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How should we interpret the latest clinical evidence for approved BCMA-directed therapeutic approaches to managing RRMM?

Practice aid for BCMA-targeting agents in RRMM

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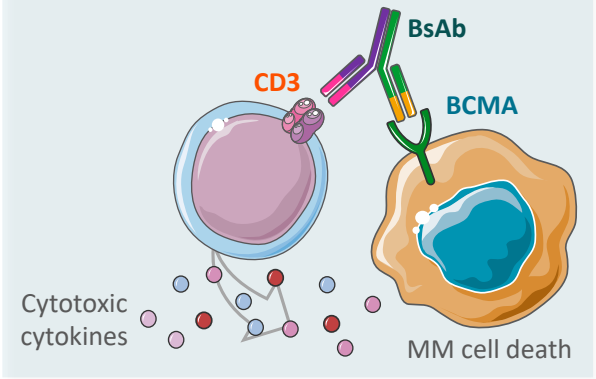
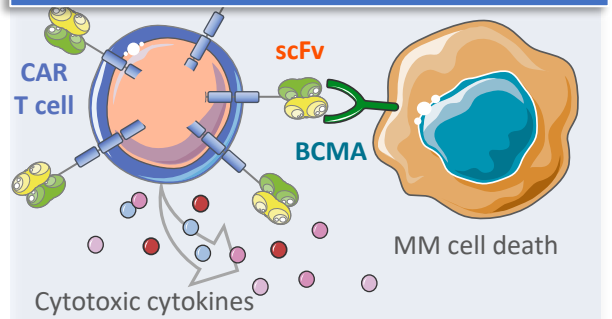
Overview of BCMA-targeting agents in the management of RRMM

Bispecific T-cell engager antibodies[1]



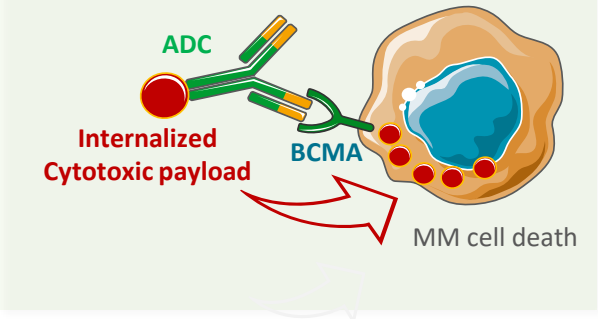
	Elranatamab[2]	Teclistamab[3]	Linvoseltamab[4]
Approved (EMA)	2024	2022	2025
Indication	≥3 prior LoT (incl. PI, IMiD, anti-CD38 mAb) and PD on last therapy		
Dosing	SUD x 2; week 2–24, QW; Q2W thereafter		SUD x 2; week 4–13, QW; Q2W to week 24; Q4W thereafter
Warnings/ precautions	CRS, NTs, infections, neutropenia and hypogammaglobulinaemia		

Chimeric antigen receptor T cells[1]



	Cilta-cel[5]*	Ide-cel[6]*
Approved (EMA)	2022	2021
Indication	≥1 prior LoT (incl. PI, IMiD), len-refractory and PD on last therapy	≥2 prior LoT (incl. PI, IMiD, anti-CD38 mAb) and PD on last therapy
Warnings/ precautions	CRS, NTs, prolonged/recurrent cytopenias, infections/febrile neutropenia, SMNs, hypogammaglobulinaemia and viral reactivation	

Antibody–drug conjugates[1]



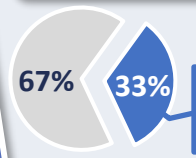
	Belantamab mafodotin
Approval status	**Monotherapy**, withdrawn (2023)[7] **Combination (BVd, DREAMM-7;[8] BPd, DREAMM-8[9]):** UK and Japan, approved, 2025;[10,11] EU, positive CHMP (2025),[12] awaiting full approval
Indication	≥1 prior LoT[10–12]
Warnings/ precautions	Corneal adverse reactions, thrombocytopenia, infusion-related reactions and pneumonitis[13]

*Must be administered in a specialized treatment centre.

