

TREATMENT UPDATE:

Multiple Myeloma

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Treatment Update: Multiple Myeloma

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Each year in the United States, approximately 30,000 people are diagnosed with multiple myeloma, a cancer of plasma cells that live in the bone marrow.

Numerous treatment options are available to people living with this form of cancer, and more are on the horizon.

Our immune system is a network of organs, cells, and molecules which protects us from bacteria and viruses that can cause infection. Plasma cells, a type of white blood cell, are an important part of this network. Normally, plasma cells make up less than 5 percent of the blood cells in the bone marrow. For reasons not completely understood, plasma cells can grow out of control. When they do and then cause problems, they are referred to as myeloma cells. These myeloma cells can fill up the bone marrow and damage the bone in multiple places.

Symptoms of multiple myeloma can include anemia, fatigue, weight loss, and bone pain. However, about 10 percent of people have either mild or no symptoms at the time of their diagnosis. In those cases, the diagnosis occurs as a result of tests for a different health issue.

Treatment Options

Multiple myeloma that is not causing symptoms (also known as “smoldering” multiple myeloma) may not initially need to be treated. Your doctor will regularly monitor your condition through blood and urine tests to determine if it is progressing, and if treatment should begin.

If treatment is recommended, you and your doctor will discuss the approach that is right for you, based on your individual circumstances. Regardless of the treatment approach, research arising from clinical trials has shown that administering a combination of drugs is usually more effective than a single drug given alone.

Stem Cell Transplant

A stem cell transplant (also known as a bone marrow transplant) is a procedure in which diseased bone marrow is replaced with healthy bone marrow. It is an important treatment option for some patients with multiple myeloma.

In the procedure, stem cells are harvested (collected) from the patient or from a donor, and then stored. The patient is given high doses of chemotherapy to destroy as many myeloma cells as possible. The previously-collected stem cells are then “infused” (transplanted) into the body, where they travel to the bones and begin rebuilding bone marrow. The stem cells help the body recover faster from the effects of the high-dose chemotherapy.

When a person with multiple myeloma receives his or her own stem cells, the procedure is called an “autologous” stem cell transplant. The procedure is known as an “allogeneic” stem cell

transplant if the stem cells are from a donor (usually a close relative, such as a brother or sister).

A stem cell transplant is an intensive treatment. To determine if it is the right treatment approach, doctors weigh a number of factors, primarily the patient's age and general physical health.

Targeted Treatments

Targeted treatments focus on binding to specific molecules thought to be important for cancer cell survival and growth.

Three “proteasome inhibitors,” a type of targeted treatment, are approved by the U.S. Food and Drug Administration (FDA) for the treatment of multiple myeloma.

The proteasome is a complex of proteins inside cells that breaks down other proteins in both healthy and cancerous cells, as part of normal cellular function. Proteasome inhibitors interfere with this action, resulting in the death of myeloma cells.

- **Bortezomib (Velcade)** was approved as a single agent (a drug used alone) in 2008. When the drug was first approved, it was given intravenously (into a vein). Currently, it is more commonly given subcutaneously (under the skin).
- **Carfilzomib (Kyprolis)** was approved as a single agent in 2012. In 2016, its approval was expanded for use in combination with the immunotherapy lenalidomide (Revlimid), and dexamethasone, a type of corticosteroid. Carfilzomib is given intravenously.
- **Ixazomib (Ninlaro)** was approved in 2015, to be taken in combination with lenalidomide and the corticosteroid dexamethasone. This combination is usually given after other drugs have been tried. Ixazomib is given in pill form.

Immunotherapy

The purpose of immunotherapy in the treatment of cancer is to modify the immune system to recognize that the cancer is foreign to the body, and needs to be attacked.

In 2015, the FDA approved two immunotherapy drugs to treat multiple myeloma. Both of these drugs are monoclonal antibodies, lab-generated molecules that target specific antigens (foreign substances that trigger an immune response) .

- **Elotuzumab (Empliciti)** was approved for patients who had received one to three previous treatments for multiple myeloma.
- **Daratumumab (Darzalex)** was approved for patients who had received at least three prior treatments for multiple myeloma, and whose cancer had become resistant to those treatments or had progressed within a short period of time after treatment. It is also now approved, in combination with lenalidomide and dexamethasone or bortezomib and dexamethasone, in patients who have relapsed after one prior treatment type.

Immunomodulatory Options

Immunomodulatory treatments are an important option for treating multiple myeloma. These types of treatments include thalidomide, lenalidomide, and pomalidomide.

