MULTIPLE MYELOMA Research Foundation

BCMA-Targeted Bispecific Antibody Therapy

March 21, 2023

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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
  - Exhibit Hall

Submit your questions throughout the program!

MM RF

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MMRF Research Initiatives

MULTIPLE MYELOMA Research Consortium

CoMMpass Study℠

CureCloud®

For more information, visit themmrf.org

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Speakers

Jesus G. Berdeja, MD
Sarah Cannon Research Institute
Nashville, Tennessee

Amrita Y. Krishan, MD
City of Hope Medical Center
Duarte, California

Tonya
Patient

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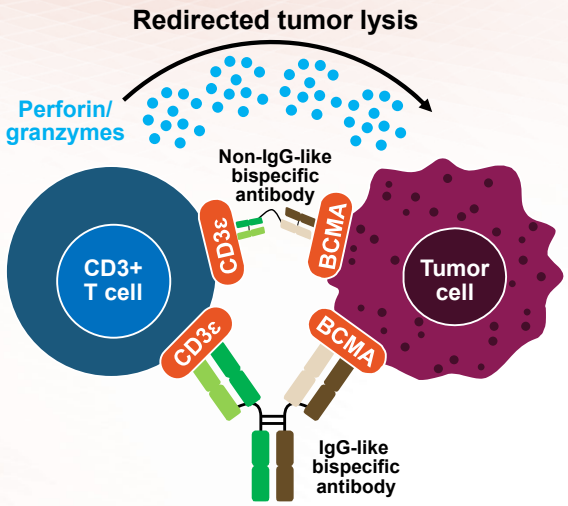
Bispecific Antibodies

- 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; one 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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BCMA-Targeted Bispecific Antibodies

Bispecific antibody	Target (on myeloma cell × T cell)	Status
Tecvayli (teclistamab)	BCMA × CD3	Approved for use in myeloma patients
Elranatamab	BCMA × CD3	Clinical studies; granted priority review by the FDA
Linvoseltamab	BCMA × CD3	Clinical studies
Alnuctamab	BCMA × CD3	Clinical studies
ABBV-383	BCMA × CD3	Clinical studies

BCMA

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

CD3

- A T cell receptor

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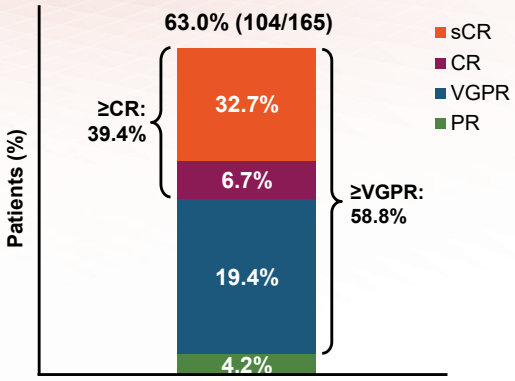
Now Approved: Tecvayli, the First Bispecific Antibody

Drug	Formulation	Approval
Tecvayli (teclistamab)*	Step-up dosing† the first week, then once weekly thereafter by subcutaneous injection	For **relapsed/refractory** myeloma (after 4 or more prior lines of therapy, including an IMiD, a PI, and an anti-CD38 mAb)

IMiD, immunomodulatory agent; PI, proteasome inhibitor; mAb, monoclonal antibody
*Black box warning: cytokine release syndrome; neurologic toxicities
†Patients are hospitalized for 48 hours after administration of all step-up doses.
Tecvayli is available only through a restricted distribution program.

	All patients (n=165)
MRD negative (10^{-5}), %	
All treated	26.7
MRD evaluable	81.5
MRD negativity with ≥CR (%)	46.2

	All patients (n=165)
Median time to first response (mos)	1.2
Median time to best response (mos)	3.8



Median duration of response 18.4 months

MajesTEC-1 Study. Moreau P et al. *N Engl J Med*. 2022;387:495.