The latest clinical evidence for approved BCMA-directed therapeutic approaches to managing RRMM

CAR T-cell therapy

CARTITUDE-1: Remission and survival ≥5 years following treatment with cilta-cel (mFU, 61.3 months)[14]



32 pts alive and progression free

Apart from tumour burden (6% vs 17%), pts who were PF for ≥5 years were comparable to pts with PD in <5 years*

Biomarkers associated with better ≥5-year survival

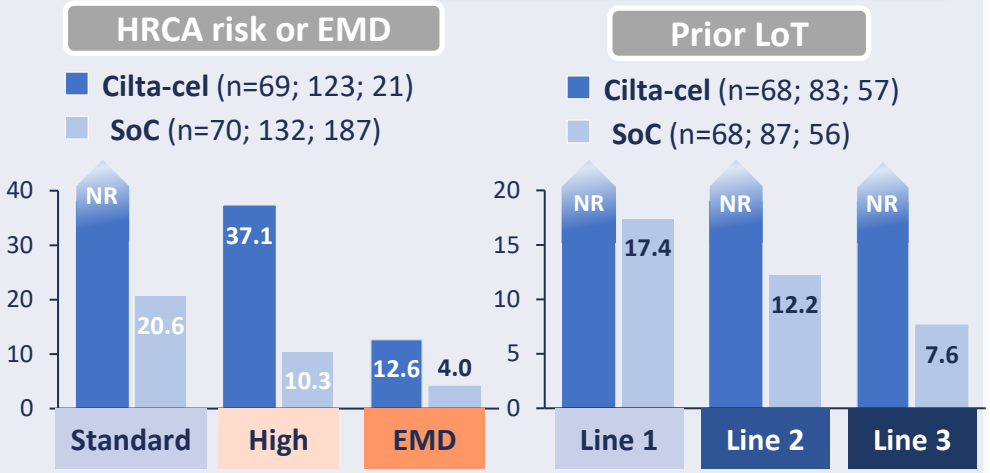
Pre-infusion:

- Higher T cell:neutrophil ratio (p=0.05)
- Fitter naive T cells in cilta-cel (p=0.003)

Post-infusion (E:T ratio at peak expansion):

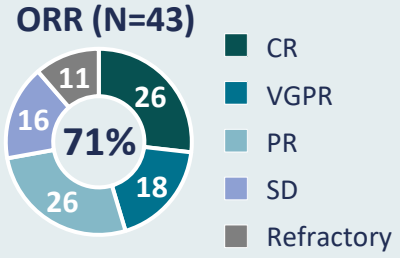
- CAR+ T cells (p=0.008)
- CAR+ CD4+ T cells (p=0.054)

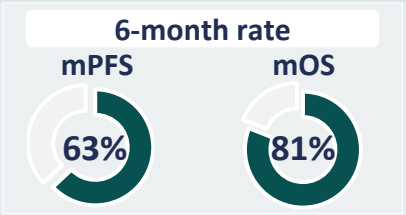
CARTITUDE-4: mPFS (months), subgroup analyses (mFU=33.6 months)[15]

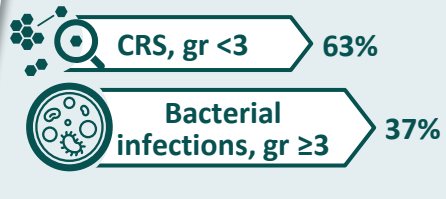


BsAbs

Elranatamab for RRMM: Real-world outcomes from five sites in the UK (mFU, 8.5 months)[16]







Teclistamab in RRMM: Real-world outcomes from the REALiTEC multi-county observational study (mFU=20.7 months)[17]

- Patients meeting MajesTEC-1 eligibility criteria[18] had better outcomes vs those who did not: **PFS**, p=0.004; **OS**, p=0.015; **DoR**, p=0.024
- Overall, outcomes were comparable to MajesTEC-1,[18] including in subgroups with historically poorer outcomes

*Serial MRD and PET/CT assessments for 12 patients in complete remission from a single centre had MRD-negativity ≥10^{-5}.
†Median time into treatment: 3 months (0.0–6.6 months).

