

APP MENTORSHIP PROGRAM

INTRODUCTION TO BISPECIFIC ANTIBODY THERAPIES

WEEK 4 CURRICULUM

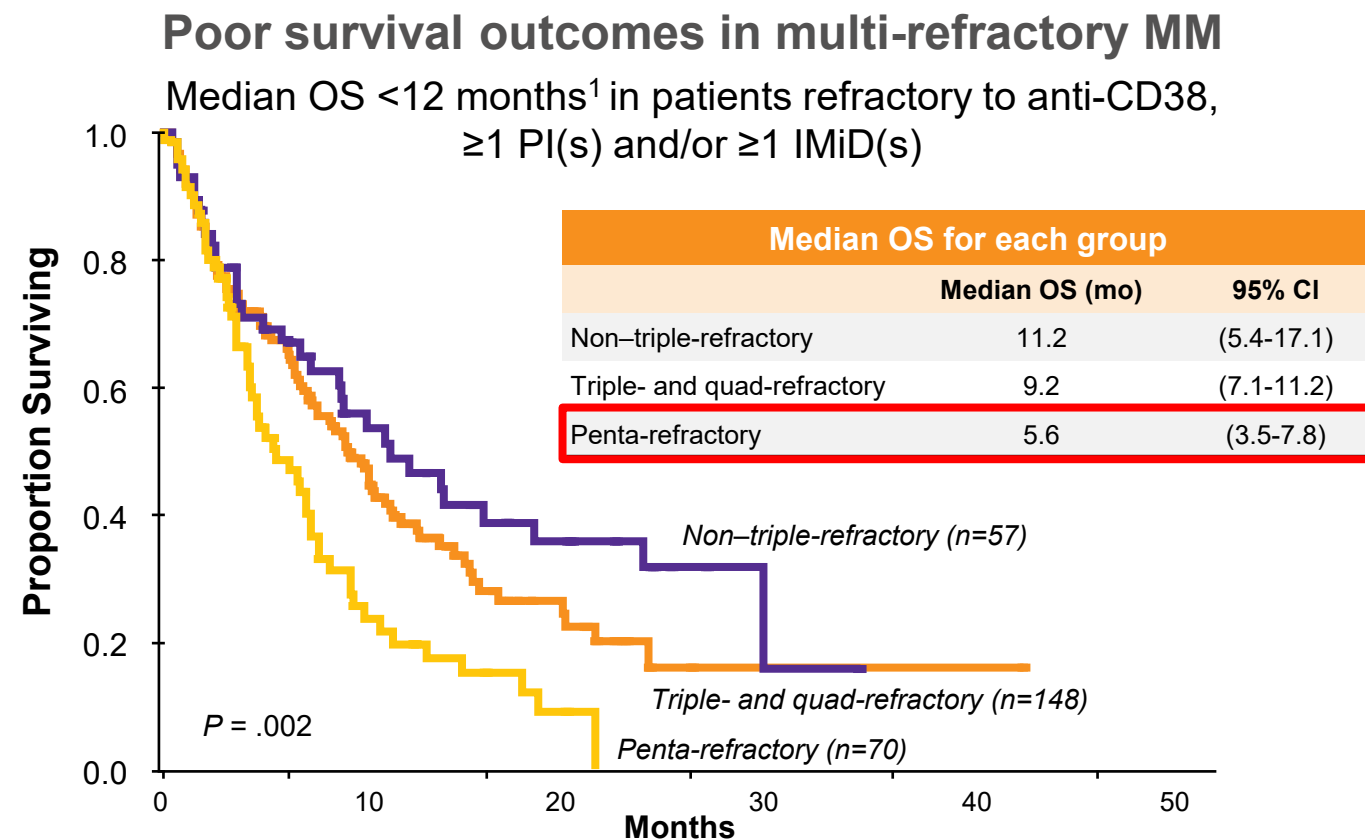


Improving Lives **Finding the Cure®**

Learning Objectives

- ✓ **Review the mechanisms of action, indications, and trial data to support the use of bispecific antibodies in myeloma**
- ✓ **Identify the clinical indications for bispecific antibodies in myeloma, including biomarker-driven eligibility.**

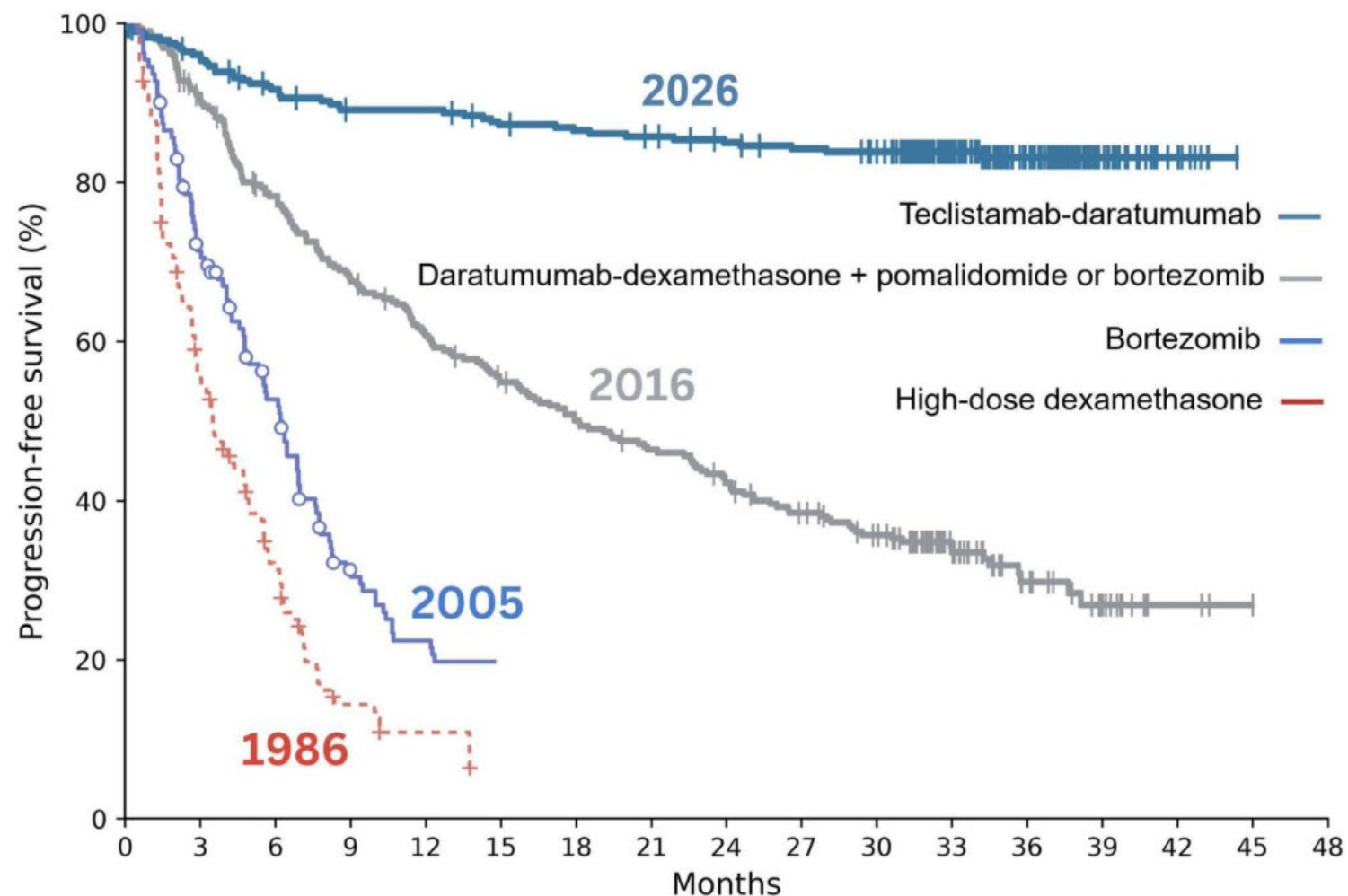
The Challenge of Treating Relapsed/Refractory MM



Treatment Options

- Participation in clinical trial
- Trial participation not always possible
 - Aggressive relapse with need to start immediately
 - Not fulfilling inclusion and exclusion criteria (renal impairment, thrombocytopenia, non-secretory disease, etc)
- Retreatment with drugs used in prior lines
- Use of recently approved drugs with novel mode of action

RRMM: How Far We Have Come

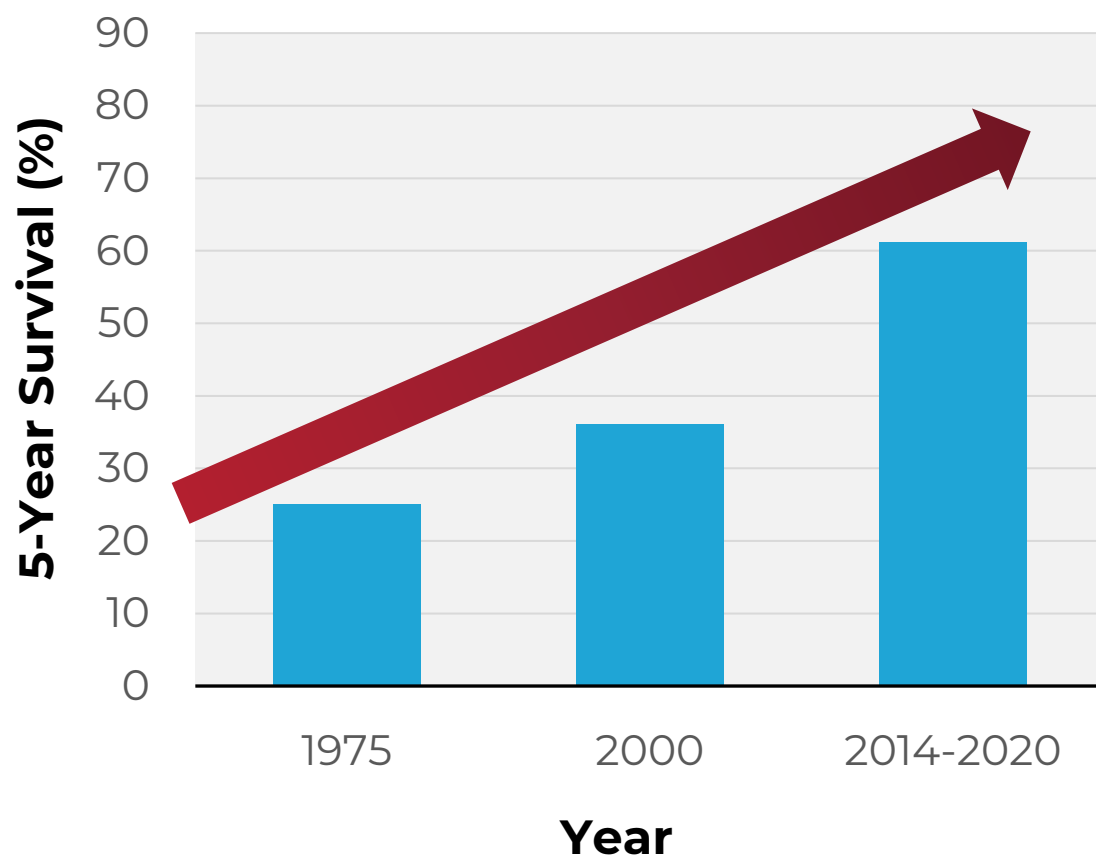


RRMM = relapsed refractory myeloma.

Dr. Samuel Hume based on Costa LJ, et al. *N Engl J Med*. 2026;394(8):739-752 and Richardson G, et al. *N Engl J Med*. 2005 Jun 16;352(24):2487-98.

