CANCERcare Connect®

Advances in the Treatment of Multiple Myeloma

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Learn about:

- Diagnosing multiple myeloma
- New treatment options
- Managing side effects
- Free support services

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Advances in the Treatment of Multiple Myeloma

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New treatments are helping people with multiple myeloma live longer after diagnosis.

Each year in the United States, approximately 20,000 people are 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.

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 multiple areas of the bones. That is why this cancer is called "multiple" myeloma.

In recent years, new medications approved by the U.S. Food and Drug Administration (FDA) have transformed the way this cancer is treated. These new drugs have doubled the survival of multiple myeloma patients, progress unmatched in any other cancer. New combinations of older drugs also are proving to be successful treatments. Researchers expect the picture for people with multiple myeloma to improve even more.

Symptoms of Multiple Myeloma

In early stages, multiple myeloma does not cause obvious symptoms. About 20 percent of people have either mild symptoms or no symptoms at the time of diagnosis. Often, these 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. Bone pain is usually treated with drugs called bisphosphonates, which stop bone cells from breaking down. They strengthen bone and can decrease the risk of fractures. For some people with bone pain, orthopedic surgery or radiation treatment also may be helpful.

Anemia (low red blood cell counts) As myeloma cells multiply, they squeeze out red blood cells, causing weakness and fatigue. Mild to moderate anemia often is treated with medications designed to promote the growth of new red blood cells. More severe anemia may require a blood transfusion.

Coping With Fatigue and Weight Loss

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, such as taking short naps, doing light exercise if possible, and asking for help with tasks you find difficult or tiring.

If weight loss is a concern, 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 various medications.

Kidney problems, due to damage from excess amounts of proteins produced by myeloma cells and high blood calcium levels caused by the breakdown of bone. Damage to the kidneys is a common complication of multiple myeloma. Drinking plenty of fluids daily is crucial 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 often have low levels of the antibodies that protect the body against disease, leaving them susceptible to infections. Infections need to be treated promptly and aggressively, usually with antibiotics.

Diagnosing Multiple Myeloma

Patients are diagnosed with multiple myeloma when at least 10 percent of their bone marrow is made up of myeloma cells or when doctors detect 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 determine the percentage of myeloma cells in the bone marrow. Blood cells are removed from the bone marrow and examined under a microscope. Doctors use high-tech tests to check the cells' genetic material for abnormalities.

- **Bone X-rays** X-ray films are examined to identify any areas of the bone that have been damaged by myeloma cells. Additional tests and procedures may provide a more detailed picture. For instance, MRI (magnetic resonance imaging) or PET (positron emission tomography) scans are used to locate

and identify 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 assess kidney and liver function, measure the amount of calcium in the blood (which rises when the bones are affected), and look for changes in the blood cells, such as anemia. Other blood tests also help doctors find and measure abnormal proteins produced by myeloma cells.
- **Urine tests** Like blood tests, urine tests can identify abnormal proteins produced by myeloma cells.

Drug Treatments for Multiple Myeloma

Doctors do not usually recommend treatment for people with multiple myeloma who have no symptoms. But once patients do experience symptoms, treatment should be started. The multiple myeloma drugs now available slow or stop the growth of this cancer in about 80 percent to 90 percent of patients. Even more encouraging, drug treatments can lead to complete remission in as many as 40 percent of people with multiple myeloma. Remission is when cancer responds to treatment or is under control. In a complete remission, all the signs and symptoms of the disease disappear. In a partial remission, the cancer shrinks, but does not completely disappear. Some cancer drugs approved to treat multiple myeloma include:

THALIDOMIDE

The drug thalidomide (Thalomid) has revolutionized the treatment of multiple myeloma. Thalidomide belongs to a class of treatments called immunomodulatory drugs. Thalidomide 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 was first introduced as a treatment for people with advanced cancer that continues to grow despite other treatments. In combination with a drug called dexamethasone, it has been approved as an effective first treatment for people with multiple myeloma, including those who will later be considered for bone marrow transplants (also referred to as stem cell transplants), discussed on page 8. (Dexamethasone belongs to the class of drugs called anti-inflammatory steroids.)

