MULTIPLE MYELOMA Research Foundation

Bispecific Antibodies

February 14, 2024

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Tech Support

1-719-234-7952

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Resources

- Resource tab includes
  - Speaker bios
  - Copy of the slide presentation

Submit your questions throughout the program!

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MMRF Research Initiatives

1. MMRF Myeloma Accelerator Challenge (MAC) Grants
   - Broad, multi-institutional research grants designed to advance clinical trial concepts in the areas of
     - High-risk newly diagnosed multiple myeloma (NDMM)
     - High-risk smoldering myeloma (SMM)
   - Each research network will be funded up to $10M over 3 years
2. MMRF Horizon Adaptive Platform Trials
   - Paired with MAC grants
   - Done in collaboration with 13 MMRC sites
   - Trials in relapsed/refractory myeloma, high-risk NDMM, high-risk SMM

For more information, visit themmrf.org

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Speakers

Noa Biran, MD
John Theurer Cancer Center
Hackensack University Medical Center
Hackensack, New Jersey

Gurbakhash Kaur, MD
UT Southwestern Medical Center
Dallas, Texas

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MULTIPLE MYELOMA Research Foundation

BCMA-Directed Bispecific Antibodies

Noa Biran, MD
John Theurer Cancer Center
Hackensack University Medical Center
Hackensack, New Jersey

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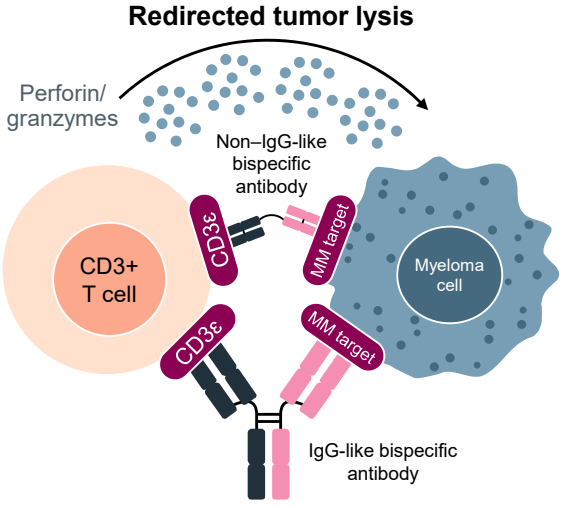
Bispecific Antibodies

- Bispecific antibodies are also referred to as *dual-specific antibodies, bifunctional antibodies,* or *T cell–engaging antibodies.*
- Bispecific antibodies can target two cell surface molecules at the same time (one on the myeloma cell and one on a T cell).
- Many different bispecific antibodies are in clinical development; three approved for use in myeloma!
- Availability is off-the-shelf, allowing for immediate treatment.



Cohen A et al. *Clin Cancer Res.* 2020;26:1541.
Singh A et al. *Br J Cancer.* 2021;124:1037.

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Myeloma Cell Targets for Bispecific Antibodies

BCMA

- Highly expressed only on the surface of plasma cells
- Myeloma patients have significantly higher serum BCMA levels than healthy individuals

GPRC5D

- High expression on myeloma cells in the bone marrow
- Low expression on hair follicles but not on other healthy cells
- Expression on myeloma cells is independent of BCMA

FcRH5

- Selectively expressed on B cells and plasma cells

GPRC5D, G protein-coupled receptor family C group 5 member D; FcRH5, Fc receptor-homolog 5

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Current State of Bispecific Antibodies

Target (MM cell × T cell)	Bispecific antibody	Status
BCMA × CD3	Tecvayli (teclistamab)	✓ Approved
	Elrexfio (elranatamab)	✓ Approved
	Linvoseltamab	Clinical studies
	Alnuctamab	Clinical studies
	ABBV-383	Clinical studies
GPRC5D × CD3	Talvey (talquetamab)	✓ Approved
	Forimtamig (RG6234)	Clinical studies
FcRH5 × CD3	Cevostamab	Clinical studies

Overall response rates 60% to 70% in heavily pretreated myeloma patients

High proportion of patients achieving VGPR or CR

GPRC5D, G protein-coupled receptor family C group 5 member D; FcRH5, Fc receptor homolog 5; VGPR, very good partial response; CR, complete response

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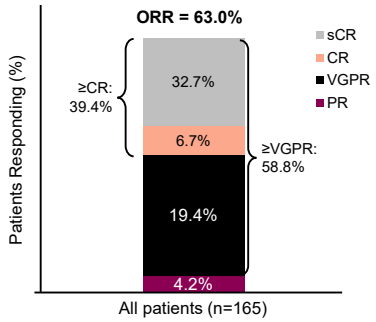
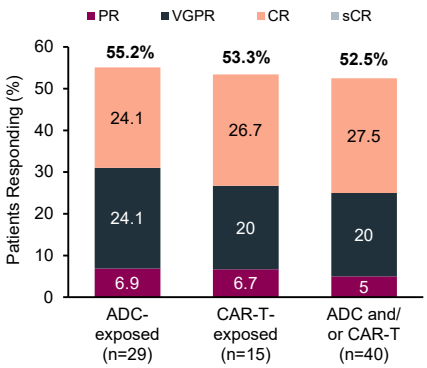
Tecvayli in Patients With RRMM

Tecvayli in patients *with no prior BCMA-targeted treatment* (MajesTEC-1 Study)[1]

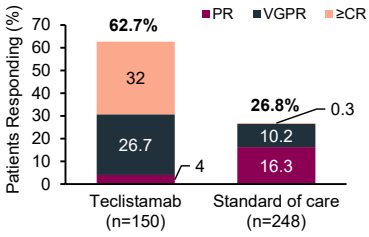


Median duration of response 18.4 months

Tecvayli in patients *with prior* BCMA-targeted treatment (MajesTEC-1 Study)[2]



Tecvayli experience vs real-world clinical practice (LocoMMotion Study)[3]



	Teclistamab	Standard of care
PFS (mos)	10.1	4.3
OS (mos)	18.3	13.0

RRMM, relapsed/refractory multiple myeloma; ORR, overall response rate

1. Moreau P et al. *N Engl J Med*. 2022;387:495. **2.** Touzeau C et al. *J Clin Oncol*. 2022;40. Abstract 8013. **3.** van de Donk NWCJ et al. *J Clin Oncol*. 2022;40. Abstract 8016.