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Fact: Patients With MM Are Living Longer Than Ever



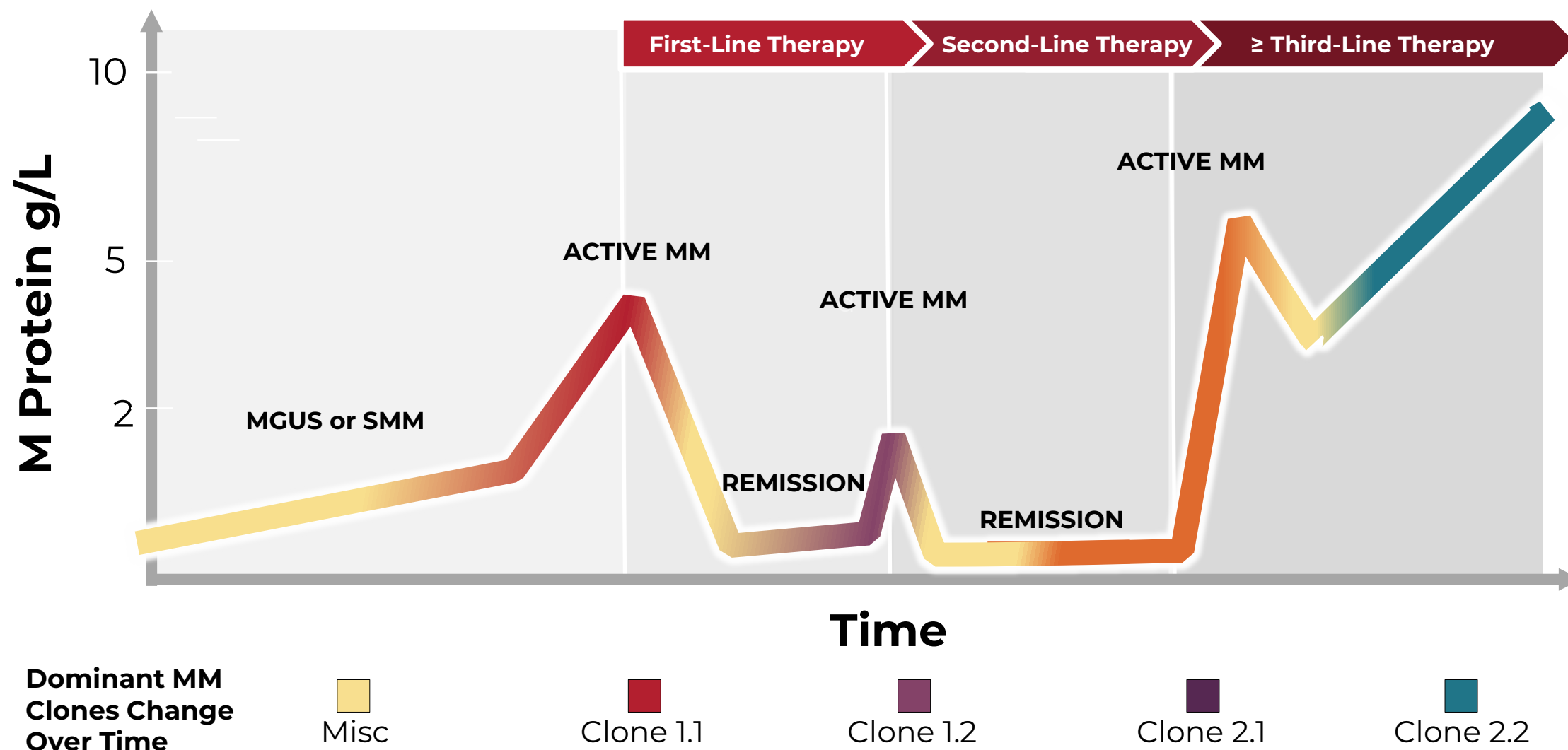
> **60%**

LIVE MORE THAN
5 YEARS
after their diagnosis

Many patients are living
10+ YEARS
after their diagnosis!

Particularly those who
are younger and/or have
standard-risk disease

Clonal Evolution: Dominant Clones Change Over Time



M protein = monoclonal protein; MGUS = monoclonal gammopathy of undetermined significance; misc = miscellaneous (no dominant clone); MM = multiple myeloma; SMM = smoldering multiple myeloma.

Adapted from Durie B. Keats JJ, et al. *Blood*. 2012;120(5):1067-1076.

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Targets of FDA-Approved Therapies for MM

Proteasome

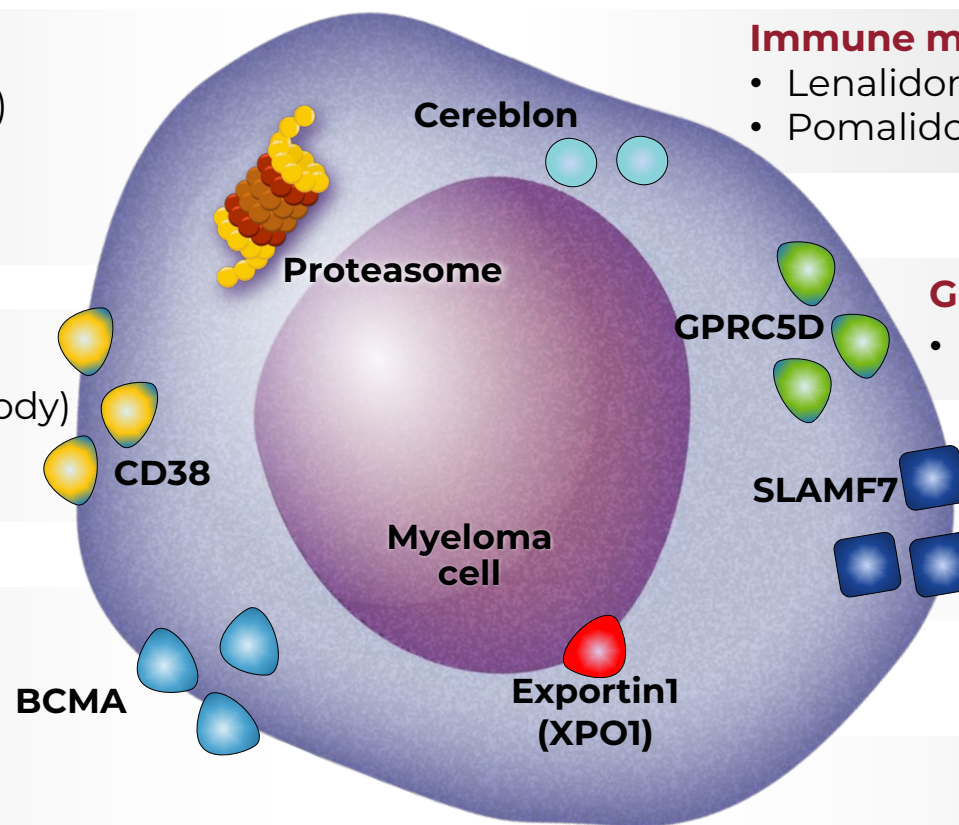
- Bortezomib (proteasome inhibitor)
- Carfilzomib (proteasome inhibitor)
- Ixazomib (proteasome inhibitor)

CD38

- Daratumumab (monoclonal antibody)
- Isatuximab (monoclonal antibody)

BCMA

- Belantamab mafodotin (ADC)
- Cilta-cel (CAR T-cell therapy)
- Ide-cel (CAR T-cell therapy)
- Elranatamab (bispecific antibody)
- Linvoseltamab (bispecific antibody)
- Teclistamab (bispecific antibody)



Immune modulation

- Lenalidomide
- Pomalidomide

GPRC5D

- Talquetamab (bispecific antibody)

SLAMF7

- Elotuzumab (monoclonal antibody)

Exportin 1 (XPO1)

- Selinexor (SINE inhibitor)

ADC = antibody drug conjugate; BCMA = B-cell maturation antigen; CAR = chimeric antigen receptor; cilta-cel = ciltacabtagene autoleucel; FDA = US Food and Drug Administration; GPRC5D = G-protein coupled receptor family C group 5 member D; ide-cel = idecabtagene vicleucel; MM = multiple myeloma; SINE = selective inhibitor of nuclear export; SLAMF7 = SLAM family member 7.

Leow CC-Y, Low MSY. *J Pers Med*. 2021;11(5):334. National Comprehensive Cancer Network® (NCCN®) NCCN Clinical Practice Guidelines In Oncology (NCCN Guidelines®) for Multiple Myeloma. Version 5.2026. To view the most recent or complete version of the guideline, go online to [NCCN.org](https://www.nccn.org).

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Treatment at Relapse: Many Combinations

Myeloma Therapy	Common Combinations or Therapy Names
Belantamab mafodotin ^a	BVd, ^a BPd, ^c BKRd ^c
Bortezomib (SC admin)	VRd, Vd, VCd
Carfilzomib	KRd, Kd, Dara-Kd, Isa-Kd
CAR T-cell therapy (BCMA)	Cilta-cel, ide-cel ^c
Daratumumab	DRd, DVd, DPd, DVMp, DKd, Tec-Dara, IBER+Dara
Elotuzumab	ERd, EPd ^a
Isatuximab	Isa-Pd, ^a Isa-Kd
Ixazomib	IRd
Lenalidomide	VRd, Rd, KRd, Dara-Rd, ERd, IRd
Pomalidomide ^a	Pd, ^a Dara-Pd, EPd, ^a PCd ^c
Selinexor	Xd, XVd, XKd, ^c Dara-Xd ^c
T-cell engager (BCMA) ^b	Teclistamab, ^b Elranatamab, ^b Linvoseltamab, ^b Tec-Dara
T-cell engager (GPRC5D) ^b	Talquetamab ^b

New agents or regimens in clinical trials may be an option

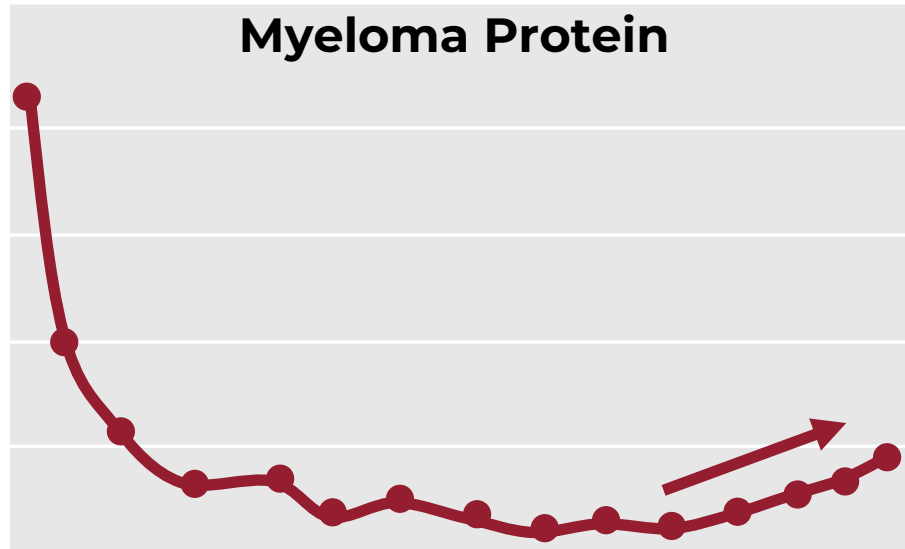
^a2 or more prior therapies. ^b4 or more prior therapies. ^cOff label; not currently FDA approved.

