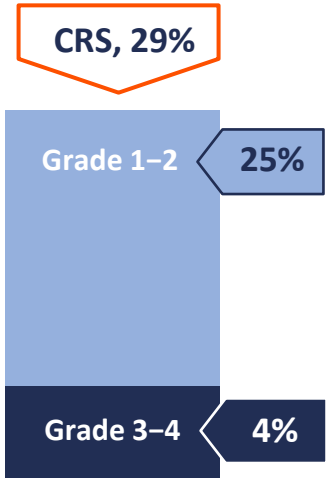
Rodriguez C, et al. Presented at ASH 2024, San Diego, CA, USA, 7–10 December 2024. Abstr. 496.

496: ABBV-383 plus daratumumab-dexamethasone in RRMM: A phase Ib dose-escalation and safety expansion study

Rodriguez C, et al.

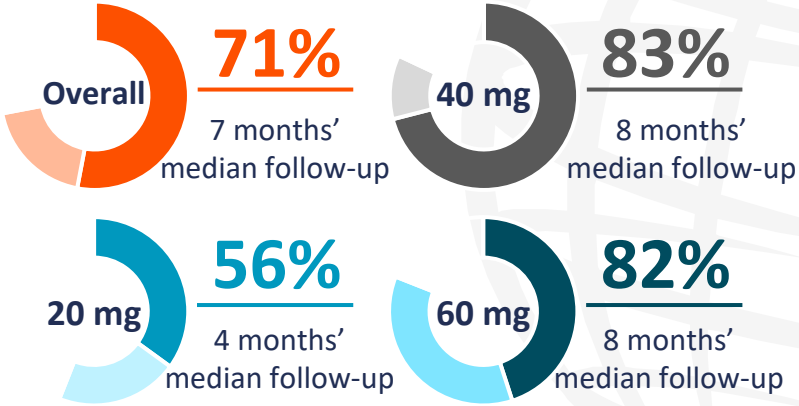
Safety profile

Any-grade TEAEs, % (>25%)	ABBV-383 + Dd (Total, N=86)
Haematologic	
Neutropenia	48
Anaemia	31
Thrombocytopenia	31
Non-haematologic	
CRS	29
Fatigue	26
Infections	67
TEAE leading to	
ABBV-383/Dd:	
Interruption	57/64
Discontinuation*	14/15
Death	14



ORR (≥VGPR, PR) by ABBV-383 dose

n=80 evaluable for disease assessment



Preliminary data suggest ABBV-383 in combination with Dd is tolerable. Incidence of CRS was only 29% and early response rates were promising in these heavily pretreated patients with MM.

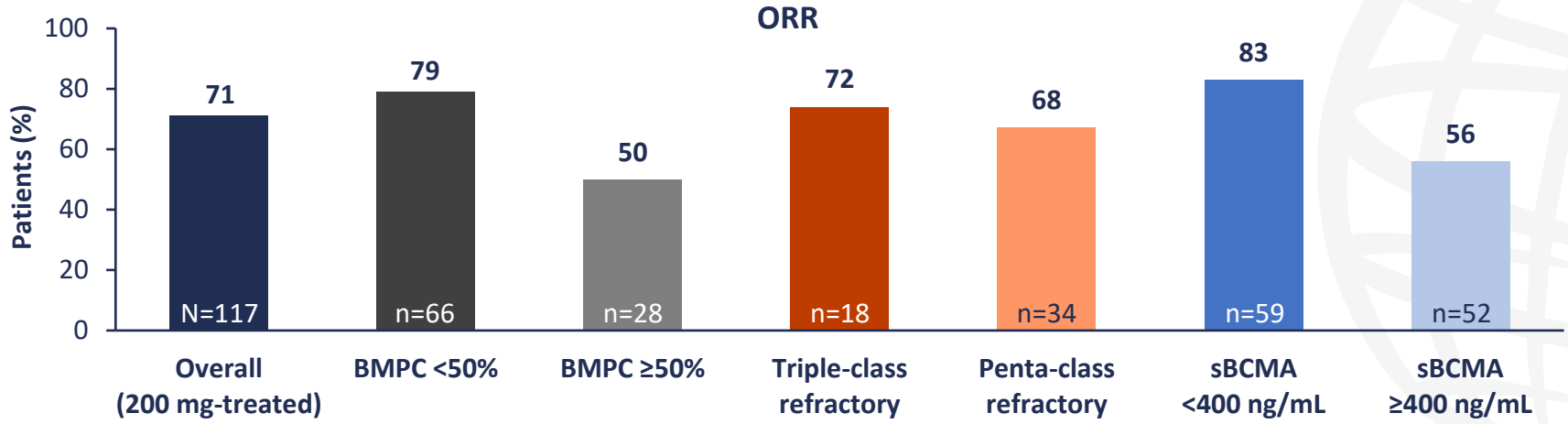
*Most common cause was disease progression (22%). CRS, cytokine release syndrome; Dd, daratumumab and dexamethasone; MM, multiple myeloma; ORR, overall response rate; PR, partial response; RRMM, relapsed/refractory MM; TEAE, treatment-emergent adverse event; VGPR, very good partial response.

