



MULTIPLE MYELOMA
Research Foundation

MULTIPLE MYELOMA IMMUNOTHERAPY

themmrf.org





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 health equity so that all myeloma patients can benefit from the scientific and clinical advances we pursue. Since our inception, the MMRF has raised over \$600 million for research, opened nearly 100 clinical trials, and helped bring 15+ FDA-approved therapies to market, which have tripled the life expectancy of myeloma patients.

To learn more about the MMRF, visit themmrf.org.

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



INTRODUCTION

Multiple myeloma is a cancer of the blood cells (specifically, **white blood cells**, one of several types of blood cell). Blood cells are formed in the **bone marrow**, the soft, spongy tissue located inside your bones. Myeloma cells grow and crowd out the normal blood cells in the bone marrow, which results in a reduction in the number of normal white blood cells. Having a reduced number of white blood cells makes infections harder to fight off.

The use of one's own **immune system** to fight cancer is a new approach to the treatment of multiple myeloma. This is called cancer **immunotherapy**. For myeloma immunotherapy treatments to work, they must be designed to recognize myeloma cells. This has long been a challenge, because myeloma cells have the ability to hide from the body's normal **immune response**. Myeloma cells also have the ability to weaken the body's immune response to such an extent that they can continue to grow and thrive. Restoring the immune protection lost to myeloma is believed to be an important potential pathway to new levels of treatment success.

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 health care provider regarding specific questions relating to your health, especially questions about myeloma diagnosis or treatment.

THE IMMUNE SYSTEM

If your immune system is primed and ready to attack and kill foreign invaders, why do cancers still grow and survive? There are a number of reasons why the immune system is ineffective against myeloma.

- Myeloma cells arise from normal **plasma cells** and therefore may not look like invaders.
- Myeloma cells can fool the immune system by disguising themselves in a way that lets them go unnoticed by immune cells.
- Myeloma cells can actively resist the immune system because they're able to produce substances that inactivate (that is, turn off) existing immune cells.

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

For more information about multiple myeloma and its treatment, refer to the other booklets in our Patient Toolkit, as well as the MMRF website, themmrf.org.

TYPES OF IMMUNOTHERAPY

The excitement that immunotherapy brings to the myeloma community is its unique approach to treatment. Immunotherapy works differently than other types of myeloma therapies, such as **chemotherapy**. Immunotherapy helps the immune system selectively target myeloma cells. In contrast, chemotherapy targets both cancer cells and healthy cells. Activated immune cells that are programmed to recognize and remember myeloma cells circulate throughout the body, inducing a long-term response to therapy 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

Immunomodulatory drugs (IMiDs) are 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 throughout myeloma treatment 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, but they interact with the immune system differently. Several CELMoDs are being studied as myeloma treatments and may soon be available.

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

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 supportive care

ANTIBODY-BASED THERAPY

Antibody-based therapy uses **monoclonal antibodies**, which are proteins engineered in a laboratory to bind to a specific protein found on the surface of a myeloma cell. In antibody therapy, monoclonal antibodies are injected or infused into the body to attack myeloma cells. The different types of antibody-based therapies used include:

1. Naked antibodies
2. Bispecific antibodies

When used on their own as a therapy, monoclonal antibodies are referred to as **naked antibodies**. Darzalex (daratumumab), Sarclisa (isatuximab), and Empliciti (elotuzumab) are naked antibodies that are currently approved to treat multiple myeloma.

Side effects of Darzalex, Sarclisa, and Empliciti 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

Other antibody-based therapies being used to treat myeloma are **bispecific antibodies**. Made from portions of two different monoclonal antibodies that have been combined, bispecific antibodies are able to recognize two different targets.

B-cell maturation antigen (BCMA) and G protein-coupled receptor class C group 5 member D (GPRC5D) are proteins found on the surface of myeloma cells that are targeted by bispecific antibodies.

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

Side effects of BCMA-directed bispecific antibodies and their management.

Side effect	Management
Cytokine release syndrome (CRS) Symptoms include fever, chills, dizziness, nausea, headache, rapid heartbeat, and low blood pressure	Step-up dosing and monitoring, tocilizumab, steroids
Immune effector cell-associated neurotoxicity syndrome (ICANS) 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, intravenous immunoglobulin (IVIG)

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

Side effects of GPRC5D-directed bispecific antibodies and their management.

Side effect	Management
Cytokine release syndrome (CRS) Symptoms include fever, chills, dizziness, nausea, headache, rapid heartbeat, and low blood pressure	Step-up dosing and monitoring, tocilizumab, steroids
Immune effector cell-associated neurotoxicity syndrome (ICANS) 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, intravenous immunoglobulin (IVIG)
Dysgeusia (altered taste)	Supportive care
Nail and skin effects like blistered or peeling skin	Supportive care

You may need to be hospitalized for several days after you receive the first few doses of treatment so that your care team can monitor for these side effects.

CAR T-CELL THERAPY

Immune cell therapy is also known as *cell-based therapy*, *cellular therapy*, or *adoptive cell therapy*. One form of cellular therapy, called **chimeric antigen receptor (CAR) T-cell therapy**, is a customized immunotherapy that is made by 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 to you. In **clinical trials**, BCMA-modified 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.