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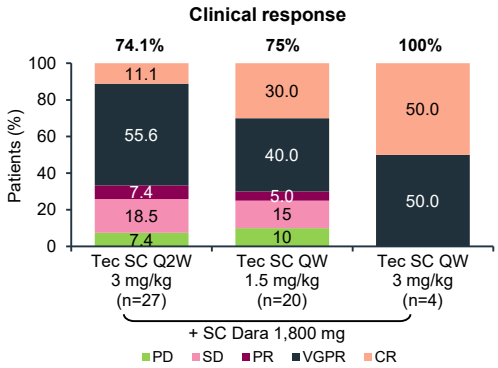
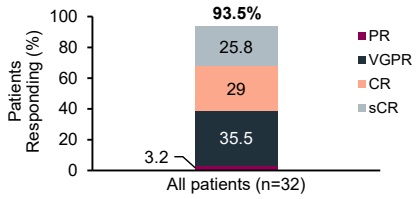
Tecvayli Combinations

Tecvayli + Darzalex in patients with 3 or more prior lines of therapy (TRIMM-2 Study)[1]



Tecvayli + Darzalex + Revlimid in patients with 1–3 prior lines of therapy (MajesTEC-2 Study)[2]



Most frequent non-hematologic adverse events, %	Any grade	Grade 3/4
CRS	81.3	0
Fatigue	46.9	6.3
Infections (≥1)	90.6	37.5

PD, progressive disease; PR, partial response; SD, stable disease; sCR, stringent complete response

1. Rodriguez-Otero P et al. *HemaSphere*. 2022;6. Abstract S188. **2.** Searl E et al. *Blood*. 2022;140. Abstract 160.

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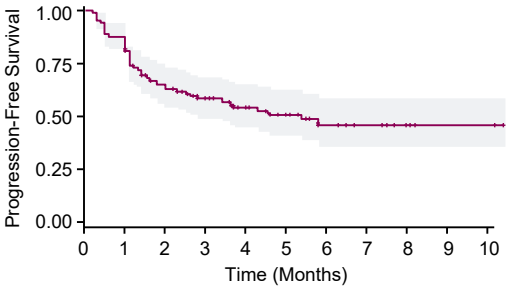
Real-World Experience With Tecvayli

Real-World Experience From 5 US Academic Centers,
Part of the US Myeloma Innovations Research Collaborative

Response (full cohort), %	RWE cohort (n=104)	MajesTec-1 (n=165)
ORR	66	63
CR or better	29	39.4
VGPR	17	19.4
PR	20	4.2
Minimal Response	0	1.2
SD	9.5	16.4
PD	24.5	14.5
NE	0	4.8

NE, not estimable; RWE, real-world experience



- Median PFS: 5.4 months
- Overall, Tecvayli was well tolerated with no major safety concerns despite worse performance status and cytopenias than the MajesTEC-1 trial population

Dima D et al. *Blood*. 2023;142. Abstract 652.

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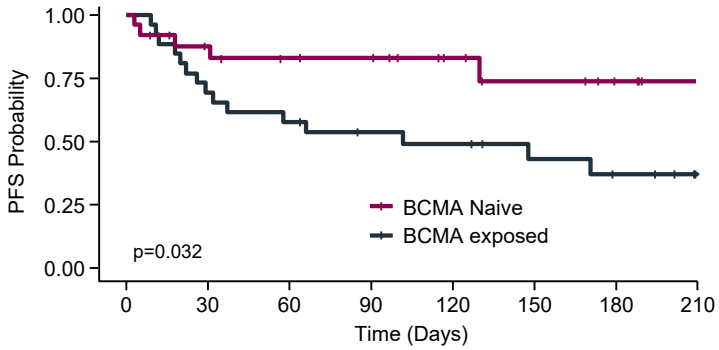
Impact of Prior BCMA Therapy on Tecvayli

- Single-center analysis of 72 patients receiving Tecvayli
- Compared to MajesTEC-1, patients were older, more heavily pretreated, and had a greater incidence of high-risk features



Firestone R et al. *Blood*. 2023;142. Abstract 333.

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Horizon Adaptive Platform Trial

- Done in collaboration with the Multiple Myeloma Research Consortium (MMRC)
- Designed to rapidly test multiple agents simultaneously while evolving in response to clinical outcomes and scientific advances
  - Teclistamab or an investigational agent
  - Additional treatment options may be added at different times
- The goal is to identify the safest and most effective therapies for multiple myeloma patients, especially the 25% of patients in the high-risk category, where need is the greatest

clinicaltrials.gov/ct2/show/NCT06171685

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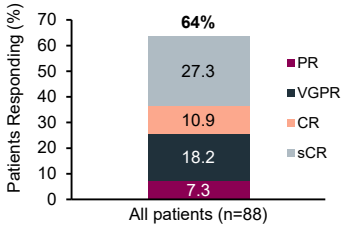
Elrexfio in Patients With RRMM

Efficacy and safety results with Elrexfio (MagnetisMM-1 Study)[1]

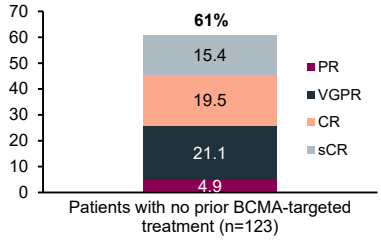
Phase 1 study in RRMM (91% triple-class refractory)



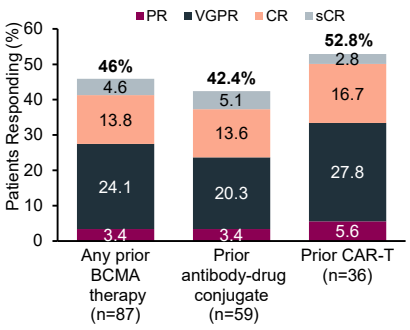
Median duration of response 17.1 months.

Elrexfio in patients with no prior BCMA-directed treatment (MagnetisMM-3 Study)[2]

Phase 2 study in RRMM refractory to at least 1 PI, 1 IMiD, and 1 anti-CD38 antibody—no prior BMCA-targeted treatment



Elrexfio in patients with prior BCMA-directed therapies (Pooled analysis of MagnetisMM studies)[3]



IMiD, immunomodulatory drug; PI, proteasome inhibitor

1. Bahlis N et al. *Nat Med*. 2023;29:2570-2576. **2.** Lesokhin A et al. *Nat Med*. 2023;29:2259-2267. **3.** Nooka AK et al. *J Clin Oncol*. 2023;41. Abstract 8008.

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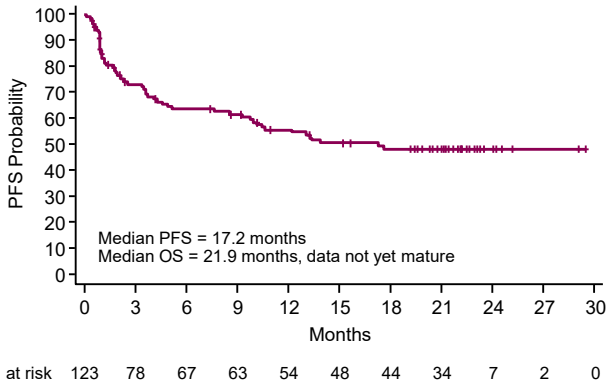
Elrexfio in Patients With RRMM: MagnetisMM-3 Updates

Lower response rates in poorer prognosis groups were primarily driven by patients with ISS stage III

Response in subgroups	ORR (%) ISS I–II	ORR (%) ISS III
High-risk cytogenetics (n=31)	71.4	0
Extramedullary disease (n=39)	47.4	0
>50% BMPCs (n=26)	84.6	7.7
Penta-refractory (n=52)	63.6	0

Progression-Free Survival



BMPC, bone marrow plasma cell; ISS, International Staging System; PFS, progression-free survival OS, overall survival

Tomasson M et al. *Blood*. 2023;142. Abstract 3385.