B = belantamab mafodotin; BCMA = B-cell maturation antigen; C = cyclophosphamide; CAR = chimeric antigen receptor; cilta-cel = ciltacabtagene autoleucel; d = dexamethasone; D = daratumumab; Dara = daratumumab; E = elotuzumab; FDA = US Food and Drug Administration; GPRC5D = G-protein coupled receptor family C group 5 member D; I = ixazomib; ide-cel = idecabtagene vicleucel; Isa = isatuximab; K = carfilzomib; M = melphalan; p = prednisone; P = pomalidomide; R = lenalidomide; SC = subcutaneous; Tec = teclistamab; V = bortezomib; X = selinexor.

National Comprehensive Cancer Network® (NCCN®) NCCN Clinical Practice Guidelines In Oncology (NCCN Guidelines®) for Multiple Myeloma. Version 5.2026. To view the most recent or complete version of the guideline, go online to [NCCN.org](https://www.nccn.org).

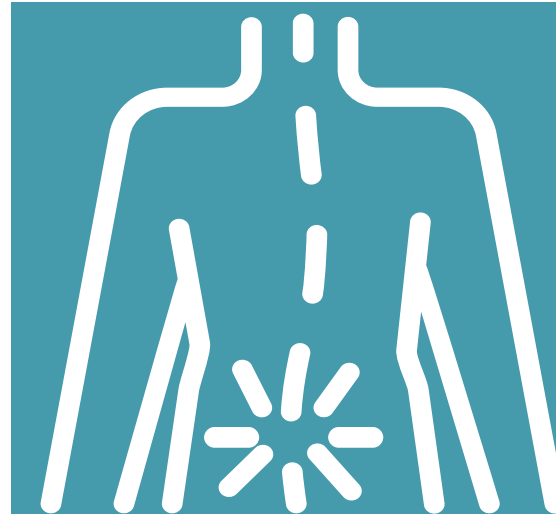
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How Patients With Myeloma Relapse



Asymptomatic Biochemical Relapse

- Sequentially rising myeloma protein or free light chain (> 25% increase from low point)
- Loss of MRD not currently defined as relapse; when to treat?
- No other symptoms
- Decisions: if, when, how to treat



Symptomatic

- New or worsening bone pain
- Increasing fatigue, anemia
- Next step: relapse workup; many therapy choices



Psychologically, many patients find their first relapse harder than their initial diagnosis. Nurses are essential for supporting patients!

MRD = minimal residual disease

Noonan K, et al. *J Adv Pract Oncol*. 2022;13(suppl 4):15-21. Faïman B, et al. *J Adv Pract Oncol*. 2016;7(suppl 1):17-29. Kurtin S, et al. *J Adv Pract Oncol*. 2016;7(suppl 1):59-70. Gerber L. *Nursing*. 2018;48(4):55-58.

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International Myeloma Working Group consensus criteria for response and minimal residual disease assessment in multiple myeloma

Shaji Kumar, Bruno Paiva, Kenneth C. Anderson, Brian Durie, Ola Landgren, Philippe Moreau, Nikhil Munshi, Sagar Lonial, Joan Bladé, Maria-Victoria Mateos, Seodis Dimopoulos, Efsthathios Kastiritsis, Mario Boccadoro, Robert Orlowski, Hartmut Goldtmidt, Andrew Spencer, Jian Hou, WeeJoo Chng, Maletzi Usamoni, Elena Zangari, Kazuyuki Shimizu, Jagan Jagannath, Hans E. Johnsen, Evangelos Terpos, Antonia Reimann, Robert A. Pertz, Pieter Smeets, Paul G. Richardson, Philip McCarthy, Heinz Ludwig, Wenming Chen, Michele Cag, Jean-Luc Harousseau, Suzanne Lentzsch, Jens Hildebrand, Antonio Palumbo, Alberto Orth, S.Vinceent Bakjumar, Iyegbe Sam Nkomo, Henne Avert-Joisneau

Treatment of multiple myeloma has substantially changed over the past decade with the introduction of several classes of new effective drugs that have greatly improved the rates and depth of response. Response criteria in multiple myeloma were developed to use serum and urine assessment of monoclonal proteins and bone marrow assessment (which is relatively insensitive). Given the high rates of complete response seen in patients with multiple myeloma with new treatment approaches, new response categories need to be defined that can identify responses that are deeper than those conventionally defined as complete response. Recent attempts have focused on the identification of residual tumour cells in the bone marrow using flow cytometry or gene sequencing. Furthermore, sensitive imaging techniques can be used to detect the presence of residual disease outside of the bone marrow. Combining these new methods, the International Myeloma Working Group has defined new response categories of minimal residual disease negativity, with or without imaging-based absence of extramedullary disease, to allow uniform reporting within and outside clinical trials. In this Review, we clarify several aspects of disease response assessment, along with endpoints for clinical trials, and highlight future directions for disease response assessments.

Introduction

The treatment landscape for multiple myeloma has been radically transformed during the past decade by the introduction of several new drugs with different mechanisms of action, which has led to improved survival for patients with multiple myeloma.^{1,2} Progress has been made in other areas, including an improved understanding of disease biology, enhanced diagnostic criteria, availability of sensitive and specific tools for disease prognostication, increasingly effective treatment

negative serum and urine immunofixation) has been confirmed.¹² The original definition of a complete response only required bone marrow with less than 5% plasma cells, irrespective of their clonal nature.¹³ The definition was further refined to stringent complete response, by the addition of the sFLC assay plus immunohistochemical clonal assessment on the trephine biopsy.^{13,14} Additional clarifications, especially with respect to the use of sFLC, were introduced during the International Myeloma Workshop in 2011.¹⁵

Lancet Oncol 2016; 17: e328-46

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Department of Hematology
and Medical Oncology, Winship
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University School of Medicine,

Progressive Disease^{a,b}

Any 1 or more of the following criteria:

- Increase of 25% from lowest confirmed response value in 1 or more of the following criteria:
- Serum M protein (absolute increase must be ≥ 0.5 g/dL)
- Serum M protein increase ≥ 1 g/dL if the lowest M protein was ≥ 5 g/dL
- Urine M protein (absolute increase must be ≥ 200 mg/24h)
- In patients without measurable serum and urine M protein levels, the difference between involved and uninvolved FLC levels (absolute increase must be > 10 mg/dL)
- In patients without measurable serum and urine M protein levels and without measurable involved FLC levels, bone marrow plasma cell percentage irrespective of baseline status (absolute increase must be $\geq 10\%$)
- Appearance of a new lesion(s) $\geq 50\%$ increase from nadir in SPD^c of > 1 lesion, or $\geq 50\%$ increase in the longest diameter of a previous lesion > 1 cm in short axis; $\geq 50\%$ increase in circulating plasma cells (minimum of 200 cells/ μ L) if this is the only measure of disease

CT = computed tomography; FLC = free light chain; h = hours; M protein = myeloma protein; MRD = minimal residual disease; MRI = magnetic resonance imaging; PET = positron emission tomography; SPD = sum of the products of the maximal perpendicular diameters of measured lesions.

^a Positive immunofixation alone in a patient previously classified as achieving a complete response will not be considered progression. For purposes of calculating time to progression and progression-free survival, patients who have achieved a complete response and are MRD-negative should be evaluated using criteria listed for progressive disease. Criteria for relapse from a complete response or relapse from MRD should be used only when calculating disease-free survival. ^bIn the case where a value is felt to be a spurious result per physician discretion (eg, a possible laboratory error), that value will not be considered when determining the lowest value. ^cPlasmacytoma measurements should be taken from the CT portion of the PET/CT, or MRI scans, or dedicated CT scans where applicable. For patients with only skin involvement, skin lesions should be measured with a ruler. Measurement of tumour size will be determined by the SPD.

Kumar S. et al. *Lancet Oncol.* 2016;17(8):e328-e346.

Relapse Workup

LAB TESTS

- CBC + differential + chemistry (metabolic panel)
- Serum free light chain (FLC) assay
- Serum protein electrophoresis (SPEP)
- Urine protein electrophoresis (UPEP)
- Immunoglobulins

CONSIDER BONE MARROW BIOPSY

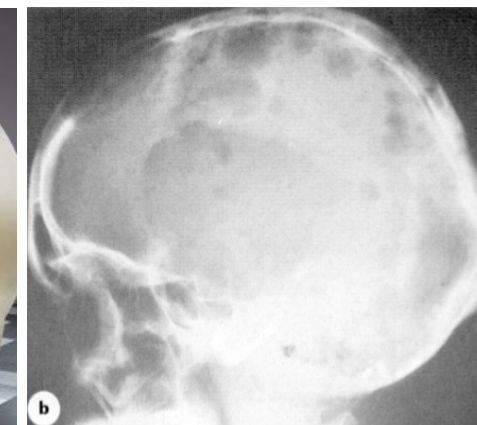
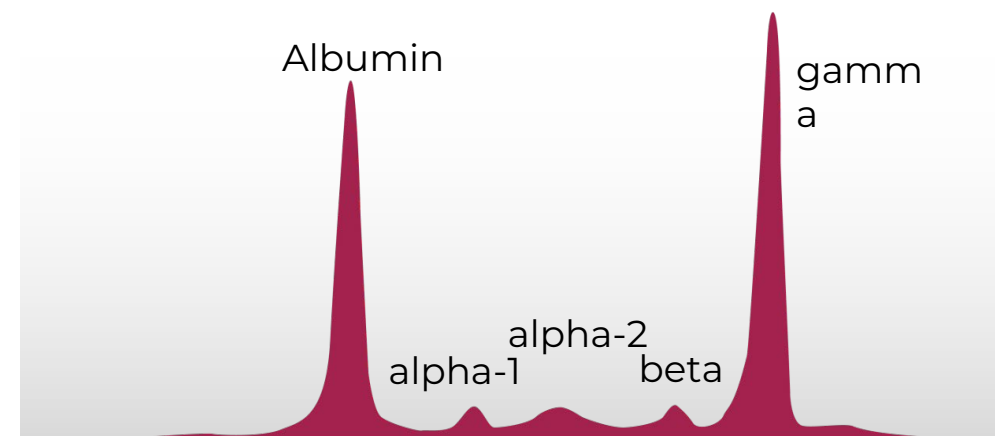
Cytogenetics and FISH (some risk factors can be acquired)

IMAGING



- PET/CT
- WBLDCT
- MRI

Imaging type depends on individual's symptoms and available testing options



CBC = complete blood count; CT = computed tomography; FISH = fluorescence in situ hybridization; FLC = free light chain; MRI = magnetic resonance imaging; PET = positron emission tomography; SPEP = serum protein electrophoresis; UPEP = urine protein electrophoresis; WBLDCT = whole-body low-dose computed tomography.

Noonan K, et al. *J Adv Pract Oncol.* 2022;13(suppl 4):15-21. Rome SI, et al. *Clin J Oncol Nurs.* 2017;21(5 suppl):47-59. Hillengass J, et al. *Lancet Oncol.* 2019;20(6):e302-e312. Ghobrial IM, et al. *Blood.* 2014;124:3380-3388. Rajkumar SV, et al. *Lancet Oncol.* 2014;15:e538-e548. Fauman B. *Clin Lymphoma Myeloma Leuk.* 2014;14:436-440.

Principles of Treatment Selection in Relapse



T

Timing of relapse



R

Response to prior therapy



A

Aggressiveness of relapse



P

Performance status



P

Patient preference

How do you address treatment selection and sequencing therapy in your practice?

ASCT = autologous stem cell transplant; mAb = monoclonal antibody.

Rajkumar SV. *Am J Hematol*. 2022;97(8):1086-1107.

