TREATMENT UPDATE:

Multiple Myeloma

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Treatment Update: Multiple Myeloma

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Each year in the United States, approximately 32,000 people are diagnosed with multiple myeloma, a cancer of a type of white blood cell that lives 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 and lead to the development of multiple myeloma.

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 the disease is progressing and if treatment is needed.

If treatment is recommended, you and your doctor will discuss the approach that is right for you, based on your 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 diseased bone marrow is replaced with healthy bone marrow. 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 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 (either a close relative, such as a brother or sister, or a donor from a registry).

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 (see the Targeted Therapy section).

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.

Targeted Therapy

Targeted therapy focuses on specific molecules and cell mechanisms thought to be important for cancer cell survival and growth, taking advantage of what researchers have learned in recent years about how cancer cells grow.

Four proteasome inhibitors, a type of targeted therapy, are approved by the FDA for the treatment of multiple myeloma. The proteasome is a complex of proteins inside cells that breaks down 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 in combination with lenalidomide and dexamethasone as first-line therapy for 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 type of 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.
- **Selinexor (XPOVIO)** In July 2019, the FDA approved selinexor (XPOVIO), in combination with dexamethasone, for people with relapsed (returned) or refractory (not responding to treatment) multiple myeloma who have received at least four specific prior therapies.

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. There are two immunotherapy drugs approved by the FDA to treat multiple myeloma:

- **Elotuzumab (Empliciti).** In November 2018, elotuzumab was approved, in combination with pomalidomide and dexamethasone, for the treatment of relapsed or refractory multiple 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.
- **Daratumumab (Darzalex)** was initially approved for people who have received at least three prior treatments for multiple myeloma, and whose cancer has become resistant to those treatments or has progressed within a short period of time after treatment. 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 in combination with lenalidomide and dexamethasone for the treatment of newly diagnosed multiple myeloma in people who are not candidates for a stem cell transplant.

Both elotuzumab and daratumumab are monoclonal antibodies, lab-generated molecules that target specific antigens (foreign substances that trigger an immune response).

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.
- **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.

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.

Treating Bone Loss

Multiple myeloma can cause bone damage, resulting in pain and an increased risk of fracture. This damage (called bone lesions) primarily affects the spine, pelvis and rib cage. Radiation therapy is one treatment option; there are also medications available to minimize the impact of 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. Bisphosphonates are eliminated from the body by the kidneys and their use is associated with a risk of kidney damage (nephrotoxicity).
- **RANK ligand inhibitors** block a factor in bone development known as RANK ligand, which stimulates cells that break down bone. By blocking RANK ligand, these drugs increase bone density and strength. In 2018, the FDA approved the RANK ligand inhibitor denosumab (Xgeva, Prolia) for the treatment of bone lesions caused by multiple myeloma. The kidneys are not involved in the elimination of RANK ligand inhibitors from the body. Unlike bisphosphonates, this type of drug is not associated with kidney damage.

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. There are additional immunotherapy approaches currently being studied:

- 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 they target a particular protein that may be found on cancer cells. These reprogrammed T-cells are infused back into the patient with the goal of improving the immune system's anti-cancer response.
- Bi-specific T-cell Engages (also called BiTEs) are artificial monoclonal antibodies that direct a person's immune system (specifically the T-cell) to link to the cancer cell, destroying it.
- Antibody Drug Conjugates (ADC) work by combining (linking) a chemotherapy with a monoclonal antibody.

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 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 cold or at room temperature, 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 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, nurse practitioners, physician assistants, 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.

Prepare a list of questions. Before your next medical appointment, write down your questions and concerns. Because your doctor may have limited time, ask your most important questions first and be as specific 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. 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. You can also ask the person who accompanies you to take notes for you, either in your journal or on a tablet or smartphone.

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.

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

Cancer*Care*'s Free Support Services and Programs

Receiving a diagnosis of multiple myeloma can be very difficult, 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, 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.

MORE ABOUT MULTIPLE MYELOMA

Frequently Asked Questions

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

A: Ibuprofen (Motrin, Advil, Nuprin) and naproxen (Aleve) 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 it is safe and will not interfere with your treatments.

Physical therapy, acupuncture and massage may also be of help in managing your pain. Consult with a member of your health care team before beginning any of these activities.

Q: I am taking a corticosteroid in combination with other drugs for the treatment of my multiple myeloma. What possible side effects should I be aware of?

A: The side effects of corticosteroids depend on the dose you receive and how long you are taking the medication, and can include:

- Elevated pressure in the eyes (glaucoma)
- High blood pressure
- High blood sugar, which can lead to or worsen diabetes
- Thinning bones (osteoporosis) and increased risk of fractures
- Increased risk of infections

Your oncologist and other members of your health care team will monitor for these side effects.

There are some side effects that may be noticeable to you. Notify your health care team right away if you experience any of the following:

- Fluid retention
- Thin skin and a tendency to bruise more easily
- Slower wound healing
- Cataracts (clouding of the eye's normally clear lens)

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 the targeted therapies carfilzomib and ixazomib) have a reduced risk of neuropathy, and neuropathy is not typically experienced with the monoclonal antibodies daratumumab and elotuzumab. Lenalidomide and pomalidomide 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 approach is best for you.

Resources

CancerCare®
800-813-HOPE (800-813-4673)
www.cancercare.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
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www.myeloma.org

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www.lls.org

Lymphoma Research Foundation
800-500-9976
www.lymphoma.org

Multiple Myeloma Research Foundation
www.themmrf.org

National Bone Marrow Transplant Link
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www.nbmtlink.org

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