



MULTIPLE MYELOMA
Research Foundation

MULTIPLE MYELOMA TREATMENT OVERVIEW

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 committed over \$500 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.



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INTRODUCTION

Patients with **multiple myeloma** have more options than ever before. Over the last two decades, several new drugs have been approved by the US Food and Drug Administration (FDA) for the treatment of myeloma, and many other therapies are under investigation.

This booklet is designed to help you better understand the current treatment options for multiple myeloma, as well as the emerging treatment options that are being tested in clinical trials. Words that may be unfamiliar are **bolded** and defined in the Glossary (page 35).

The information in this booklet is not intended to replace the services or advice of trained health professionals. Consult with your health care professional or contact the MMRF Patient Navigation Center (1-888-841-6673) if you have specific questions relating to your health, especially questions about myeloma diagnosis or treatment.

For more information about how myeloma develops, as well as its symptoms, diagnosis, and **prognosis**, refer to the companion booklet *Multiple Myeloma Disease Overview* and the MMRF website, themmrf.org.

WHO GETS TREATED?

Generally, you will not receive treatment for myeloma until you develop symptoms.

There are two myeloma **precursor conditions**, **monoclonal gammopathy of undetermined significance (MGUS)** and **smoldering multiple myeloma (SMM)**, in which **monoclonal (M) protein** is detectable in your blood and **clonal plasma cells** are present in your **bone marrow** but usually cause no symptoms or organ damage.

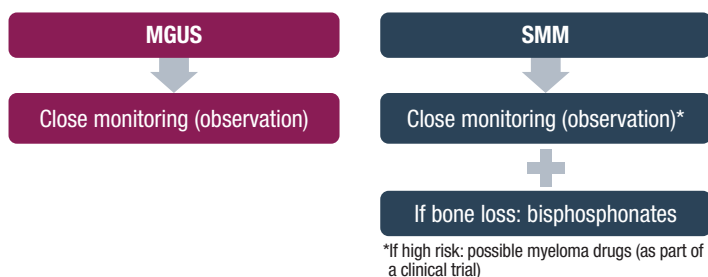
For more information on precursor conditions, refer to the companion booklet *Multiple Myeloma Precursor Conditions* and the MMRF website, www.themmr.org.

If you have MGUS or SMM, typical follow up (in the absence of disease progression) with your doctor will look as follows:

- MGUS: 6 months following diagnosis, then every 1 to 3 years depending on risk
- SMM: 2 to 3 months following diagnosis, then every 4 to 6 months for 1 year, then every 6 to 12 months

If you have both SMM and bone loss (**osteoporosis** or **osteopenia**), you will receive **bisphosphonates** to reduce your risk of fractures and other bone problems.

Treatment approach to myeloma precursor conditions.



Clinical trials are currently studying whether patients with high-risk SMM—that is, those who are at greater risk of rapidly progressing to **active multiple myeloma**—do better when they receive earlier treatment and also what type of treatment is best. A **phase 3** clinical trial has shown that treatment with Revlimid delayed progression to active multiple myeloma in patients with high-risk SMM. However, information on the benefits and risks—such as side effects or the possibility that receiving Revlimid for high-risk SMM will reduce its effectiveness in the future—of this approach is not yet complete, so this therapy is still considered experimental.

Researchers are also investigating ways to delay, and ultimately, prevent active multiple myeloma from developing in patients who have SMM. In particular, studies designed to identify these patients earlier in their disease course are under way. Data collected from patients in these studies will help researchers identify clinical factors that may be associated with progression to active multiple myeloma.

Generally, only patients with active multiple myeloma require treatment with myeloma drugs. When patients with SMM or MGUS do receive treatment, it is usually through a clinical trial.

WHAT FACTORS ARE CONSIDERED IN DEVELOPING A TREATMENT PLAN FOR ACTIVE MULTIPLE MYELOMA?

There is no one standard treatment for myeloma. Each patient's treatment plan is based on a number of factors specific to them.

Your personal treatment plan: partnering with your health care team.



When you receive a diagnosis of multiple myeloma, it is extremely important for you to commit to partnering with your doctor and health care team to review all of the factors of your disease and determine what treatment will work best. You should also share your treatment goals. Depending on the characteristics of the disease and your wishes, treatment plans may be designed to meet one or more goals.

In the MMRF, you have an advocate by your side—one who is an expert on all things myeloma, who is committed to helping you get the care and support you need, and who understands what you’re going through. The Patient Navigation Center is available to answer 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

GOALS OF MYELOMA THERAPY

The treatment of your active multiple myeloma is usually aimed at reducing—or at least providing relief from—your symptoms and reducing the number of myeloma cells in your bone marrow, which is determined by measuring the level of M protein in your blood. Achieving a response as quickly as possible—keeping safety in mind—is also a priority.

The guiding principles for treatment include using a three-drug (triplet) or four-drug (quadruplet) regimen as initial therapy (also called **induction therapy** or **frontline therapy**), aiming for as deep a treatment response as possible (reducing plasma cells and M protein to a very low level), and considering an **autologous stem cell transplant (ASCT)** or **maintenance therapy**. These principles are described later in this booklet.

Goals and guiding principles of myeloma therapy.

Goals of therapy	Guiding principles
1 Induce response (a reduction in plasma cells/M protein to a very low level)	1 Use three or four drugs for induction therapy
2 Produce a rapid response	2 Aim for the deepest response
3 Improve your daily functioning	3 Consider stem cell transplant either now or later (if eligible)
4 Lessen the impact of side effects	
5 Prolong overall survival and preserve function and quality of life	

If one regimen stops working, another one can be used. There are many choices available today—and treatments continue to improve.

INDUCTION THERAPY OPTIONS

The choice of initial treatment depends on many factors, including the features of your myeloma, the anticipated risk of **adverse events**, convenience for you, and the familiarity of the doctor with the given regimen. One of the first questions that must be answered, by both you and your doctor, is whether you are a candidate for high-dose chemotherapy followed by ASCT.

If you are a candidate for ASCT, you may choose to have a transplant after three to six cycles of induction therapy or you may decide to complete induction therapy and consider transplant later. Maintenance therapy—a stage of treatment designed to preserve your response to a previous therapy—is the next step after induction therapy, depending on your response to induction therapy and/or transplant.

Clinical trials that address the most appropriate duration of therapy for patients who do not undergo ASCT are still ongoing. In the meantime, some doctors recommend continuous treatment until there is evidence of myeloma progression. The specific characteristics of your myeloma, as well as your preferences and the doctor's perspective, are considerations that influence how long you receive a particular therapy.

Key questions to ask your health care team when preparing for induction therapy.

