



MULTIPLE MYELOMA  
Research Foundation

# MULTIPLE MYELOMA IMMUNOTHERAPY

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## ABOUT THE **MMRF**

The Multiple Myeloma Research Foundation® (MMRF®) is the largest nonprofit in the world solely focused on accelerating a cure for each and every multiple myeloma patient. We drive the development and delivery of next-generation therapies, leverage data to identify optimal and more personalized treatment approaches, and empower myeloma patients and the broader community with information and resources to extend their lives.

Central to our mission is our commitment to advancing access for all so that every myeloma patient can benefit from the scientific and clinical advances we pursue. Since our inception, the MMRF has raised over \$600 million for research, opened over 100 clinical trials, and helped bring more than 15 FDA-approved therapies to market, which have tripled the life expectancy of myeloma patients.

To learn more about the MMRF, visit [themmrf.org](https://themmrf.org).

To speak to a patient navigator at the Patient Navigation Center, call **1-888-841-6673** or email [patientnavigator@themmrf.org](mailto:patientnavigator@themmrf.org).

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# INTRODUCTION

**Multiple myeloma** is a cancer of the blood cells (specifically, **plasma cells**, which produce **antibodies** to fight infections). Blood cells are formed in the **bone marrow**, the soft, spongy tissue located inside your bones. **Malignant** plasma cells (that is, myeloma cells) grow and crowd out the normal blood cells in the bone marrow.

The use of one's own **immune system** to fight cancer is a new approach to myeloma treatment. This is called cancer **immunotherapy**.

There are many types of immunotherapy that can rev up or improve your **immune response**, including:

- **Immunomodulatory drugs**
- Antibody-based treatments
- Cell-based treatments, such as those that use your own immune cells or those from a donor

This booklet is designed to help you better understand the concept and the promise of immunotherapy. Words that may be unfamiliar are **bolded** and defined in the Glossary (page 9).

The information in this booklet is not intended to replace the services or advice of trained health care professionals. Please consult with your care provider regarding specific questions relating to your health, especially questions about myeloma diagnosis or treatment.

# THE IMMUNE SYSTEM

If your immune system is ready to attack and kill foreign invaders, why do cancers still grow and survive?

Some of the reasons why the immune system is ineffective against myeloma are that myeloma cells:

- Arise from normal plasma cells and therefore may not look like invaders
- Fool the immune system by disguising themselves in a way that lets them go unnoticed by immune cells
- Resist the immune system by producing substances that inactivate (that is, turn off) immune cells

Immunotherapy is a treatment approach that is designed to overcome these tactics used by myeloma cells.

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For more information about multiple myeloma and its treatment, refer to the other booklets in our Patient Toolkit, as well as the MMRF website, [themmr.org](http://themmr.org).

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## TYPES OF IMMUNOTHERAPY

Immunotherapy works differently than other types of myeloma treatment, such as **chemotherapy**. Where chemotherapy targets both cancer cells and healthy cells, immunotherapy selectively targets myeloma cells.

For an overview of immunotherapy, see the *Immunotherapy High-Impact Topic* video.

[bit.ly/Immunotherapy\\_HIT](http://bit.ly/Immunotherapy_HIT)



In immunotherapy, immune cells are programmed to recognize and remember myeloma cells. These programmed immune cells remain in the body, providing a long-term response and helping to hold off a myeloma **relapse**.

There are three main types of immunotherapy currently being used or studied in patients with multiple myeloma.

## Types of immunotherapy.

Immunomodulatory  
drugs

Antibody-based  
therapy

CAR T-cell therapy

### IMMUNOMODULATORY DRUGS

Immunomodulatory drugs (IMiDs) are oral drugs that work against myeloma cells partly by boosting a patient's immune system. IMiDs currently used to treat myeloma include Revlimid (lenalidomide) and Pomalyst (pomalidomide). IMiDs are used for both newly diagnosed myeloma (including **induction therapy** and **maintenance therapy**) and relapsed or **refractory** myeloma.

Cereblon E3 ligase modulators (CELMoDs) are similar to IMiDs, though they tend to be stronger and more effective in clearing myeloma cells. Iberdomide and mezigdomide are CELMoDs that are being studied in clinical trials as myeloma treatments and may soon be broadly available if the trials are successful.