Thalidomide also has been shown to be remarkably effective in treating myeloma and increasing survival in older people with newly diagnosed multiple myeloma. In these patients, thalidomide is added to chemotherapy, typically with the drugs melphalan (Alkeran and others) and prednisone, a type of steroid like dexamethasone.

Side effects of thalidomide may include blood clots, which can be prevented with aspirin or prescription blood thinners such as warfarin (Coumadin and others); constipation; and fatigue. Thalidomide may also lead to peripheral neuropathy, a nerve condition that causes tingling sensations, weakness, or numbness, typically in the hands and feet. Neuropathy can be treated with medications including gabapentin (Neurontin and others), duloxetine (Cymbalta), and pregabalin (Lyrica). Vitamin supplements, particularly B vitamins, and physical therapy may also help.

LENALIDOMIDE

A newer, stronger immunomodulatory drug for treating multiple myeloma is called lenalidomide (Revlimid). It was originally approved, in combination with dexamethasone, for people whose myeloma returns after at least one prior treatment. Doctors also have found that this combination seems to be effective as an early treatment for young people with newly diagnosed multiple myeloma who are candidates for stem cell transplants. In addition, lenalidomide is being

tested to see whether it can delay early-stage multiple myeloma from progressing into a more advanced stage of the disease. Like thalidomide, lenalidomide is effective when combined with melphalan and prednisone for older people with newly diagnosed multiple myeloma.

Lenalidomide is also being used as a "maintenance" therapy after initial treatment with the combination of melphalan, prednisone, and lenalidomide. Used this way, low doses of the drug have been shown to be very effective at keeping tumors from growing after treatment.

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

BORTEZOMIB

Another drug, bortezomib (Velcade), is approved for people with newly diagnosed multiple myeloma. The first of a new class of drugs called proteasome inhibitors, bortezomib blocks the actions of a large group of proteins in myeloma cells called proteasomes. Proteasomes rid cells of substances they no longer need; blocking the proteasomes disrupts myeloma cells, killing them. In so doing, bortezomib overcomes the tumor's resistance to traditional chemotherapy.

Bortezomib is also approved and is especially effective for treating multiple myeloma tumors that have returned or do not respond to other medications. For these types of tumors, bortezomib is even more effective when combined with a long-acting form of doxorubicin (Doxil), a drug used to treat a number of different cancers. Researchers have shown that this combination is an effective treatment for newly diagnosed multiple myeloma as well. In addition, combining bortezomib with dexamethasone has been shown to be superior to traditional chemotherapy in preparing people for stem cell transplants.

Bortezomib has also been combined with melphalan and prednisone and used to treat older adults with newly diagnosed multiple myeloma. This combination of drugs has been highly effective, often leading to complete remission of the cancer.

Finally, one of the most exciting developments for people with myeloma is the combination of bortezomib, lenalidomide, and dexamethasone. This combination has been shown to be at least somewhat effective for everyone with multiple myeloma—an unprecedented success rate. Nearly 75 percent of patients treated with this combination of drugs experience a partial remission, and nearly 50 percent have a complete remission.

Side effects of bortezomib may include peripheral neuropathy.

The Role of Stem Cell Transplants

Stem cell transplants are an important treatment option for people with multiple myeloma. Transplants often lead to longer remissions and longer survival than other types of treatments.

For this procedure, stem cells are taken from either the person with cancer or from a donor. Keeping the stem cells on reserve, doctors then give the patient high doses of chemotherapy to destroy myeloma cells. The stem cells are then transplanted to the patient to grow into healthy blood cells, forming new blood cells and a new immune system.

When a patient receives his 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, typically a brother or sister, the procedure is known as an allogeneic stem cell transplant.

Many factors are considered to determine whether a patient is a good candidate for a stem cell transplant. These factors include the type of myeloma, the cancer stage, how aggressive it is, and how it has responded to prior treatment. A patient's age and general physical condition are also taken into account. Generally, transplants are appropriate for people under the age of 70 whose kidneys, lungs, liver, and heart are considered healthy enough.

Stem cells

Allogeneic transplants tend to produce the longest remissions, but they also are associated 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.

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, bone breaks (fractures), and the need for radiation. And, 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 jaw.

Currently, 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 maintain excellent oral

hygiene and have dental checkups every six to 12 months. Your dentist and your physician can work with you to develop the best plan for dental checkups and treatment.