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Elrexfio in Patients With RRMM: MagnetisMM-3 Updates

Most frequent adverse events, %	n=123	
	Any grade	Grade 3/4
Hematologic		
Neutropenia	49.2	49.6
Anemia	48.8	37.4
Thrombocytopenia	31.7	23.6
Non-hematologic		
Infections	66.9	47.2
CRS	57.7	0
ICANS	4.9	0
Diarrhea	44.7	3.3
Fatigue	33.3	4.1
Decreased appetite	33.3	0.8
Pyrexia	32.5	4.1
Nausea	26.8	0

ICANS, immune effector cell-associated neurotoxicity syndrome

- No new safety signals with additional follow-up

Tomasson M et al. *Blood*. 2023;142. Abstract 3385.

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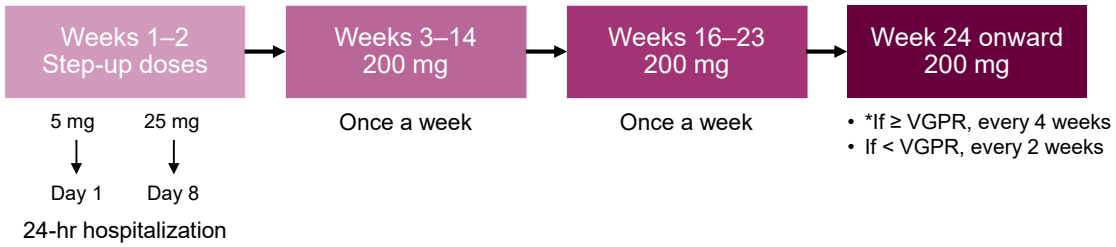
Linvoseltamab in Patients With RRMM: LINKER-MM1 Update

- Phase 2 of open-label LINKER-MM1 study: 200-mg expansion cohort
- Active MM per IMWG criteria: previous ≥3 lines of therapy and triple-exposed or triple-refractory disease (to ≥1 IMiD, PI, and anti-CD38 mAb)



IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; mAb, monoclonal antibody; PI, proteasome inhibitor; VGPR, very good partial response

Jagannath S et al. *Blood*. 2023. Abstract 4746.

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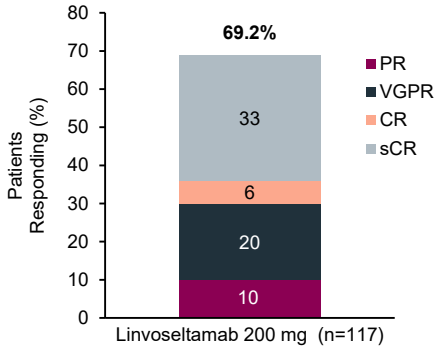
Linvoseltamab in Patients With RRMM: LINKER-MM1 Update: Response



- Median time to ≥PR was 1 month, to ≥VGPR was 2 months, and to ≥CR 7.6
- In 10 patients with previous exposure to belantamab mafodotin, ORR was 70%
- Among 37 patients with CR/sCR and available MRD data, 50% had no measurable residual disease at 10^{-5}

Jagannath S et al. *Blood*. 2023. Abstract 4746.

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Linvoseltamab in Patients With RRMM: LINKER-MM1 Update: Adverse Events

- Patients in 200-mg cohort received median of 35 weeks of treatment exposure (range: 1–137)

Nonhematologic TEAEs, %	Any Grade	Grade 3/4
CRS	46.2	0.9
Diarrhea	35	1.7
Cough	34.2	0
Fatigue	32.5	0
Arthralgia	29.1	0
Hypokalemia	22.2	2.6
Headache	21.4	0.9
Nausea	21.4	0
Dyspnea	19.7	0.9
Back pain	17.9	1.7
Vomiting	17.9	0
Constipation	16.2	0
Pyrexia	16.2	0

Hematologic TEAEs, %	Any Grade	Grade 3/4
Neutropenia	38.5	37.6
Anemia	38.5	30.8
Thrombocytopenia	17.9	14.5
Lymphopenia	12	11.1

Infection TEAEs, %	Any Grade	Grade 3/4
Opportunistic infections	8.5	6
PJP	4.3	2.6
CMV infections	1.7	1.7
CMV reactivations	2.6	1.7
Other infections of interest	69.2	36.8
Pneumonia	15.4	13.7
COVID-19	14.5	5.1
Upper respiratory tract	12.8	1.7

AE, adverse event; CRS, cytokine-release syndrome; ICANS, immune effector cell–associated neurotoxicity syndrome; TEAE, treatment-emergent adverse event

Jagannath S et al. *Blood*. 2023. Abstract 4746.

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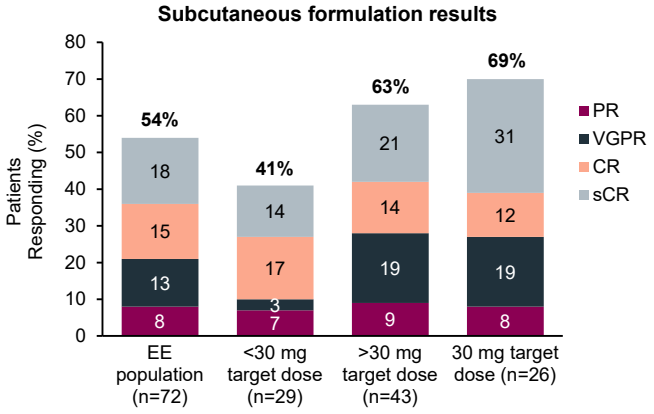
Alnuctamab in Patients With RRMM: Phase 1 Response and Adverse Events



Most frequent adverse events (%)	Any grade	Grade 3/4
Hematologic		
Anemia	47	27
Neutropenia	55	45
Thrombocytopenia	37	16
Non-hematologic		
CRS	56	0
Infections	62	16

Bar N et al. *Blood*. 2023;142. Abstract 2011.