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SHARE Approach to Shared Decision-Making



Benefits to Healthcare Professionals

- Improved quality of care delivered
- Increased patient satisfaction

Benefits to Patients

- Improved patient experience of care
- Improved patient adherence to treatment recommendations using the SHARE Approach builds a trusting and lasting relationship between healthcare professionals and patients

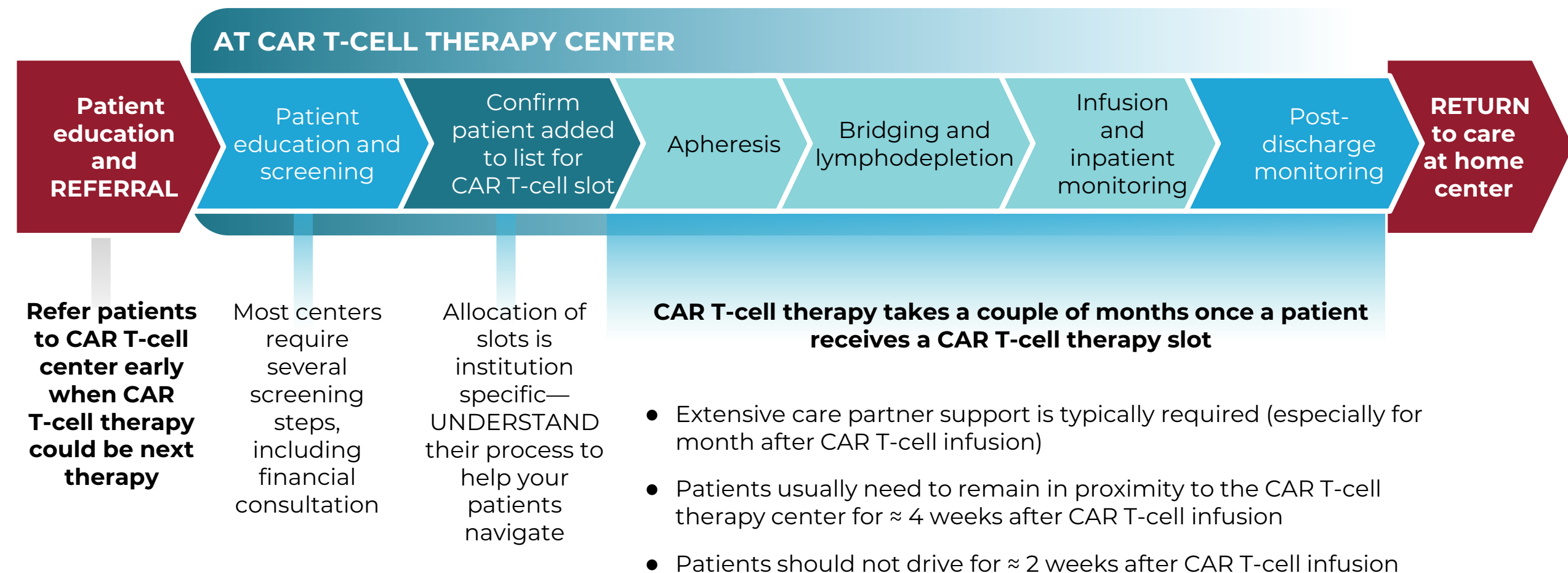


FREE Professional Education and Training

<https://www.ahrq.gov/health-literacy/professional-training/index.html>

CAR T-Cell Therapy: Steps

All patients should be referred to specialty centers at diagnosis for transplant evaluation, or first relapse due to the complexity of myeloma care



CAR = chimeric antigen receptor.

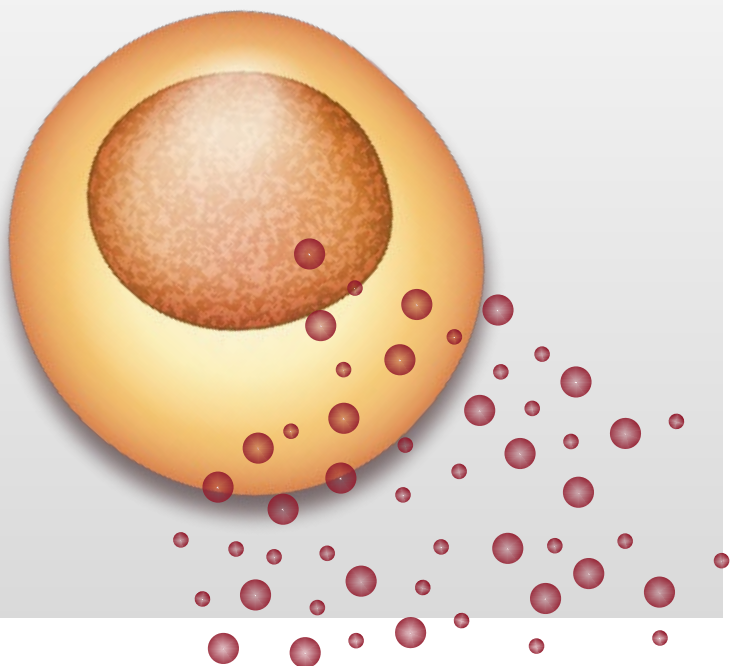
Catamero D, et al. *J Adv Pract Oncol*. 2022;13(suppl 4):31-43. Teoh PJ, Chng WJ. *Blood Cancer J*. 2021;11(4):84. Shah UA, Mailankody S. *BMJ*. 2020;370:m3176. <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/fda-eliminates-risk-evaluation-and-mitigation-strategies-rems-autologous-chimeric-antigen-receptor>

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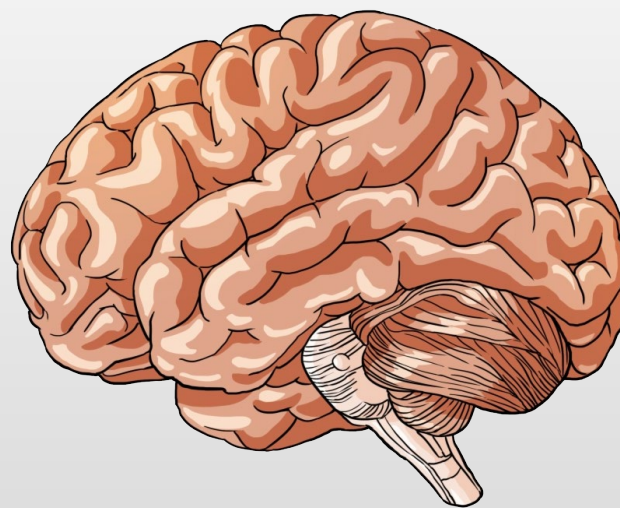
CAR T Therapy and Bispecific Antibodies Share

Key Side Effects

**Cytokine release
syndrome (CRS)**

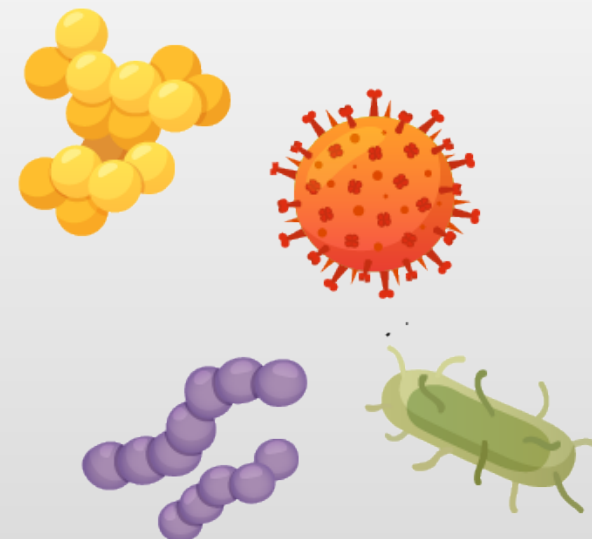


**Immune effector cell-
associated neurotoxicity
syndrome (ICANS)**



Neurotoxicity

Infection



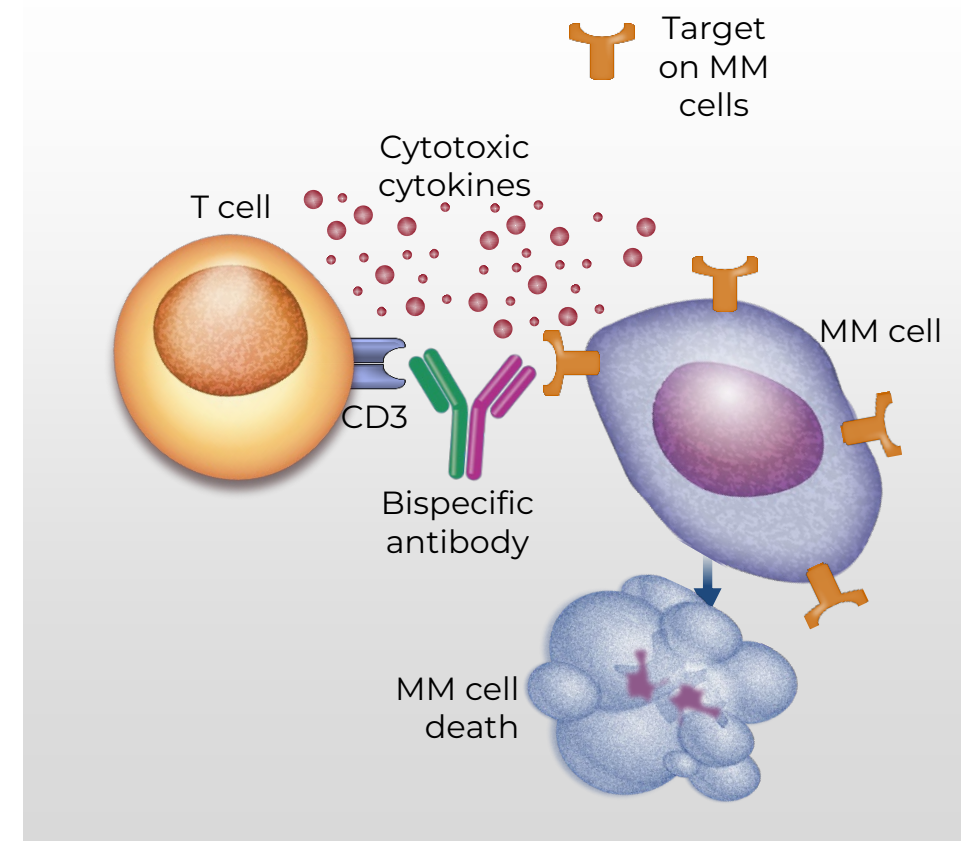
WHAT ARE BISPECIFIC ANTIBODIES

Mechanism of Action for Bispecific Antibodies: T-Cell Immune Activity Triggered Killing of MM Cells

- CD3-targeted bispecific antibodies recruit T-cells to target cancer cells
 - 1 arm of the bispecific molecule binds to CD3 (antigen on T-cells)
 - The other arm binds to a tumor-associated antigen (eg, BCMA, GPRC5D)
- Once bound, a synapse forms and T-cells release perforin, forming pores in the cell membrane
- Granzymes flow through open pores, leading to cell death

Bispecific antibodies are off-the-shelf therapeutics.

