touch™ HAEMATOLOGY

Targeting BCMA in multiple myeloma: Insights from COMy and EHA 2024

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

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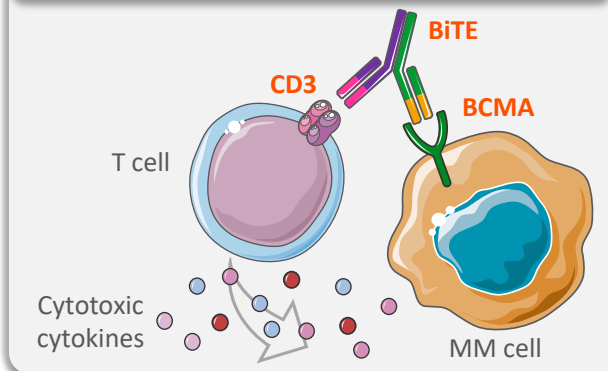
Role of BCMA-targeted agents in the management of relapsed or refractory multiple myeloma

Bispecific T-cell engager antibodies[1]



Elranatamab[2,3]

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

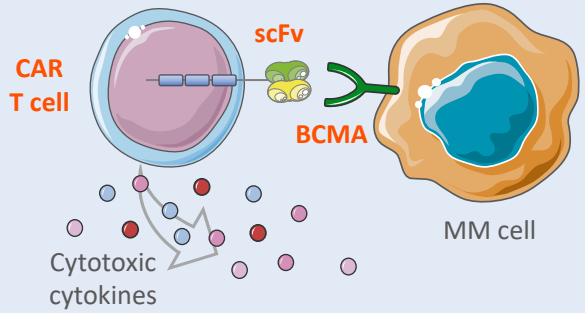
- **≥3 prior lines** (incl. PI, IMiD, anti-CD38 mAb) and disease progression on last therapy[2] → Subject to additional monitoring[2]
- **≥4 prior lines** (incl. PI, IMiD, anti-CD38 mAb)[3] → Only available through REMS[3]

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

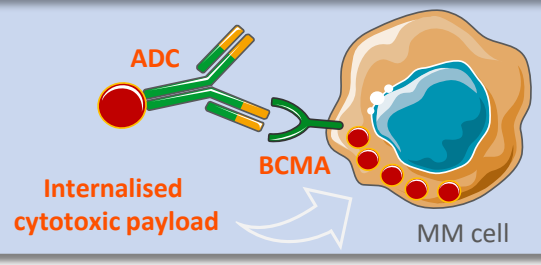
- **≥1 prior line** (incl. PI, IMiD), **lenalidomide refractory**, disease progression on last therapy[6] → Subject to additional monitoring[6]
- **≥1 prior line** (incl. PI, IMiD) and **refractory to lenalidomide**[7] → Only available through REMS[7]

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 with pomalidomide and dexamethasone (BPd) for the treatment of patients with RRMM[12]

Regulatory body

- EMA
- FDA

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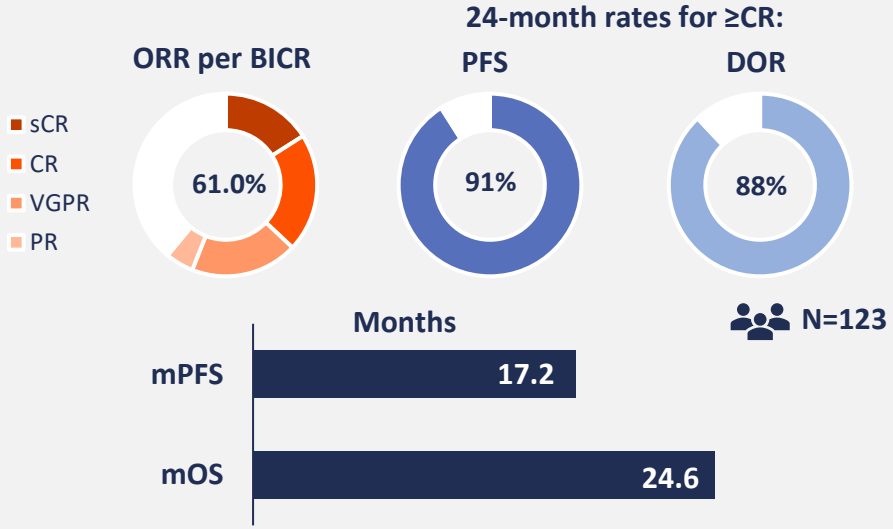
Summary of latest data for approved BCMA-targeted antibodies in multiple myeloma*

Elranatamab: MagnetisMM-3[13]

Elranatamab continued to demonstrate deep and durable responses in heavily pretreated BCMA-naive patients with RRMM refractory to prior PI, IMiD and anti-CD38 therapies



No new safety signals observed with extended follow-up

With an additional 6 months' follow-up:

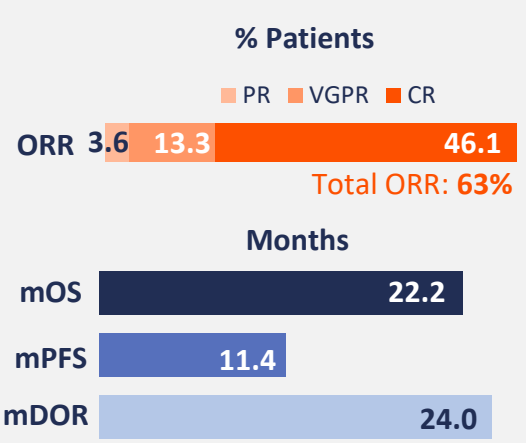
- **4 new deaths** had occurred
- **5 patients** had **secondary primary malignancies**
  - **All** were cutaneous squamous cell carcinoma
  - **All** received prior lenalidomide and a stem cell transplant
  - **No haematological** SPMs were observed

Teclistamab: MajesTEC-1[14]

Teclistamab continued to demonstrate deep and durable responses, even with less frequent (Q2W) dosing, and can provide clinical benefit to patients with some high-risk features

30.4-month follow-up

- N=165 (weekly); n=65 (transitioned to Q2W)
- Patients still on treatment: n=38 (n=37 on Q2W)



High-risk features	ORR, %
Total	63.0
Penta-drug refractory	60.0
High-risk cytogenetics	60.5
Age ≥75 years	54.2
BMPCs ≥60%	44.4
EMD	35.7
ISS stage III	35.0

No new safety signals and a manageable safety profile

Infections

- **78.8%** of patients (grade 3/4, 55.2%)
- No new grade 5 COVID-19 TEAEs
- Onset of new grade ≥3 infections declined over time:
  Transitioning to Q2W dose and increased use of Ig replacement may contribute to this trend

CRS and ICANS

- **CRS: 72.1%** of patients (grade 3/4, 0.6%)
- **No changes** at 30.4-month follow-up

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

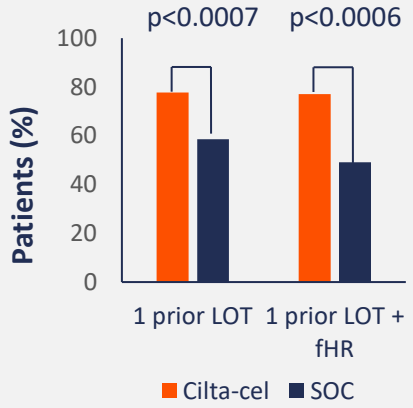
Summary of latest data for approved BCMA-targeted CAR T-cell therapy in multiple myeloma*

Cilta-cel: CARTITUDE-4[15]

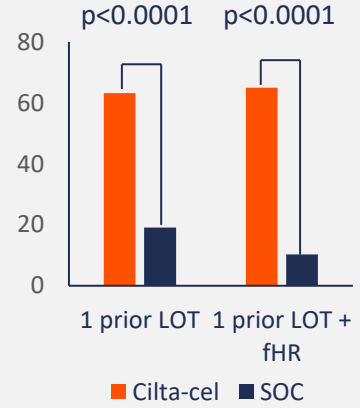
A single cilta-cel infusion improved PFS vs SOC in lenalidomide-refractory patients with MM, regardless of functional risk strata, after 1 prior LOT

- 1 prior LOT: **Cilta-cel n=68; SOC n=68**
- 1 prior LOT+ fHR: **Cilta-cel n=40; SOC n=39**

12-month mPFS



MRD negativity (10^{-5} threshold)



AEs were generally similar between 1 prior LOT vs 1 prior LOT and fHR cohorts

	1 prior LOT		1 prior LOT + fHR	
Grade ≥3 TEAEs, %	Cilta-cel	SOC	Cilta-cel	SOC
	95.6	95.6	100	97.4

- **No grade 3/4 ICANS, MNT or PN** in patients with 1 prior LOT and fHR
- **Grade 3/4 CRS** only in **1 patient**; **CNP** in **2 patients** with 1 prior LOT

Cilta-cel: CARTITUDE-4[16]

Cilta-cel demonstrated favourable efficacy outcomes vs SOC in patients with standard and high-risk cytogenetics†

	Median PFS, months (range)	ORR, %
Cilta-cel standard risk n=69	NE (NE–NE)	85.5
Cilta-cel high-risk n=123	NE (18.4–NE)	85.4
SOC standard risk n=70	20.6 (11.2–NE)	71.4
SOC high-risk n=132	10.3 (7.6–12.5)	65.9

Cilta-cel lessens the impact of high-risk cytogenetics on PFS, and improved PFS compared with SOC

mPFS, months

t(4;14) NE vs 6.7 HR 0.37

Del 17p 19.3 vs 8.7 HR 0.48

*Not all congress data are included in this practice aid. Data included here were selected by faculty for discussion within the accompanying educational activity.
†High-risk cytogenetic abnormalities, including t(4;14), del(17p), t(14;16), and gain/amp(1q).