As with all treatments, IMiDs have side effects that may require management. It's important to communicate with your care team about any side effects you experience, so they can determine the best way to address them.

#### Potential side effects of IMiDs and their management.

Side effect	Management
Fatigue and weakness	Sleep hygiene; regular exercise; dose adjustment, if needed; adjusting the time of day the dose is taken
Blood clots	Blood thinners, aspirin
Diarrhea	Imodium, cholestyramine
Constipation	Stool softeners, laxatives, fiber, increased fluid intake
Muscle cramping and back pain	Tonic water/hydration
Rash	Topical treatments and/or dose adjustment
Shortness of breath	Rule out blood clot; dose adjustment
Upper respiratory Infections	Antibiotics, antivirals, and/or <b>supportive care</b>

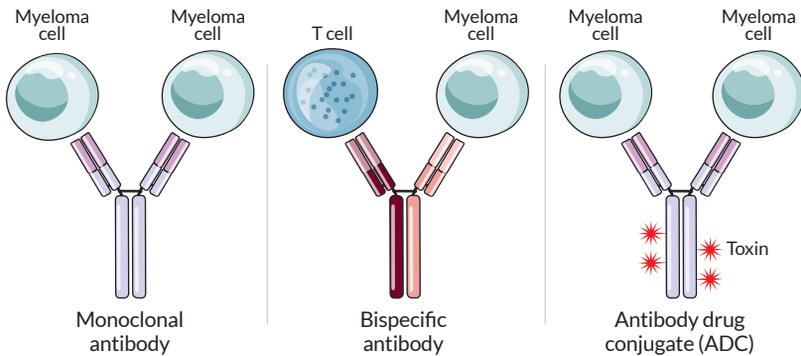
## ANTIBODY-BASED THERAPIES

Antibodies are unique, Y-shaped proteins designed to target and destroy anything foreign to the body.

Antibody-based therapies use antibodies that are designed to target certain proteins found on the surface of myeloma cells. In targeting myeloma cells, antibodies act like locks that fit a specific key—and the targeted proteins on the myeloma cell are those keys.

Once the antibody finds its target, the myeloma cell is destroyed based on the type of antibody therapy used.

### The different types of antibody-based therapies.



### Monoclonal Antibodies

**Monoclonal antibodies** attach to one specific protein on myeloma cells, for example CD38 or SLAMF7. Darzalex (daratumumab), Sarclisa (isatuximab), and Emluciti (elotuzumab) are the monoclonal antibodies currently approved by the FDA to treat multiple myeloma.

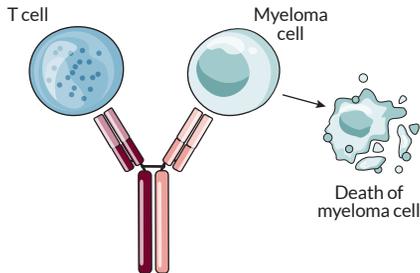
**Potential side effects of monoclonal antibodies used in myeloma and their management.**

Side effect	Management
Infusion reaction	Supportive care
Fatigue	Sleep hygiene, regular exercise, dose adjustment
Upper respiratory infection	Antibiotics, antivirals, and/or supportive care

## Bispecific Antibodies

**Bispecific antibodies** are another type of antibody used in antibody-based therapy. They are made by combining parts of two regular antibodies. One part attaches to and “tags” myeloma cells (making them easier for your immune system to find). The other attaches to your immune cells—specifically, **T cells**—and helps them find and fight the tagged myeloma cells.

### Bispecific antibody.



BCMA and GPRC5D are proteins found on the surface of myeloma cells that are targeted by bispecific antibodies.

For an overview of bispecific antibody therapy, see the ***Bispecific Antibodies High-Impact Topic*** video.

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Tecvayli (teclistamab), Elrexfio (elranatamab), and Lynozyfic (linvoseltamab) are BCMA-directed bispecific antibodies that are FDA-approved for patients with relapsed or refractory myeloma. Several other bispecific antibodies that target BCMA are being studied.

Talvey (talquetamab) is a bispecific antibody that targets GPRC5D. It's FDA-approved for patients with relapsed or refractory myeloma.

