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Targeting BCMA in multiple myeloma: Insights from ASH 2024

Practice aid for the role of BCMA-targeting agents in relapsed/refractory multiple myeloma

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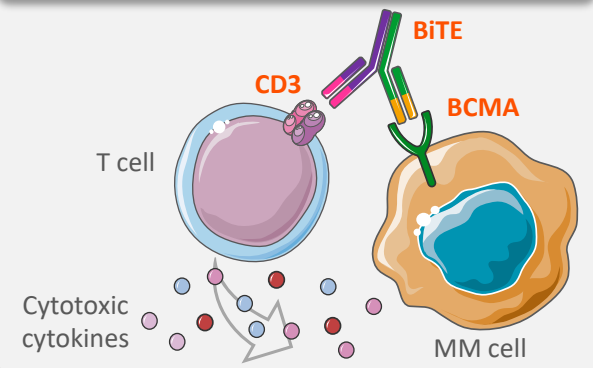
Role of BCMA-targeted agents in the management of relapsed or refractory multiple myeloma

Bispecific T-cell engager antibodies[1]



Elranatamab[2,3]

Warning:[2,3] CRS and neurotoxicity incl. ICANS

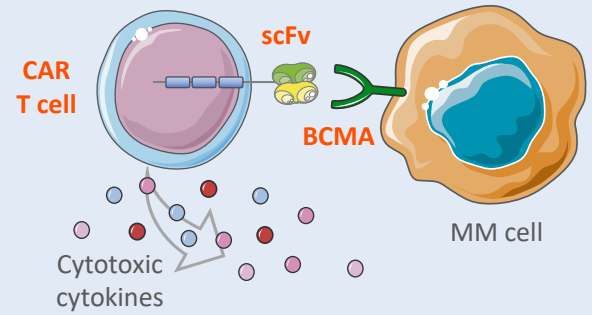
- **≥3 prior lines** (incl. PI, IMiD, anti-CD38 mAb) and disease progression on last therapy[2] → Subject to additional monitoring[2]
- **≥4 prior lines** (incl. PI, IMiD, anti-CD38 mAb)[3] → Only available through REMS[3]

Teclistamab[4,5]

Warning:[4,5] CRS and neurotoxicity incl. ICANS

- **≥3 prior lines** (incl. PI, IMiD, anti-CD38 mAb) and disease progression on last therapy[4] → Subject to additional monitoring[4]
- **≥4 prior lines** (incl. PI, IMiD, anti-CD38 mAb)[5] → Only available through REMS[5]

Chimeric antigen receptor T cells[1]



Cilta-cel[6,7]

Warning:[6,7] CRS, neurotoxicities, HLH/MAS, prolonged and recurrent cytopenia, SHMs

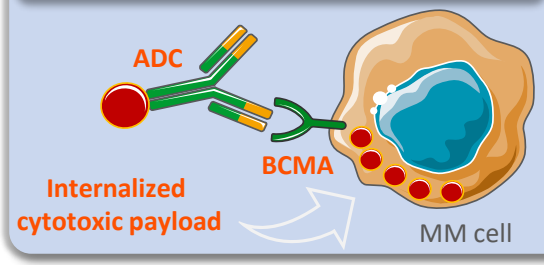
- **≥1 prior line** (incl. PI, IMiD), **lenalidomide refractory**, disease progression on last therapy[6] → Subject to additional monitoring[6]
- **≥1 prior line** (incl. PI, IMiD) and **refractory to lenalidomide**[7] → Only available through REMS[7]

Ide-cel[8,9]

Warning:[8,9] CRS, neurotoxicities, HLH/MAS, prolonged and recurrent cytopenia, SHMs

- **≥2 prior lines** (incl. PI, IMiD, anti-CD38 mAb) and disease progression on last therapy[8] → Subject to additional monitoring[8]
- **≥2 prior lines** (incl. PI, IMiD, anti-CD38 mAb)[9] → Only available through REMS[9]

Antibody–drug conjugates[1]



Belantamab mafodotin — WITHDRAWN[10,11]

July 2024

The EMA accepted an MAA seeking approval of belantamab mafodotin in combination with bortezomib and dexamethasone (BVd) or pomalidomide and dexamethasone (BPd) for the treatment of patients with RRMM[12]

November 2024

The FDA has accepted a BLA for belantamab mafodotin in combination with bortezomib and dexamethasone (BVd), or pomalidomide and dexamethasone (BPd), for the treatment of MM in patients who have received ≥1 prior line of therapy[13]

Regulatory body
EMA
FDA

Summary of latest data for approved BCMA-targeted bispecific antibodies in multiple myeloma*

Elranatamab: MagnetisMM-3[14]

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

N=123

SC elranatamab step-up priming doses; then 76 mg QW

Q2W dosing

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

Q4W dosing

Patients with ≥6 cycles of QW dosing achieving PR or better for ≥2 months were transitioned to Q2W

58 switched to **Q2W**

28 switched to **Q4W**

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

- **Maintained response** for **≥6 months** post-switch: **93%**
- **Maintained** a **complete response or better**: **88%**
- Had **progressive disease**: **4%**

mPFS 17.2 months | **mOS** 24.6 months | **MRD-negativity** 90%

Grade 3/4 TEAEs, %	Before Q4W	After 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

Teclistamab: Real-world data[15,16]

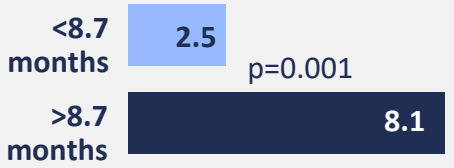
Effect of prior BCMA-DT[15]

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.