Bispecific Antibodies



Approved Bispecific Antibodies for Myeloma

Bispecific	Teclistamab	Elranatamab	Linvoseltamab	Talquetamab
Target	BCMA	BCMA	BCMA	GPRC5D
First Approved	October 2022	August 2023	July 2025	August 2023
Indication(s) Combination	With daratumumab in patients with at least 1 prior line of therapy, including a PI and an IMiD			
Monotherapy	At least 4 prior lines of therapy, including a PI, IMiD, and anti-CD38 mAb	At least 4 prior lines of therapy, including a PI, IMiD, and anti-CD38 mAb	At least 4 prior lines of therapy, including a PI, IMiD, and anti-CD38 mAb	At least 4 prior lines of therapy, including a PI, an IMiD, and an anti-CD38 mAb
Key AEs	CRS, neurotoxicity, ICANS, cytopenias, infection			CRS, neurotoxicity, ICANS, cytopenias, skin/nail, oral

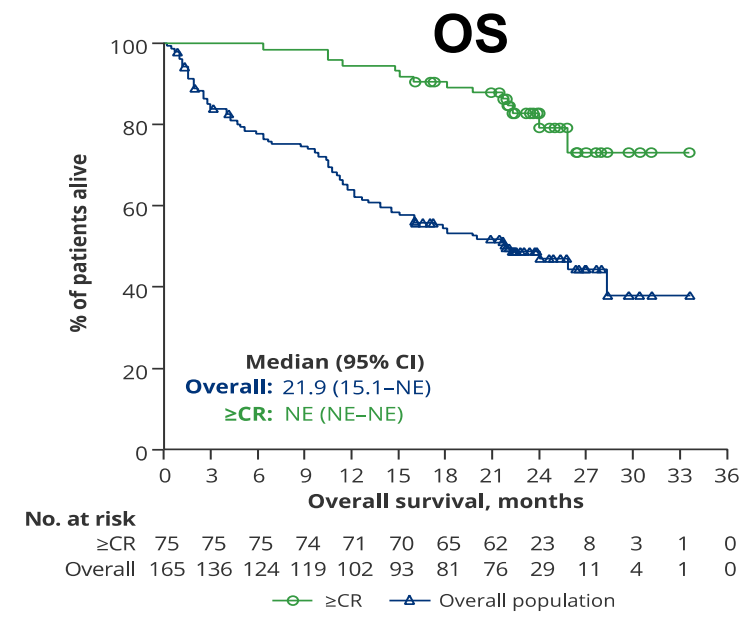
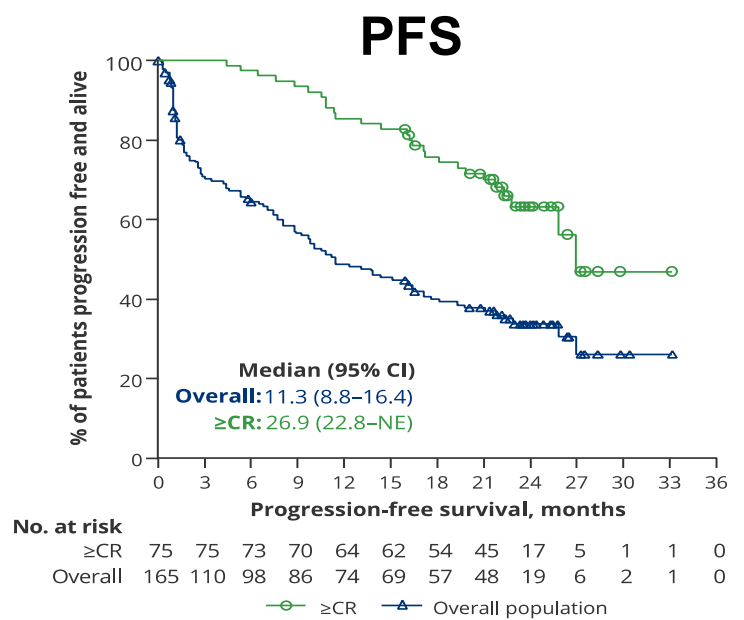
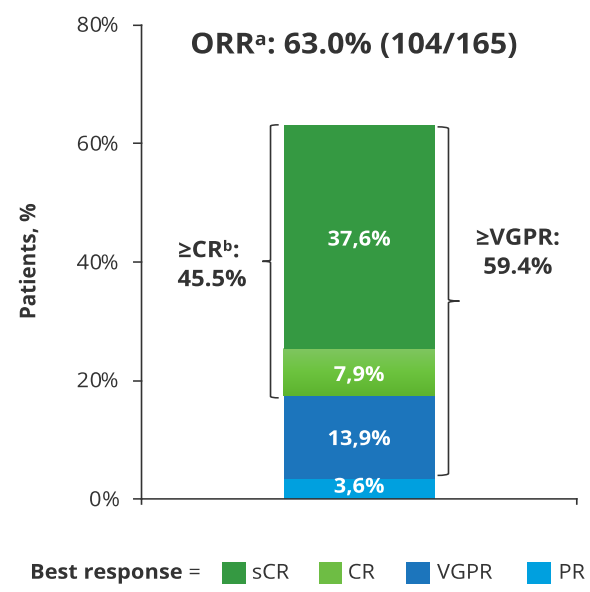
AE = adverse event; BCMA = B-cell maturation antigen; CRS = cytokine release syndrome; GPRC5D = G-protein coupled receptor family C group 5 member D; GI = gastrointestinal; ICANS = immune effector cell-associated neurotoxicity syndrome; IMiD = immunomodulatory drug; mAb = monoclonal antibody; PI = proteasome inhibitor.
TECVAYLI® (teclistamab-cqyv) Prescribing Information. ELREXFIO® (elranatamab-bcmm) Prescribing Information. LYNOZYFIC™ (linvoseltamab-gcpt) Prescribing Information. TALVEY® (talquetamab-tgvs) Prescribing Information.
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MajesTEC-1: Teclistamab Monotherapy in RRMM

Long-Term Outcomes

- 165 patients with RRMM after median 5 prior lines (77.6% triple-class refractory; no prior BCMA-targeted therapy)
- After 2 years median f/u, 47 patients remain on treatment and 41 of them maintain a deep

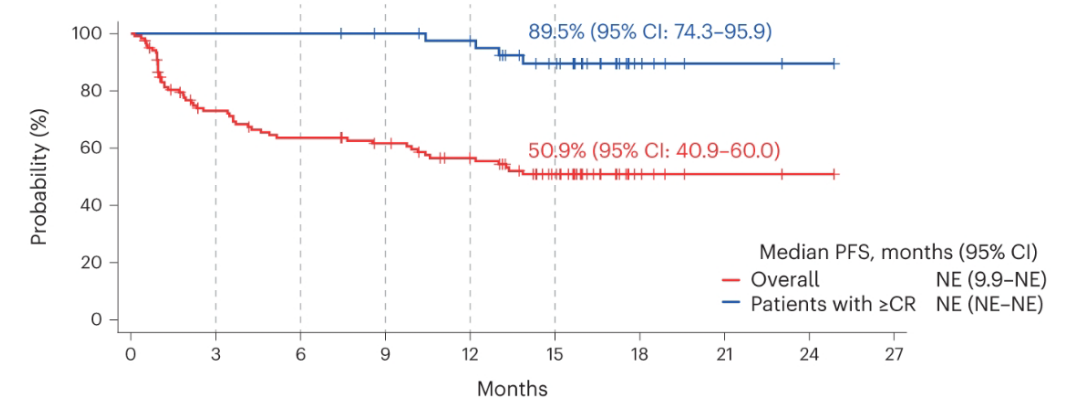
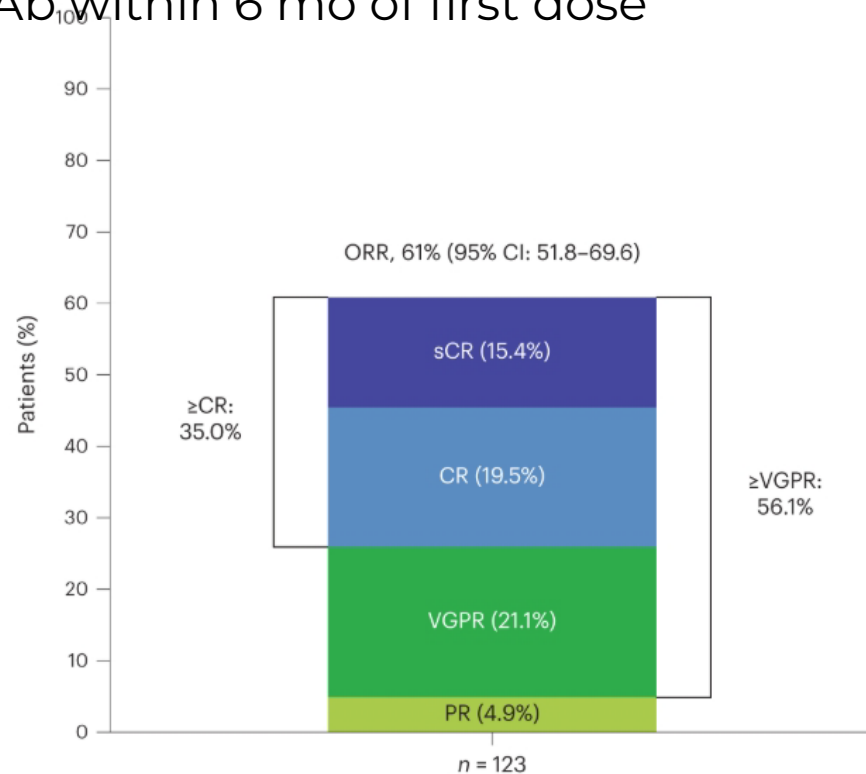
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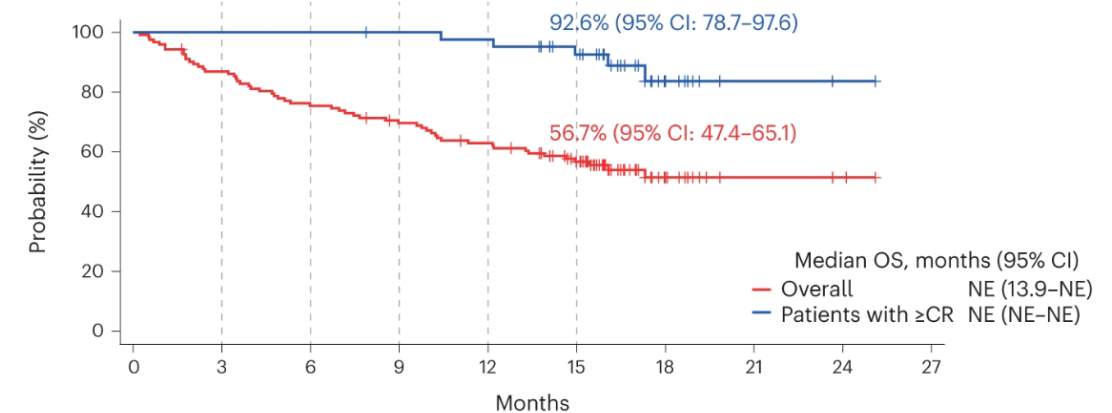
^aORR assessed by IRC. ^bFor the phase 2 efficacy population (patients enrolled in cohort A on or before March 18, 2021), ≥CR rate is 46.4% (51/110).
CR: complete response; IRC: independent review committee; NE: not evaluable; PR: partial response; sCR: stringent complete response; VGPR: very good partial response.