Abecma (idecabtagene vicleucel) is approved for patients with relapsed or refractory multiple myeloma who have received at least two prior treatments; Carvykti (ciltacabtagene autoleucel) is approved for patients with relapsed or refractory myeloma who have received at least one prior treatment. Both Abecma and Carvykti target the BCMA protein found on the surface of most myeloma cells.

Side effects of CAR T-cell therapy and their management.

Side effect	Management
Cytokine release syndrome (CRS) Symptoms include fever, chills, dizziness, nausea, headache, rapid heartbeat, and low blood pressure	Monitored while hospitalized, tocilizumab, steroids
Immune effector cell-associated neurotoxicity syndrome (ICANS) Symptoms include headache, confusion, language disturbance, seizures, delirium, and brain swelling	Anakinra and/or steroids
Infection	Monitor for signs of infection, medications to prevent infection, good hygiene, vaccines, IVIG

You'll be monitored closely at the treatment facility for 10–14 days after infusion for these serious side effects.

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 is only available at cancer centers that have experts in this therapy on staff. Because this treatment is in high demand, you may need to get on a waiting list before you can begin this therapy, though this is becoming less of an issue.

Immunotherapy as a treatment option is an exciting and fast-developing area of myeloma management. However, some immunotherapies are not approved for use in myeloma patients. Not all experimental immunotherapies are appropriate for all myeloma patients. Talk with your health care team about your disease and what options are best for you.

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, Derrick Blakely of Evanston, Illinois, for their contributions to this booklet.

MMRF PATIENT SUPPORT AND RESOURCES

The MMRF is dedicated to supporting 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

Speak to an MMRF patient navigator at the Patient Navigation Center for answers to your questions about disease management, treatments, clinical trials, and assistance with finding financial and other available resources.

Telephone: 1-888-841-6673

Monday–Friday, 9:00 AM to 7:00 PM ET

Email: patientnavigator@themmrf.org

Online: themmrf.org/support/patient-navigation-center

Connect with an MMRF Myeloma Mentor:

themmrf.org/resources/myeloma-mentors

This is a phone-based program offering the opportunity for patients and/or caregivers to connect one-on-one with a trained patient and/or caregiver mentor to share their patient journeys and experiences.

FIND AND PARTICIPATE IN A CLINICAL TRIAL

Search for a clinical trial in your area or let an MMRF patient navigator help guide you through the process.

Clinical Trial Finder: themmrf.org/resources/clinical-trial-finder

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: Visit themmrf.org/get-involved

GLOSSARY

adaptive immunity Part of the immune system composed of highly specialized cells designed to recognize foreign invaders and attack them any time they enter the body

antibody Protein produced by plasma cells that helps protect the body from infection and disease (also called immunoglobulin; see also *monoclonal antibody*)

bispecific antibody Monoclonal antibody that can simultaneously bind to two different cell surface proteins

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

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 trial Study of the safety and effectiveness of a therapeutic agent using consenting human subjects

comorbidity Disease that is 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) Common, flu-like side effect following treatment with bispecific antibodies or infusion of CAR T cells in which a patient experiences fevers, chills, and low blood pressure

dysgeusia Condition that distorts the sense of taste, causing foods to taste metallic, foul, rancid, or salty

frontline therapy Initial treatment given to a newly diagnosed patient (also known as *induction therapy*, *first-line therapy*, or *frontline treatment*)

immune effector cell–associated neurotoxicity syndrome (ICANS) Common side effect of the nervous system observed 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 altering the function of 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 (see also *frontline therapy*)

intravenous immunoglobulin (IVIG) Biologic agent consisting of pooled antibodies used to treat immunodeficiencies and other conditions

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

monoclonal antibody Antibody produced in a laboratory that is 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

naked antibody Monoclonal antibody that can bind to a cell surface protein and that has no drug or *toxin* attached

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

plasma cell Antibody-secreting immune cell that develops from a B cell; in myeloma, it is this type of cell that has become cancerous or abnormal

refractory Progression of a disease during therapy

relapse Progression of a disease that has initially responded to therapy

step-up dosing Method of giving a drug treatment 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 cell 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 are killers of 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 RESOURCES IN PERSON OR ONLINE



Attend a Multiple Myeloma Patient Summit

Learn about standard and emerging therapies, including stem cell transplants, promising clinical trials, and more for optimal disease management. Attend a complimentary symposium for all the information you need to make well-informed decisions about your treatment and care.

To register or to view the complete calendar, visit:
themmrf.org/resources/education-programs



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, at:
themmrf.org/resources/education-programs



Find a Clinical Trial Near You

Clinical trials are critically important to developing new myeloma treatments and better understanding the biology of the disease. The more people who enroll, the faster we can find answers. Patients who enroll in clinical trials have the opportunity to be among the first to receive the newest drugs or drug combinations in development and receive close monitoring.

To find a clinical trial near you, visit:
themmrf.org/resources/clinical-trial-finder

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

Name: _____

Address: _____

City: _____ State: _____ ZIP: _____

Telephone: _____ Mobile: _____

Email: _____

Or sign up at themmrf.org

I AM A:

- Myeloma Patient
- Myeloma Patient Caregiver
- Myeloma Patient Family Member (non-caregiver)
- Health Care Professional or Researcher
- Biopharma, Medical Device, or Health Care Technology Industry Professional

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