To minimize side effects, bispecific antibodies are typically given in doses that start small and gradually ramp up to a full dose. This is referred to as **step-up dosing**. You may need to be hospitalized for several days after you receive these step-up doses, and for the first full treatment dose, so that your care team can monitor for side effects.

**Potential side effects of bispecific antibodies and their management.**

Treatment	Side effect	Management
Tecvayli, Elrexmio, Lynozytic, Talvey	<b>Cytokine release syndrome (CRS):</b> symptoms include fever, chills, dizziness, nausea, headache, rapid heartbeat, and low blood pressure	Step-up dosing and monitoring, tocilizumab*, steroids
	<b>Immune effector cell-associated neurotoxicity syndrome (ICANS):</b> symptoms include headache, confusion, language disturbance, seizures, delirium, and brain swelling	Anakinra*, antiseizure medication, steroids
	Infection	Monitor for signs of infection, medications to prevent infection, good hygiene, vaccines, <b>intravenous immunoglobulin (IVIG)<sup>†</sup></b>
Talvey	<b>Dysgeusia</b> (altered taste)	Maintain oral hygiene; enhance flavor of food (for example, with oils, herbs, and spices); stay hydrated
	Nail and skin effects like blistered or peeling skin	Apply thick, fragrance-free moisturizers; use topical steroids for rash or itchiness
	<b>Cerebellar toxicity:</b> symptoms include dizziness, <b>ataxia</b> (loss of coordination), slurred speech, and trouble with balance while walking	Step-up dosing and monitoring, dose modification, steroids

\*Tocilizumab and Anakinra are drugs used to treat inflammatory and autoimmune conditions.

<sup>†</sup>IVIG is a treatment used to boost the immune system, treat autoimmune disorders, and prevent infections in patients with weakened immunity.

**Antibody-Drug Conjugates**

Another type of antibody-based treatment uses a monoclonal antibody that is linked to a cancer drug or a **toxin**; this type of agent is called an **antibody–drug conjugate** or **ADC**. The antibody part binds to a myeloma cell—just as monoclonal antibodies do—and the attached drug kills the myeloma cell.

Blenrep (belantamab mafodotin) is an ADC that is FDA-approved for use in patients with relapsed or refractory myeloma. Blenrep targets BCMA on myeloma cells and delivers a toxin to destroy the myeloma cells.

Blenrep is given as an intravenous infusion that can be administered at a doctor’s office or a cancer center, making it more easily available than myeloma treatments that must be administered at specialized centers (for example,

CAR T-cell or bispecific antibody therapy) or require hospitalization to manage side effects like CRS or ICANS.

**Potential side effects of Blenrep and their management.**

Side effect	Management
Diarrhea	Imodium*
Eye-related problems (blurred vision, dry eyes)	Preservative-free eye drops, treatment breaks, close monitoring, dose adjustments
Fatigue	Sleep hygiene, regular exercise
Upper respiratory infection	Antibiotics, antivirals, and/or supportive care

\*Imodium is a drug used to control diarrhea symptoms.

**CAR T-CELL THERAPY**

**Chimeric antigen receptor (CAR) T-cell therapy** is a customized immunotherapy that involves collecting your own T cells, engineering them in a lab so they're better able to identify and attack myeloma cells, and then returning them back to your body.

In **clinical trials**, CAR T-cell therapies produced high response rates; that is, most patients responded to the treatment. CAR T-cell therapy is available for patients who have relapsed from prior therapies.

CAR T-cell therapy is administered as a one-time infusion and does not require additional treatments.

For an overview of CAR T-cell therapy, see the **CAR T-Cell Therapy High-Impact Topic** video. [bit.ly/CART-CellTherapy\\_HIT](https://bit.ly/CART-CellTherapy_HIT)



Abecma (idecabtagene vicleucel) is FDA-approved for patients with relapsed or refractory myeloma who have received at least two prior treatments.

Carvykti (ciltacabtagene autoleucel) is FDA-approved for patients with relapsed or refractory myeloma who have received at least one prior treatment.

Both Abecma and Carvykti target BCMA.

During CAR T-cell therapy, you'll be monitored closely at the treatment facility for at least 7 days after infusion for any serious side effects.