Prior BCMA-DT (n=193)
No prior BCMA-DT (n=192)

ORR 49% vs 62% p=0.012

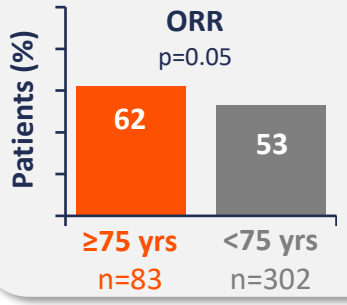
PFS (months) by time gap between last exposure to prior BCMA-DT and teclistamab initiation

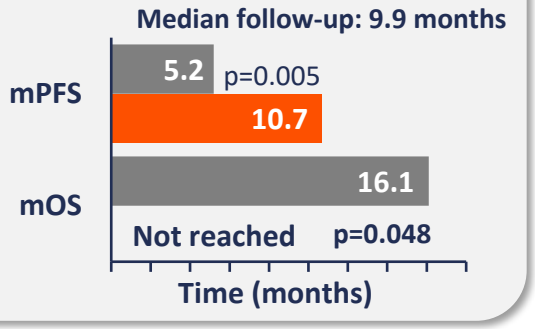


PFS (months) by number of prior BCMA-DT

Outcomes in elderly patients[16]

Teclistamab demonstrates comparable efficacy and safety in patients aged ≥75 years to that in MajesTEC-1 overall. Multivariate analysis showed patients aged ≥75 years had no significant impact on survival outcomes.





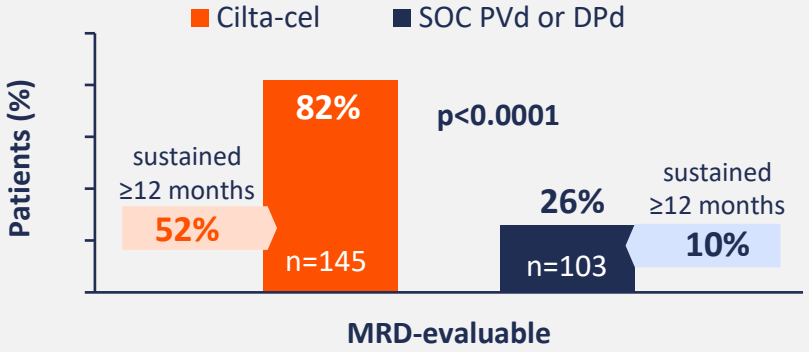
*Not all congress data are included in this practice aid. Data included here were selected by faculty for discussion within the accompanying educational activity.
†Responders per blinded independent central review who switched to Q4W dosing ≥6 months before the data cut-off.

Summary of latest data for approved BCMA-targeted CAR T-cell therapy in multiple myeloma*

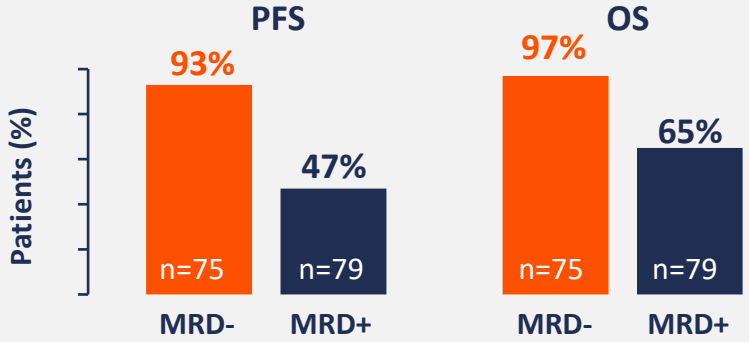
Cilta-cel: CARTITUDE-4[17]

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 CAR T-cell-treated patients treated

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



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

Cilta-cel vs ide-cel: Real-world use[18]

Comparing cilta-cel vs ide-cel in SOC setting for RRMM showed a higher efficacy (responses and survival)

	Treatment response	OR (95% CI)
Cilta-cel (n=236) vs Ide-cel (n=350)	Best ≥CR	2.42‡ (1.63–3.60)
	Best ORR (≥PR)	1.60 (0.90–2.83)

Infused		HR (95% CI)
	PFS	0.48‡ (0.36–0.63)
	OS	0.67 (0.46–0.97)

Cilta-cel was associated with higher toxicities (severe CRS, delayed NT, infections, trend for SPMs) but no difference in other toxicities. No difference in non-relapse mortality.

