TREATMENT UPDATE:

Multiple Myeloma

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Treatment Update: Multiple Myeloma

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Each year in the United States, approximately 35,000 people—most over the age of 60—are diagnosed with multiple myeloma, a cancer of a type of white blood cell that lives in the bone marrow.

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 and lead to the development of multiple myeloma.

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. The person's condition is regularly monitored through blood and urine tests and imaging to determine if the disease is progressing and if treatment is needed.

If treatment is recommended, approaches are discussed based on the person's individual circumstances. Research arising from clinical trials has shown that administering a combination of drugs is usually more effective than a single drug given alone. However, the benefit of such an approach must be weighed against the potentially higher risk of side effects.

Stem Cell Transplant

A stem cell transplant (also known as a bone marrow transplant) is a procedure in which stem cells are used to aid bone marrow recovery. It is an important treatment option for some people 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 stem cells are then infused (transplanted) into the body, where they travel to the bones and begin rebuilding bone marrow.

When a person with multiple myeloma receives their own stem cells, the procedure is called an autologous stem cell transplant. If the stem cells are from a donor (either a close relative, such as a brother or sister, or a donor from a registry), the procedure is known as an allogeneic stem cell transplant. In multiple myeloma, autologous stem cell transplant is much more commonly used than allogeneic stem cell transplant.

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

Immunomodulatory Options

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 and/or monoclonal antibodies.

Immunomodulatory drugs are an important option for treating multiple myeloma. Lenalidomide (Revlimid) was approved by the U.S. Food and Drug Administration (FDA) in 2006 for relapsed (recurring) multiple myeloma. It was approved for newly-diagnosed patients in 2015 and as a maintenance therapy (continued treatment designed to prevent relapse) in 2017. Pomalidomide (Pomalyst) was approved in 2013 for the treatment of relapsed disease.

Proteasome Inhibitors

Proteasome inhibitors are approved by the FDA for the treatment of multiple myeloma. The proteasome is a complex of proteins inside cells that break down unneeded or damaged proteins in healthy cells and cancer cells. 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 and is now often given as part of combination therapy for the first-line treatment of multiple myeloma. It is typically given as a shot 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 immunomodulatory drug lenalidomide and dexamethasone, a corticosteroid. Carfilzomib is given intravenously (through a needle into a vein).
- **Ixazomib (Ninlaro)** was approved in 2015 to be taken in combination with lenalidomide and dexamethasone. Given in pill form, this combination is usually given after other drugs have been tried.

Monoclonal Antibodies

Monoclonal antibodies are lab-generated proteins that target specific antigens on the surface of the myeloma cell, triggering an immune response. There are four monoclonal antibodies approved by the FDA to treat multiple myeloma.

- **Elotuzumab (Empliciti)** was approved in 2018, in combination with pomalidomide and dexamethasone, for the treatment of relapsed or refractory (resistant to treatment) myeloma in people who have received at least two prior therapies, including lenalidomide and a proteasome inhibitor. Elotuzumab had previously been approved in combination with lenalidomide and dexamethasone to treat people with multiple myeloma who have received one to three prior therapies. This drug is given intravenously.
- **Daratumumab (Darzalex)** was initially approved for people who have received at least three prior treatments for multiple myeloma. It was subsequently approved in combination with lenalidomide plus dexamethasone (or bortezomib plus dexamethasone) in people whose cancer has returned after one prior treatment type. In June 2019, the FDA approved daratumumab for treatment of newly-diagnosed multiple myeloma, in combination with lenalidomide and dexamethasone in people who are not candidates for a stem cell transplant. This drug is given intravenously or subcutaneously.
- **Isatuximab (Sarclisa)** was approved in March 2020, in combination with pomalidomide and the corticosteroid dexamethasone, for the treatment of people with multiple myeloma who have received at least two prior therapies, including lenalidomide and a proteasome inhibitor. In 2021, the approval was extended for use in combination with carfilzomib and dexamethasone for previously-treated multiple myeloma. This drug is given intravenously.

Antibody Drug Conjugates (ADCs)

Antibody drug conjugates work by combining (linking) a chemotherapy with a monoclonal antibody. The ADC belantamab mafodotin-blmf (Blenrep) was approved by the FDA in August 2020 as therapy for relapsed or refractory multiple myeloma that was treated with at least four prior therapies, including an anti-CD38 monoclonal antibody, a proteasome inhibitor and an immunomodulatory agent. This drug is given intravenously.