## Potential side effects of CAR T-cell therapy and their management.

Side effect	Management
CRS	Monitored while hospitalized, tocilizumab, steroids
ICANS	Anakinra and/or steroids
Infection	Monitor for signs of infection, medications to prevent infection, good hygiene, vaccines, IVIG

In rare cases, longer-term side effects of CAR T-cell therapy can include neurological problems like **parkinsonism** (which involves slow movements, tremors, or stiffness), development of new cancers (such as certain blood cancers or **lymphomas**), and **enterocolitis** (inflammation of the gut that may cause ongoing diarrhea and abdominal pain). Most patients never experience these side effects. Researchers are studying why these side effects occur and who may be at risk.

Currently, CAR T-cell therapy is limited to patients whose myeloma returns after treatment or does not respond to one or more prior treatments. Eligibility for CAR T-cell therapy depends on **comorbidities**, risk factors, and your ability to perform certain daily activities without help (**performance status**).

CAR T-cell therapy is a specialized treatment that's only available at cancer centers that have experts in this therapy on staff. However, it's possible to be treated at a cancer center and still be followed by your own doctor for routine care and to manage your health during and after CAR T-cell therapy.

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**Immunotherapy is an exciting and fast-developing area of myeloma management. However, not all immunotherapies are appropriate for all myeloma patients. Talk with your care team about your disease and what options are best for you.**

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The MMRF would like to thank Joshua Richter, MD, Associate Professor of Medicine, Hematology and Oncology, in the Myeloma Division at the Tisch Cancer Institute at the Icahn School of Medicine at Mount Sinai and Director of Myeloma at the Blavatnik Family Chelsea Medical Center at Mount Sinai, and our patient advocate, Kerri Hoffman of Carlsbad, California, for their contributions to this booklet.

## GLOSSARY

**adaptive immunity** Part of the immune system that is made up of specialized cells that recognize and attack foreign invaders

**antibodies** Proteins produced by plasma cells that help protect the body from infection and disease (also called immunoglobulins; see also *monoclonal antibodies*)

**antibody-drug conjugate (ADC)** Monoclonal antibody that is coupled to a cancer drug; an example is Blenrep

**ataxia** Condition that causes poor muscle coordination and balance that leads to slurred speech, unsteady movements (like wobbling when walking), and trouble with fine tasks (like buttoning clothes)

**bispecific antibodies** Monoclonal antibodies that can bind to two different proteins at the same time

**bone marrow** Soft, spongy tissue found in the center of many bones and the site of blood cell production

**cerebellar toxicity** Damage to the part of the brain that controls balance and coordination, which can cause unsteady walking, poor coordination, or slurred speech

**chemotherapy** Use of drugs to kill rapidly dividing cells, such as cancer cells

**chimeric antigen receptor T (CAR T)-cell therapy** A form of immunotherapy in which a patient's immune cells (mostly T cells) are collected, engineered in a lab to be better able to identify and attack myeloma cells, and then returned to the patient; examples are Abecma and Carvykti

**clinical trials** Studies of the safety and effectiveness of a drug using consenting human participants

**comorbidities** Diseases that are present at the same time as another disease

**cytokine** Protein produced and secreted by cells of the immune system (for example, interleukins)

**cytokine release syndrome (CRS)** Flu-like reaction that can develop as a result of treatment; it may cause fevers, chills, and low blood pressure

**dysgeusia** Condition that causes foods to taste metallic, foul, rancid, or salty

**enterocolitis** Inflammation of the small and large intestines that causes belly pain, diarrhea, fever, and nausea

**immune effector cell–associated neurotoxicity syndrome (ICANS)** Side effect of the nervous system seen after certain immunotherapies (such as CAR T-cell therapy and bispecific antibody therapy) that can include confusion or delirium, speech problems (expressive aphasia), motor weakness, tremor, headache, seizures, and reduced level of consciousness

**immune response** Reaction of the cells and fluids of the body against a substance or agent (for example, bacteria, a virus, or a foreign cell) that is not recognized as part of the body

**immune system** Network of cells that protect the body from foreign substances and destroy infected and cancerous cells

**immunomodulatory drugs** Drugs that fight cancer by boosting the immune system; examples include Thalomid, Revlimid, and Pomalyst

**immunotherapy** Prevention or treatment of disease with drugs that stimulate the immune system

**induction therapy** The first treatment a patient receives for myeloma after he or she is diagnosed; also refers to the use of anti-myeloma drugs prior to high-dose chemotherapy and stem cell transplant