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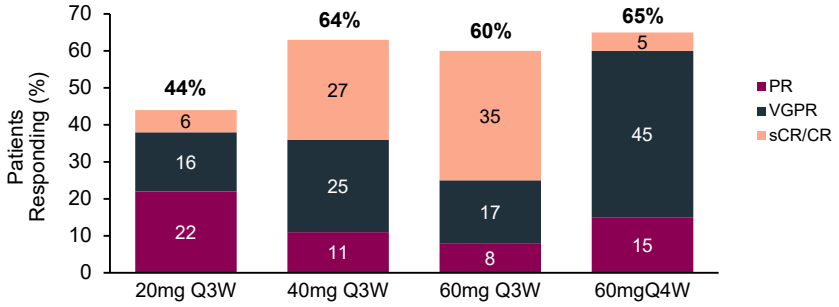
ABBV-383 in Patients With RRMM: Phase 1 Response

- ABBV-383 is a BCMA-directed bispecific with a bivalent BCMA domain and low CD affinity
- Phase 1 trial with patients (n=220) who had previous ≥3 lines of therapy



Q3W, every 3 weeks; Q4W, every 4 weeks

Jagannath S et al. *Blood*. 2023. Abstract 4746.

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ABBV-383 in Patients With RRMM: Phase 1 Adverse Events

Non-hematologic adverse events	ABBV-383 every 3 weeks*						ABBV-383 monthly†	
	20 mg (n=32)		40 mg (n=55)		60 mg (n=61)		60 mg (n=21)	
	Any grade	Grade 3/4	Any grade	Grade 3/4	Any grade	Grade 3/4	Any grade	Grade 3/4
Grade 3/4 infection	–	22	–	24	–	34	–	10
Pneumonia	25	9	33	5	30	10	10	0
CRS	50	3	71	0	70	2	43	0
ICANS	3	0	5	0	5	2	5	0

*Premeds included 10 mg dexamethasone; hospitalization 48 hr, dose 1 only.
†Premeds included 36 mg dexamethasone; hospitalization 24 hr, dose 1 only.

Jagannath S et al. *Blood*. 2023. Abstract 4746.

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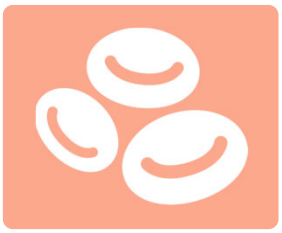
Expected Toxicities With BCMA-Directed Bispecific Antibodies

Cytokine release syndrome (CRS)

Infections



Cytopenias

Neurotoxicity (ICANS)

ICANS, immune effector cell-associated neurotoxicity syndrome

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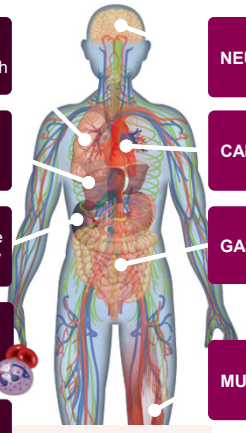
CRS Severity Is Typically Mild: Early Recognition and Treatment Is Key

RESPIRATORY	• Difficulty breathing • Shortness of breath
HEPATIC	• Altered liver function tests in the blood
RENAL	• ↑ Serum creatinine • Renal insufficiency
HEMATOLOGIC	• Anemia • Thrombocytopenia • Neutropenia
CONSTITUTIONAL	• Fever • Fatigue • Headache



NEUROLOGIC	• Tremors • Altered wakefulness • Difficulty speaking
CARDIOVASCULAR	• Rapid heart rate • Low blood pressure • Arrhythmias
GASTROINTESTINAL	• Nausea • Vomiting • Diarrhea
MUSCULOSKELETAL	• Weakness

Mitigation and monitoring for CRS

- Step-up dosing with hospitalization for monitoring
- Frequent vital signs
- Rule out infection
- Laboratory monitoring
- Early intervention with tocilizumab

ALP, alkaline phosphatase; CPK, creatine phosphokinase; CRP, C-reactive protein; CRS, cytokine release syndrome; LDH, lactate dehydrogenase; O_2, oxygen; TLS, tumor lysis syndrome

Oluwole OO, Davila ML. *J Leukoc Biol*. 2016;100:1265. June CH, et al. *Science*. 2018;359:1361. Brudno JN, Kochenderfer JN. *Blood*. 2016;127(26):3321. Brudno JN, Kochenderfer JN. *Blood Rev*. 2019:34:45. Shimabukuro-Vornhagen, et al. *J Immunother Cancer*. 2018;6:56. Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;25:625.

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Infection Prevention

Avoid crowds	Ensure handwashing, hygiene	Growth factors	IVIG for hypo-gammaglobulinemia
Immunizations (no live vaccines)	COVID-19 prevention	Zoster and PJP prophylaxis	Monitor CD4 count

IVIG, intravenous immunoglobulin; PJP, *Pneumocystis jirovecii* pneumonia

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Key Points

- Approved BCMA bispecifics offer patients expanded access to BCMA therapy because of the “off-the-shelf” nature of treatment
  - Tecvayli
  - Elrexfio
- Differentiating factors between BCMA bispecifics include
  - Route of administration
  - Step-up dosing schedule, hospitalization requirements, dosing frequency
- Infection management: use preventive strategies, treat accordingly
- Ongoing clinical trials continue to evaluate newer BCMA-directed bispecific antibodies

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MULTIPLE MYELOMA Research Foundation

Non–BCMA-Directed Bispecific Antibodies

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UT Southwestern Medical Center
Dallas, Texas

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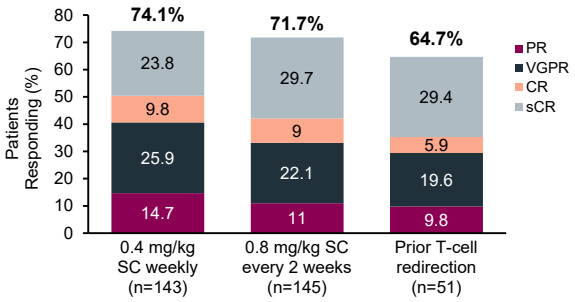
Talvey in Patients With RRMM: Response

Phase 1/2 study (MonumenTAL-1) in RRMM

288 patients—with or without prior T-cell–redirecting therapies—received treatment with Talvey at 2 different doses (0.4 mg/kg every week and 0.8 mg/kg every other week) subcutaneously.



Now approved for patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a PI, an IMiD, and an anti-CD38 monoclonal antibody!

IMiD, immunomodulatory drug; PI, proteasome inhibitor
Schinke CD et al. *J Clin Oncol*. 2023;41. Abstract 8036.

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Talvey in Patients With RRMM: Adverse Events

Most frequent adverse events, %	0.4 mg/kg		0.8 mg/kg	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Hematologic				
Anemia	44.8	31.5	45.5	27.6
Neutropenia	35.0	30.8	28.3	22.1
Thrombocytopenia	27.3	20.3	29.7	18.6
Non-hematologic				
CRS	79.0	2.1	74.5	0.7
Taste disorder (dysgeusia)*	72.0	NA	71.0	NA
Infections	58.7	19.6	66.2	14.5
Skin related*	55.9	0	73.1	0.7
Nail related	54.5	0	53.8	0
Weight decreased	41.3	2.1	41.4	5.5
Fatigue	24.5	3.5	27.6	0.7

*Taste- and skin-related side effects led to discontinuations in 5 patients

Schinke CD et al. *J Clin Oncol*. 2023;41. Abstract 8036.