Chimeric Antigen Receptor T-cell (CAR T-cell) Therapy

In March 2021, the FDA approved idecabtagene vicleucel (Abecma) for the treatment of relapsed or refractory multiple myeloma after four or more prior therapies. Idecabtagene vicleucel is a CAR T-cell therapy, an approach in which T-cells are collected from the patient (in a process similar to donating blood) and genetically modified so that they target a particular protein that may be found on cancer cells. Vicleucel targets BCMA, which is found on the surface of myeloma cells. These reprogrammed T-cells are infused back into the patient and then attack the cancer cells.

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.

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)**. Given in high doses, melphalan is used in association with a stem cell transplant.
- **Melphalan flufenamide (Pepaxto)**. This new, modified form of melphalan was approved in February 2021 for multiple myeloma that has progressed after four prior lines of treatment.
- **Cyclophosphamide (Cytoxan)**. Cyclophosphamide is frequently given as a high-dose monotherapy (treatment given alone) or in combination with other types of treatments.
- **Panobinostat (Farydak)**. Panobinostat is approved, in combination with bortezomib and dexamethasone, for people who have received at least two prior multiple myeloma treatments. It is used less often than melphalan and cyclophosphamide.

Selective Inhibitor of Nuclear Export (SINE) compounds work by inhibiting the action of proteins involved in cancer cell growth. Selinexor (Xpovio), a type of SINE called an XPO1 inhibitor, was approved in 2019 for people with relapsed or refractory multiple myeloma who have received at least four prior therapies. Initially approved for use in combination with dexamethasone, it may be combined with proteasome inhibitors for the treatment of multiple myeloma. Selinexoris given orally.

Radiation therapy 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). The course of treatment can last several weeks.

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.

People with multiple myeloma have an increased risk of infection, both from the disease itself and its treatment. When white blood cells are abnormally low (a condition called neutropenia), an infection may progress rapidly and become serious. For this reason, it's important that people being treated for multiple myeloma immediately report fevers or other signs of infection to their health care team.

Side Effects of Immunomodulatory Options, Targeted Therapy and Immunotherapy

The side effects of these approaches in the treatment of multiple myeloma vary based on the specific therapy used. Common side effects of immunomodulatory options include fatigue, blood clots and rash. Targeted therapy approaches can result in peripheral neuropathy (numbness or tingling in hands and feet), an increased risk of shingles and an increased risk of cardiovascular disease or pulmonary side effects. The side effects that may be experienced with immunotherapy include fatigue, decreased appetite and digestive tract symptoms.

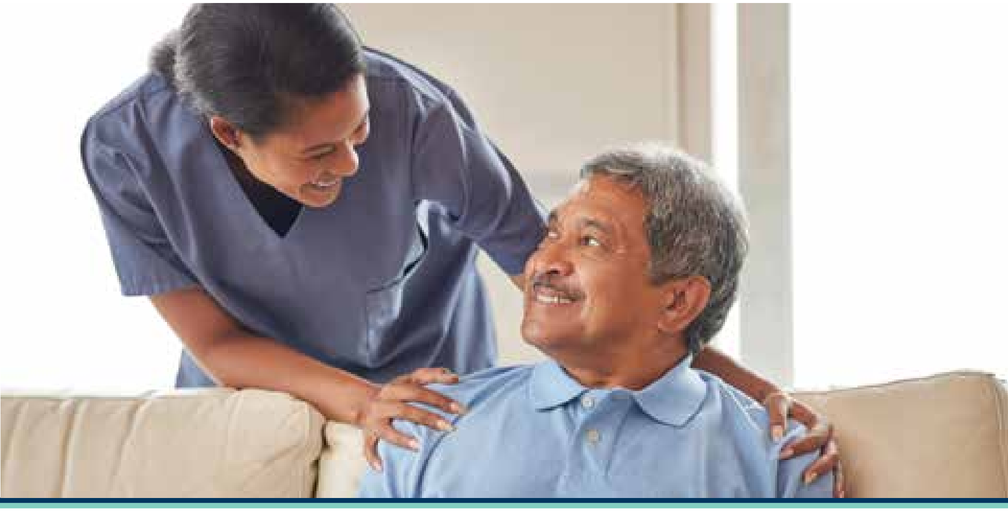
Side Effects of Chemotherapy

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
- Edema (swelling)
- Mouth sores

Side Effects of Radiation Therapy

Changes to the skin are the most common side effects of radiation therapy. The 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.