	OR (95% CI)
Grade ≥3 CRS	6.80‡ (2.28–20.33)
Infections	2.03‡ (1.41–2.92)
Delayed NT	20.07‡ (4.46–90.20)
Grade ≥3 ICANS	1.54 (0.53–4.48)
Any SPMs	1.77 (0.89–3.56)

Non-relapse mortality
HR 1.24
(95% CI 0.67–2.30)
p=0.49

*Not all congress data are included in this practice aid. Data included here were selected by faculty for discussion within the accompanying educational activity.
†Defined as confirmed MRD negativity ≥12 months apart and without MRD positivity in between.
‡Statistical significance p<0.001.

New horizons for BCMA-targeting agents in multiple myeloma

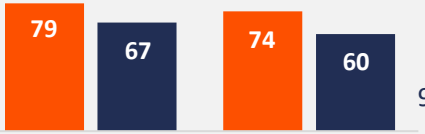
Belantamab mafodotin: DREAMM-7[19]

Favourable survival outcomes and MRD-negativity observed with BVd vs DVd, suggesting that BVd could become a new SOC treatment option for patients with RRMM

≥1 prior LOT; PD on/after latest therapy

BVd vs **DVd:** **ITT (treated):** n=243 (242); n=251 (246)

OS rate (% patients)



mOS

NR in both arms
HR 0.58
95% CI 0.43–0.79
p=0.00023

MRD-negativity

≥CR
25% vs **10%**

≥VGPR
39% vs **18%**

Safety and tolerability of BVd was consistent with the primary analysis

Safety summary, % patients	BVd (n=242)	DVd (n=246)
Permanent discontinuation of study drug due to AEs	32	19
Any SAE	53	38
Fatal SAE	11	8

Blurred vision was the **most common AE in BVd arm** affecting 68% (any grade) and 24% (3/4 grade) of BVd-treated patients

Congress snapshot: Emerging agents and indications

Bispecific antibodies

- **ABBV-383 (etentamig): Phase Ib study[20]** — Preliminary data suggest ABBV-383 plus Dd is tolerable. Low incidence of CRS and early response rates were promising in these heavily pretreated patients with MM.
- **Linvoseltamab: LINKER-MM1[21]** — Linvoseltamab may provide meaningful clinical benefit in hard to treat and high-risk patients with limited treatment options.
- **Teclistamab: MajesTEC-2/TriMM-2[22]** — 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. No fatal infections occurred following the implementation of an intensified infection prophylaxis plan, including Ig replacement.
- **Teclistamab: MajesTEC-4[23]** — TEC-R and TEC may be safely administered as maintenance therapy following ASCT in NDMM. These data informed the randomized part of the MajesTEC-4/EMN30 trial.
- **Teclistamab: MajesTEC-5[24]** — 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.

CAR T

- **Anito-cel: iMMagine-1[25]** — 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.

ADC

- **Belantamab mafodotin: DREAMM-9[26]** — 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.

*Not all congress data are included in this practice aid. Data included here were selected by faculty for discussion within the accompanying educational activity.

Abbreviations and references

Abbreviations

ADC, antibody–drug conjugate; AE, adverse event; ASCT, autologous stem cell transplant; B, belantamab mafodotin; BCMA, B cell maturation antigen; BCMA-DT, BCMA-directed therapy; BCVA, best-corrected visual acuity; BiTE, bispecific T cell engager; BLA, biologics license application; CAR, chimeric antigen receptor; CI, confidence interval; cilta-cel, ciltacabtagene autoleucel; CR, complete response; CRS, cytokine release syndrome; CTD, connective tissue disorders; d, dexamethasone; D, daratumumab; EMA, European Medicines Agency; FDA, US Food and Drug Administration; HLH/MAS, haemophagocytic lymphohistiocytosis/macrophage activation syndrome; HR, hazard ratio; ICANS, immune effector cell-associated neurotoxicity syndrome; ide-cel, idecabtagene vicleucel; Ig, immunoglobulin; IMiD, immunomodulatory drug; ITT, intention-to-treat; LOT, line of therapy; m, median; MAA, marketing authorization application; mAb, monocolonal antibody; MM, multiple myeloma; MRD, minimal residual diseases; NDMM, newly diagnosed MM; NR, not reached; NT, neurotoxicities; OR, odds ratio; ORR, overall response rate; OS, overall survival; P, pomalidomide; PD, progressive disease; PFS, progression-free survival; PI, proteasome inhibitor; PR, partial response; QW, every week; Q2W, every 2 weeks; Q4W, every 4 weeks; R, lenalidomide; REMS, Risk Evaluation and Mitigation Strategies; RRMM, relapsed/refractory MM; SAE, serious adverse event; SC, subcutaneous; SHM, secondary haematological malignancies; SOC, standard of care; SPM, second primary malignancies; TEAE, treatment-emergent AE; TEC, teclistamab; V, bortezomib; VGPR, very good partial response.

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*EMA Summary of product characteristics available at: www.ema.europa.eu/en/medicines.

†FDA prescribing information available at: www.accessdata.fda.gov/scripts/cder/daf/index.cfm.
All URLs accessed 20 January 2025.

‡Presented at the 66th American Society of Hematology Annual Meeting and Exposition (San Diego, CA, USA, 7–10 December 2024).