TREATMENT UPDATE

Multiple Myeloma
Treatment Update: Multiple Myeloma

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All people depicted in the photographs in this booklet are models, used for illustrative purposes only.
New treatments are helping people with multiple myeloma live longer after diagnosis.

This year, nearly 27,000 people in the United States will be diagnosed with multiple myeloma, a cancer of the bone marrow. Bone marrow contains plasma cells, a type of white blood cell that is an important part of the immune system, which protects the body from infection.

Normally, plasma cells make up less than five percent of the blood cells in the bone marrow. For reasons not completely understood, plasma cells can grow out of control. When they do, they are referred to as myeloma cells. These myeloma cells can fill up the bone marrow and damage the bone. Over time, they collect and form tumors in several (multiple) areas of the bones. That is why this cancer is called multiple myeloma.

Over the past 20 years, new medications approved by the U.S. Food and Drug Administration (FDA) have transformed the way multiple myeloma is treated. This progress is unmatched in any other type of cancer. Doctors report that some patients have gone into remission (a state in which all signs and symptoms of cancer have disappeared) for 10 or even 20 years. Researchers expect the picture for people with multiple myeloma to improve even more as new drugs and drug combinations are studied in clinical trials.

Symptoms of Multiple Myeloma

In its early stages, multiple myeloma does not cause obvious symptoms. About 20 to 25 percent of people have either mild symptoms or no symptoms at the time of diagnosis. Often, people are diagnosed when a doctor is looking at another health problem. But as multiple myeloma progresses, it begins to affect the bone and other parts of the body. Possible symptoms include:

**Bone pain**, often in the spine, hip bones and skull. As multiple myeloma progresses, it begins to wear down bone. This breakdown may cause pain, weakness and fractures (breaks). Bone disease is usually treated with drugs called bisphosphonates, which stop bone from breaking down. They strengthen bone and can decrease the risk of fractures. Denosumab (Xgeva), a different type of bone-preserving drug, is being studied for use in bone disease caused by multiple myeloma. This medication is already approved for other types of bone conditions.
Anemia (low red blood cell counts). As myeloma cells multiply in the marrow, they squeeze out red blood cells, causing weakness and fatigue. Mild to moderate anemia is often treated with epoetin, which is designed to promote the growth of new red blood cells. Epoetin can raise the risk of blood clots, so using this drug is something to consider carefully with your doctor. More severe anemia may require a blood transfusion.

Kidney problems, due to damage from proteins produced by myeloma cells and high blood calcium levels caused by the breakdown of bone. It’s important to drink plenty of fluids (between two and three quarts a day) to help keep the kidneys working properly and to prevent damage.

Infections, particularly pneumonia, as myeloma cells interfere with the body’s immune system. People with multiple myeloma must take fevers (a sign of infection) seriously. If you develop a fever, contact your health care team right away. Infections should be treated promptly, usually with antibiotics.

Diagnosing Multiple Myeloma

Patients are considered to have multiple myeloma when at least 10 percent of their bone marrow is made up of plasma cells or when doctors find a tumor containing myeloma cells. Doctors use a number of tests to detect multiple myeloma:

Bone marrow biopsy. This is the most important test used to figure out the percentage of myeloma cells in the bone marrow. Blood cells are removed from the bone marrow and examined under a microscope. Doctors use other tests to check the cells’ genetic material for anything out of the ordinary.

Bone X-rays. X-ray films are examined to find any areas of the bone that have been damaged by myeloma cells. Other tests may provide a more detailed picture. For instance, MRI or PET scans are used to locate tumors that may be affecting tissues outside of the bone, pressing on the nerves or the spinal cord.

Blood tests. Blood samples are taken to measure liver and kidney function, as well as the amount of calcium in the blood (which rises when the bones are affected), and to look for changes in the blood cells, such as anemia. Other blood tests help doctors find and measure abnormal proteins produced by myeloma cells.

Urine tests. Like blood tests, urine tests can find any abnormal proteins produced by myeloma cells.
Treatment of Multiple Myeloma

A number of advances have made treatment of multiple myeloma much more effective. Over the past 10 years, drugs for multiple myeloma have been able to target not only the tumors in the bones but also the bone marrow where the tumors begin. Medications that help the body’s immune system destroy myeloma cells are now being used. And we are learning more about how the genetic makeup of myeloma differs from one patient to another. This will help pinpoint the best treatment for each person. Also, patients may be taking drugs by mouth more often than intravenously or by injection under the skin, as these become more available.