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Talvey in Patients With RRMM: Efficacy in TAL-Responsive, Dose-Reduction Cohorts

- Talvey dose reduction typically occurred after achieving a response
- Median time to dose reduction following response:
  - QW 3.2 mo, Q2W 4.5 mo, prior TCR 4.7 mo
- Response maintained following prospective dose reduction, with some patients achieving deepening responses:
  - ORR: 79.2%; sCR: 25%; CR: 29.2%; VGPR: 20.8%; PR: 4.2%

Outcome	Responders with dose reduction		
	QW* (n=24)	Q2W† (n=13)	Prior TCR‡ (n=10)
Median follow-up, mo	27.6	20.8	21.3
Median DoR, mo	19.8	NE	24.2
12-mo DoR, %	78.3	84.6	100

*Dose reduction for AE (n=21), dose reduction for response only (n=3); †Dose reduction for AE (n=11), dose reduction for response only (n=2); ‡Dose reduction for AE (n=9), dose reduction for response only (n=1).

Chari A et al. *Blood*. 2023;142. Abstract 1010.

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Talvey in Patients With RRMM: Safety in Prospective Dose-Reduction Cohorts

Patients, %	Change in AE status in prospective dose-reduction cohorts after switch vs matched nonswitch cohort							
	Resolved		Improved but not resolved		No change		Worsened	
	Prospective	Without DR	Prospective	Without DR	Prospective	Without DR	Prospective	Without DR
Skin toxicity (rash)	66.7	41.2	0	0	33.3	58.8	0	0
Skin toxicity (nonrash)	50.0	15.3	0	4.7	50.0	74.1	0	5.9
Oral toxicity	33.3	26.9	6.7	3.1	60.0	66.9	0	3.1
Nail toxicity	11.1	12.0	11.1	3.3	77.8	81.5	0	3.3
Weight loss	12.5	18.9	12.5	6.5	37.5	53.8	37.3	20.8

- Most GPRC5D-related AEs trended toward improvement or resolution, except for weight loss

Patient numbers: skin toxicity (rash): prospective, n=3; no dose reduction, n=17. Skin toxicity (nonrash): prospective, n=6; no dose reduction, n=85. Oral toxicity: prospective, n=15; no dose reduction, n=160. Nail toxicity: prospective, n=9; no dose reduction, n=92. Weight loss: prospective, n=8; no dose reduction, n=106.

Chari A et al. *Blood*. 2023;142. Abstract 1010.

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GPRC5D-Associated Side Effects

Affected area	Symptoms and effects	Management
Skin	Rash, skin peeling	Relatively benign, not painful, self-limiting, and manageable with emollients
Nails	Nail thinning and loss	Mostly aesthetic but take time to resolve
Oral	Difficulty swallowing, dry mouth, taste changes	Can lead to weight loss; have longer duration and can affect quality of life. Most successfully managed with dose modification. Supportive measures may be used (eg, NaCl mouth rinse, artificial saliva spray, diet modification)

Myeloma patients respond well to treatment, and GPRC5D-associated side effects improve over time, becoming more tolerable; notable reduction in side effects is seen with dose modification.

Catamero D et al. *Clin Lymphoma Myeloma Leuk*. 2023;23. Abstract NSP-03.

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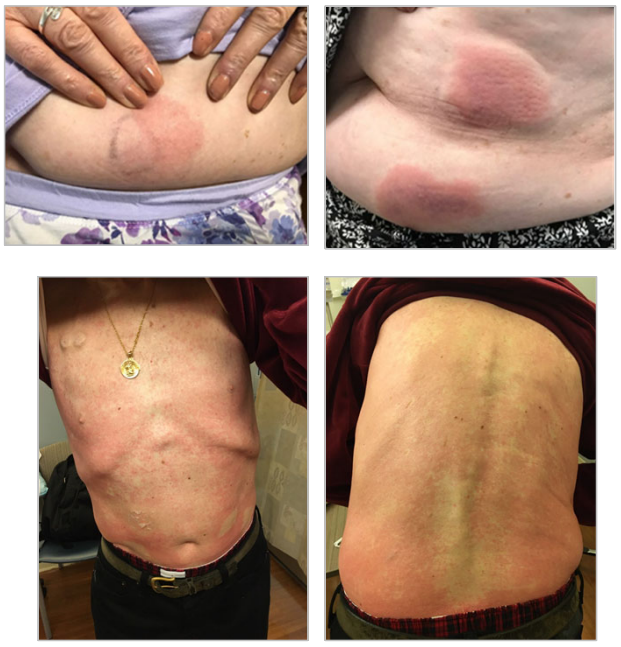

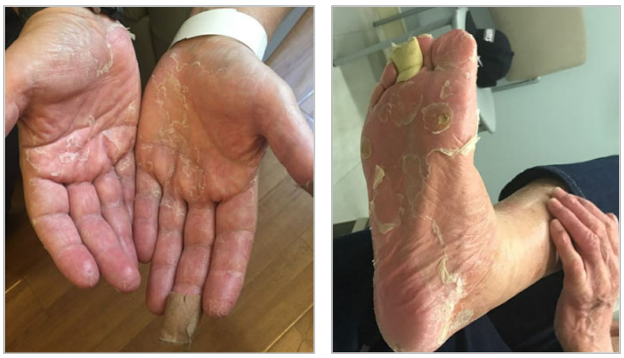

Products applied twice daily
- Ammonium lactate 12% cream
- Triamcinolone 0.1% cream
- Emollients
- Oral antihistamines as needed

5 patients who had grade 3 rash

Images courtesy of Dr. Ajay Chari.

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- Starts ~C2, lasts for months
- Avoid frequent/long durations of water immersion
- Frequent application of emollients (Vaseline, Aquaphor)
- Vitamin E oil
- File to smooth the edges and corners of the nail plates
- Clear nail polish or nail hardeners
- Biotin supplements may be helpful

Images courtesy of Dr. Ajay Chari.