- What treatment options should I consider? What are the treatment choices? What are the risks and benefits of each?
- What can I do to prepare for treatment?
- How will treatment affect my normal routine?
- What lab values and test results are important to track for a response or to monitor for side effects?
- Is there a clinical trial that might be better suited for my type of myeloma or prognosis?
- What resources are available for me and my family?
- What is the best way to get in touch with you for questions or emergencies?
- Should I ask for genomic sequencing?



TRIPLET REGIMENS

Because they involve combinations of three myeloma drugs, triplet regimens offer the promise of greater effectiveness and have been the standard for treating newly diagnosed multiple myeloma patients.

Triplets include:

- Revlimid, Velcade, and dexamethasone (RVD)
- Kyprolis, Revlimid, and dexamethasone (KRD)
- Ninlaro, Revlimid, and dexamethasone (IRD)
- Velcade, cyclophosphamide, and dexamethasone (VCD or CyBorD)
- Darzalex, Revlimid, and dexamethasone (Darzalex-RD)

QUADRUPLET REGIMENS

Like triplet regimens, quadruplet regimens offer the promise of greater effectiveness, with deeper responses and higher rates of minimal (measurable) residual disease (MRD) negativity, at the risk of increased side effects.

Quadruplet therapies typically add an anti-CD38 **monoclonal antibody** (Darzalex or Sarclisa) to triplet therapies like the RVD and KRD regimens

described above and are rapidly becoming a standard of care for newly diagnosed patients.

REVLIMID

Revlimid (lenalidomide) is an **immunomodulatory drug** approved by the FDA for multiple myeloma patients with newly diagnosed or **relapsed or refractory disease** (myeloma that has recurred after initially responding to therapy or that has progressed during therapy). Revlimid is also approved for use as maintenance therapy following ASCT. It is given orally and is usually taken once a day. Cycles are typically 4 weeks, with treatment on days 1–21 and no treatment for days 22–28.

Revlimid (lenalidomide).

Current indications**	How is Revlimid administered?	What are the possible side effects?
<ul style="list-style-type: none">• For newly diagnosed myeloma in combination with dexamethasone• For relapsed/refractory myeloma in combination with dexamethasone• As maintenance therapy following ASCT	<ul style="list-style-type: none">• Oral capsule• For relapsed/refractory or newly diagnosed myeloma: 25 mg[†] once daily for 21 days out of a 28-day cycle (3 weeks on, 1 week off)• For myeloma maintenance therapy: 10 mg[†] once daily continuously for 28 days of repeated 28-day cycles	<ul style="list-style-type: none">• Potential for blood clots• Reduced blood counts• Rash• Fatigue• Muscle pain or muscle cramping• Diarrhea• Small chance of second new cancers when given with melphalan

*Black box warnings:

- Embryo-fetal toxicity; Revlimid is available only through a restricted distribution program
- Hematologic toxicity

• Venous and arterial thromboembolism

[†]Generic version now available.

[‡]Dose may be adjusted as needed

Fatigue is a common side effect of Revlimid that can sometimes be managed by adjusting the dose.

Revlimid can also decrease blood counts. When this occurs, medications like **growth factors** are sometimes given to bring your blood counts up. You may develop a rash when taking Revlimid, sometimes (though not frequently) to an extent where it is necessary to stop taking the drug.

Also, Revlimid can increase the risk of blood clots. Because of this, your treatment will also include, at the very least, a baby aspirin daily to prevent blood clots. If you have other blood clotting risk factors (for example, if you previously developed a blood clot or are sedentary), you might need to take something stronger than aspirin, such as Lovenox or an oral or injectable blood thinner.

VELCADE

Velcade (bortezomib) was the first **proteasome inhibitor** to be approved by the FDA for multiple myeloma patients with newly diagnosed or relapsed or refractory disease.

Velcade (bortezomib).

Current indications*	How is Velcade administered?	What are the possible side effects?
<ul style="list-style-type: none">• For newly diagnosed myeloma• For relapsed/refractory myeloma	<ul style="list-style-type: none">• 1.3, 1.0, or 0.7 mg/m² once or twice a week:<ul style="list-style-type: none">– Injection under the skin (subcutaneous)– Intravenous	<ul style="list-style-type: none">• Peripheral neuropathy<ul style="list-style-type: none">– Occurs less often when subcutaneous or once weekly dosing is used• Low platelets: blood clotting problems• Gastrointestinal problems: nausea, diarrhea, vomiting, loss of appetite• Fatigue• Rash

*Generic version now available.

Velcade can be given either **intravenously** or as an injection under the skin (**subcutaneously**). Because subcutaneous injection is associated with less peripheral **neuropathy** than intravenous injection, you are more likely to receive this drug subcutaneously. Its most common side effects are gastrointestinal symptoms (for example, nausea or diarrhea), but these are usually mild. Velcade can lower the **platelet** count, but the effect does not usually last long. You may develop a rash and become fatigued when taking Velcade, but these symptoms are less common.

The most common side effect of Velcade is peripheral neuropathy, which is damage to the peripheral nerves that can produce numbness, tingling, and in some cases pain in your arms, legs, and feet that can become disabling. If you experience these symptoms, it is important to notify your doctor, as adjusting the dose can prevent the neuropathy from getting worse.

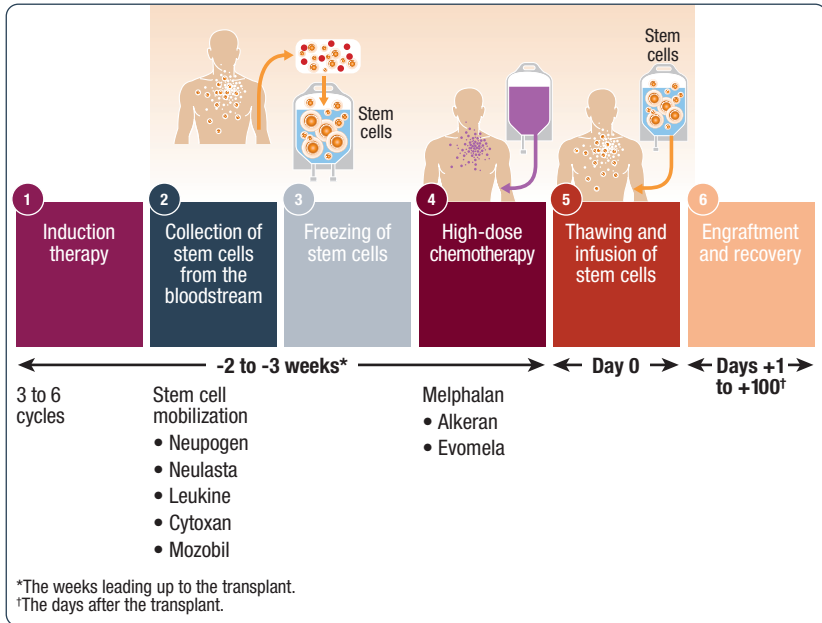
GENERIC

In the first half of 2022, the FDA approved generic versions of Revlimid (generic name: lenalidomide) and Velcade (generic name: bortezomib). To be approved, a generic drug must use the same active ingredients and work the same way as—and demonstrate that it can be substituted for—the brand-name version that it copies.