Doctors do not usually recommend treatment for people with multiple myeloma who have no symptoms. However, this is changing and patients with factors that suggest that their disease may progress sooner might be treated earlier. Once patients do experience symptoms, treatment should be started. Some cancer drugs approved to treat multiple myeloma include:

**Thalidomide**

Thalidomide (Thalomid) works with the body’s immune system to fight cancer. It prevents myeloma cells from binding to bone and forming tumors. It also blocks the growth of blood vessels that tumors need to grow. Thalidomide is used as a treatment for people with advanced cancer that continues to grow despite other treatments. In 2006, the FDA approved the use of thalidomide with a type of steroid called dexamethasone (Decadron and others) for newly diagnosed multiple myeloma. This combination is an effective first treatment for people with multiple myeloma, including those who later may have a stem cell transplant (discussed on page 10).

Thalidomide is also an effective treatment for older people with newly diagnosed multiple myeloma. In these patients, thalidomide is combined with the steroid prednisone (Deltasone) and melphalan (Alkeran and others).

Possible side effects of thalidomide include blood clots, which can be managed with low-dose aspirin and prescription blood thinners such as warfarin (Coumadin and others). Other possible side effects include constipation and fatigue. Thalidomide may also lead to nerve damage, which causes tingling, weakness or numbness, usually in the hands and feet. This condition, called peripheral neuropathy, can be treated with medications that include gabapentin (Neurontin and others), duloxetine (Cymbalta) and pregabalin (Lyrica and others). Vitamin supplements, especially B vitamins, and physical therapy also may help.

**Lenalidomide**

Originally approved by the FDA in 2006, lenalidomide (Revlimid) is used in combination with dexamethasone to treat people whose myeloma returns after at least one previous treatment. Doctors have found that these two drugs together can also be effective as an early treatment for young people with newly diagnosed multiple myeloma who are able to have a stem cell transplant. After treatment, low doses of lenalidomide have been shown to be effective at keeping tumors from growing. This use is known as maintenance therapy.

Side effects of lenalidomide may include low blood cell counts, which can be corrected by adjusting the dose. Like thalidomide, lenalidomide may cause blood clots.
**Pomalidomide**

A new form of the immunomodulatory drugs, pomalidomide (Pomalyst), is effective when combined with dexamethasone. This combination has been studied in a number of large clinical trials and has shown long-lasting effects in about one-third of people whose multiple myeloma does not respond to any other drugs. Pomalidomide stops the growth of blood vessels that feed tumors. It also boosts the immune system and may kill cancer cells directly.

**Bortezomib**

Bortezomib (Velcade) inhibits a molecule in cells called the proteasome. It not only kills myeloma tumor cells but also overcomes the tumors’ resistance to chemotherapy. In 2005, bortezomib was approved by the FDA for the treatment of multiple myeloma tumors that have returned or do not respond to other medications. The drug is especially effective when added to other medications such as cyclophosphamide plus dexamethasone, melphalan plus prednisone or lenalidomide plus dexamethasone. Bortezomib can be helpful as maintenance therapy after a stem cell transplant.

Side effects of bortezomib may include peripheral neuropathy. But in the past few years, doctors have found a way to greatly reduce the risk of nerve damage by giving it as an injection under the skin rather than as an infusion. Another way to reduce side effects is to give bortezomib once a week instead of twice a week.

**Carfilzomib**

In 2012, the FDA approved carfilzomib (Kyprolis) to treat people whose multiple myeloma comes back or does not respond to at least two previous treatments, including bortezomib and thalidomide. Carfilzomib is similar to bortezomib in that it inhibits the proteasome, but researchers consider it to be more potent. It is given intravenously (in a vein) and does not cause neuropathy. The most common side effects of carfilzomib are fatigue, low blood cell count and blood platelet levels, shortness of breath, diarrhea and fever. In rare cases, it can cause or worsen heart problems, so patients must be watched closely.

**Panobinostat**

The FDA approved a new drug, panobinostat (Farydak), in 2015 for people whose multiple myeloma comes back after at least two previous treatments, including bortezomib and thalidomide, lenalidomide, or pomalidomide. This drug is prescribed along with bortezomib and dexamethasone. In some people, panobinostat has caused severe diarrhea and in rare cases, has been linked to heart attacks, so patients will need to be carefully monitored by their doctor.
The Role of Stem Cell Transplants

Stem cell transplants are an important treatment option for people with multiple myeloma. Transplants often lead to long remissions and long survival.