On the Horizon

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

- **Monoclonal antibodies** Often compared to guided missiles, monoclonal antibodies zero in on cancer cells whose surfaces have a "target molecule." For example, the combination of lenalidomide with a monoclonal antibody called elotuzumab holds promise in treating multiple myeloma that comes back after traditional treatments.

- **Growth blockers** These drugs are designed to block the growth of myeloma cells by depriving them of substances they need, such as vascular endothelial growth factor (VEGF). When tumor cells spread through the body, they release VEGF to create new blood vessels. These blood vessels supply oxygen, minerals, and other nutrients to feed the tumor.
- **Proteasome inhibitors** Bortezomib was the first in its class of proteasome inhibitors. Another promising drug, called carfilzomib, appears to work the same way as bortezomib.
- **Immunomodulators** A new form of the drug thalidomide is showing promise in people whose multiple myeloma has returned after previous treatment. Called

pomalidomide (Actimid), this medication stops the growth of blood vessels that feed tumors. It also boosts the immune system and may kill cancer cells directly.

- **Histone deacetylase (HDAC) inhibitors** This class of drugs works by killing cancer cells or stopping their growth. Two HDAC inhibitors, vorinostat (Zolinza) and panobinostat, have been combined with bortezomib. This combination has been shown to be effective in many people whose tumors resist treatment with bortezomib alone.
- **Akt inhibitors** These drugs aim to disrupt cancer cell membranes and block the actions of proteins involved in cancer growth. An Akt inhibitor called perifosine holds promise as a treatment for multiple myeloma, when combined with bortezomib.
- **Heat shock protein-90 (Hsp90) inhibitors** Heat shock proteins are key players in a number of processes that cancer cells use to survive and grow. Multiple myeloma cells contain more of a heat shock protein, called Hsp90, than normal cells. Two drugs—alvespimycin and tanespimycin—block the actions of Hsp90. Research suggests that combining these drugs with bortezomib may be more effective than treatment with bortezomib alone.
- **mTOR inhibitors** This class of drugs blocks a mechanism called the mammalian target of rapamycin (mTOR) pathway, which promotes tumor growth. Preliminary research suggests that combining lenalidomide with an mTOR inhibitor called everolimus (Afinitor) may stall the growth of multiple myeloma.
- **Cyclin-dependent kinase (CDK) inhibitors** CDK inhibitors, such as the drug flavopiridol, block proteins that promote the growth of multiple myeloma cells.
- **Telomerase inhibitors** One drug, known as imetelstat, blocks an important enzyme found to be active in

myeloma cells. This enzyme allows cancer cells to resist chemotherapy.

- **RANK ligand inhibitors** This new class of drugs works differently from other types of drugs that treat bone complications. They are designed to block a factor in bone development known as RANK ligand. RANK ligand stimulates cells that break bone down. By blocking RANK ligand, RANK ligand inhibitors may increase bone density and strength. Denosumab (Xgeva) is being tested in people with multiple myeloma for the treatment of bone complications. The FDA has recently approved denosumab to help prevent bone fractures and bone pain in non-myeloma patients whose cancer has spread (metastasized) and damaged the bone.

How Cancer*Care*® Helps

When you are being treated for multiple myeloma, you may have many concerns. It's perfectly normal to feel sad, worried, or upset. But the more you learn about what's involved and what to expect, the better you'll feel about your particular situation. Your most important support will likely come from your health care team, family members, and friends. But Cancer*Care* offers these free resources as well:

Counseling Our oncology social workers can speak with you one-on-one to help you find ways to cope with the emotional and practical challenges of cancer. Counseling services are available in person or over the phone.

Support groups Connect with other people who are in a similar situation in our free support groups, led by professional oncology social workers.

Connect Education Workshops Leading experts in oncology provide up-to-date information in these free, one-hour workshops over the telephone. Listen in live to learn about cancer-related issues from the convenience of your

Tips for Coping With Multiple Myeloma

CancerCare's *Multiple Myeloma Fact Sheet Series* offers tips on coping with the diagnosis and treatment of multiple myeloma. Titles in this series include:

- Coping with Multiple Myeloma
- Multiple Myeloma: Finding Resources and Support
- Multiple Myeloma: Making the Most of Your Medical Appointments

To order free copies of these publications, call **1-800-813-HOPE (4673)** or use the online order form on our website, ***www.cancercare.org.***

home or office. Past workshops are also available as podcasts on our website and on telephone replay 24 hours a day, seven days a week.