Rodriguez C, et al. Presented at EHA2024, Madrid, Spain, 13–16 June 2024. Abstr. S211.

3369: Linvoseltamab in patients with RRMM: Longer follow-up and selected high-risk subgroup analyses of the LINKER-MM1 study

Shah MR, et al.

ORR and mDOR by patient subgroup



	Overall (200 mg-treated)	BMPC <50%	BMPC ≥50%	Triple-class refractory	Penta-class refractory	sBCMA <400 ng/mL	sBCMA ≥400 ng/mL
≥CR	52%		39%		41%		40%
mDOR	29 months		19 months		29 months		29 months

BMPC, bone marrow plasma cell; CR, complete response; mDOR, median duration of response; ORR, overall response rate; RRMM, relapsed/refractory multiple myeloma; sBCMA, soluble B-cell maturation antigen.

Shah MR, et al. Presented at ASH 2024, San Diego, CA, USA, 7–10 December 2024. Abstr. 3369.

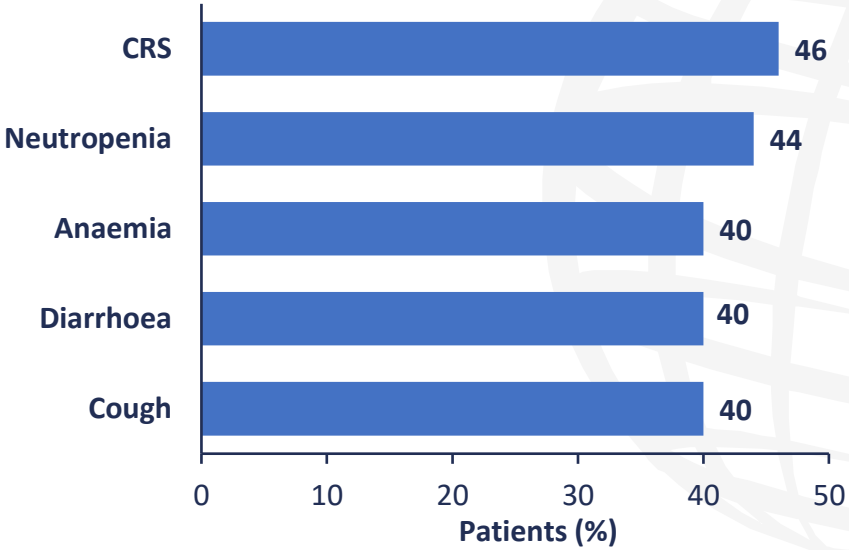
3369: Linvoseltamab in patients with RRMM: Longer follow-up and selected high-risk subgroup analyses of the LINKER-MM1 study

Shah MR, et al.

Survival outcomes (months) by patient subgroup

Patient subgroup	mPFS, months (95% CI)	mOS, months (95% CI)
Overall (200 mg-treated)	**NR** (17.3–NE)	**31.4** (23.8–NE)
BMPC <50%	**NR** (NE–NE)	**31.4** (27.8–NE)
BMPC ≥50%	**17.3** (2.5–20.8)	**21.6** (10.2–NE)
Triple-class refractory	**NR** (7.6–NE)	**21.7** (11.7–NE)
Penta-class refractory	**NR** (6.4–NE)	**31.4** (10.2–NE)
sBCMA <400 ng/mL	**NR** (NE–NE)	**NR** (27.8–NE)
sBCMA ≥400 ng/mL	**15.7** (3.0–NE)	**23.8** (11.7–NE)

Common TEAEs (any grade; all patients, n=117)



Linvoseltamab may provide meaningful clinical benefit in high-risk and other hard to treat patients with limited treatment options.

BMPC, bone marrow plasma cell; CI, confidence interval; CRS, cytokine release syndrome; m, median; NE, non-evaluable; NR, not reached; OS, overall survival; PFS, progression-free survival; RRMM, relapsed/refractory multiple myeloma; sBCMA, soluble B-cell maturation antigen; TEAE, treatment-emergent adverse event.

Shah MR, et al. Presented at ASH 2024, San Diego, CA, USA, 7–10 December 2024. Abstr. 3369.