HIGH-DOSE CHEMOTHERAPY AND STEM CELL TRANSPLANTATION

High-dose chemotherapy (usually melphalan) with ASCT is a treatment that, for many eligible myeloma patients, offers the best chance for long-lasting response. High-dose chemotherapy, though effective in killing myeloma cells, also destroys normal blood-forming cells (called **hematopoietic stem cells**) in the bone marrow. Stem cell transplantation replaces these important cells. Results of this approach to myeloma therapy have improved with the release of several newer drugs.

Autologous stem cell transplant.



MAINTENANCE (OR CONTINUOUS) THERAPY

Myeloma is not yet curable, so it can recur even if you achieve a complete response (CR). The goal of maintenance therapy is to maintain the response for as long as possible and hopefully improve survival. There is increasing evidence supporting the role of maintenance therapy after the completion of induction therapy or after transplantation.

Several phase 3 trials indicate that Revlimid (at 10 mg per day) provides significant benefits following transplant. This finding is the basis for the FDA's approval of Revlimid as maintenance therapy in patients following ASCT. Revlimid is given until your myeloma progresses or you experience unacceptable toxicity.

An analysis of the data from these studies demonstrated that disease progresses later in patients receiving Revlimid maintenance than in those not receiving Revlimid. However, low blood counts are commonly seen with Revlimid maintenance. If your blood counts get too low, it may be necessary for the doctor to reduce your dose. Overall, more severe side effects are seen with Revlimid than without. A small increase in second cancers (such as acute myeloid leukemia or various solid tumors), likely related to maintenance therapy and any doses of melphalan, was seen in all trials, but the current consensus among most researchers is that the benefits likely outweigh the risks for most patients.

Several smaller (**phase 2**) trials have shown that maintenance therapy with Velcade can also improve outcomes. If you have high-risk myeloma or are unable to tolerate Revlimid, your doctor may recommend maintenance therapy with Velcade.

Ninlaro, an oral drug in the same class as Velcade, was studied as maintenance therapy for patients following ASCT in a phase 3 trial. The results showed that more patients lived longer without disease progression on Ninlaro maintenance therapy (as compared to patients who received no maintenance therapy); additionally, Ninlaro maintenance helped to deepen the treatment response. If you are unable to tolerate Revlimid for an extended time, Ninlaro may be a suitable alternative.

The improvement seen in the length of time patients remain without relapse has prompted many doctors to discuss Revlimid maintenance therapy with their patients.

For high-risk patients, there is no standard treatment approach for maintenance, but treatment will usually be a combination of therapies (typically Revlimid plus at least one other agent). Alternatively, high-risk patients are encouraged to enroll in a clinical trial.

Maintenance therapy options.

Revlimid	Velcade-based treatment	Ninlaro
<ul style="list-style-type: none">• Reduction in myeloma progression• Improved survival (1 of 3 studies, meta-analysis)• Increased risk of second cancers when used after melphalan• Approved for use as maintenance treatment after ASCT	<ul style="list-style-type: none">• Supported by several smaller studies	<ul style="list-style-type: none">• Oral proteasome inhibitor• Reduction in myeloma progression (1 large study)

Additional agents under investigation: Kyprolis, Darzalex, Emlliciti

HOW DO I KNOW IF A TREATMENT IS WORKING?

During and after treatment, doctors monitor your symptoms and may also perform some of the same tests that were done when you were initially diagnosed with myeloma. The results of these tests show how well the treatment is working and may detect side effects. These tests also help determine if, after an initial response to treatment, your myeloma relapses.

The outcome of treatment in myeloma is defined using very specific standards or criteria. A stronger or deeper response is usually associated with better prognosis. However, you can do well even if you never achieve a CR.

Response to treatment is defined using the following criteria:

- Sustained MRD negativity
 - Multiple MRD negativity results as measured in the bone marrow and by imaging-confirmed minimum of 1 year apart

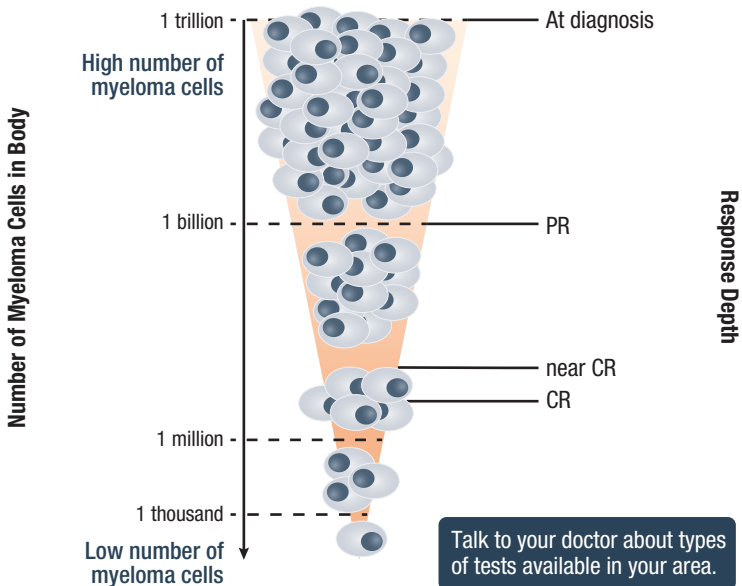
- MRD negativity
 - Absence of clonal plasma cells in bone marrow samples
 - Disappearance of lesions found at baseline as determined by **positron emission tomography (PET)** or **computed tomography (CT)** imaging (for example, imaging plus MRD negativity)
- **Stringent complete response (sCR)**
 - A CR plus normal **free light chain** levels and absence of clonal cells in bone marrow by immunohistochemistry
- **Complete response (CR)**
 - Negative **immunofixation** on serum and urine
 - Disappearance of any soft tissue **plasmacytomas**
 - Less than 5% plasma cells in bone marrow
- **Very good partial response (VGPR)**
 - Serum and urine M protein detectable by immunofixation (but not on **electrophoresis**), or
 - At least 90% reduction in serum M protein plus urine M protein level to less than 100 mg per 24 h
- **Partial response (PR)**
 - At least 50% reduction in serum M protein plus urine M protein level to less than 200 mg per 24 h (or reduction in 24-hour urinary M protein by at least 90%)
- **Minimal response (MR)**
 - At least 25% but no more than 49% reduction of serum M protein and reduction in 24-hour urine M protein by 50% to 89%
- **Stable disease (SD)**
 - Does not meet criteria for response or progressive disease
- **Progressive disease (PD)**
 - An increase of 25% in M protein
 - An increase of 10% in bone marrow plasma cells

For newly diagnosed myeloma patients, the goal of treatment is typically a VGPR or better. That is, you have no (or only a very small amount of) M protein detectable in your blood or urine. Luckily, with the treatments that are available today, more and more patients are achieving a CR.

