

T-cell re-directional therapy considerations from real world cases

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The IMWG immunotherapy committee recommends that CAR T-cell therapy is pursued first, where available*¹

Recommendations for sequencing immunotherapies*

- BCMA-targeting CAR-T should be pursued before T-cell engagers or ADCs,¹ given the deep responses, long PFS and QoL benefits associated with not requiring continuous treatment^{1,2}
 - Except for patients with rapidly progressing disease and those who are unlikely to transit through apheresis and bridging therapy without disease-related morbidity

Recommendations for treatment after BCMA-targeting CAR-T*

- Both BCMA and GPRC5D immunotherapy are active, with acceptable safety profiles
 - However, responses to BCMA-targeting therapies are likely less frequent and durable than in patients not previously treated with BCMA-targeting CAR-T

Recommendations for treatment after BCMA-targeting T-cell engagers*

- Therapy with a different mechanism of action or immunotherapy targeting a different antigen should be pursued
 - Efficacy data for sequencing BCMA-targeting treatments of different modalities are limited

***All recommendations assume equal access and that the patient is eligible/suitable for all therapy types.**

ADC, antibody-drug conjugate; BCMA, B-cell maturation antigen; GPRC5D, G-protein-coupled receptor class C group 5 member D; IMWG, International Myeloma Working Group; PFS, progression-free survival; QoL, quality of life.

1. Costa LJ, et al. Leukemia 2025;doi: 10.1038/s41375-024-02482-6; 2. Speaker's personal opinion, March 2025.



Case #1

[FF]

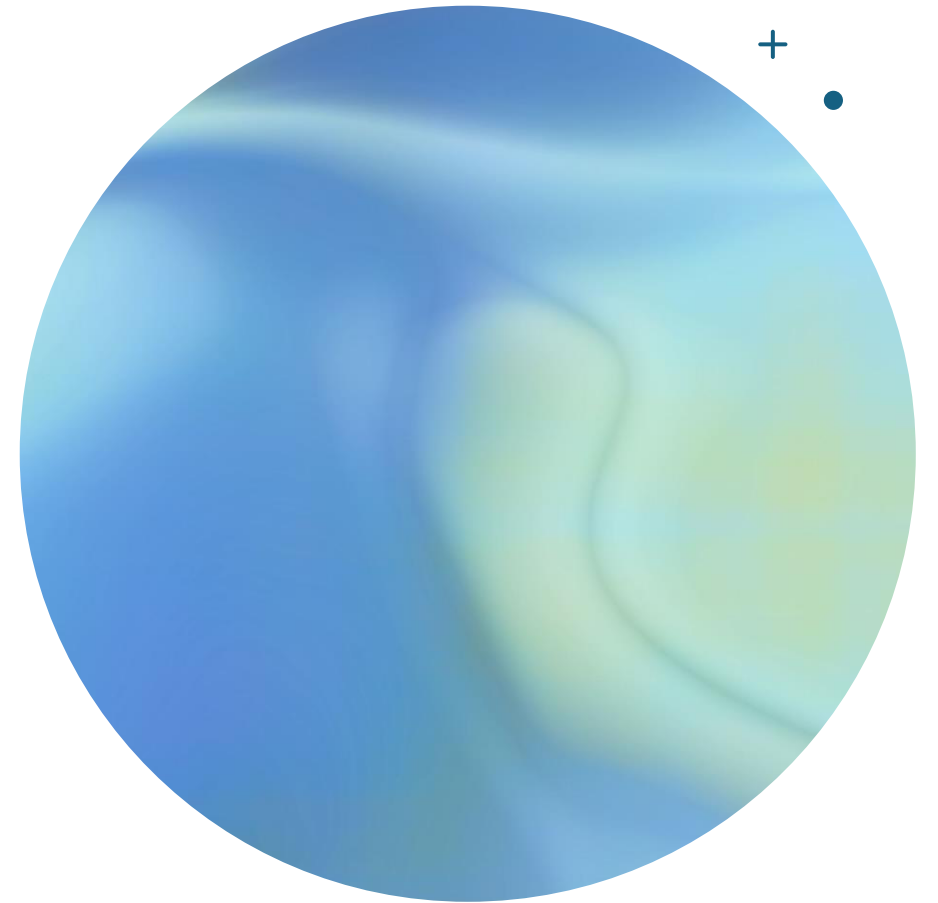
Oligo-secretory IgG-K MM diagnosed 9/2019 (male, age 65), with extensive bone involvement, plasmacytosis 90% in BM, del17p(33%) and t(11:14)