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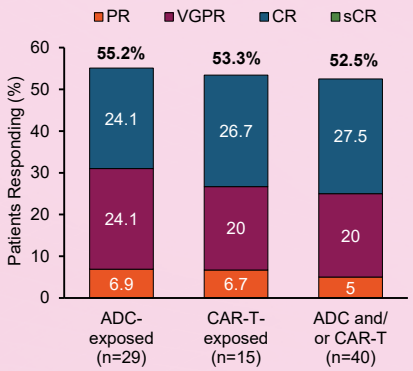
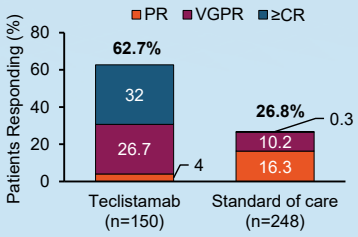
Additional Studies of Tecvayli in Patients With Relapsed/Refractory Myeloma

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



Teclistamab experience vs real world clinical practice (LocoMMotion Study)[2]



	Teclistamab	Standard of Care
Progression-free survival (mos)	10.1	4.3
Overall survival (mos)	18.3	13.0

1. Touzeau C et al. *J Clin Oncol*. 2022;40. Abstract 8013.
2. van de Donk NWCJ et al. *J Clin Oncol*. 2022;40. Abstract 8016.

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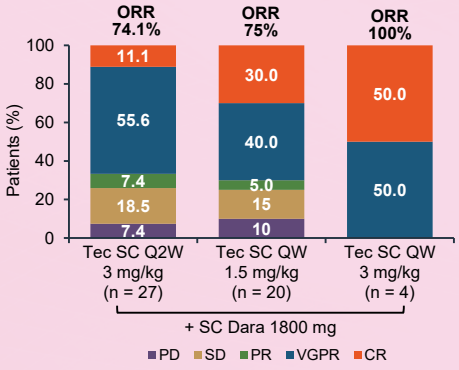
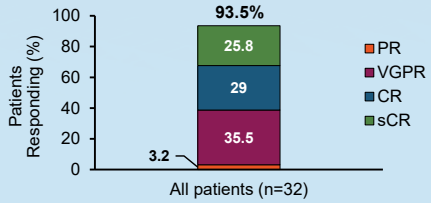
Tecvayli Combinations

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

Clinical Response



Teclistamab + 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

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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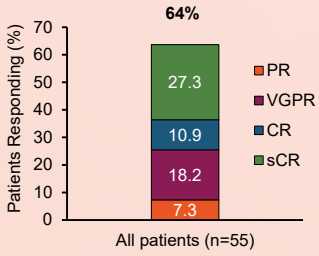
Elranatamab in Patients With Relapsed/Refractory Myeloma

Updated efficacy and safety results with elranatamab (MagnetisMM-1 Study)[1]

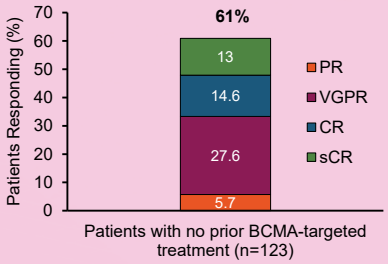
Phase 1 study in RRMM
(91% triple-class refractory)



Median duration of response 17.1 months.

Elranatamab 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



Elranatamab to be investigated alone and in combination with other drugs in phase 3 studies.

The FDA has granted priority review for elranatamab for the treatment of patients with relapsed or refractory multiple myeloma.

IMiD, immunomodulatory drug; PI, proteasome inhibitor
1. Raje N et al. *Blood*. 2022;140. Abstract 158. **2.** Bahlis NJ et al. *Blood*. 2022;140. Abstract 159.

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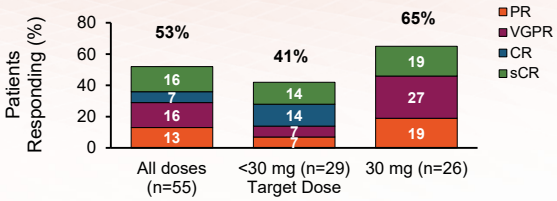
Phase 1 Study of Alnuctamab in Patients With Relapsed/Refractory Myeloma

Intravenous Formulation Results

	IV alnuctamab (n=70)
Median follow-up (months)	8.0
Overall response rate (%)	39
Median duration of response (months)	33.6
Responses ongoing (%)	48
Median PFS (months)	
All patients	3.1
Responders	36.4
Nonresponders	1.7

Subcutaneous Formulation Results



Most frequent adverse events, %	Any grade	Grade 3/4
Hematologic		
Anemia	38	25
Neutropenia	37	32
Thrombocytopenia	24	9
Non-hematologic		
CRS	53	0
Infections	34	9
ICANS	3	0
ALT increase	12	6

Wong SW et al. *Blood*. 2022;140. Abstract 162.