WHAT IS MINIMAL (MEASURABLE) RESIDUAL DISEASE (MRD)?

Treatment advances have increased the likelihood that you will achieve a CR. However, achieving a CR does not eliminate all myeloma in your body; some myeloma cells can remain. This is called **minimal (or measurable) residual disease (MRD)** and is reported as MRD positive.

Minimal (measurable) residual disease.



Conventional blood tests are not sensitive enough to detect these remaining cells, but this is changing. MRD measurement aims to detect any myeloma cells that remain in your body after a CR is achieved.

Studies using newer, more sensitive tests to detect MRD have shown that patients who achieve deeper responses with fewer remaining myeloma cells may have better outcomes. With today's therapies, more and more patients are achieving deep responses. Thus, interest in the assessment of MRD is growing. MRD monitoring is now being adopted in cancer centers, especially in clinical trials.

An FDA-approved molecular test called the clonoSEQ assay is available to detect and monitor MRD in bone marrow samples from patients with myeloma.

The extent of MRD positivity or negativity depends on the MRD test used and how sensitive it is in detecting myeloma cells in the sample (for example, one myeloma cell out of 100,000 normal cells or one myeloma cell out of 1,000,000 normal cells).

Currently, measurement of MRD depends on detecting myeloma cells in samples from your bone marrow and not other areas of your body. Therefore, imaging (for example, PET or CT scans) is also required to detect any myeloma cells that continue to be present outside of your bone marrow. Also, it may be premature to base treatment decisions on the results of MRD testing; for example, it is unclear whether patients who are MRD positive should get more treatment or if patients who are MRD negative no longer need treatment. Also, some patients may never achieve MRD negativity and continue to live without major complications. MRD is an area of ongoing investigation in clinical trials.

WHAT ARE MY OPTIONS IF I RELAPSE OR IF I DON'T RESPOND TO THERAPY?

If you relapse or become refractory to therapy, you have the benefit of having many novel agents available as options for your treatment—including molecularly targeted and immunotherapeutic agents. In some cases, older treatments (such as Thalomid, Doxil, and older chemotherapies) may be appropriate, particularly if you do not respond to other agents.

FDA-approved myeloma drugs.

Immunomodulatory drugs	Revlimid (lenalidomide)	Pomalyst (pomalidomide)	
Proteasome inhibitors	Velcade (bortezomib)	Kyprolis (carfilzomib)	Ninlaro (ixazomib)
Chemotherapy alkylators	Cytoxan (cyclophosphamide)	Melphalan	
Steroids	Dexamethasone	Prednisone	
Monoclonal antibodies	Empliciti (elotuzumab)	Darzalex (daratumumab)	Sarclisa (isatuximab)
Bispecific antibodies	Tecvayli (teclistamab)		
Other mechanism of action	XPOVIO (selinexor)		
Cellular therapy (eg, CAR-T)	Abecma (idecabtagene vicleucel)	Carvykti (ciltacabtagene autoleucel)	

If your myeloma relapses or is refractory to treatment, several factors need to be taken into account to select a regimen that balances effectiveness and the risk of toxicity.

Factors to consider in choosing therapy for relapsed or refractory myeloma.



Many treatments are available for relapsed or refractory myeloma, and many potential new drugs are currently being studied. If your myeloma does not respond to induction therapy, or you relapse soon after induction therapy is completed, your myeloma is considered to be refractory. However, if you are refractory to a particular drug, you may respond if the drug is used in combination with other myeloma medications.

Treatment options include:

- Any myeloma drug that has not been previously used
- A different combination of myeloma medications (which can include a previously used drug)
- High-dose chemotherapy and stem cell transplant (if appropriate)
- Participation in a clinical trial

To accelerate development of new therapies for myeloma, all eligible patients should consider participating in a clinical trial.

REVLIMID AND VELCADE REGIMENS

Treatment regimens in which Revlimid is combined with Velcade and dexamethasone (RVD) may be options depending on whether you received them previously and how you responded.

Combining current and new drugs in development with treatment regimens based around Revlimid or Velcade is continually being evaluated in clinical trials.

PROTEASOME INHIBITORS

Proteasome inhibitors slow myeloma cell growth and kill myeloma cells by interfering with processes that play a role in cell function.

Kyprolis

Kyprolis (carfilzomib) is approved for patients with relapsed or refractory myeloma.

Kyprolis (carfilzomib).

Current indications	How is Kyprolis administered?	What are the possible side effects?
<ul style="list-style-type: none">• For relapsed/refractory myeloma alone or in combination with dexamethasone or Revlimid and dexamethasone or Darzalex and dexamethasone	<ul style="list-style-type: none">• Intravenously• Once weekly or twice weekly as a 10- or 30-minute infusion	<ul style="list-style-type: none">• Fatigue• Anemia• Nausea• Low platelet count• Shortness of breath• Diarrhea• Fever• Hypertension• Cardiac symptoms

The benefit of Kyprolis-based treatment in patients with relapsed or refractory disease was shown in a phase 2 study; Kyprolis is commonly given in combination (with Revlimid or Pomalyst and dexamethasone) to improve effectiveness.

Common side effects of Kyprolis include nausea, diarrhea, fever, headache, infections, shortness of breath, and reductions in some blood cell counts. The incidence of peripheral neuropathy was notably low (14% of patients) in the phase 2 study; when it occurred, it tended to be mild.

Although uncommon, there is a risk of cardiovascular side effects with Kyprolis, including congestive heart failure. If you have a heart condition, you will be evaluated to determine whether Kyprolis is an appropriate treatment. If you have any heart problems, your doctor will monitor you closely while you take Kyprolis.

Studies are ongoing to evaluate Kyprolis in combination with other myeloma drugs and to assess its potential for use in additional types of patients.

Ninlaro

Ninlaro (ixazomib) is the first oral proteasome inhibitor approved for patients with relapsed or refractory myeloma.

Ninlaro (ixazomib).

Current indications	How is Ninlaro administered?	What are the possible side effects?
<ul style="list-style-type: none">• For relapsed/refractory myeloma in combination with Revlimid and dexamethasone	<ul style="list-style-type: none">• Oral capsule	<ul style="list-style-type: none">• Diarrhea• Constipation• Low platelet counts• Peripheral neuropathy• Nausea• Peripheral edema• Vomiting• Back pain

A regimen of Ninlaro, Revlimid, and dexamethasone was compared to Revlimid and dexamethasone in a phase 3 trial. On average, patients receiving Ninlaro in combination with Revlimid and dexamethasone lived significantly longer without their disease worsening compared to patients receiving Revlimid and dexamethasone. Responses also lasted longer in the group receiving Ninlaro.