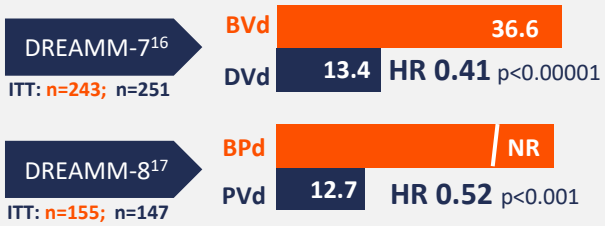
New horizons for BCMA-targeting agents in multiple myeloma

Belantamab mafodotin: DREAMM-7,[17] -8[18]

Favourable survival outcomes and treatment response with belantamab mafodotin-based regimens vs comparator arms (pomalidomide or daratumumab); OS follow-up is ongoing

≥1 prior LOT; PD on/after latest therapy

mPFS (months)



Safety profile broadly consistent with known profiles of individual regimen components

	DREAMM-7		DREAMM-8	
Ocular AEs (any grade), %	BVd n=242	DVd n=246	BPd n=150	PVd n=145
	79	29	89	30

Ocular AEs led to low (9%) rate of treatment discontinuations in both the DREAMM-7 and DREAMM-8 trials

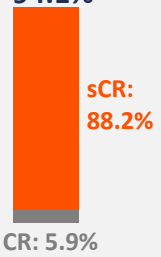
Management of ocular AEs
- Dose holds
- Dose reductions
- Dose delays/interruptions
- ↓ dose frequency

Cilta-cel: CARTITUDE-2[19]

Cilta-cel ± lenalidomide maintenance is promising in newly diagnosed patients with poor response to frontline ASCT, especially given the historically poorer clinical outcomes

N=17

ORR: 94.1%



18-month rates for:

DOR	93.3%
PFS	93.8%
OS	93.8%

AEs were consistent with known safety profile of cilta-cel

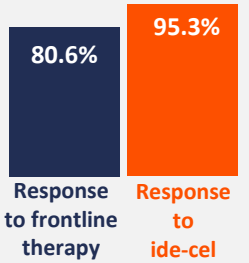
- **No cases** of **MNT/parkinsonism** were observed
- **1 patient with ICANS**, which **resolved**
- **6 patients** with **other neurotoxicities** (mostly grade 1/2)
- **No grade 3/4 CRS** (82.4% grade 1/2)

Ide-cel: KarMMa-2[20]

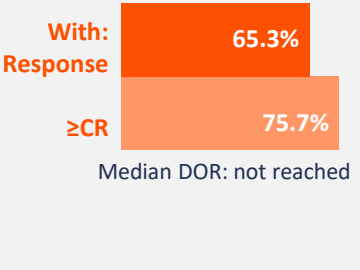
Ide-cel showed a favourable risk–benefit profile in in clinical high-risk early relapse MM without frontline ASCT

N=31

ORR



DOR rate at 24 months



Median DOR: not reached

Ide-cel showed a favourable risk-benefit profile; no grade 3/4 CRS or iiNTs occurred

Grade 1/2 CRS occurred in **83.9%** of patients
- 94.4% managed with tocilizumab

Grade 1/2 iiNT occurred in **9.7%** of patients and managed with:
- Tocilizumab (33.3%)
- Steroids (33.3%)
- Anakinra (33.3%)

Grade 3/4 infection and infestations occurred in 19.4% of patients

Emerging agents

Bispecific antibodies
- ABBV-383[21]
- Linvoseltamab[22]

CAR Ts
- Anitocabtagene autoleucel (anito-cel)[23]
- Equecabtagene autoleucel (eque-cel)[24]

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Abbreviations and references

Abbreviations

ADC, antibody–drug conjugate; AE, adverse event; ASCT, autologous stem cell transplant; B, belantamab mafodotin; BCMA, B cell maturation antigen; BICR, blinded independent central review; BiTE, bispecific T cell engager; BMPC, bone marrow plasma cell; CAR, chimeric antigen receptor; cilta-cel, ciltacabtagene autoleucel; CNP, cranial nerve palsy; CR, complete response; CRS, cytokine release syndrome; d, dexamethasone; DOR, duration of response; EMD, extramedullary disease; fHR, functionally high risk; HLH/MAS, haemophagocytic lymphohistiocytosis/macrophage activation syndrome; HR, hazard ratio; ICANS, immune effector cell-associated neurotoxicity syndrome; ide-cel, idecabtagene vicleucel; iiNT, investigator-identified neurotoxicity; IMiD, immunomodulatory drug; ISS, international staging system; ITT, intention-to-treat; LOT, line of therapy; m, median; MAA, marketing authorization application; MM, multiple myeloma; MNT, movement and neurocognitive TEAE; MRD, minimal residual diseases; NE, not evaluable; NR, not reached; ORR, overall response rate; OS, overall survival; P, pomalidomide; PD, progressive disease; PFS, progression-free survival; PI, proteasome inhibitor; PN, peripheral neuropathy; PR, partial response; Q2W, every 2 weeks; REMS, Risk Evaluation and Mitigation Strategies; RRMM, relapsed/refractory MM; scFV, single-chain variable fragment; sCR, stringent CR; SHM, secondary haematological malignancy; SOC, standard of care; SPM, second primary malignancies; TEAE, treatment-emergent AE; 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 10 September 2024.

‡EHA 2024 was held in Madrid, Spain, 13-16 June 2024.