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Talvey Use in Practice

Administered subcutaneously according to step-up dosing schedule and then weekly or every 2 weeks thereafter

Patients are hospitalized for 48 hours for monitoring of side effects after they have completed their step-up dosing at a REMS-certified facility

REMS, risk evaluation and mitigation strategy

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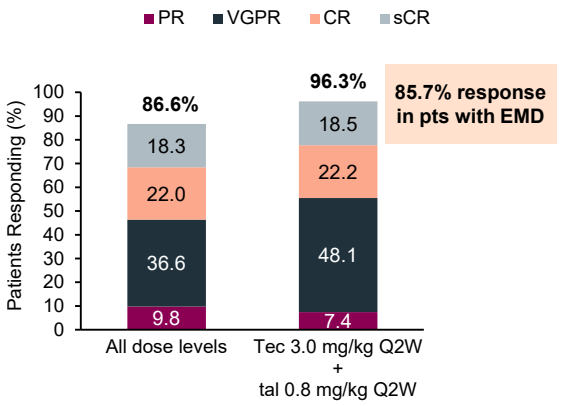
Talvey Combinations: Tecvayli + Talvey in Patients With RRMM



Most frequent adverse events (%)	All dose levels (n=93)		Tec + Tal at RP2R dose levels (n=34)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Hematologic				
Neutropenia	65.6	61.3	55.9	44.1
Anemia	50.5	34.4	32.4	23.5
Thrombocytopenia	43.0	29.0	32.4	23.5
Non-hematologic				
CRS	76.3	3.2	73.5	0
Dysgeusia	61.3	–	47.1	–
Pyrexia	50.5	2.2	38.2	2.9
Skin toxicity	53.8	0	52.9	0
Nail disorders	46.2	0	41.2	0

Progression-free survival, 20.9 months; duration of response, not yet evaluable.

PR, partial response; VGPR, very good partial response; CR, complete response; sCR, stringent complete response; CRS, cytokine release syndrome; EMD, extramedullary disease
Cohen YC et al. *J Clin Oncol*. 2023;41. Abstract 8002.

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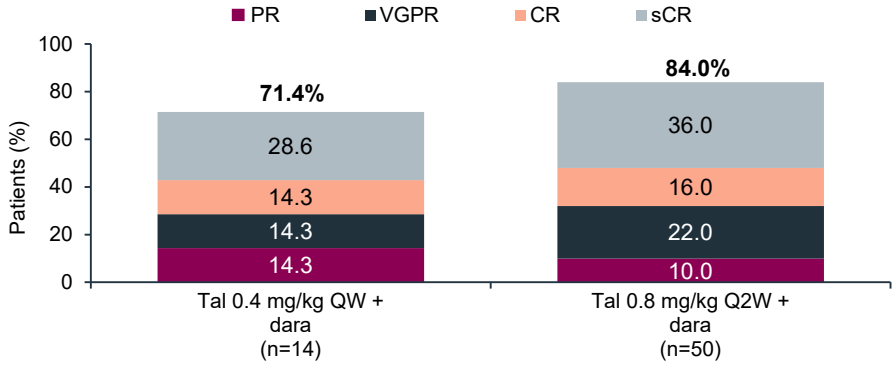
Talvey Combinations: Talvey + Darzalex in Patients With 3 or More Prior Lines of Therapy



Progression-free survival, 19.4 months; duration of response, 20.3 months.

PR, partial response; VGPR, very good partial response; CR, complete response; sCR, stringent complete response

TRIMM-2 Study. Dholaria BR et al. *J Clin Oncol*. 2023;41. Abstract 8003.

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Future Direction With Talvey

- Phase 2 pilot study of Talvey + Darzalex and Tecvayli + Darzalex in patients with high-risk* newly diagnosed multiple myeloma, with an early rescue intervention guided by minimal residual disease (MRD) assessment (GEM-TECTAL)

*One or more of the following high-risk features: del(17p), t(4;14), t(14;16), or 1q amplifications detected by fluorescence in situ hybridization, Revised ISS stage 3, and presence of extramedullary disease.

Rodríguez-Otero P et al. *Clin Lymphoma Myeloma Leuk*. 2023;23. Abstract NSP-03.

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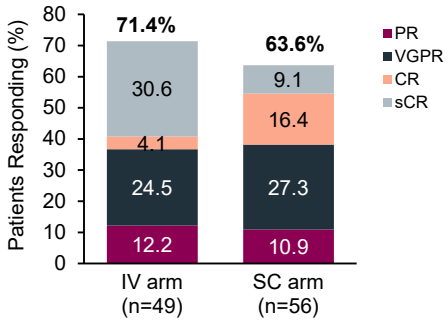
Forimtamig: A GPRC5D × CD3 Bispecific Antibody in Patients With RRMM

Phase 1 study of 105 patients[1]



Subgroup analysis[2]	Number of patients	Overall response rate (%)
Age ≥65 years	52	71.2
>4 Prior lines of therapy	49	63.3
Triple-class refractory	81	60.5
Penta-drug refractory	45	57.8
Prior BCMA-targeted therapy	29	51.2
Antibody-drug conjugate	19	47.7
Bispecific antibody	5	42.9
CAR T cells	5	66.7
High risk cytogenetics (include del(17p), t(4;14), t(14;16))	33	63.4
1q21 gain	15	86.7
ISS III	24	70.8
Soluble BCMA >327 ng/mL	54	55.6
Soluble BCMA <327 ng/mL	55	80.0
Extramedullary disease	28	50.0

1. Carlo-Stella CA et al. *Blood*. 2022;140. Abstract 161.
2. Harrison SJ et al. *Clin Lymphoma Myeloma Leuk*. 2023. Abstract OA-05.

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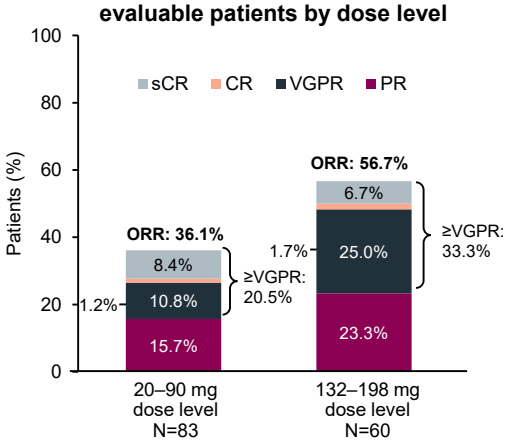
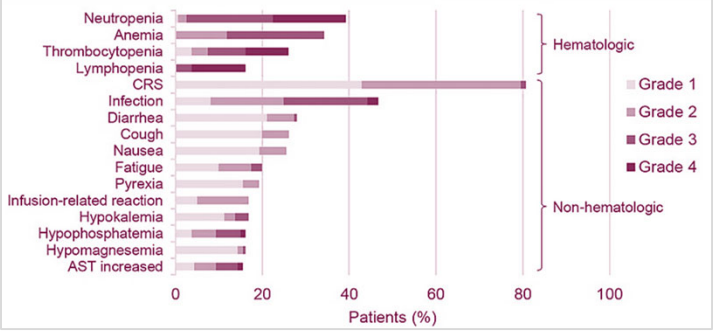
Cevostamab: A FcRH5 × CD3 Bispecific Antibody in Patients With RRMM

Best response rates in efficacy-evaluable patients by dose level



Common (≥15%) hematologic and non-hematologic AEs in all patients by Grade‡



Trudel S et al. *Blood*; 2021;138. Abstract 157.