The most common side effects include gastrointestinal effects (diarrhea, constipation, nausea, or vomiting), **thrombocytopenia**, peripheral neuropathy, **peripheral edema**, and back pain. The most common serious side effects were thrombocytopenia and diarrhea.

Ninlaro is being evaluated in phase 3 trials in newly diagnosed myeloma in combination with Revlimid and dexamethasone and as maintenance therapy.

IMMUNOMODULATORY DRUGS (IMiDs)

The drug listed below is in the same class as Revlimid.

Pomalyst

Pomalyst (pomalidomide) is more potent than Revlimid and is approved for patients with relapsed or refractory myeloma.

Pomalyst (pomalidomide).

Current indications*	How is Pomalyst administered?†	What are the possible side effects?
<ul style="list-style-type: none">• For relapsed/refractory myeloma in combination with dexamethasone, or Darzalex and dexamethasone, or Emlipicit and dexamethasone, or Sarclisa and dexamethasone	<ul style="list-style-type: none">• Oral capsule	<ul style="list-style-type: none">• Fatigue and weakness• Low white blood cell counts• Anemia• Gastrointestinal effects (constipation, nausea, or diarrhea)• Shortness of breath• Upper respiratory infection• Back pain• Fever• Blood clots

*Black box warnings:

- Embryo-fetal toxicity; Pomalyst is available only through a restricted distribution program
- Venous and arterial thromboembolism

†Dosing can be adjusted if needed.

Side effects vary by patient and are considered manageable. The most common include fatigue and loss of strength, low white cell blood counts, **anemia**, constipation, nausea, diarrhea, shortness of breath, upper respiratory tract infections, back pain, and fever. Similar to other IMiDs, some patients who received Pomalyst in clinical trials developed blood clots. For this reason, aspirin or another blood thinner is given with Pomalyst.

Pomalyst has been approved for use in combination with dexamethasone and certain monoclonal antibodies as a treatment for some myeloma patients.

Numerous clinical trials are continuing to evaluate the use of Pomalyst in other types of patients and in combination with other myeloma drugs.

MONOCLONAL ANTIBODIES

Monoclonal antibodies can kill myeloma cells by targeting myeloma cell surface proteins.

Darzalex

Darzalex (daratumumab) is an anti-CD38 antibody and is the first monoclonal antibody approved for use in patients with newly diagnosed myeloma who are not eligible for ASCT and those with relapsed or refractory myeloma.

Darzalex (daratumumab).

Current indications	How is Darzalex administered?*	What are the possible side effects?
<ul style="list-style-type: none">• For newly diagnosed myeloma patients who are ineligible for ASCT, in combination with Revlimid and dexamethasone or Velcade, melphalan, and prednisone• For relapsed/refractory myeloma alone or in combination with Revlimid and dexamethasone, or Velcade and dexamethasone, or Kyprolis and dexamethasone, or Pomalyst and dexamethasone	<ul style="list-style-type: none">• Intravenous injection• Subcutaneous injection†• Once a week for the first 8 weeks then every 2 weeks for 4 months, then monthly<ul style="list-style-type: none">– The first prescribed dose may be split over 2 consecutive days	<ul style="list-style-type: none">• Infusion reactions• Fatigue• Nausea• Back pain• Fever• Cough• Upper respiratory tract infection

*Dose schedule varies slightly depending on combination and **formulation**.

†Subcutaneous formulation is named Darzalex-Faspro

These combinations have proven to be effective in patients with relapsed or refractory myeloma:

- Darzalex plus Revlimid and dexamethasone or Velcade and dexamethasone
- Darzalex plus Pomalyst and dexamethasone
- Darzalex plus Kyprolis and dexamethasone

The most common side effects included fatigue, low **red blood cell** and platelet counts, and nausea. Some patients in clinical trials experienced **infusion reactions** (chills and low-grade fever) while receiving the drug. For this reason, you will receive medications before and after administration of Darzalex to reduce your risk of these reactions.

Sarclisa

Sarclisa (isatuximab) is an anti-CD38 antibody approved for use—in combination with Pomalyst or Kyprolis and dexamethasone—in multiple myeloma patients with relapsed or refractory disease who have received at least two previous lines of treatment including Revlimid and a proteasome inhibitor.

Sarclisa (isatuximab).

Current indications	How is Sarclisa administered?	What are the possible side effects?
<ul style="list-style-type: none">• For relapsed/refractory myeloma in combination with Pomalyst or Kyprolis and dexamethasone	<ul style="list-style-type: none">• Intravenously• Once a week for the first 4 weeks then every 2 weeks thereafter• Premedication for infusion reactions	<ul style="list-style-type: none">• Low numbers of white blood cells known as neutrophils (neutropenia)• Infusion-related reactions• Pneumonia• Upper respiratory tract infection• Diarrhea• Anemia• Low numbers of white blood cells known as lymphocytes (lymphopenia)• Low platelet counts (thrombocytopenia)

A regimen of Sarclisa, Pomalyst, and dexamethasone was compared to Pomalyst and dexamethasone in a phase 3 trial. On average, patients receiving Sarclisa in combination with Pomalyst and dexamethasone lived significantly longer without their disease worsening than did patients receiving Pomalyst and dexamethasone.

The most common side effects included infusion-related reactions, pneumonia, diarrhea, and low blood counts.

Empliciti

Empliciti (elotuzumab) is approved for multiple myeloma patients with relapsed or refractory disease.

Empliciti (elotuzumab).

Current indications	How is Empliciti administered?	What are the possible side effects?
<ul style="list-style-type: none">• For relapsed/refractory myeloma in combination with Revlimid or Pomalyst and dexamethasone	<ul style="list-style-type: none">• Intravenous injection• Once a week for the first 8 weeks then every 2 weeks	<ul style="list-style-type: none">• Fatigue• Diarrhea• Fever• Constipation• Cough• Peripheral neuropathy• Infusion reactions• Nasopharyngitis• Upper respiratory tract infection• Decreased appetite• Pneumonia• Small chance of second new cancer

Empliciti plus Revlimid and dexamethasone was compared to Revlimid and dexamethasone in a phase 3 trial. The three-drug regimen reduced the risk of disease progression or death compared to Revlimid and dexamethasone.

Empliciti, Pomalyst, and low-dose dexamethasone was compared to Pomalyst and low-dose dexamethasone, also in a phase 3 trial. The addition of Empliciti resulted in a reduction in risk of disease progression or death compared to Pomalyst and low-dose dexamethasone alone.

The most common side effects included fatigue, diarrhea, fever, constipation, cough, infection of the nose and throat (nasopharyngitis), upper respiratory tract infection, pneumonia, peripheral neuropathy, and decreased appetite.