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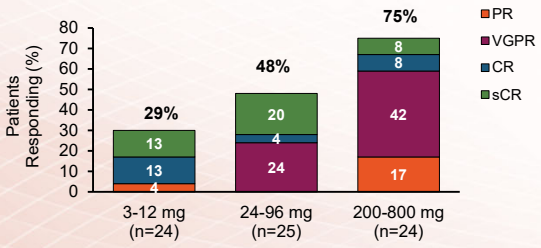
Phase 1/2 Study of Linvoseltamab in RRMM

Patients who were refractory or intolerant to two or more prior lines of systemic therapy, including a PI, IMiD, and anti-CD38 mAb



Most frequent adverse events, %	Any grade	Grade 3/4
Hematologic		
Anemia	32	23
Lymphopenia	23	20
Neutropenia	23	22
Thrombocytopenia	21	13
Non-hematologic		
Fatigue	45	3
CRS	38	0
Pyrexia	36	4
Nausea	33	0
Dyspnea	26	0
Diarrhea	25	3
Back pain	25	5
Vomiting	25	0
Pneumonia	23	11
Chills	22	1

Zonder J et al. IMS 2022 . Abstract OAB-056.

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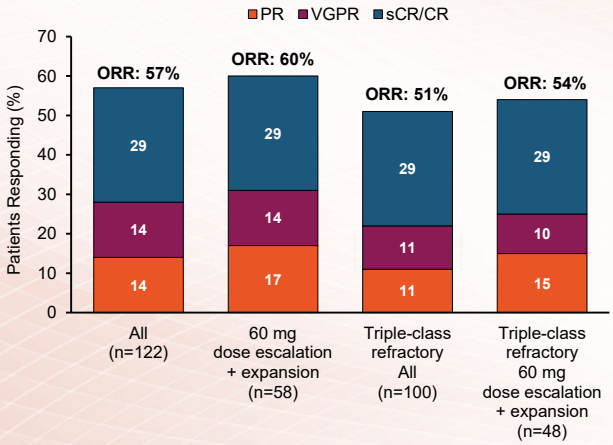
Phase 1 Study of ABBV-383 in RRMM



Cytokine release syndrome, %	60 mg dose escalation + expansion (n=60)	All patients (n=124)
All grades	72	57
Grade 1	48	35
Grade 2	22	19
Grade ≥3	2	2
Serious	27	18

Voorhees P et al. IMS 2022 . Abstract OAB-55.

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Bispecific Antibody Therapy Expected Toxicities

Cytokine release syndrome

Neurotoxicity (ICANS)

Cytopenias

Infections

ICANS, immune effector cell-associated neurotoxicity syndrome

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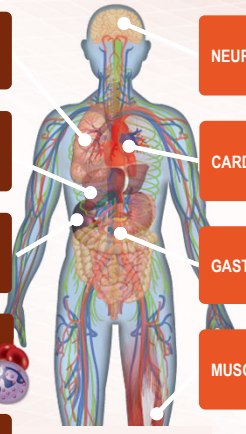
CRS Severity Is Typically Mild: Early Recognition and Treatment Is Key



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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Neurotoxicity With Bispecific Antibodies

Neurotoxicity was observed in 5% to 28% of patients in clinical trials, with most cases being mild.

Symptoms include headache, confusion, difficulty with comprehension (aphasia), cognitive disorder, and encephalopathy.

Many symptoms occur with CRS and typically resolve after CRS treatment.

Lancman G et al. *Blood Cancer Disc*. 2021;2:423.

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BCMA-Targeted Therapies Are Associated With an Increased Risk of Infections

A pooled analysis of 1,185 RRMM patients in 11 different clinical trials treated with single agent bispecific antibodies (with no prior use of different bispecifics)

Majority of patients (72%) treated with BCMA-targeted bispecific antibodies

	Patients (%)	
Adverse event	**All grades**	**Grade 3/4**
Neutropenia	38.6	34.8
Infections	50	24.5
CRS	59.6	NR
Pneumonia	NR	10
COVID-19	NR	11.4

Hypogammaglobulinemia occurred in 75.3% of patients with intravenous immunoglobulin used in 48%.

Death was reported in 110 patients of which 28 (25.5%) were reported to be secondary to infections.

Certain precautions should be used when using BsAbs to mitigate the risk and/or identify and treat infections promptly.

NR, not reported.

Lancman G et al. *Blood Adv.* March 1, 2023 [Online ahead of print].

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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**
- **Consider CMV monitoring**

IVIG. intravenous immunoglobulin; PJP, *Pneumocystis jiroveci* pneumonia; CMV, cytomegalovirus.