Through a complicated mechanism that was only recently discovered, immunomodulatory drugs lead to the degradation (reduction) of growth signals in myeloma cells. These medications are taken by mouth as capsules, typically in combination with corticosteroids like dexamethasone and frequently in combination with proteasome inhibitors.

Lenalidomide (Revlimid) was approved in 2006 for relapsed disease and then in 2015 for newly-diagnosed patients. In 2017, it was approved for use as a maintenance therapy. Pomalidomide (Pomalyst) was approved in 2013 for treatment of relapsed disease.

Other Treatment Options for Multiple Myeloma

Corticosteroids, such as prednisone and dexamethasone, control inflammation in the body and can also fight myeloma cells.

Corticosteroids can be taken in pill form or given intravenously. In combination with other drugs, corticosteroids are often used throughout the course of multiple myeloma treatment.

Traditional chemotherapy drugs, given intravenously or in pill form, can destroy myeloma cells. The types of chemotherapy most often given to treat multiple myeloma are melphalan (Alkeran) and cyclophosphamide (Cytoxan). High-dose melphalan is used in association with autologous stem cell transplants. Cyclophosphamide is frequently given in combination with other drugs.

In May 2015, the FDA approved panobinostat (Farydak) for patients who have received at least two prior multiple myeloma treatments. Panobinostat inhibits the activity of enzymes known as histone deacetylases (HDACs); by doing so, it may slow the over-development of plasma cells, or cause these cells to die. Panobinostat is used in combination with bortezomib and dexamethasone.

Radiation Therapy

Radiation is often used to shrink myeloma cells in a specific area, such as a plasmacytoma (a collection of myeloma cells that create a bone tumor that can be uncomfortable or lead to a fracture). The course of treatment can last several weeks.

“External beam” is the type of radiation most often used to treat multiple myeloma. It uses a machine to direct a beam (or multiple



beams) of radiation to the cancer. The use of CT, MRI, and PET scans allows radiation oncologists to accurately target tumors, shaping the radiation beams to the size and dimensions of the tumor to help spare healthy tissues.

Treating Bone Pain

Multiple myeloma can cause bone damage, resulting in pain and an increased risk of fracture. This damage, also called “lesions,” primarily affects the spine, pelvis, and rib cage. Radiation therapy is one treatment option; there are also medications called bisphosphonates available to minimize the impact of this bone damage.

Bisphosphonates, which include drugs such as zoledronic acid (Zometa) and pamidronate (Aredia), slow the process by which bone wears away and breaks down. These medications belong to a class of drugs called osteoclast inhibitors, which are also used to treat osteoporosis.

Should a fracture of the vertebrae occur, there are minimally invasive surgical procedures available:

- **Vertebroplasty** is a procedure in which a special cement is injected into a fractured vertebra, to relieve spinal pain and restore mobility.
- **Kyphoplasty** is similar to vertebroplasty, with the additional step of creating space for the special cement by using a balloon-like device.

Treatment Approaches Being Studied

As outlined earlier, immunotherapy is currently being used as a treatment approach for multiple myeloma. Additional immunotherapy approaches are being studied, including adoptive T cell transfer.

Adoptive T cell transfer (also called CAR-T cell therapy) is an approach in which T cells are removed from the patient and genetically modified so that the T cells target a particular protein often found on cancer cells. These reprogrammed T cells are re-introduced into the patient with the goal of improving the immune system's anti-cancer response.



The Importance of Clinical Trials

Clinical trials are the standard by which we measure the worth of new treatments and the quality of life of patients as they receive those treatments. For this reason, doctors and researchers urge people with cancer to take part in clinical trials.

Your doctor can guide you in making a decision about whether a clinical trial is right for you. Here are a few things that you should know:

- Often, people who take part in clinical trials gain access to and benefit from new treatments.
- Before you participate in a clinical trial, you will be fully informed as to the risks and benefits of the trial, including any possible side effects.
- Most clinical trials are designed to test a new treatment against a standard treatment to find out whether the new treatment has any added benefit.
- You can stop taking part in a clinical trial at any time for any reason.

Treatment Side Effects

All cancer treatments can cause side effects. It's important that you report any side effects that you experience to your health care team so they can help you manage them. Report them right away—don't wait for your next appointment. Doing so will improve your quality of life and allow you to stick with your treatment plan. It's important to remember that not all patients experience all side effects, and patients may experience side effects not listed here.

Side Effects of Targeted Treatments

Drugs used in targeted treatments don't have the same effect on the body as do chemotherapy drugs, but they can still cause side effects. Common side effects of targeted therapy include rashes, diarrhea, liver problems (such as elevated liver enzymes), problems with blood clotting and wound healing, and high blood pressure.