BISPECIFIC ANTIBODIES

Bispecific antibodies are another type of **antibody**-based **immunotherapy** and are made by fusing together fragments from two regular antibodies—like those normally produced by your **immune system**. One fragment attaches to proteins on the myeloma cells (making them easier for your immune system to find). The other fragment attaches to proteins found on your immune cells—specifically, **T cells**—and helps these T cells find and fight the tagged myeloma cells.

Tecvayli

Tecvayli (teclistamab) is a **B-cell maturation antigen (BCMA)**-directed bispecific antibody. Tecvayli targets both BCMA on the surface of multiple myeloma cells and CD3 receptors expressed on the surface of T cells.

In one clinical trial, 165 patients whose disease had come back after at least four prior lines of treatment received two small doses of Tecvayli followed by larger doses once per week until their disease progressed or until they experienced unacceptable side effects. Approximately two thirds of patients had a PR or better and nearly 40% had CR. The most common side effects included **cytokine release syndrome**, fever, low blood counts, and musculoskeletal pain.

Tecvayli (teclistamab).

Current indications*	How is Tecvayli administered?	What are the possible side effects?
<ul style="list-style-type: none">• For patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody.	<ul style="list-style-type: none">• Subcutaneous injection• Two step-up[†] doses on day 1 and day 4, followed by the first full treatment dose on day 7; Tecvayli is given once weekly thereafter until disease progression• Hospitalization required for each step-up dose and first full treatment dose	<ul style="list-style-type: none">• Cytokine release syndrome• Neurotoxicity• Low blood counts• Fever• Musculoskeletal pain• Injection site reaction• Fatigue

*Black box warnings:

- Cytokine release syndrome
- Neurologic toxicities
- Tecvayli is available only through a restricted distribution program

[†]Step-up doses are smaller initial doses that gradually increase to the full dose to minimize adverse effects.

OTHER MECHANISMS OF ACTION

Drugs with other **mechanisms of action** work in different ways than drugs in the other classes. Myeloma drugs with novel mechanisms of action target proteins involved in cell growth and division. These drugs may target proteins that are specific to myeloma cells or common to all cells.

Xpovio

Xpovio (selinexor) is the first in a new drug class called nuclear export inhibitors. Xpovio targets—and disrupts the function of—a protein called XPO1, which ultimately leads to myeloma cell death.

Xpovio (selinexor).

Current indications	How is Xpovio administered?	What are the possible side effects?
<ul style="list-style-type: none">• In combination with dexamethasone for relapsed/refractory myeloma patients who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, at least two immunomodulatory agents, and an anti-CD38 monoclonal antibody• In combination with Velcade and dexamethasone for patients who have received at least 1 prior therapy	<ul style="list-style-type: none">• Oral tablet• Taken once or twice a week	<ul style="list-style-type: none">• Low platelet count• Low white blood cell counts• Fatigue• Anemia• Decreased appetite• Decreased weight• Diarrhea• Vomiting• Low sodium levels• Constipation• Shortness of breath• Upper respiratory infection

In a phase 2 trial of Xpovio-based treatment, one quarter of patients responded. These were heavily pretreated patients who had received at least four prior anti-myeloma treatments and were refractory to at least two proteasome inhibitors, at least two immunomodulatory drugs, and an anti-CD38 monoclonal antibody.

Xpovio plus Velcade and dexamethasone was compared to Velcade and dexamethasone in a phase 3 trial of patients who had been treated with one to three lines of therapy, including a proteasome inhibitor. The three-drug regimen reduced the risk of disease progression or death compared to Velcade and dexamethasone.

The most common side effects included diarrhea, nausea and vomiting, fatigue, and reductions in platelets, **white blood cells**, and red blood cells.

CELLULAR THERAPY

Immune cell therapy is the process of extracting your own immune cells, engineering them in a laboratory to be better able to identify and attack myeloma cells, and then returning them to you.

Abecma

Abecma (idecabtagene vicleucel) is a first-in-class BCMA-directed personalized immunotherapy called **chimeric antigen receptor (CAR) T-cell therapy**. Abecma is manufactured using T cells that have been collected from your blood. The T cells are modified in a laboratory to recognize BCMA, a protein expressed on multiple myeloma cells. CAR T cells are then infused back into you—now with an enhanced ability to find and kill myeloma cells.

Abecma (idecabtagene vicleucel).

Current indications*	How is Abecma administered?	What are the possible side effects?
<ul style="list-style-type: none">• For patients who have relapsed/refractory myeloma and have received at least four prior therapies, including an anti-CD38 monoclonal antibody, a proteasome inhibitor, and an immunomodulatory agent	<ul style="list-style-type: none">• Intravenously• One-time infusion 2 days after completing lympho-depleting chemotherapy (cyclophosphamide IV and fludarabine)• Hospitalization required for treatment infusion	<ul style="list-style-type: none">• Low blood counts• Cytokine release syndrome• Neurotoxicity• Infection• Fatigue• Musculoskeletal pain• Hypogammaglobulinemia• Diarrhea

*Black box warnings:

- Cytokine release syndrome
- Neurologic toxicities
- Hemophagocytic lymphohistiocytosis/ macrophage activation syndrome
- Prolonged cytopenia
- Abecma is available only through a restricted distribution program

The efficacy of Abecma was studied in a clinical trial of 100 patients with relapsed or refractory myeloma who received CAR-positive T cells. Patients in this study had received three to sixteen previous therapies, with most patients receiving six. Nearly all had received a previous ASCT. Treatment response lasted around 1 year.

The most common side effects included low blood counts, cytokine release syndrome, **neurotoxicity**, infection, and fatigue.

Carvykti

Carvykti (ciltacabtagene autoleucl) is another CAR T cell therapy that uses T cells that have been modified to recognize BCMA.

The efficacy of Carvykti was studied in a clinical trial of 97 patients with relapsed or refractory myeloma who received CAR T cells. Patients in this study had received four to eight previous therapies, with most patients receiving six. Treatment response lasted nearly 2 years.

The most common side effects include low blood counts, cytokine release syndrome, fever, low blood pressure, and **hypogammaglobulinemia**.

Carvykti (ciltacabtagene autoleucl).

Current indications*	How is Carvykti administered?	What are the possible side effects?
<ul style="list-style-type: none">• For patients with relapsed or refractory multiple myeloma after four or more prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.	<ul style="list-style-type: none">• Intravenously• One-time infusion after completing lymphodepleting chemotherapy (cyclophosphamide IV and fludarabine IV daily for 3 days)• Hospitalization required after treatment infusion	<ul style="list-style-type: none">• Low blood counts• Cytokine release syndrome• Neurotoxicity• Infection• Fever• Musculoskeletal pain• Fatigue• Hypogammaglobulinemia• Hypotension

*Black box warnings:

- Cytokine release syndrome
- Neurologic toxicities
- Hemophagocytic lymphohistiocytosis/ macrophage activation syndrome
- Prolonged cytopenia
- Carvykti is available only through a restricted distribution program

For more information about the different types of immunotherapy, refer to the companion booklet **Multiple Myeloma Immunotherapy** and the MMRF website, themmrf.org.