Publications Our free booklets and fact sheets offer up-to-date, easy-to-read information on topics such as the latest treatments, managing side effects, and coping with cancer.

Financial help Our staff helps you manage financial concerns and provides referrals. Limited aid also is available to eligible individuals through CancerCare's Door to Door Program. This program provides individual grants to patients with multiple myeloma, covering transportation costs such as the price of gasoline or taxi, bus, or train fare to and from their doctor's office.

Referrals to resources CancerCare can help you learn about other organizations in your community and nationwide that can assist you in finding information and help.

To learn more about how we help, call us at **1-800-813-HOPE (4673)** or visit our website, ***www.cancercare.org.***

Frequently Asked Questions

Q What are the causes of multiple myeloma, and are there any ways to prevent it?

A The cause of multiple myeloma is unknown. But we do know some of the factors that may increase a person's risk of developing multiple myeloma, including exposure to pesticides and radiation. Researchers are working on studies of the genes involved in multiple myeloma to try to find the cause.

Although we haven't found a way to prevent multiple myeloma, we have identified stages of the disease. Multiple myeloma usually begins with an increase in abnormal proteins in the blood. Next, the disease progresses to "smoldering myeloma." At this stage, people have unusually high levels of proteins in the blood and excess plasma cells in the bone marrow, but they still don't experience symptoms. Traditionally, smoldering myeloma wasn't treated. Today, researchers are testing whether new drugs such as lenalidomide can prevent smoldering myeloma from moving into active myeloma, which is the next stage. Typically, people with active multiple myeloma experience symptoms and require treatment.

Q I am in the middle of treatment for multiple myeloma and have to relocate. I have a terrific health care team, and I'm concerned about leaving them. How can I find a good oncologist in a new city?

A First, ask your current physicians for a recommendation. They may know specialists in different areas of the country and may be able to make a referral. If they're unable to help,

there are several organizations you can turn to for assistance, such as the International Myeloma Foundation. Contact information for these organizations is listed on page 16.

Q Is it safe to take antioxidant supplements while I'm having chemotherapy?

A In general, there is no reason not to take antioxidant supplements while you're having chemotherapy. But throughout your treatment, it is important to tell your health care team about any nutritional supplements that you're taking. Some supplements, including herbs, may interact with certain medications. For example, some research suggests that taking vitamin C at the same time as bortezomib may decrease the effectiveness of the drug.

Q I was diagnosed with multiple myeloma in 2001, and I had a stem cell transplant in 2003. Since that time, I've had no signs of multiple myeloma. Is there a point at which my doctors could say I'm cured?

A Although it's too early to use the word "cure" for people with multiple myeloma, there are many people like you who live for many, many years without experiencing a recurrence. Regardless of how long you live without signs of active myeloma, it's always important to have your blood tested regularly. If the cancer comes back, there are more ways than ever to treat it effectively.

Resources

Cancer*Care*®
1-800-813-HOPE (4673)
www.cancercare.org

American Cancer Society
1-800-227-2345
www.cancer.org

Blood & Marrow Transplant Information Network
1-888-597-7674
www.bmtinfonet.org

Bone and Cancer Foundation
1-888-862-0999
www.boneandcancerfoundation.org

Cancer.Net
Patient information from the American Society of Clinical Oncology
www.cancer.net

International Myeloma Foundation
1-800-452-2873 in the United States and Canada
www.myeloma.org

National Bone Marrow Transplant Link
1-800-546-5268
www.nbmtlink.org

National Cancer Institute
Cancer Information Service
1-800-422-6237
www.cancer.gov

National Coalition for Cancer Survivorship
1-888-650-9127
www.canceradvocacy.org

National Marrow Donor Program
1-800-627-7692 in the United States and Canada
www.marrow.org

To find out about clinical trials:
Coalition of Cancer Cooperative Groups
www.CancerTrialsHelp.org

National Cancer Institute
www.cancer.gov/clinicaltrials

The information presented in this patient booklet is provided for your general information only. It is not intended as medical advice and should not be relied upon as a substitute for consultations with qualified health professionals who are aware of your specific situation. We encourage you to take information and questions back to your individual health care provider as a way of creating a dialogue and partnership about your cancer and your treatment.