For this procedure, patients first receive standard chemotherapy to reduce the number of cancer cells. Then, stem cells are taken from either the person with multiple myeloma or from a donor. Keeping the stem cells on hold, doctors then give the patient high doses of chemotherapy to destroy as many myeloma cells as possible. The stem cells are then transplanted to the patient to grow into healthy blood cells, forming new blood cells and boosting the person’s defense against infection.

When a person with multiple myeloma receives his or her own stem cells, the procedure is called an autologous stem cell transplant. For some people, two autologous transplants given within six months of each other (called tandem transplants) are more effective than single transplants. When a patient gets stem cells from a donor (usually a brother or sister), the procedure is known as an allogeneic stem cell transplant.

To figure out whether a stem cell transplant is right for a patient, doctors weigh several factors: the type of myeloma, the cancer stage, how aggressive the cancer is and how it has responded to treatment before. A patient’s age and general physical health also are taken into account. Most patients who are candidates for a stem cell transplant are aged less than 70 years, but some patients older than 70 years who are in good health could get a stem cell transplant.

Allogeneic transplants are generally reserved for patients whose disease has come back after treatment. These kinds of transplants tend to lead to the longest remissions because the donor’s cells attack any remaining cancer cells, leading to long-term remissions. However, they also are linked with more risks. For example, in some people, transplanted cells from the donor’s bone marrow see the patient’s body tissues as “foreign” and attack them. This serious complication in the skin, mouth, digestive system and liver is called graft-versus-host disease (GVHD). Steroids often are given to treat GVHD. Therefore allogeneic transplants should be considered in the context of a clinical trial.
Living With Multiple Myeloma

It is very important to involve all of the professionals you need in your care. If you have symptoms or side effects from treatment or mental issues related to coping with your cancer, it is important to seek help. Many things can be done to improve your quality of life and help you manage your treatment.

Your medical team will include your medical oncologist as well as other physicians such as a radiation therapist or orthopedic surgeon. You may also be directly involved with an advance practice provider, usually a nurse practitioner or a physician’s assistant, as well as nurses, dietitians, a physical therapist, and a pharmacist.

Professional oncology social workers and other mental health professionals can help with the emotional and financial challenges related to your diagnosis.

Medications for Bone Health

To strengthen bone, bisphosphonates such as pamidronate (Aredia and others) or zoledronic acid (Zometa) are often recommended as part of the treatment for multiple myeloma. These medications reduce pain and bone breaks, as well as the need for radiation. According to one clinical trial, treatment with zoledronic acid also helps people with multiple myeloma live longer. However, as people with this type of cancer survive longer, many are developing long-term side effects from the use of bisphosphonates, including the rare side effect of damage to the jawbone.

The American Society of Clinical Oncology recommends using bisphosphonates for at least two years and then considering stopping them. If you are taking bisphosphonates, it’s important to keep your teeth and mouth clean and have dental checkups every six to 12 months. Your dentist and doctor can work with you to develop the best maintenance plan. It is also important to keep up with calcium supplementation and adequate vitamin D for good bone health.

In the meantime, researchers continue to study new drugs such as denosumab to strengthen and heal bone. Denosumab is used to reduce fractures from cancer that began in another part of the body but has spread to the bones. It has not yet been approved by the FDA for treatment of bone breaks from multiple myeloma. This drug works by decreasing the breakdown of bone and increasing bone strength and thickness. Other drugs in clinical trials block proteins in myeloma cells that break down bone. In this way, these drugs help strengthen the bone. Aside from medications, there are types of surgery that can relieve pain from fractures in the lower back, for instance. Talk to your doctor about whether surgery is right for you.
On the Horizon

Researchers are developing a number of new drugs to treat multiple myeloma. Some of the most promising of these new medications include:

**Immunotherapy.** There are new antibodies and drugs becoming available that can help reveal cancer cells to the body’s immune system by blocking receptors on the T cells and in the bone marrow. Ongoing trials in myeloma will help determine which of these drugs work best and in which combinations. One type of immunotherapy is monoclonal antibodies. It’s likely there will be a monoclonal antibody for myeloma approved within the next year.

**Monoclonal antibodies.** Often compared to guided missiles, monoclonal antibodies zero in on cancer cells whose surface has a “target molecule.” For example, elotuzumab blocks SLAMF7, which is a substance on the surface of myeloma cells. This drug has been shown to kill myeloma cells, including those that resist other treatments.

Elotuzumab and daratumumab have both been awarded “breakthrough therapy” status by the FDA, meaning that they can be approved more quickly and may be available for multiple myeloma treatment soon.