SHOULD I PARTICIPATE IN A CLINICAL TRIAL?

Clinical trials are essential to the development of new myeloma treatments, providing new therapeutic options for myeloma patients at all stages of the disease. The greater the number of people there are enrolling in clinical trials, the faster new treatments can be made available to patients. It is only through patient participation in clinical trials that we have achieved the high number and various types of myeloma treatments available today.

Clinical trials compare new treatments or combinations with current standards of care. If you enroll in a clinical trial, you have the opportunity to be among the first to receive the newest drugs and therapies in development—before they are available commercially.

However, it is important to understand that new treatments may be equivalent to, more effective than, or not as effective as standard treatment options. They may also have unexpected side effects.

Before any drug is considered for testing in people, evidence of activity against the disease must have been demonstrated in laboratory and animal studies—these are called **preclinical studies**.

In all myeloma clinical trials, participants receive the experimental therapy being tested or the best available standard treatment.

Clinical trials take place in different stages, with each phase serving a distinct purpose.

Clinical trial stages.

	Phase 1	Phase 2*	Phase 3†
Objectives	Optimal dose Side effects Metabolism	Preliminary effectiveness Additional safety	Definitive effectiveness and safety
Treatment	Single arm (all patients receive experimental therapy)	Single arm Two arms of different treatments or doses: patients randomly assigned to an arm	Two arms: patients randomly assigned to receive experimental therapy or standard therapy
Study size	Small (<50)	Varies	>200

*When no standard treatment is available, FDA may approve drugs based on trial results

†Conducted to receive FDA approval of new drugs, in most cases

Based on the results of clinical trials, the FDA approves treatments that are safe, effective, and shown to be better than the standard treatments available.

Clinical trials take place at cancer centers, hospitals, clinics, or doctors' offices. Before you enroll in a clinical trial, all details of the treatment are explained, and you must consent to participate. If you agree to participate in a clinical trial, you are free to withdraw at any time.

Most research foundations fund—but don't actually conduct—research. The Multiple Myeloma Research Consortium (MMRC), a sister organization to the MMRF, actually does conduct research. The MMRC is a unique collaboration of academic medical centers in North America that evaluates new agents and drug combinations for their safety, efficacy, and feasibility in early-stage clinical trials.

FINDING A CLINICAL TRIAL

The MMRF Patient Navigation Center is designed to match patients with appropriate clinical trials. To take advantage of this program, you (or your caregiver or family member) can complete a simple questionnaire online at [themmr.org/resources/clinical-trial-finder](https://www.themmr.org/resources/clinical-trial-finder). Or you can call 888-841-6673 to speak with an MMRF patient navigator, who will ask you questions and talk to you about clinical trials in your area or ones that may be appropriate for you.

How do I find a clinical trial?

- 1** Ask your treating hematologist or oncologist about any available trials
- 2** Check with any academic medical centers close to your home
- 3** Search for a clinical trial in your area, or let an MMRF patient navigator help guide you through the process at themmrf.org/resources/clinical-trial-finder

WHAT ARE THE MOST PROMISING AGENTS IN CLINICAL TRIALS?

There are a variety of new agents in various stages of development for myeloma. Agents in development may act in different ways against myeloma than currently available drugs, may have fewer side effects, or may have more convenient dosing. However, the availability of some of these drugs may be limited to individuals at particular stages of disease, and the drugs are not without side effects of their own.

Enrolling in a clinical trial may provide additional treatment options. Your doctor can determine which trials are appropriate and available in your area.

The MMRF would like to thank Jesus G. Berdeja, MD, Director of Multiple Myeloma Research and Senior Investigator, Hematologic Malignancies at the Sarah Cannon Research Institute in Nashville, Tennessee, and Faith E. Davies, MBBCh, MRCP, MD, FRCPath, Director of the Center for Blood Cancers and Director of the Clinical Myeloma Program at the Perlmutter Cancer Center at New York University Langone Health in New York, New York, and our patient advocates Allan and Deb Osborne of Millis, Massachusetts, and Cindy Chmielewski of Lawrenceville, New Jersey, 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

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

The MMRF has partnered with Lazarex Cancer Foundation to help patients access clinical trials by helping with travel expenses. Patients who qualify will be reimbursed for out-of-pocket travel expenses for themselves and a travel companion. To learn more about this program, contact the MMRF Patient Navigation Center (1-888-841-6673 or patientnavigator@themmrf.org).

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

REIMBURSEMENT-ASSISTANCE PROGRAMS

Patient Access Network

Website: www.panfoundation.org

Services: Help and hope to people with chronic or life-threatening illnesses for whom cost limits access to critical medical treatments

Phone: 1-866-316-PANF (1-866-316-7263)

Contact: www.panfoundation.org/contact

Amgen Inc

Products: Neupogen/Neulasta/Kyprolis/Xgeva

Website: www.amgenassist360.com

Phone: 1-888-4ASSIST (1-888-427-7478)

Bristol-Myers Squibb

Products: Empliciti/Pomalyst/Revlimid/Thalomid/Abecma

Website: www.bmsaccesssupport.bmscustomerconnect.com/patient

Phone: 1-800-861-0048

Janssen

Product: Darzalex

Website: www.janssencarepath.com/patient/darzalex/patient-support

Phone: 1-844-55DARZA (1-844-553-2792)

Product: Carvykti

Website: www.carvykti.com/resources-and-support

Phone: 1-800-559-7875

Product: Tecvayli

Website: www.janssencarepath.com/patient/tecvayli/patient-support

Phone: 1-877-227-3728

Karyopharm

Product: XPOVIO

Website: www.karyforward.com

Phone: 1-877-KARY4WD (1-877-527-9493)

Novartis**Product:** Zometa**Website:** www.patientassistancenow.com**Phone:** 1-800-245-5356**Sanofi****Product:** Sarclisa**Website:** www.sanoficareassist.com**Phone:** 1-833-WE+CARE (1-833-930-2273)**Takeda Oncology Company****Product:** Velcade/Ninlaro**Website:** www.here2assist.com/patient/home**Phone:** 1-844-817-6486, Option 2

GLOSSARY

active multiple myeloma Multiple myeloma in which the percentage of plasma cells in the bone marrow is greater than 10% and in which the patient shows one or more CRAB symptoms (see definition at CRAB)

adaptive immunity The part of the immune system that is composed of specialized cells designed to recognize foreign invaders and attack them any time they enter the body

adverse event Any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease that occurs after a medical treatment or procedure; adverse events may or may not be related to the treatment or procedure

anemia Decrease in the number of red blood cells in the blood

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

autologous stem cell transplant (ASCT) Procedure in which stem cells collected from a patient are transplanted back into that patient; the most common type of transplant performed in myeloma