All people depicted in the photographs in this booklet are models and are used for illustrative purposes only.

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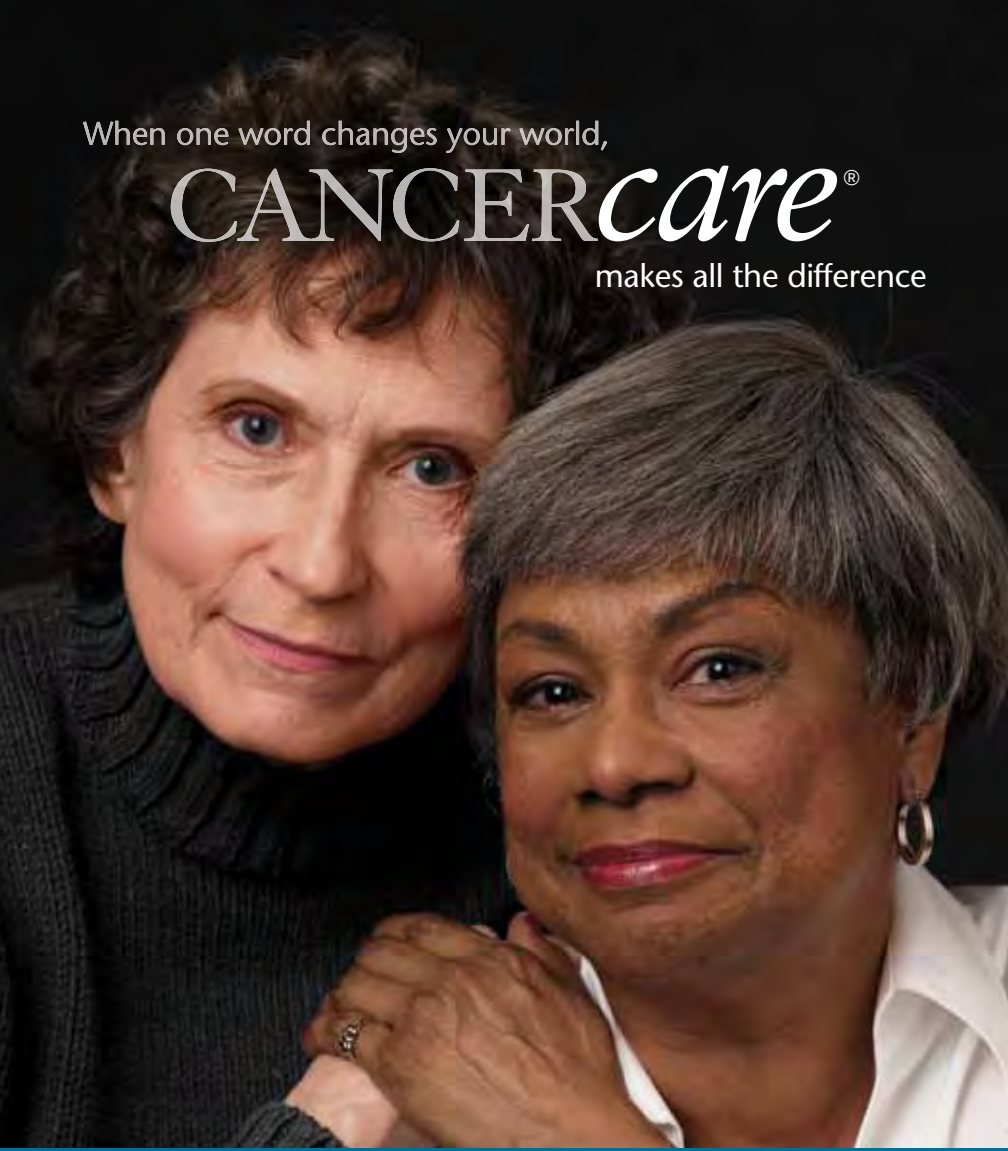

With Cancer*Care*, the difference comes from:

- Professional oncology social workers
- Free counseling for you and your loved ones
- Education and practical help
- Up-to-date information

Our trusted team of professionally trained oncology social workers provides free counseling, education and practical help for you and your loved ones.

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