Side Effects of Immunotherapy

Immunotherapy travels through the bloodstream, helping to prompt an immune response against the cancer cells. Because the immune system may attack healthy cells as well as cancer cells, certain side effects may be experienced, including fatigue, decreased appetite, and digestive tract symptoms.

Guidance for coping with these potential side effects is discussed in the "General Side Effects" section of this booklet.

Side Effects of Immunomodulatory Options

While the side effects of immunomodulatory options can vary depending on the specific drug, common side effects include headache, nausea, vomiting, and diarrhea.

Side Effects of Chemotherapy

The side effects of chemotherapy depend on the type and dose of drugs given and the length of time they are used, and can include:

- Hair loss
- Increased risk of infection (from having too few white blood cells)
- Easy bruising or bleeding
- Changes in memory or thinking
- Peripheral neuropathy (numbness or tingling in hands and feet)
- Edema (swelling)

Side Effects of Radiation Therapy

Changes to the skin are the most common side effects of radiation therapy; those changes can include dryness, swelling, peeling, redness, and blistering. If a reaction occurs, contact your health care team so the appropriate treatment can be prescribed. It's especially important to contact your health care team if there is any open skin or painful areas, as this could indicate an infection. Infections can be treated with an oral antibiotic or topical antibiotic cream.



General Side Effects

Some side effects may occur across treatment approaches; this section provides tips and guidance on how to manage these side effects should they occur.

Managing Digestive Tract Symptoms

Nausea and vomiting

- Avoid food with strong odors, as well as overly sweet, greasy, fried, or highly seasoned food.
- Nibble on dry crackers or toast. These bland foods are easy on the stomach.
- Having something in your stomach when you take medication may help ease nausea.

Diarrhea

- Drink plenty of water. Ask your doctor about using drinks such as Gatorade which provide electrolytes as well as liquid. Electrolytes are body salts that must stay in balance for cells to work properly.
- Over-the-counter medicines such as loperamide (Imodium A-D and others) and prescription drugs are available for diarrhea but should be used only if necessary. If the diarrhea is bad enough that you need medicine, discuss it with your doctor or nurse.
- Choose foods that contain soluble fiber—for example beans, oat cereals, oranges, and flaxseeds. High-pectin foods such as peaches, apples, oranges, grapefruit, bananas, and apricots can also help to avoid diarrhea.

Loss of appetite

- To help maintain your weight, eat small meals throughout the day. That's an easy way to take in more protein and calories. Try to include protein in every meal.
- To keep from feeling full early, avoid liquids with meals or take only small sips (unless you need liquids to help swallow). Drink most of your liquids between meals.
- Keep high-calorie, high-protein snacks on hand such as hard-boiled eggs, peanut butter, cheese, ice cream, granola bars, liquid nutritional supplements, puddings, nuts, canned tuna, or trail mix.
- If you are struggling to maintain your appetite, talk to your health care team about whether appetite-building medication could be right for you.



Managing Fatigue

Fatigue (extreme tiredness not helped by sleep) is one of the most common side effects of many cancer treatments. If you are taking a medication, your doctor may lower the dose of the drug, as long as it does not make the treatment less effective. If you are experiencing fatigue, talk to your doctor about whether taking a smaller dose is right for you.

There are a number of other tips for reducing fatigue:

- Take several short naps or breaks.
- Take short walks or do some light exercise, if possible.
- Try easier or shorter versions of the activities you enjoy.
- Ask your family or friends to help you with tasks you find difficult or tiring.



Communicating With Your Health Care Team

As you manage your cancer, it's important to remember that you are a consumer of health care. The best way to make decisions about health care is to educate yourself about your diagnosis and get to know the members of your health care team, including doctors, nurses, dietitians, social workers and patient navigators.

Here are some tips for improving communication with your health care team:

Start a health care journal. Having a health care journal or notebook will allow you to keep all of your health information in one place. You may want to write down the names and contact information of the members of your health care team, as well as any questions for your doctor. Keep a diary of your daily experiences with symptoms related to your illness or treatment. You can separate your journal or notebook into different sections to help keep it organized.

Prepare a list of questions. Before your next medical appointment, write down your questions and concerns. Because your doctor may have limited time, you should ask your most important questions first, and be as specific and brief as possible.

Bring someone with you to your appointments. Even if you have a journal and a prepared list of questions or concerns, it's always helpful to have support when you go to your appointments. The person who accompanies you can serve as a second set of ears. He or she may also think of questions to ask your doctor or remember details about your symptoms or treatment that you may have forgotten.