**intravenous immunoglobulin (IVIG)** Pooled antibodies used to treat immunodeficiencies and other conditions

**lymphomas** Blood cancers that develop in the lymph nodes

**maintenance therapy** Treatment given over a long period of time to patients in remission to reduce the risk of relapse

**malignant** Cancerous; able to grow and spread to other parts of the body

**monoclonal antibodies** Antibodies produced in a lab that are used to diagnose and treat some diseases

**multiple myeloma** Blood cancer that develops in the bone marrow as a result of plasma cells transforming into myeloma cells

**parkinsonism** Any of a group of conditions that produce movement-related symptoms similar to those associated with Parkinson's disease (tremors, stiff muscles, slow movements, and trouble with balance) but have different causes

**performance status** Score that estimates a patient's ability to perform certain daily activities without help

**plasma cells** Antibody-secreting immune cells that develop from B cells; in myeloma, it is these cells that have become cancerous or abnormal

**refractory** Not responding to therapy

**relapse** Progression of a disease that has initially responded to therapy

**step-up dosing** Method of giving a drug in doses that start small and gradually increase to a full dose to minimize side effects

**supportive care** Treatment that addresses the symptoms and complications of a disease rather than the disease itself

**T cells** Type of *white blood cell* that can be divided into two subgroups, helper and cytotoxic T cells; helper T cells are responsible for *adaptive immunity*; cytotoxic T cells kill cells that have been targeted for death

**toxin** A poisonous substance

**white blood cell** One of the major cell types in the blood; attacks infection and cancer cells as part of the immune system

## NOTES



# MMRF PATIENT SUPPORT AND RESOURCES

The MMRF supports the myeloma community by providing a broad range of resources for myeloma patients and their family members and caregivers. The MMRF is available to help guide you through your multiple myeloma journey every step of the way.



## YOUR QUESTIONS ANSWERED

The Patient Navigation Center is available to answer your questions about disease management and treatments, help you find clinical trials, and connect you with financial and other resources.

Telephone: 1-888-841-6673

Monday—Friday, 9:00 AM to 7:00 PM ET

Email: [patientnavigator@themmrf.org](mailto:patientnavigator@themmrf.org)

[themmrf.org/support/patient-navigation-center](https://themmrf.org/support/patient-navigation-center)

## CONNECT WITH AN MMRF MYELOMA MENTOR

Connect one-on-one with a trained patient and/or caregiver mentor that can share their patient journeys and experiences.

[themmrf.org/support/myeloma-mentors](https://themmrf.org/support/myeloma-mentors)



## FIND A CLINICAL TRIAL

The MMRF Clinical Trial Finder lets you search for a clinical trial in your area.

[themmrf.org/diagnosis-and-treatment/clinical-trials-and-emerging-therapies/clinical-trial-finder/](https://themmrf.org/diagnosis-and-treatment/clinical-trials-and-emerging-therapies/clinical-trial-finder/)

## VIEW PAST PROGRAMS ON DEMAND

Access our archive of recorded Patient Summits and webcasts. Hear expert perspectives on key clinical research and the rapidly evolving myeloma treatment landscape. All available online, and free.

[themmrf.org/educational-resources](https://themmrf.org/educational-resources)



## SUPPORT THE MMRF

Help support the MMRF's efforts to accelerate research and find a cure! Participate in an event or donate today.

Telephone: 1-203-229-0464

Donate now/Take action: [themmrf.org/get-involved](https://themmrf.org/get-involved)

## ATTEND A MULTIPLE MYELOMA PATIENT SUMMIT

Available in-person and virtually, MMRF Patient Summits discuss new treatments, promising clinical trials, and all the information you need to make well-informed decisions about your treatment and care.

[themmrf.org/educational-resources](https://themmrf.org/educational-resources)



# Don't miss out on the latest myeloma updates! Sign up today to receive news updates and notice of educational programs.

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## Or sign up at [themmrf.org](http://themmrf.org)

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- Myeloma Patient Family Member (non-caregiver)
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- Healthcare Professional or Researcher
- Biopharma, Medical Device, or Healthcare Technology Industry Professional
- None of the Above

*\*Please tear off reply card and tape all three sides before mailing.*

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