MagnetisMM-3: Elranatamab Monotherapy in RRMM

Part 1 enrolled 34 adults with R/R MM with ≥ 3 lines of therapy, including lenalidomide and a PI and no history of treatment with a BCMA-targeting agent, and no anti-CD38 mAb within 6 mo of first dose



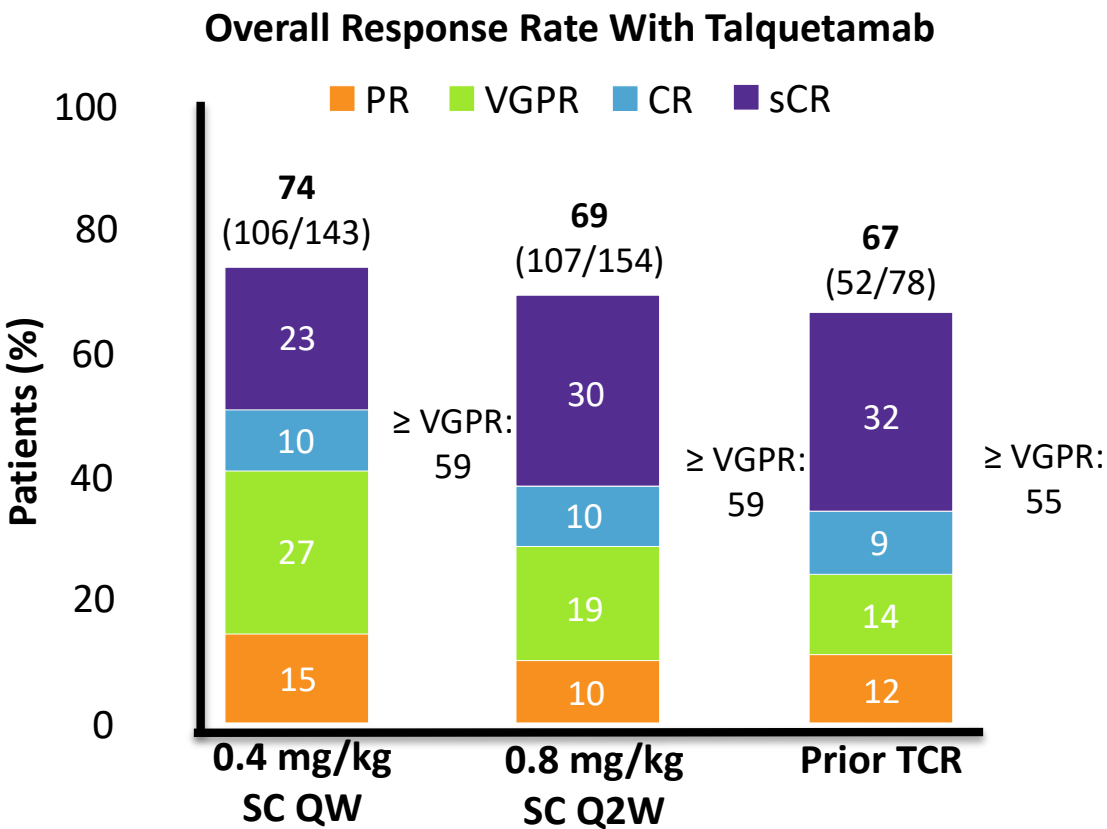
No. at risk										
Overall	123	78	67	62	52	37	6	2	1	0
Patients with $\geq$ CR	43	43	43	41	38	29	6	2	1	0



No. at risk										
Overall	123	106	92	83	74	58	12	3	2	0
Patients with $\geq$ CR	43	43	43	42	41	35	9	2	1	0

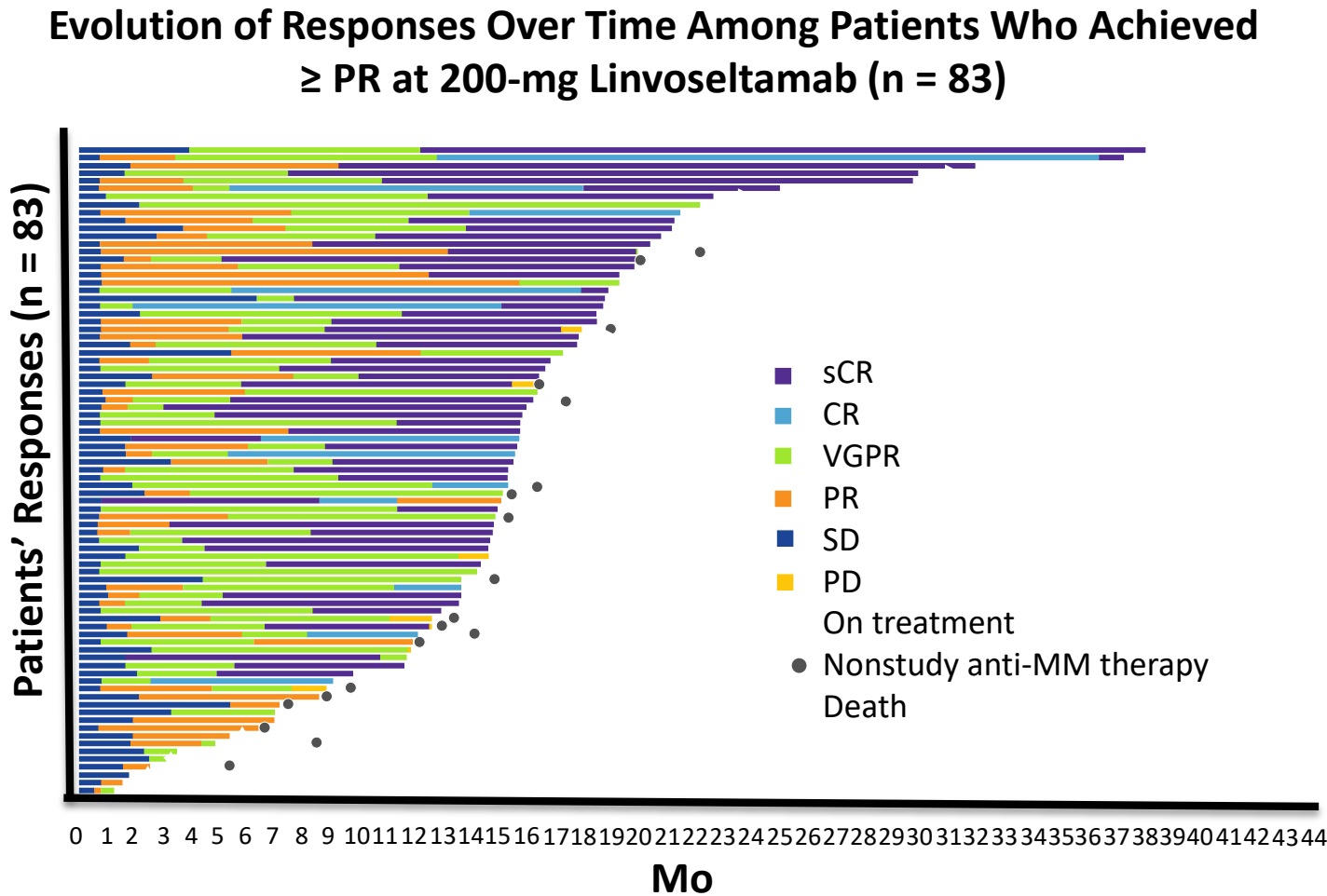
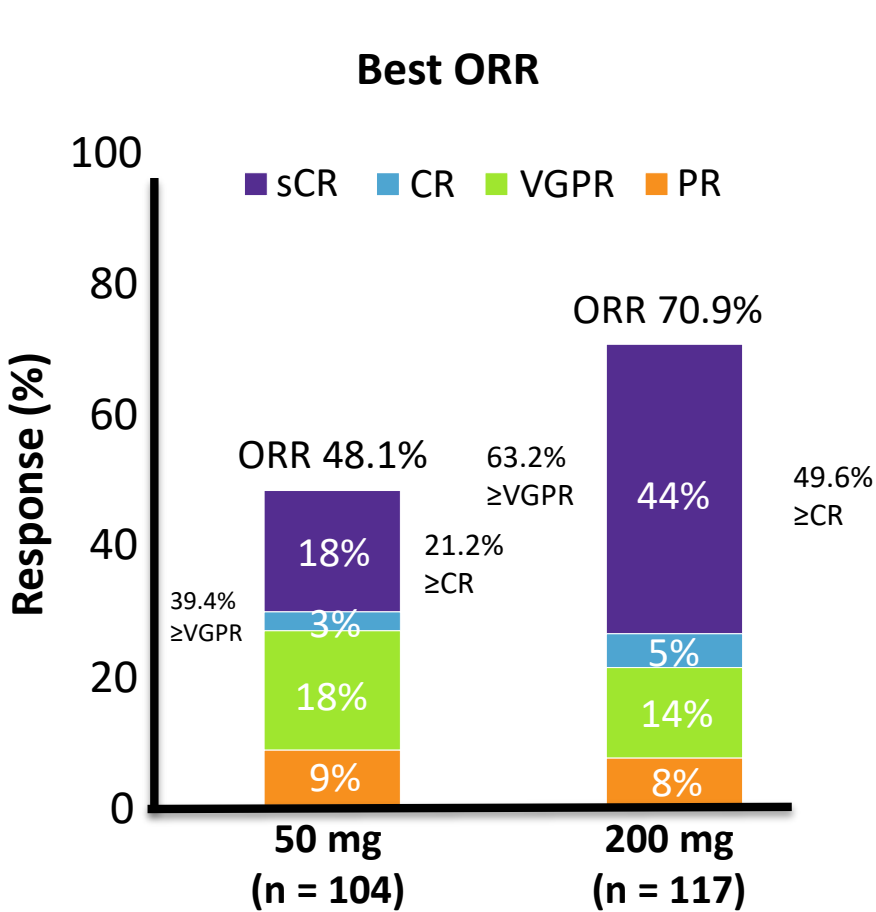
MonumenTAL-1: Talquetamab Monotherapy in R/R MM

Outcome	0.4 mg/kg QW (n = 143)	0.8 mg/kg Q2W (n = 154)	Prior T-Cell Redirection Tx (n = 78)
Median f/u, mo	29.8	23.4	20.5
Median DoR, mo (95% CI)	9.5 (6.7-13.4)	17.5 (12.5-NE)	N/A
Median PFS, mo (95% CI)	7.5 (5.7-9.4)	11.2 (8.4-14.6)	7.7 (4.1-14.5)
24-mo OS, %	60.6	67.1	57.3



In post hoc analyses, ORR was 72% in patients receiving previous CAR-T therapy and 58 in patients receiving previous bispecific antibody therapy

LINKER-MM1: Linvoseltamab Monotherapy for R/R MM



Bispecific Antibodies for MM: Monotherapy Data

Bispecific	Teclistamab	Elranatamab	Linvoseltamab	Talquetamab	
Target	BCMA	BCMA	BCMA	GPRC5D	
Clinical Trial	MajesTEC-1	MagnetisMM-3	LINKER-MM1	MonumenTAL-1	
Dose	1.5 mg/kg weekly	76 mg weekly	200 mg weekly, then bi-weekly	0.4 mg/kg weekly	0.8 mg/kg Q2W
Population	N = 165	N = 123	N = 117	N = 143	N = 154
ORR (%)	63%	61%	70%	74%	69%
PFS, median	11.3 mo	17.2 mo	NR	7.5 mo	11.2 mo
DOR, median	18.4 mo	NR	29.4 mo	9.5 mo	16.9 mo
OS, median		24.6 mo		NR	NR

BCMA = B-cell maturation antigen; DOR = duration of response; GPRC5D = G-protein coupled receptor family C group 5 member D; MM = multiple myeloma; mo = months; NR = not reached; ORR = overall response rate; OS = overall survival; PFS = progression-free survival; Q2W = every 2 weeks.