**Histone deacetylase (HDAC) inhibitors.** This class of drugs works by killing cancer cells or stopping their growth. Because combinations of drugs often are so much more effective than single drugs, the HDAC inhibitor vorinostat (Zolinza) has been combined with bortezomib, lenalidomide and dexamethasone in clinical trials. Ongoing studies also are testing the HDAC inhibitor ACY-1215 in combination with lenalidomide and bortezomib.

**Proteasome inhibitors.** Proteasomes are proteins that play a role in the development of cancer and can make myeloma cells resist chemotherapy. Proteasome inhibitors block the action of these proteins and allow chemotherapy to kill the cancer cells. Bortezomib is a proteasome inhibitor, and now there are new generations of this type of drug being studied in clinical trials.

The proteasome inhibitor ixazomib (MLN9708) has shown positive results in a clinical trial. It is taken in pill form and does not have many side effects. Oprozomib is another new oral proteasome inhibitor being studied in clinical trials. Also in this class is marizomib, which is being tested in multiple myeloma patients whose cancer has returned or has resisted other treatments.
Your Support Team

When you are diagnosed with multiple myeloma, you’re faced with a series of choices that will have a major effect on your life, and you may not be sure where to turn. Because many people live with multiple myeloma for decades, these challenges can affect families over the long term. But help is available. Your health care team, family members and friends will likely be invaluable sources of support at this time.

Oncology social workers provide emotional support for people with cancer and their loved ones. These professionals can help you cope with the challenges of a multiple myeloma diagnosis.

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

The Importance of Clinical Trials

None of the advances in the treatment of multiple myeloma would be possible without clinical trials. People who take part in these studies receive state-of-the-art care and often gain access to and benefit from new medicines, which are being developed every year.

Your doctor can guide you in making a decision about whether a clinical trial is right for you. Before you take part in a clinical trial, you will be fully informed of the risks and benefits of the trial.

No patient receives a placebo (a look-alike containing inactive ingredients) when there is a standard treatment available. Most clinical trials are designed to compare a new treatment with a standard treatment to find out whether the new treatment has any added benefit.

You can choose to stop taking part in a clinical trial at any time for any reason—you are always in control of your voluntary participation.
MORE ABOUT MULTIPLE MYELOMA

Frequently Asked Questions

Q. Do the newer treatments cause fewer cases of neuropathy (nerve damage)?
A. Yes, the newer drug carfilzomib (Kyprolis) does not cause neuropathy. There are other newer drugs not yet approved by the FDA, such as MLN9708, that do not cause as much nerve damage as some currently approved treatments. Lenalidomide (Revlimid) and pomalidomide (Pomalyst), which are approved for treatment of multiple myeloma, 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.

Q. How do doctors treat older people with multiple myeloma who can’t tolerate a stem cell transplant?
A. All patients with multiple myeloma can benefit from combinations of very effective newer drugs. For example, the combination of lenalidomide, bortezomib and dexamethasone at slightly lower doses can achieve remarkable success, even in older people with multiple myeloma. For the past 50 years, melphalan (Alkeran and others) and prednisone have been given to multiple myeloma patients. Today, we add newer drugs to that combination—either thalidomide (Thalomid), lenalidomide or bortezomib. There are exciting studies showing that people of all ages with multiple myeloma live much longer when treated with these drugs. So whether you’re younger and a transplant candidate or older and cannot have a stem cell transplant, everyone with multiple myeloma should be receiving these newer drugs as part of their first treatment as well as long term.

Q. Is the hope for a vaccine against multiple myeloma any closer to becoming a reality?
A. There are a couple of different kinds of vaccines that are showing great promise in people with multiple myeloma. In early studies, one type of vaccination seems to stop the myeloma cells from growing. But the most exciting work being done in this area is focusing on people with smoldering multiple myeloma—that is, cancer in the earliest stages that doesn’t need treatment yet. Because a patient with smoldering myeloma still has a strong immune system, the goal of this research is to help the patient’s own body destroy the myeloma cells. These vaccines are tailored to each person to make it much more likely that he or she will be able to fight off the cancer. The hope is that doctors can delay or even prevent the development of active myeloma.
Q. Can you suggest ways to cope with some of the side effects of my treatment?

A. As in many types of cancer, people with multiple myeloma may experience fatigue and weight loss. Some causes of fatigue, such as anemia, can be treated. There are also practical things you can do to cope with fatigue, including taking short naps, doing light exercise if possible and asking for help with tasks you find difficult or tiring. If you are experiencing weight loss, talk to your doctor about working with a registered dietitian. These professionals can suggest ways to maintain your weight with nutritious foods. If your treatment is causing nausea that discourages you from eating, your doctor can treat that symptom with medication.
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