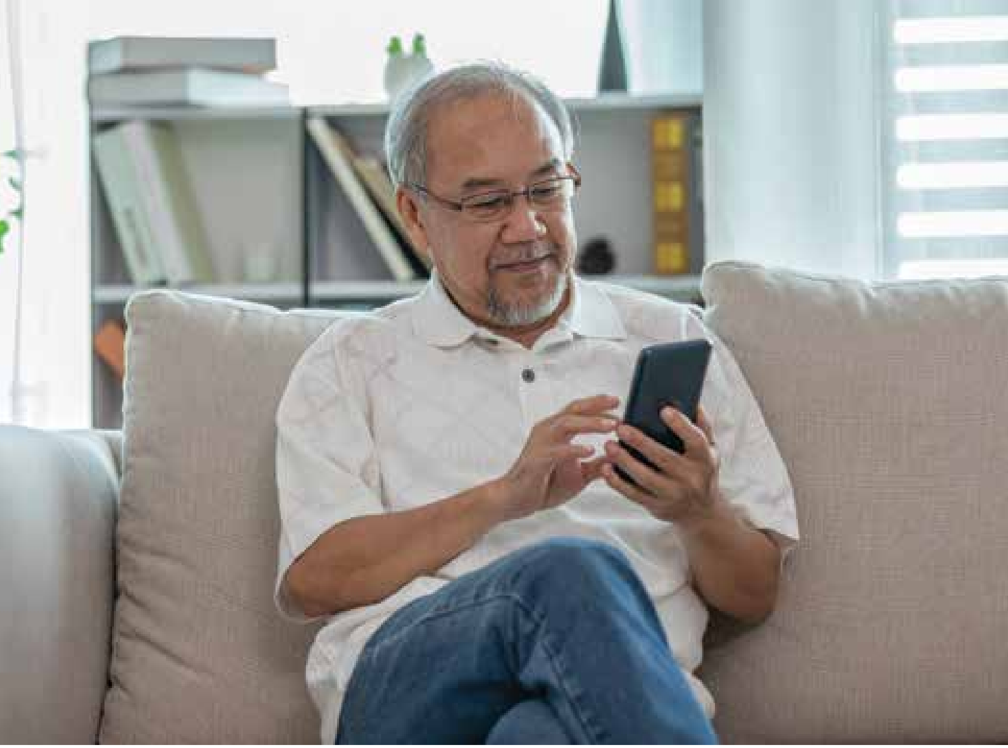
Managing Digestive Tract Symptoms

Nausea and vomiting

- Avoid food with strong odors, as well as overly sweet, greasy, fried or highly seasoned food.
- Eat meals that are chilled, which often makes food more easily tolerated.
- 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.
- 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 and after having a discussion with a member of your health care team.
- Choose fiber-dense foods such as whole grains, fruits and vegetables, all of which help form stools.
- Avoid food high in refined sugar and those sweetened with sugar alcohols such as sorbitol and mannitol.



Loss of appetite

- Eating small meals throughout the day is an easy way to take in more protein and calories, which will help maintain your weight. 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).
- Keep high-calorie, high-protein snacks on hand such as hard-boiled eggs, peanut butter, cheese, granola bars, liquid nutritional supplements, nuts and canned tuna.
- 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 during the day.
- 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.

Fatigue can be a symptom of other illnesses, such as anemia, diabetes, thyroid problems, heart disease, rheumatoid arthritis and depression. So be sure to ask your doctor if he or she thinks any of these conditions may be contributing to your fatigue.

Communicating With Your Health Care Team

As you manage your multiple myeloma, 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 the members of your health care team, including doctors, nurses, nurse practitioners, physician assistants, 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 (either on paper or in a digital format) 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 your multiple myeloma and its 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 as possible.

Bring someone with you to your appointments or have them be present during telehealth sessions. Even if you have a journal and a prepared list of questions or concerns, it's always helpful to have support during your appointments. The other person can serve as a second set of ears. They 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, like a tablet or smartphone, ask if you can use it to take notes. Writing notes will help you review the information later.