Moreau P, et al. *N Engl J Med*. 2022;387(6):495-505. Lesokhin AM, et al. *Nat Med*. 2023;10.1038/s41591-023-02528-9. Prince HM, et al. ASH 2024 #4738. Bumma N, et al. *J Clin Oncol*. 2024;42, 2702-2712. Chari A, et al. *N Engl J Med*. 2022;387(24):2232-2244. Chari AJ, et al. *Lancet Haematol*. 2025;12(4):e269-e281.

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Bispecific Antibodies for MM: Dosing

Bispecific	Teclistamab	Elranatamab	Linvoseltamab	Talquetamab	
Target	BCMA	BCMA	BCMA	GPRC5D	
Administration	SC	SC	IV	SC	
Step-Up Dosing Schedule	D1: 0.06 mg/kg (SUD1) D4: 0.3 mg/kg (SUD2) D7: 1.5 mg/kg (1st full)	D1: 12 mg (SUD1) D4: 32 mg (SUD2) D8: 76 mg (1st full)	D1: 5 mg (SUD1) D8: 25 mg (SUD2) D15: 200 mg (1st full)	Weekly D1: 0.01 mg/kg (SUD1) D4: 0.06 mg/kg (SUD2) D7: 0.4 mg/kg (1st full)	Q2W D1: 0.01 mg/kg (SUD1) D4: 0.06 mg/kg (SUD2) D7: 0.4 mg/kg (SUD3) D10: 0.8 mg/kg (1st full)
Institutions may have their own step-up protocols					
Subsequent Doses	1.5 mg/kg weekly	76 mg weekly for 24 weeks	200 mg weekly through week 13 - For week ≥ 14, switch to Q2W	0.4 mg/kg weekly	0.8 mg/kg weekly
Reduced Dosing (Based on Response)	Q2W dosing after 24 weeks for patients with $\geq$ CR	Q2W dosing after 24 weeks for patients who respond ($\geq$ PR)	Q4W dosing in patients with $\geq$ VGPR at or after week 24 and ≥ 17 full doses	NA	NA
Duration	Until PD or unacceptable toxicity	Until PD or unacceptable toxicity	Until PD or unacceptable toxicity	Until PD or unacceptable toxicity	

BCMA = B-cell maturation antigen; CR = complete response; D = day; GPRC5D = G-protein coupled receptor family C group 5 member D; IV = intravenous; MM = multiple myeloma; NA = not applicable; PD = progressive disease; PR = partial response; Q2W = every 2 weeks; Q4W = every 4 weeks; SC = subcutaneous; SUD = step-up dose; VGPR = very good partial response.

TECVAYLI® (teclistamab-cqyv) Prescribing Information. ELREXFIO® (elranatamab-bcmm) Prescribing Information. LYNZOZYFIC™ (linvoseltamab-gcpt) Prescribing Information. TALVEY® (talquetamab-tgvs) Prescribing Information.

Safety of Approved Bispecific Antibodies for Multiple Myeloma

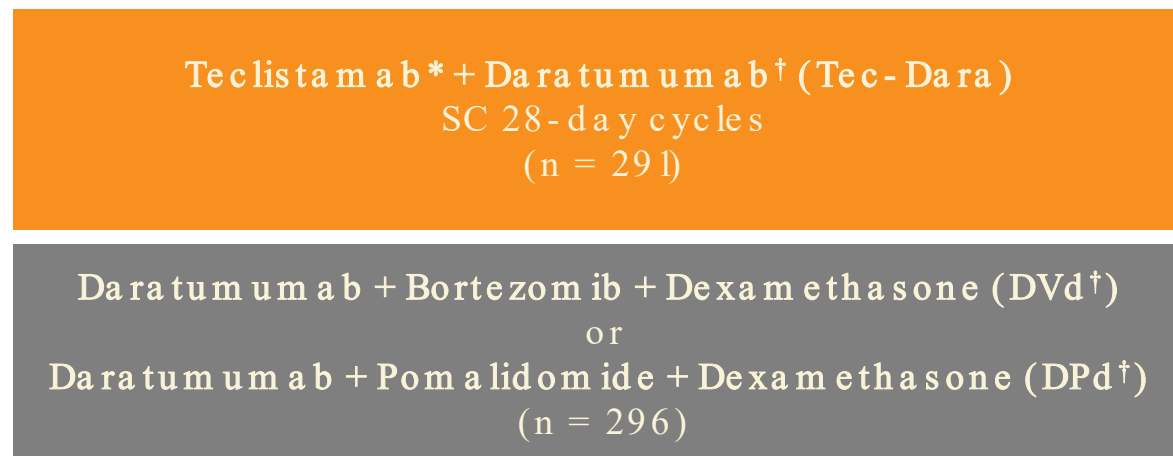
Parameter	Teclistamab ¹⁻³	Talquetamab ⁴⁻⁷	Elranatamab ⁸⁻⁹	Linvoseltamab ¹⁰
Target	CD3/BCMA	CD3/GPRC5D	CD3/BCMA	CD3/BCMA
CRS occurrence	72%: Gr 1: 50% Gr 2: 21%	76%: Gr 1: 57% Gr 2: 17%	58%: Gr 1: 44% Gr 2: 14%	46%: Gr 1: 35% Gr 2: 10%
ICANS occurrence	Gr 1/2: 3% Gr 3/4: 0%	Gr 1/2: 3% Gr 3/4: 3%	Gr 1/2: 3% Gr 3/4: 0%	Gr 1/2: 5.4% Gr 3: 2.6%
Neutropenia	Gr 3/4: 56%	Gr 3/4: 35%	Gr 3/4: 51%	Gr 3/4: 47%
Infection	Gr 3/4: 35%	Gr 3/4: 17%	Gr 3/4: 31%	Gr 3/4: 38%
Skin/nail toxicity	Not reported	62%	Not reported	15%
Oral toxicity	Not reported	80% (dysgeusia: 49%, dry mouth: 34%, dysphagia: 23%, ageusia: 18%)	Not reported	Not reported

1. Moreau. NEJM. 2022;387:495. 2. van de Donk. ASCO 2023. Abstr 8011. 3. Teclistamab-cqyv PI. 4. Chari. NEJM. 2022;387:2232. 5. Touzeau. EHA 2023. Abstr S191. 6. Talquetamab-tgvs PI. 7. Chari. Lancet. 2025;V12:E269. 8. Lesokhin. Nat Med. 2023;29:2259. 9. Elranatamab-bcmm PI. 10. Linvoseltamab PI.

MajesTEC-3: Teclistamab + Daratumumab in R/R MM

International, open-label, randomized phase III trial

Adults with MM previously treated with 1-3 prior LoT including a PI and lenalidomide; PD on/after most recent therapy; no prior treatment with BCMA-targeted therapy; not refractory to anti-CD38 therapy or any study drug; ECOG PS 0-2 (N = 587)



***1.5 mg/kg QW cycle 1 (preceded by step-up dose schedule) and cycle 2, 3 mg/kg Q2W cycles 3-6, and 3 mg/kg Q4W cycles 7+.**

†Dosed according to approved schedules.

NOTE SOME CENTERS STAY AT 1.5mg/kg

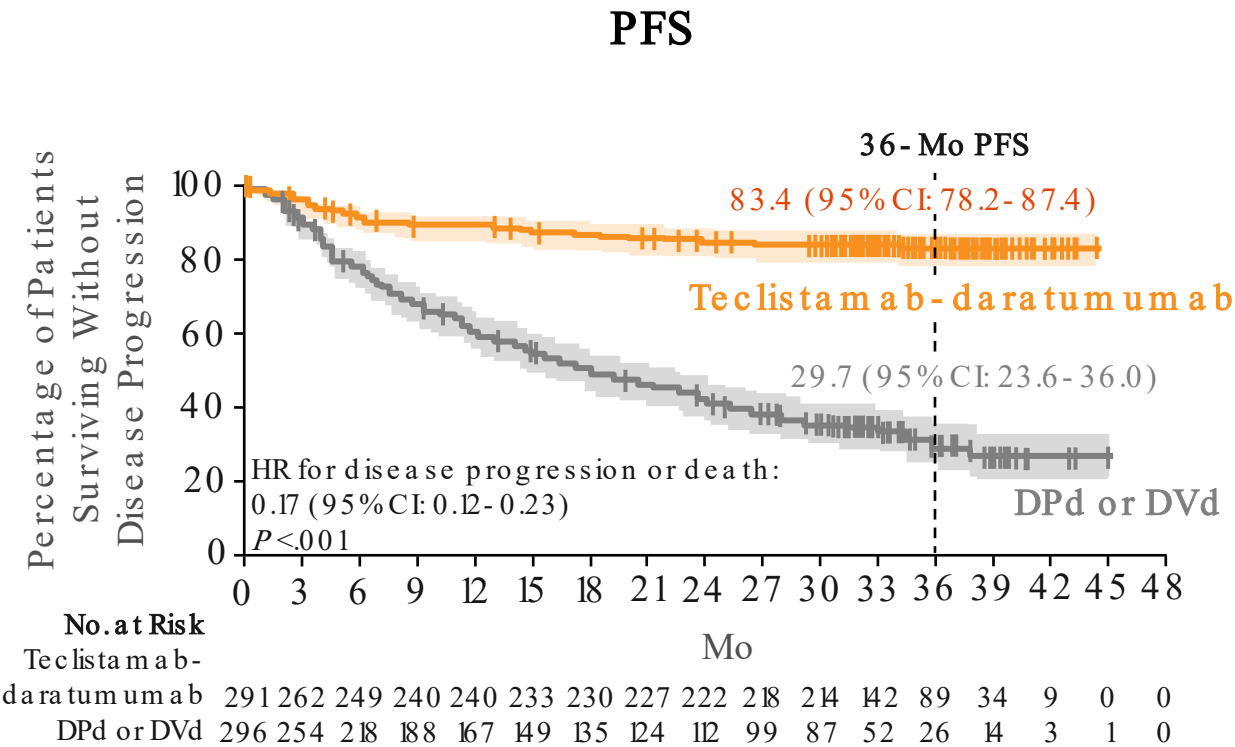
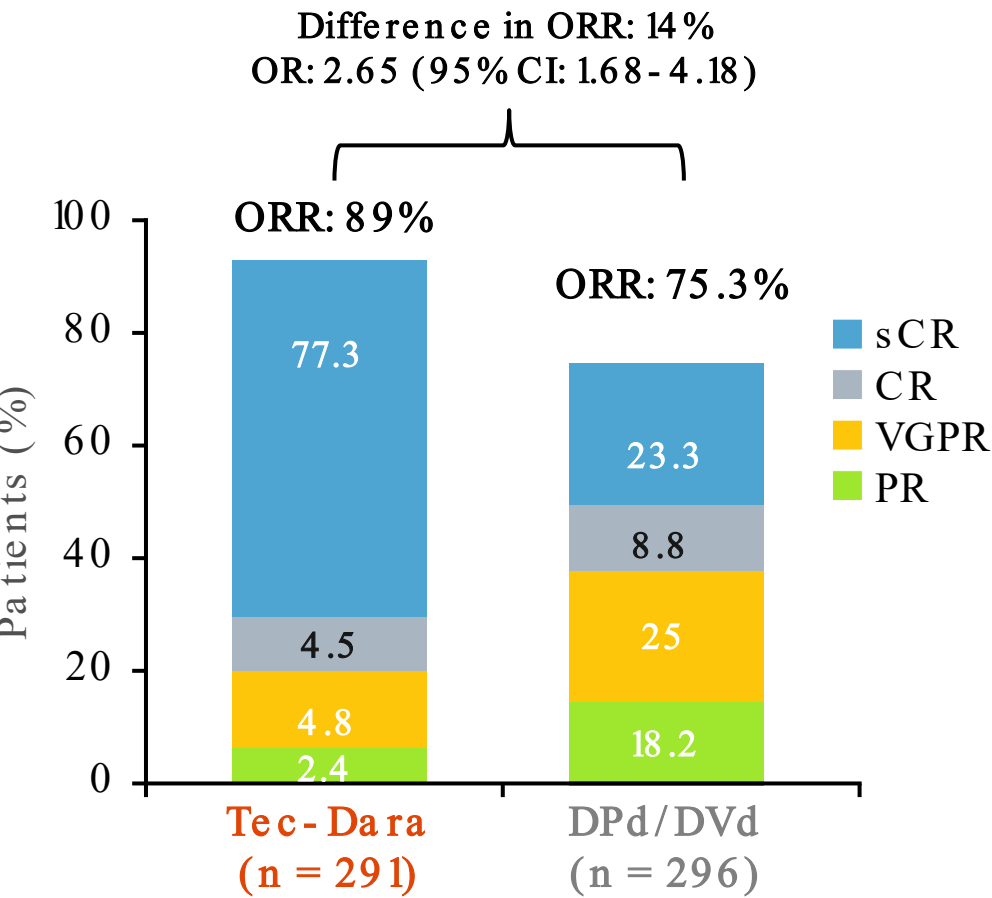
*Until PD,
unacceptable
toxicity, end of
study, or consent
withdrawal*