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Similarities and Differences Between CAR T-Cell Therapy and Bispecific Antibodies

	CAR T-cell therapy	Bispecific antibody
Approved product	Abecma, Carvykti	Tecvayli
Efficacy	++++	+++
How given	One-and-done	IV or SC, weekly to every 3 weeks until progression
Where given	Academic medical centers	Academic medical centers
Notable adverse events	CRS and neurotoxicity	CRS and neurotoxicity
Cytokine release syndrome	+++	++
Neurotoxicity	++	+
Availability	Wait time for manufacturing	Off-the-shelf, close monitoring for CRS and neurotoxicity

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BCMA Therapeutics: Advantages/Disadvantages

	CAR T cells	Bispecific antibodies
Advantages	Personalized	Off the shelf
	Targeted immunocytotoxicity	Targeted immunocytotoxicity
	Single infusion (one and done)	No lymphodepletion Minimal steroids
	Potentially persistent	
Disadvantages	FACT-accredited center required (hospitalization likely required)	Initial hospitalization required
	CRS and neurotoxicity; requires ICU and neurology services	CRS and neurotoxicity possible
	Dependent on T-cell health (manufacturing failures)	Dependent on T-cell health (T-cell exhaustion)
	Requires significant social support; caregiver required	Requires treatment until disease progression
	$$$$	$$$

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Key Points

- **Bispecific antibodies are very active even in heavily pre-treated patients.**
- **Side effects of bispecific antibodies include cytokine release syndrome, confusion, infection, and low blood counts, all of which are treatable.**
- **Tecvayli is the first BCMA-targeted bispecific antibody approved for use in myeloma patients. Different bispecifics and different targets are on the way.**

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Patient Experience

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Questions & Answers

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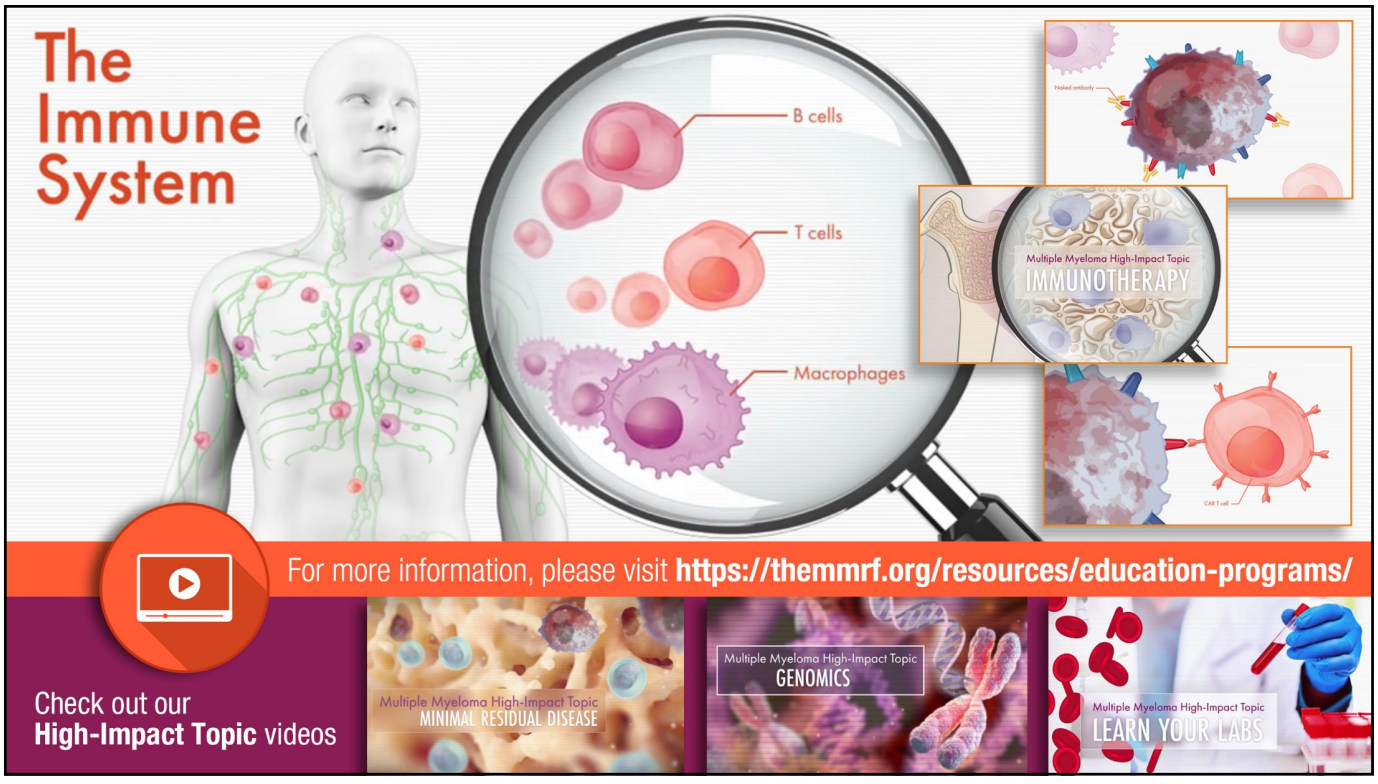