Record your visit if your doctor allows it. Recording the conversation with your doctor gives you a chance to hear specific information again or share it with family members or friends.

Incorporate other health care professionals into your team. Your medical oncologist is an essential member of your health care team, but there are other health care professionals who can help you manage your diagnosis and treatment:

- Your primary care physician should be kept updated about your multiple myeloma treatment and any test results.
- Your local pharmacist is a great source of knowledge about the medications you are taking. Have all of your prescriptions filled at the same pharmacy to avoid the possibility of harmful drug interactions.
- Make sure your oncologist knows of any other medical conditions you have, or any pain you are experiencing, so that they can consult with your primary care physician or your specialist if needed.
- Ask your oncologist to send a summary of your visits to your primary care physician and all doctors involved in your care.

Remember, there is no such thing as over-communication.

Cancer*Care*'s Free Support Services and Programs

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

Cancer*Care*® 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 offer information on support groups and other resources.

To learn more about how Cancer*Care* helps, call us at 800-813-HOPE (4673) or visit www.cancercare.org.

You will likely also build your own personal support network composed 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, or ask a friend who's a good listener to come over for a chat.

Frequently Asked Questions

Q: I have recently been diagnosed with multiple myeloma. What questions should I ask my oncologist about their recommended treatment approach?

A: Here are some questions you should ask; others will likely arise in the course of your discussions.

- What are the goals of treatment?
- How long will treatment last?
- Do you have any written information about this treatment?
- What medical procedures and expenses does my insurance plan cover?
- What are the side effects of this treatment?
- Are there any ways to help manage side effects?
- How do we know if a side effect is severe enough to call you?
- Are there any other treatment options?
- Are there any clinical trials we should be aware of?
- What is the best way to let you know when we have questions about treatment?

Q: I know that multiple myeloma can cause bone damage and an increased risk of fracture. What information should I be aware of?

A: There are medications that are available to minimize the impact of bone damage (also called bone lesions):

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

- **RANK ligand inhibitors** block a factor in bone development known as RANK ligand, which stimulates cells that break down bone. By blocking RANK ligand, drugs such as denosumab (Xgeva, Prolia) increase bone density and strength.

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.

There are also lifestyle choices that you can make to improve the health (density) of your bones:

- **A diet high in calcium and vitamin D.** Foods that are high in calcium include dairy products, spinach, kale, okra and certain fish (sardines, salmon, perch and rainbow trout). Foods that provide Vitamin D include fatty fish (tuna, mackerel and salmon), cheese, egg yolks and beef liver. Some other foods come in versions fortified with calcium and/or Vitamin D.
- **Exercise.** Although high-impact exercise should be avoided, some forms of exercise can be beneficial for bone health, including flexibility, endurance, aerobic and strengthening exercises. Importantly, exercise is also known to have a positive impact on physical function, mood, sleep and overall quality of life.
- **Eliminate smoking.** Even minimal smoking has a negative effect on bone density.
- **Avoid or reduce alcohol consumption.** Alcohol intake has been shown to decrease bone density.

It’s important that you consult a member of your health care team before making any changes to your diet or exercise routine.

Q: What is a treatment summary and why is it important?

A: Keeping your own records up-to-date in the form of a treatment summary can be helpful, as it allows you and your family members to have instant access to the specifics of your multiple myeloma diagnosis and treatment. A treatment summary should include:

- Your name and date of birth
- Date of diagnosis
- Prescribed therapy/therapies, including dates started and stopped and dosages when appropriate
- Dates and types of baseline and post-diagnosis testing and the results of these tests
- Other medications and supplements you are taking
- Names, affiliations and contact information of all members of your health care team

Ask the members of your health care team what they suggest be included. Take your personal record with you when you visit any doctor, not just your oncologist.

Q: My sister has multiple myeloma. I want to help with caregiving, but I live far away. What can I do?

A: Even from a distance, you can provide ongoing emotional support to your sister and to her primary caregiver. It is sometimes easier for people to talk about difficult topics over the phone than in person, so be willing to have in-depth and serious conversations. You can also help coordinate medical appointments (and send reminders to your sister and her caregiver about those appointments), provide verbal updates to other family members, and share information on how your sister is feeling (if she agrees) in an on-line journal such as CaringBridge.

Resources

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