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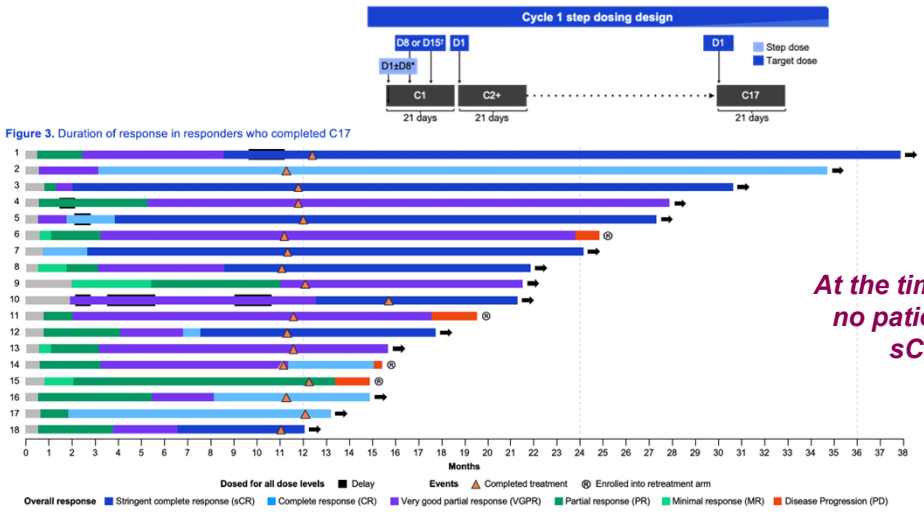
Fixed-Duration Therapy With Cevostamab



At the time of this presentation, no patients who achieved an sCR have relapsed!

Lesokhin AM et al. *Blood*. 2022;140. Abstract 1924.

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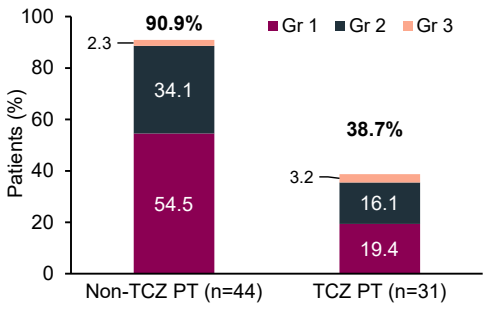
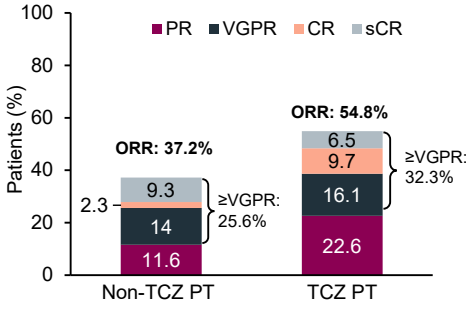
Pretreatment With Tocilizumab Reduces Incidence and Severity of Cytokine Release Syndrome With Cevostamab

Phase 1 study evaluating the use of tocilizumab (an IL-6 antibody) prior to the first dose of cevostamab.



Significantly lower rate of CRS in patients pretreated with tocilizumab



Patients pretreated with tocilizumab had no negative impact on response rates

Trudel S et al. *Blood*; 2022;140. Abstract 567.

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Cevostamab Combinations: Cevostamab + Pomalyst + Dexamethasone in RRMM

Phase 1b study (CAMMA 1) in RRMM (≥2 prior lines of therapy, including ≥1 IMiD and ≥1 proteasome inhibitor)

8 patients received treatment with cevostamab (intravenously), Pomalyst, and dex.

	Cevostamab-Pom-Dex (n=8)
Overall response rate, n	8 (100%)
CR	1 (12.5%)
VGPR	3 (37.5%)
PR	4 (50%)
Adverse events (grade 3/4), n	7 (87.5%)
Neutropenia	Gr 3: 1 (12.5%) Gr 4: 3 (37.5%)
CRS	All Gr: 7 (87.5%) Gr 3: 2 (25%)

Jelinek T et al. *Clin Lymphoma Myeloma Leuk*. 2023;23. Abstract P-019.

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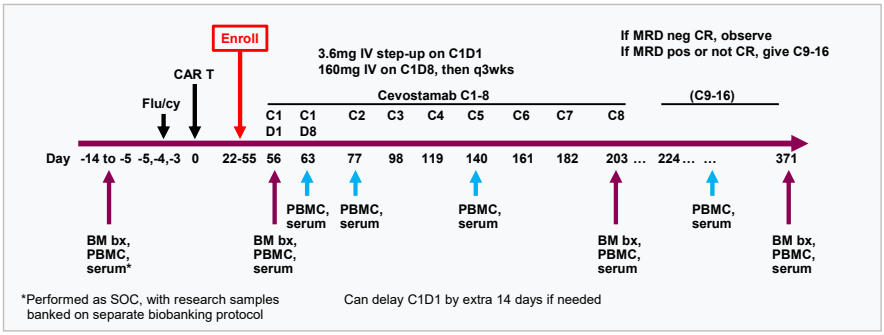
Cevostamab Consolidation Post–CAR T-Cell Therapy

Phase 2 investigator-initiated study

8 cycles of cevostamab starting 8 weeks to 10 weeks after commercial CAR T-cell infusion
(Exclusion criteria include significant immune-related events associated with CAR T cells)

Key inclusion criteria
- RRMM, ≥ 4 prior lines
- Triple-class exposed
- ≥ SD after CAR T
- ECOG PS 0-1

Primary end point
MRD-negative CR rate at 12 mo post-CAR T



Accrual began in July 2023 for planned 26 patients

Bx, bone marrow biopsy; C, cycle; Cy, cyclophosphamide; D, day; ECOG PS, Eastern Cooperative Oncology Group performance status; Flu, fludarabine; PBMC, peripheral blood mononuclear cells; SD, stable disease; SOC, standard of care

Cohen AD et al. *Blood*. 2023;142. Abstract 3389.

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Key Points

- Bispecific antibodies are very active even in heavily pretreated patients.
- Side effects of bispecific antibodies include cytokine release syndrome, low blood counts, and confusion (rare)—all of which are treatable.
- Infections have emerged as a more challenging toxicity, but—with experience—strategies are forming to mitigate the risks.
- Bispecific antibodies represent an off-the-shelf immunotherapy; three bispecific antibodies have been approved since October 2022.
- Several additional bispecific antibodies are under clinical evaluation. Different bispecifics and different targets are on the way.