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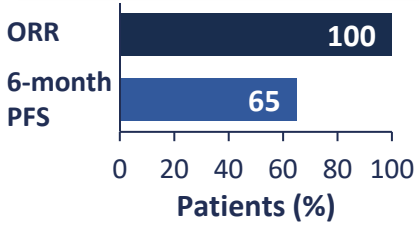
Practical considerations for BCMA-targeted CAR T-cell therapies to manage RRMM

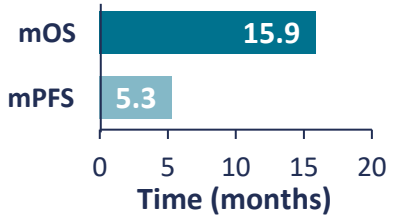
Studies investigating treatment sequencing

Ide-cel → cilta-cel (N=10, mFU: 8.8 months)[19]



No new safety signals or grade ≥3 CRS/ICANS

GPRC5D-BsAb → BCMA-BsAb (N=26; mFU: 20.0 months)[20]



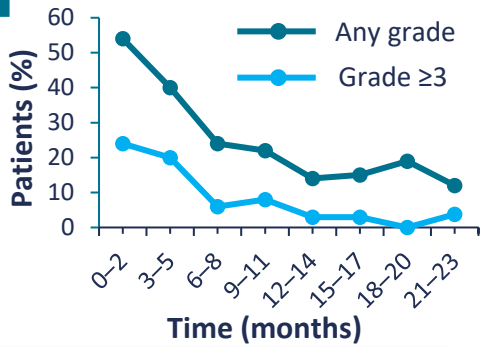
CRS, grade <3: 50%
Infections, grade ≥3: 38%

Sequencing of CAR T cell or BsAb therapy appears to be viable

REALiTEC: The safety profile of teclistamab in the real world[21]

TEAEs, %	Any grade	Grade ≥3
CRS	56	2
ICANS	4	0
Infections	71	39
Haematological		
Anaemia	26	17
Neutropenia	35	33
Thrombocytopenia	19	15

Toxicity-related discontinuations 16%



Up to 60% of patients were treated with supportive IVIg

Management of OEs: Recommendations from the Belamaf Expert Experience Program[22]

11 Recommendations

01 Screening, identifying and monitoring BL OCs and classifying belamaf-OEs

- Specialist eye evaluation is recommended before each of the first four cycles

02 Dose adjustments

- Dosing should be based on the KVA scale
- Tailor dosing to mitigate risk of MM relapse

03 Effective MDT working

- Shared learning is important due to varying experience with belamaf in the MDT

04 Patient-centric approaches in managing OEs

- Communicate the benefits and risks of belamaf
- Support SDM

The guidance that has been developed through the Belamaf Expert Experience Program is a key resource for clinicians to support the effective use of belamaf, while minimizing OEs

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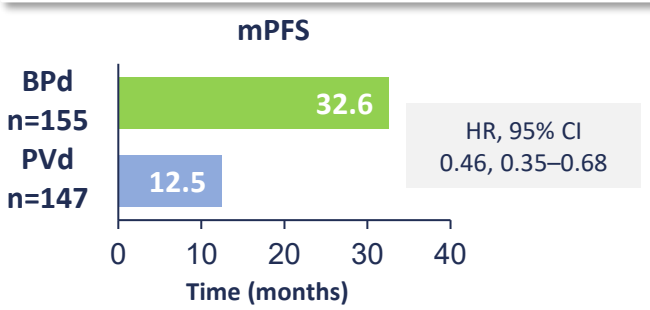
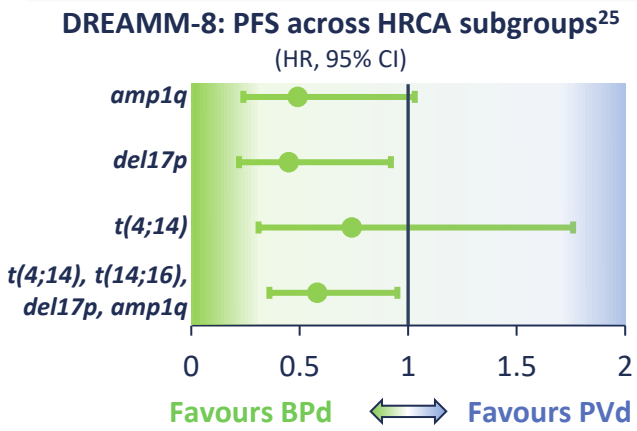
Congress snapshot of selected emerging agents and indications for treating RRMM

DREAMM-8 (mFU, 28.0 months)[23]



- A similar treatment benefit was observed for all subgroups analysed
- The updated safety results were consistent with the primary analysis

DREAMM-7 and -8: HRCAs[24,25]



- A similar treatment benefit was observed in DREAMM-7 (BVd vs DVd)[24]
- The data support BPd or BVd as potential SoC for patients with HRCAs[24,25]