- 1st Ln: **VCD X 4 – ASCT [1/2020] – VR maintenance** →
5/2021 PD new lytic lesions; Kappa LC 54mg/L, BM w/ 20%PCs
- 2nd Ln: **DPd** → VGPR → **8/2021 PD** w/ extensive bone disease
- 3rd Ln: **K-Veneto-d** → VGPR → **PD 11/2022**, extensive BM involvement, pancytopenia, bone disease (Kappa 94mg/L)
- 4th Ln: **DPACE** with stem cell support
 - Intended as bridge to CART. remained in response until **4/2023 PD** including EMD, BM heavy infiltration, pancytopenia
 - Lymphopheresis (Hadassah)
- 5th Ln: DCEP as bridging → **HBI101 BCMA CART [7/2023]**

May 2025 – MRD negative CR

Case #2 [SO]

Women aged 52, diagnosed with Kappa LC Myeloma **7/2022**, 1q amplification, presented with anemia, AKI, extensive bone disease



Case #3 [IB]

- Diagnosed 2015 (male, aged 59) with IgA-Kappa MM, Anemia, 1q21 gain. Medical Hx: heavy smoker.

Line #	PI	IMiD	ChemoT	CS	mAB	Other	start date	stop date	best rspns	stop d/t
1	BORT		Cyclo	dexa			01/06/2015	07/10/2015	VGPR	
1			autoSCT				28/10/2015	28/10/2015		
1	BORT		Cyclo	dexa		Consolidation	01/11/2015	04/05/2016	MRDneg	
1	BORT			dexa		Maintenance	18/05/2016	16/10/2017		end of Tx
2		LEN		dexa	DARA		19/10/2020	29/11/2021	PR	PD
3	IXA	POM		dexa			04/01/2022	05/02/2023	PR	PD
4	BORT		Cyclo	dexa			05/03/2023	28/03/2023		
4						Trial - CART PHE885	18/04/2023	18/04/2023	MRDneg	→5 mo.
5	CARF			dexa		Selinexor	19/09/2023	26/12/2023	PR	PD →3 mo.
6						Trial - GO43980 Cevostamab XmAb24306	08/02/2024	28/02/2024		PD →//
7						Belantamab	13/03/2024	01/12/2024	VGPR	PD → 8.5 mo
8						Talquetamab	23/12/2024			→6 mo

Case #4 [TM]

MM IgG Kappa diagnosed 2018 (male, aged 65) with anemia, FLCr>100. FISH: t(11:14)

- Ln1: VRD – AST (4.2019) – KRD X 6 --> PR → Len MTNS → 5/2020 PD
 - Ln2: DKd → biochem PD → DKd+ Veneto → CR
 - Ln3: Elo-Pom-Dex (MMY3009) 7/2024 → 10/2024 PD
pancytopenia / new focal lesions / heavy BM infiltration. On FISH del17 detected in 60% of PCs
Patient requested Ciltacel, pending approval in Israel ... Tal “bridging” was initiated
 - Ln4: Talquetamab (12.2024) → non-response
 - Ln5: Salvage ASCT (16/1/2025 , as bridging to Cilta...) → non-response
 - Ln6: Teclistamab (13/2/2024) → CR
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Case #5 [PZ]

MM diagnosed 11.2018 (female, age 58) AKI, hypercalcemia, bone disease, anemia. High disease burden, FISH: 1q21+ and t(11;14), ISS III