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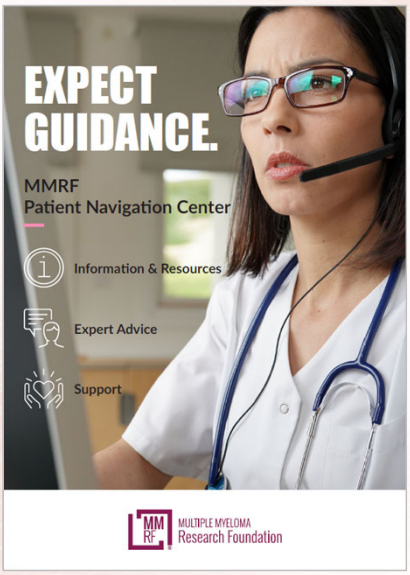
MMRF Patient Resources



MMRF Patient Navigation Center

You and your care team will have many decisions to make along your treatment journey. The Patient Navigation Center is a space for multiple myeloma patients and their caregivers to connect with patient navigators — who are professionals specializing in oncology — for guidance, information, and support. You can connect with a patient navigator via phone, or email. Whatever questions you may have, our patient navigators are here to help.

MMRF Patient Navigators include:
- Grace Allison, RN, BSN, OCN, RN-BC
- Brittany Hartmann, RN-BSN
- Erin Mensching, RN-BSN, OCN

THE RIGHT TRACK

Get on the right track for you

The MMRF's Right Track program puts you on the path to the best results for you.

Right Team
Access experts and centers that have extensive experience treating multiple myeloma.

Right Tests
Get the information, tests, and precise diagnoses to make the right treatment decisions.

Right Treatment
Work with your team to consider the best treatment plan and identify clinical trials that are right for you.

Contact the Patient Navigation Center Today

Looking for guidance? We're here to help.

Monday – Friday | 9:00AM – 7:00PM ET

Phone: 1-888-841-MMRF (6673) Online: TheMMRF.org/PatientNavigationCenter

Email: patientnavigator@themmrf.org

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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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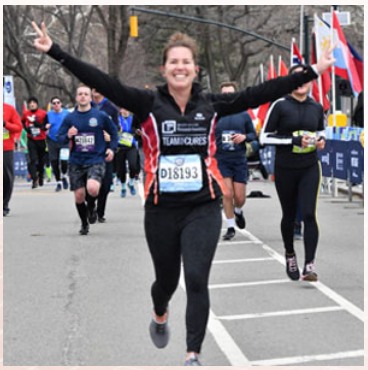
MMRF Events

Our events are returning live and in-person, and there are so many ways to get involved. Most have a virtual option, too. Join us today!

Endurance Events



5K Walk/Run Events

Independent Events

FIND AN EVENT AND JOIN US: themmrf.org/get-involved/mmrf-events/

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Upcoming Patient Education Events

Save the Date

Topic	Date and Time (ET)	Speakers	
Patient Summit Scottsdale, AZ *In collaboration with Arizona Myeloma Network*	Saturday, March 25 9:00 AM to 3:45 PM MT	Leif Bergsagel, MD Clarence Adoo, MD Jonathan Keats, PhD Sumit Madan, MD	Suzanne Hyde, MSW, LCSW Barbara Kavanagh, MSW, LCSW Joan Koerber-Walker William Brown
Facebook Live FAQs	Tuesday, March 28 2:00 to 3:00 PM ET	Brandon Blue, MD Dana Spiak, RN	
Webinar (rebroadcast): *Multiple Myeloma Precursor Conditions*	Wednesday, April 5 2:30 to 3:30 PM ET	Sagar Lonial, MD Omar Nadeem, MD	

For more information or to register, visit themmrf.org/resources/education-program

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