ADC	Phase I/IIa HDP-101[26]	HDP-101 is a novel ADC that targets BCMA with a synthetic amanitin payload. Results are promising and support further dose optimization and investigation.
CAR T	iMMagine-1[27] phase II anito-cel	Anito-cel demonstrates deep and durable efficacy and manageable safety for in a high-risk, ≥4 LoT, RRMM population. A global, phase III study (iMMagine-3, NCT06413498) is now enrolling.
BsAbs	Phase Ib[28] etentamig (ABBV-383)	Long-term efficacy and safety for etentamig (1 SUD, Q4W) demonstrates low CRS incidence and durable response. Efficacy was comparable across all subgroups, suggesting therapeutic benefits among a broad RRMM population.
BsAbs	LINKER-MM2[29,30] phase Ib LINVO + CFZ or BTZ	LINVO + CFZ or BTZ show potential as suitable combination therapies for patients with RRMM. Investigation is ongoing.
BsAbs	MagnetisMM-20[31] phase Ib ELRA + CFZ + d	ELRA + CFZ + d demonstrated a predictable safety and efficacy profile (pts: BCMA-naive, median 2 LoT). Responses deepened over time and, in some cases, persisted following treatment discontinuation. The study is ongoing.
BsAbs	Phase I/II FiH OM336[32]	OM336 is a BCMA x CD3 BsAb with a detuned CD3 platform that is administered subcutaneously. It shows promising initial efficacy and safety, warranting further investigation.
TsAbs	Phase I JNJ-5322[33]	Dual targeting of BCMA and GPRC5D with low affinity CD3 binding. Intended as an off-the-shelf agent for outpatient dosing. Early data suggest JNJ-5322 offers ORRs that are similar to CAR T-cell therapy.
TsAbs	Phase I ISB 2001[34]	Tuned BCMA>CD38>CD3 binding and distal positioning of CD38 vs CD3 enhance tumour killing and minimize CD38-related toxicities. Initial data demonstrate deep and durable responses with robust activity across key subgroups.

Abbreviations and references

Abbreviations

ADC, antibody–drug conjugate; anito-cel, anitocabtagene autoleucel; BCMA, B-cell maturation antigen; BL, baseline; BPd, belantamab mafodotin, pomalidomide and d; BsAb, bispecifc antibody; BTZ, bortezomib; BVd, belantamab mafodotin, bortezomib and d; CAR, chimeric antigen receptor; CFZ, carfilzomib; CHMP, Committee for Medicinal Products for Human Use; CI, confidence interval; cilta-cel, ciltacabtagene autoleucel; CR, complete response; CRS, cytokine release syndrome; d, dexamethasone; DoR, duration of response; DVd, daratumumab, bortezomib and d; ELRA, elranatamab; EMA, European Medicines Agency; EMD, extramedullary disease; FiH, first-in-human; FU, follow-up; GI, gastrointestinal; GPRC5D, G protein-coupled receptor, family C, group 5, member D; gr, grade; HR, hazard ratio; HRCA, high-risk cytogenetic abnormalities; ICANS, immune effector cell-associated neurotoxicity syndrome; ide-cel, idecabtagene vicleucel; Ig, immunoglobulin; IMiD, immunomodulatory drug; IVIg, intravenous Ig; KVA, Keratopathy and Visual Acuity; Len, lenalidomide; LINVO, linvoseltamab; LoT, line of therapy; m, median; mAb, monoclonal antibody; MDT, multidisciplinary team; MHRA, Medicines and Healthcare products Regulatory Agency; MM, multiple myeloma; MRD, minimal residual disease; NR, not reached; NT, neurotoxicity; OC, ocular conditions; OE, ocular event; ORR, objective response rate; OS, overall survival; PD, progressive disease; PET/CT, positron emission tomography/computerized tomography; PF, progression free; PFS, PF survival; PI, proteasome inhibitor; PR, partial response; pts, patients; PVd, pomalidomide, bortezomib and d; Q2W, every 2 weeks; Q4W, every 4 weeks; QW, every week; RRMM, relapsed/refractory MM; scFV, single-chain variable fragment; SD, stable disease; SDM, shared decision-making; SMN, secondary myeloid neoplasm; SoC, standard of care; SUD, step-up-dose; TEAE, treatment-emergent adverse event; TsAb, trispecific antibody; VGPR, very good PR.

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