Write down your doctor's answers. Taking notes will help you remember your doctor's responses, advice, and instructions. If you cannot write down the answers, ask the person who accompanies you to do that for you. If you have a mobile device, ask if you can use it to take notes. Writing notes will help you review the information later.

Remember, there is no such thing as asking too many questions.



CancerCare's Free Support Services and Programs

It is very difficult to receive a diagnosis of cancer, and adjusting to the necessary changes in your life can be challenging.

CancerCare can help. We are a national nonprofit organization providing free, professional services to anyone affected by cancer. Our licensed oncology social workers can provide support and education, help in navigating the complicated health care system, and provide information on support groups and other resources.

To learn more about how CancerCare helps, call us at 800-813-HOPE (4673) or visit www.cancercares.org.

You will likely also build your own personal support network, comprised of family and friends. In doing so, it's best to take some time to think about the people in your life and how they are best suited to help. Match the task to their strengths—ask a family member who loves to shop to pick up something for you at the store; ask a friend who's a good listener to come over for a chat.

Frequently Asked Questions

Q. My doctor said I should not take ibuprofen for pain. Why is that?

A. Ibuprofen (Motrin, Advil, Nuprin, others) and Aleve (naproxen) are non-steroidal anti-inflammatory drugs (NSAIDs) that work by reducing cytokines (substances secreted from the immune system) that can cause inflammation and pain. NSAIDs should be avoided by people with multiple myeloma, as they can be harmful to the kidneys. There are a number of other options for pain relief, including prescription and over-the-counter medications. It's important to talk to a member of your health care team before taking any over-the-counter medication, to determine if they are safe and will not interfere with your treatments.

Q. I have mouth sores as a result of my chemotherapy treatment. What can I do?

A. It is not unusual to experience mouth sores as a side effect of chemotherapy. Your doctor may recommend treatments such as:

- **Coating agents.** These medications coat the entire lining of your mouth, forming a film to protect the sores and minimize pain.
- **Topical painkillers.** These are medications that can be applied directly to your mouth sores.
- **Over-the-counter treatments.** These include rinsing with baking soda or salt water, or “magic mouthwash,” a term given to a solution to treat mouth sores. Magic mouthwash usually contains at least three of these ingredients: an antibiotic, an antihistamine or local anesthetic, an antifungal, a corticosteroid, and/or an antacid.

Q. Is neuropathy a side effect of all multiple myeloma treatments?

A. Neuropathy (numbness and tingling in the hands and feet) can be a side effect of a number of cancer treatments. However, some of the newer drugs used to treat multiple myeloma, such as carfilzomib (Kyprolis) and ixazomib (Ninlaro) have a reduced risk of neuropathy, and neuropathy is not typically experienced seen with the monoclonal antibodies daratumumab and elotuzumab. Lenalidomide (Revlimid) and pomalidomide (Pomalyst) also cause less neuropathy than some other drugs. It's worth noting that a protein produced by myeloma cells can lead to neuropathy in some people. However, treatments are available that can help; your health care team can provide guidance on what may be best for you.

Q. What is maintenance therapy and is it valuable?

A. Across many types of cancer, maintenance therapy is designed to help the primary treatment(s) succeed, and to prevent relapse (the cancer returning). The drug lenalidomide (Revlimid) is most commonly used as a maintenance therapy for multiple myeloma. It is important to discuss the possible side effects of any drug with your health care team before undergoing treatment.

Notes

Resources

CancerCare®

800-813-HOPE (800-813-4673)
www.cancercares.org

American Cancer Society

800-227-2345
www.cancer.org

Cancer.Net

Patient information from
the American Society of
Clinical Oncology
888-651-3038
www.cancer.net

National Cancer Institute

800-422-6237
www.cancer.gov

Cancer Support Community

888-793-9355
www.cancersupportcommunity.org

**National Coalition
for Cancer Survivorship**

877-622-7937
www.canceradvocacy.org

CLINICAL TRIALS WEBSITES**Coalition of Cancer
Cooperative Groups**

www.cancertrialshelp.org

EmergingMed

www.emergingmed.com

National Cancer Institute

www.cancer.gov

Be The Match®

800-627-7692
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BMT InfoNet

888-597-7674
www.bmtinfonet.org

**International Myeloma
Foundation**

800-452-2873
www.myeloma.org

**Multiple Myeloma
Research Foundation**

www.themmr.org

**National Bone Marrow
Transplant Link**

800-546-5268
www.nbmtlink.org

This booklet was made possible by AbbVie, Celgene Corporation, Takeda Oncology, and an educational donation provided by Onyx Pharmaceuticals, an Amgen Subsidiary.



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