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MULTIPLE MYELOMA Research Foundation

Questions & Answers

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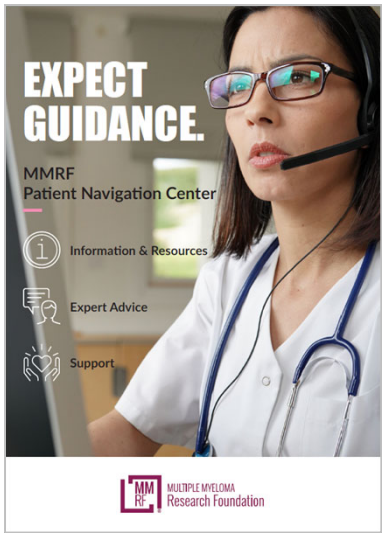
MMRF Patient Resources



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Myeloma Mentors®

Myeloma Mentors® allows patients and caregivers the opportunity to connect with trained mentors. This is a phone-based program offering an opportunity for a patient and/or caregiver to connect one-on-one with a trained patient and/or caregiver mentor to share his or her patient journeys and experiences.

No matter what your disease state—smoldering, newly diagnosed, or relapsed/refractory—our mentors have insights and information that can be beneficial to both patients and their caregivers.

Contact the Patient Navigation Center at 888-841-6673 to be connected to a Myeloma Mentor or to learn more.

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Join the MMRF Community!

National Walk/Run Program

Atlanta | 10.26.24
Boston | 10.12.24
Chicago | 9.8.24
Dallas | 11.16.24
Houston | 11.23.24
Los Angeles | 8.17.24
National Virtual | 12.14.24
New York City | 10.5.24
Philadelphia | 10.19.24
San Francisco | 8.24.24
Scottsdale | 12.7.24
Southeast Michigan | TBD
Tampa | TBD
Twin Cities | 9.14.24
Washington, D.C. | 9.28.24

Other MMRF Event Programs

Moving Mountains for Multiple Myeloma

Half and Full Marathons

Bike/Road to Victories

Create Your Own Fundraiser

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Upcoming Patient Education Events
Save the Date

Program	Date and Time	Speakers
Biomarkers *Patient Webinar*	Monday, February 19, 2024 1:00 PM – 2:00 PM (ET) 10:00 AM – 11:00 AM (PT)	Ben Diamond, MD Francesco Maura, MD
Bispecific Antibodies *Livestream*	Monday, February 26, 2024 11:00 AM – 12:00 PM (ET) 8:00 AM – 9:00 AM (PT)	Jesus Berdeja, MD Melissa Alsina, MD
Biomarkers *Livestream*	Tuesday, March 5, 2024 1:00 PM – 2:00 PM (ET) 10:00 AM – 11:00 AM (PT)	Joshua Richter, MD Alexander Lesokhin, MD

For more information or to register,
visit **https://themmrf.org/educational-resources**

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Resources

- Resource tab includes
  - Speaker bios
  - Copy of the slide presentation

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Need help with travel to a clinical study?

- The MMRF has partnered with the Lazarex Cancer Foundation to help provide more equitable access to clinical studies for multiple myeloma patients
- This partnership is one facet of the MMRF's commitment to improve diversity and representation in myeloma clinical studies
- MMRF has provided $100,000 over 2 years to Lazarex to fund travel, lodging, and food for patients (and a travel companion) so that they can participate in clinical studies that are appropriate for them
- Patients are funded according to income guidelines and will be reimbursed for allowed expenses
- For more information on this program and to be connected with Lazarex, call our Patient Navigation Center at 1-888-841-6673

It's About Living
Lazarex
CANCER FOUNDATION

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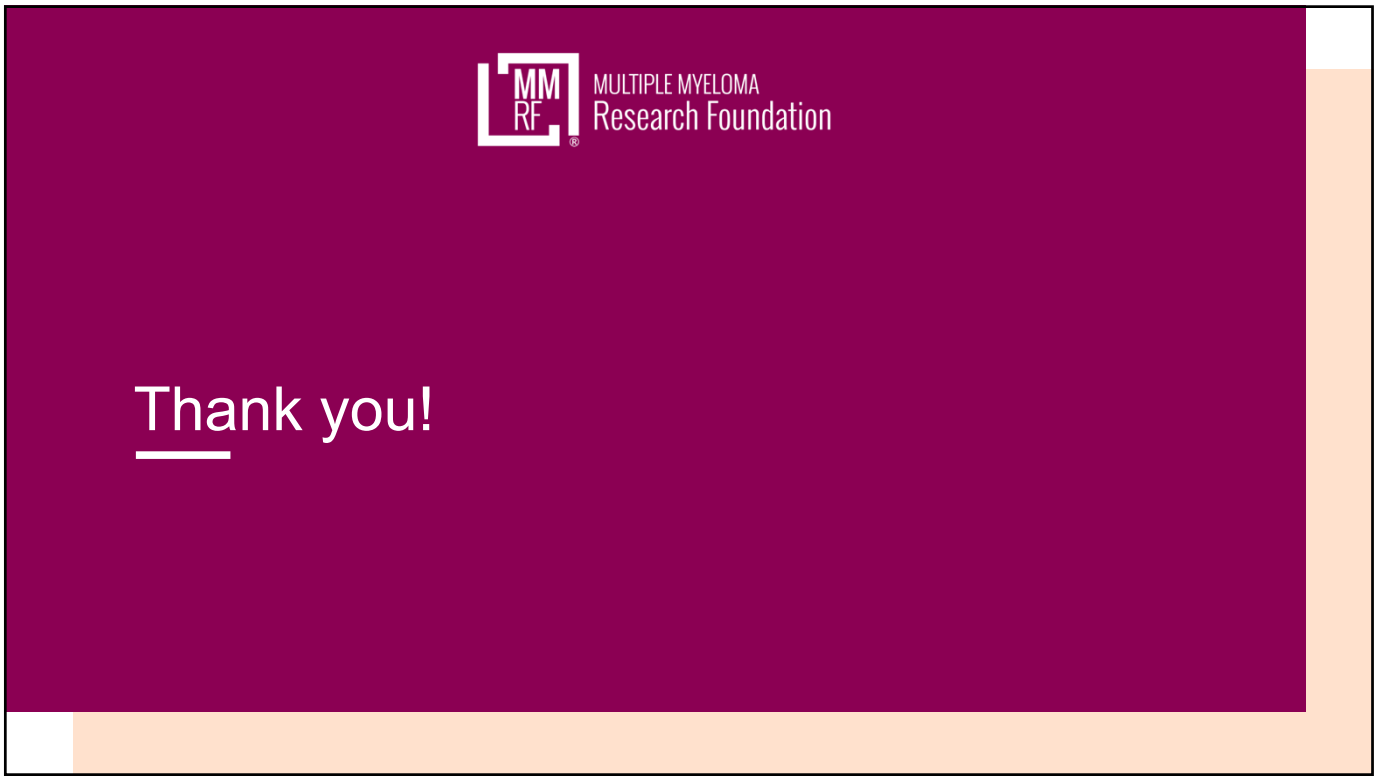

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