B-cell maturation antigen (BCMA) A protein found on the surface of myeloma cells

bisphosphonate Type of drug used to treat osteoporosis and bone disease

bispecific antibody Engineered therapy created by fusing two antibody fragments together; one fragment binds to surface proteins on cancer cells and the other binds to a protein found on the surface of immune cells

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

chimeric antigen receptor T (CAR-T) cell therapy 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

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

clonal Derived from a single mutated cell

complete response (CR) Treatment outcome in which the level of plasma cells in the bone marrow is no more than 5%, there is no evidence of myeloma proteins in the serum or urine as measured by standard laboratory techniques, and all signs and symptoms of cancer have disappeared (though cancer still may be in the body); also called complete *remission*

computed tomography (CT) Imaging technique that uses a computer to generate three-dimensional x-ray pictures (also referred to as *computerized axial tomography [CAT]*)

CRAB Acronym for the following group of clinical indicators of organ damage: increased calcium level, renal (kidney) failure, anemia, bone lesions; the presence of one or more of these indicators can help establish a diagnosis of multiple myeloma

cytokine release syndrome Common, infection-like side effect following infusion of CAR T cells in which a patient experiences fevers, chills, and low blood pressure

electrophoresis Laboratory test used to measure the levels of proteins in the blood or urine; uses an electrical current to sort proteins by their charge

formulation The preparation of a drug

free light chain (FLC) Short protein (immunoglobulin light chain) that is produced by myeloma cells and found in the blood

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

growth factor Substance that stimulates cells to multiply

hematopoietic stem cell Cell that grows and divides to produce red blood cells, white blood cells, or platelets; found in bone marrow and blood

hypogammaglobulinemia Condition in which the levels of serum immunoglobulin or antibodies in the body are reduced

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

immunofixation Test to measure immunoglobulins in blood

immunoglobulin (Ig) Protein that helps protect the body from infection (also called *antibody*)

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; also refers to the use of anti-myeloma drugs prior to high-dose chemotherapy and stem cell transplant (see also *frontline therapy*)

infusion reaction Symptoms that sometimes develop after a patient receives intravenous drugs; commonly include chills, fever, nausea, weakness, headache, skin rash, and/or itching; although rare, severe reactions such as difficulty breathing or low blood pressure can occur

intravenous Administration of a drug directly into a vein

maintenance therapy Treatment that is given to patients following a response to induction therapy over a long period of time to reduce the risk of relapse

mechanism of action The specific biochemical process through which a drug produces an effect on the body

minimal (measurable) residual disease (MRD) Presence of small numbers of myeloma cells in the bone marrow during or after treatment, even when the patient shows no symptoms or signs of disease

minimal response Treatment outcome in which there is at least 25% but no more than 49% reduction of serum M protein

monoclonal antibody Antibody produced in a laboratory that is used to diagnose and treat some diseases

monoclonal gammopathy of undetermined significance (MGUS) A condition that can occur before a patient develops or shows any symptoms of cancer; indicated by the presence of M protein in the serum or urine, MGUS may eventually progress to myeloma

monoclonal (M) protein Abnormal antibody found in large quantities in the blood and urine of individuals with myeloma

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

neuropathy Disorder of the nerves that can disrupt sensation or cause burning/tingling; when the hands and feet are affected, it is referred to as *peripheral neuropathy*

neurotoxicity Damage to nervous system including brain and/or nerves

osteopenia Decreased bone density

osteoporosis Bone loss typically associated with old age; can occur in myeloma

partial response (PR) Treatment outcome where there is a greater than 50% decrease in M protein and disappearance of some (but not all) signs and symptoms of cancer

peripheral edema Abnormally large amount of fluid in the circulatory system or in tissues

phase 1 The first round of a clinical trial, conducted with a small number of participants to assess a drug's safety and dosage levels

phase 2 The second stage of a clinical trial, conducted with a larger number of participants to assess a drug's effectiveness and further evaluate its safety

phase 3 The most advanced stage of drug development, conducted with a large number of participants to confirm a drug's effectiveness, identify and monitor its side effects, compare it to commonly used treatments, and collect information that will allow the drug to be used safely; usually required for FDA approval of drugs

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

plasmacytoma Tumor made up of cancerous plasma cells that occurs in bone or soft tissue; patients with a plasmacytoma may develop multiple myeloma

platelets Small cell fragments in the blood that help it to clot

positron emission tomography (PET) Imaging technique in which radioactive glucose (sugar) is used to highlight cancer cells

preclinical studies Experiments conducted in the laboratory and in animals to identify a target for therapy and to confirm its anticancer activity

precursor conditions Any of the preceding phases of multiple myeloma, called monoclonal gammopathy of undetermined significance (MGUS) or smoldering multiple myeloma (SMM), which are characterized by changes in the cells and the presence of materials in the bone marrow, but no symptoms or organ damage

progressive disease Increase of 25% in M protein or an increase of 10% in bone marrow plasma cells

prognosis Prediction of the course and outcome of a disease

proteasome inhibitors Drugs that slow myeloma cell growth and kill myeloma cells by interfering with processes that play a role in cell function; examples include Velcade, Ninlaro, and Kyprolis

red blood cell Blood cell that carries oxygen

refractory disease Myeloma that does not respond to therapy

relapsed disease Myeloma that progresses after initially responding to therapy

smoldering multiple myeloma (SMM) Myeloma characterized by increased M protein and slightly increased numbers of plasma cells in the bone marrow and an absence of symptoms; patients with SMM are monitored and only treated if their disease progresses

stable disease Disease that does not meet criteria for response or progressive disease

stem cell Cell that grows and divides to produce red blood cells, white blood cells, and platelets; found in bone marrow and blood

step up Smaller doses that gradually increase to the full dose to minimize adverse effects

stringent complete response (sCR) A treatment outcome in which there are no detectable abnormal plasma cells in the bone marrow or M protein in the serum or urine and in which free light chain ratio test is normal

subcutaneous Drug or treatment that is given under the skin

T cell (or T lymphocyte) Type of white blood cell that can be subdivided into two main groups called helper T cells and cytotoxic T cells; helper T cells are responsible for *adaptive immunity*; cytotoxic T cells kill cells that have been marked by the immune system as enemies, including cancer cells

thrombocytopenia Decrease in the number of platelets (small cell fragments in the blood that help it to clot)

tissue A group of structurally and functionally similar cells

very good partial response (VGPR) Treatment outcome in which there is a greater than 90% decrease in M protein

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



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.

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Or sign up at **themmrf.org**

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