Study unblinded:
36-mo PFS HR = 0.17

Primary endpoint: PFS by IRC

Key secondary endpoints: CRR, ORR, MRD (10^{-5} by NGS), OS, safety, time to worsening of symptoms

MajesTEC-3: Teclistamab + Daratumumab in RRMM



	Tec-Dara (n = 291)	DPd/DVd (n = 296)
36-mo PFS, % (95% CI)	83.4 (78.2-87.4)	29.7 (23.6-36)
HR: 0.17 (95% CI: 0.12-0.23; P<.001)		

MajesTEC-3: Tec-Dara Combination for RRMM

MajesTEC-3: Phase 3, open-label, multicenter, randomized clinical trial

- Patients with 1 to 3 prior lines of therapy (N = 587)
- Tec-Dara (n = 291) vs DPd or DVd (n = 296)

Results

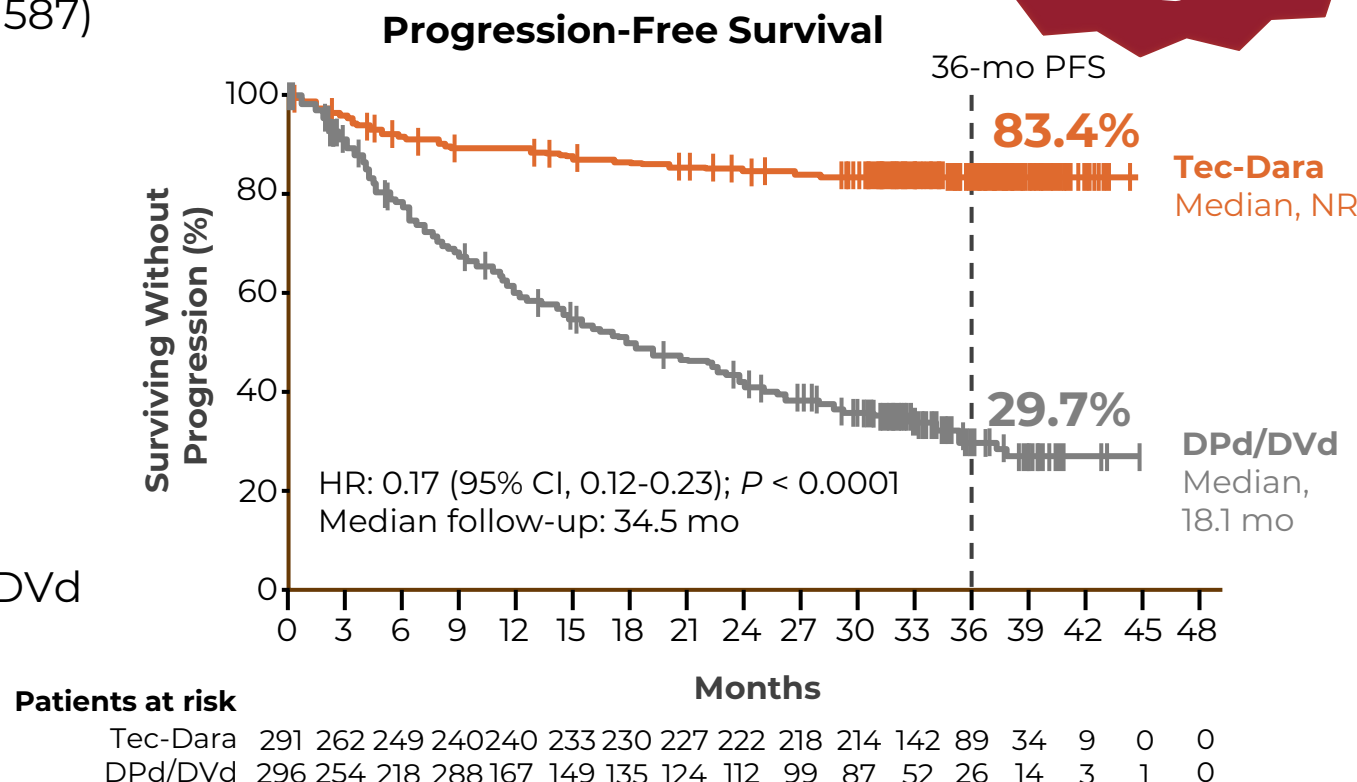
- Median follow-up 34.5 months
- **Estimated 36-month PFS**
 - **Tec-Dara: 83.4%**
 - **DPd or DVd: 29.7%**
 - **HR: 0.17 (95% CI, 0.12-0.23); $P < 0.001$**
- CR or better: 81.8% Tec-Dara vs 32.1% DPd or DVd
- ORR: 89.0% Tec-Dara vs 75.3% DPd or DVd
- MRD negative: 10^{-5} : 58.4% Tec-Dara vs 17.1% DPd or DVd
- SAEs: 70.7% Tec-Dara vs 62.4% DPd or DVd

CR = complete response; DPd = daratumumab, pomalidomide, dexamethasone; DVd = daratumumab, bortezomib, dexamethasone; FDA = US Food and Drug Administration; HR = hazard ratio; IMiD = immunomodulatory drug; LOT = line of therapy; MRD = minimal residual disease; NR = not reached; ORR = overall response rate; PFS = progression-free survival; PI = proteasome inhibitor; RRMM = relapsed/refractory multiple myeloma; SAE = adverse event; Tec-Dara = teclistamab, daratumumab.

Costa LJ, et al. *N Engl J Med*. 2026;394(8):739-752.

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**FDA approved
Tec-Dara for
RRMM with 1+
prior LOT,
including PI,
IMiD**



TEC+DARA Now FDA Approved After 1 Prior Line; Promising Single Agent Activity; MAJESTEC 9 Shows Promising Activity in Earlier Lines

The NEW ENGLAND JOURNAL of MEDICINE

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Teclistamab plus Daratumumab in Relapsed or Refractory Multiple Myeloma

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ABSTRACT

BACKGROUND
In a phase 1–2 trial, teclistamab, a bispecific antibody targeting CD3 on T-cell sur-

The authors' full names, academic degrees

Abstract #: 7510

Rapid Oral Abstract Session

Optec/Optal: A phase 2 study to evaluate outpatient (OP), step-up administration of teclistamab (Tec) or talquetamab (Tal) with prophylactic tocilizumab (prophyToci) in patients (pts) with relapsed/refractory multiple myeloma (RRMM).

Authors: Peter Forsberg, David Andorsky, Robert M. Rifkin, Christopher A. Yasenachak, Mohit Narang, Jason M. Melear, Henning H. Schade, Mitul Gandhi, Gary Simmons, Muhamed Baljevic, Habte A. Yimer, Kruti Patel, Amanda L. Gillespie-Twardy, Sudhir Manda, John S. Renshaw, Jessica Fowler, Thomas S. Lin, Tonya Le Blanc, Weiming Xu

Organizations: Colorado Blood Cancer Institute, Denver, CO, Sarah Cannon Research Institute at Rocky Mountain Cancer Centers, Boulder, CO, UCHealth Yampa Valley Medical Center, Steamboat Springs, CO, Willamette Valley Cancer Institute and Research Center, Eugene, OR, Maryland Hematology Oncology Associates, Columbia, MD, Texas Oncology PA, Austin, TX, Virginia Cancer Specialists, Gainesville, VA, Virginia Oncology Associates, Norfolk, VA, Vanderbilt University Medical Center, Nashville, TN, Texas Onc Tyler, Tyler, TX, OHC (Oncology Hematology Care)/US Oncology Network, Cincinnati, OH, Blue Ridge Cancer Care, Roanoke, VA, TMC Health Cancer Center, Tucson, AZ, Texas Oncology–San Antonio Medical Center, The US Oncology Network, San Antonio, TX, Johnson & Johnson US Hematology Medical Affairs, Horsham, PA, Sarah Cannon Research Institute, Development Innovations, Nashville, TN

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Teclistamab in Multiple Myeloma with One to Three Previous Lines of Therapy

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ORIGINAL ARTICLE

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Talquetamab–Daratumumab in Relapsed or Refractory Myeloma

Authors: Roberto Mina, M.D., Meral Beksac, M.D., Paula Rodríguez-Otero, M.D., Ph.D., Wenming Chen, M.D., Ph.D., María-Victoria Mateos, M.D., Ph.D., Jian Li, M.D., Philippe Moreau, M.D., +51 , for the MonumentAL-3 Investigators* Author Info & Affiliations

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Earlier Use of Immunotherapy After First Relapse

Among the ASCO meeting's most significant findings were **new data supporting earlier use of immunotherapy after first relapse**. Results from the **MonumenTAL-3 trial** showed that talquetamab-based combinations achieved an approximately 81% progression-free survival (PFS) rate at 2 years.

Meanwhile, the **MajesTEC-9 study** demonstrated strong activity with single-agent teclistamab in patients previously treated with daratumumab. The experts emphasized that **treatment goals at first relapse should mirror those used in NDMM—achieving the deepest and most durable remissions possible**.

Factors Driving Selection Between CAR T and BsAbs

Disease factors

- Urgency and aggressiveness of relapse
- Prior response to therapy
- Extramedullary disease (EMD)

Host factors

- Patient preference for treatment length and treatment-free intervals
- Social support and proximity to treatment centers
- Organ function: BsAb for a frail patient

Non-BCMA Options After CAR-T

- Talquetamab can be used after CAR-T to avoid further BCMA loss, preserving the option for future BCMA-targeted therapies

CAR-T vs BsAb for BCMA loss

- BCMA loss occurs less frequently after CAR-T compared to BsAb, suggesting CAR-T before BsAb may better retain efficacy for future BCMA-targeted therapies

Conclusion

- Bispecific antibodies are now an established treatment option for relapsed multiple myeloma, and the combination of teclistamab and daratumumab is approved for use in the second-line setting
- Selection between bispecific antibodies, CAR T-cell therapy, and other treatment options depends on a variety of factors, including timing and aggressiveness of relapse, patient performance status and comorbidities, and patient preference
- Bispecific antibodies are associated with a risk of potentially serious adverse events, including cytokine release syndrome, ICANs, and infections

OUR MISSION:

Improving the quality of life of myeloma patients while working toward prevention and a cure.

OUR VISION:

A world where every myeloma patient can live life to the fullest, unburdened by the disease.