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Update on Metastatic Breast Cancer

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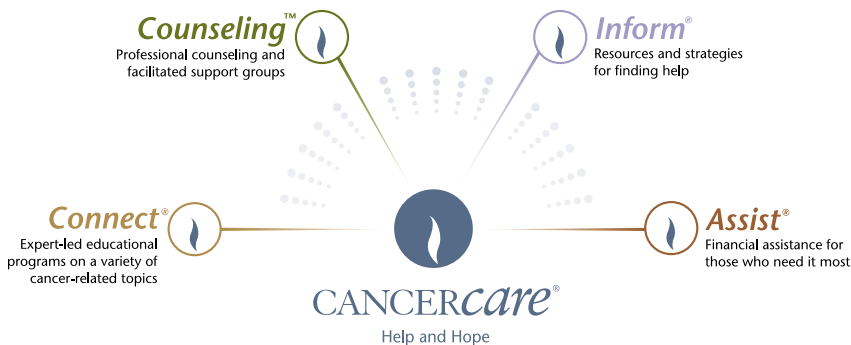
- Treatments for metastatic breast cancer
- New drugs in clinical trials
- Managing side effects
- Communicating with your health care team



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INTRODUCTION

page 2

FREQUENTLY ASKED QUESTIONS

page 12

GLOSSARY (definitions of blue boldfaced words in the text)

page 14

RESOURCES

page 16

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Today, women with metastatic breast cancer have more treatment options than ever before.

Metastatic breast cancer is cancer that has spread beyond the breast and **lymph nodes** in the armpit to another part of the body. Breast cancer cells can spread by moving into blood vessels or **lymph vessels**—a series of connections among the lymph nodes. The most common places that breast cancer cells spread to are the bones, lungs, liver, and brain. Most women who develop metastatic breast cancer have already been treated with chemotherapy or anti-estrogen treatments for their original breast cancer. But these treatments were not successful, and breast cancer cells either returned or continued to grow. But today, women with metastatic breast cancer have more treatment options than ever before.

Treating Metastatic Breast Cancer

Doctors prescribe a variety of treatments for metastatic breast cancer. The type of treatment used depends on whether the tumor growth is fueled by hormones. Choice of treatment is also affected by where in the body the cancer cells have spread.

HORMONAL THERAPY

Some breast tumors, labeled “estrogen receptor-positive,” grow in response to the hormone estrogen. In women with these types of tumors, anti-estrogen drugs are often effective at shrinking breast cancer, including metastatic breast cancer, and preventing its growth. These medications prevent estrogen from promoting cancer growth in one of several ways.

Some anti-estrogen drugs block breast cancer cell **receptors**—substances that work like doorways, allowing the female hormone estrogen to enter the cell and promote its growth. An example of an estrogen-blocking drug is tamoxifen (Nolvadex), which can be taken in pill form.

Other drugs, called **aromatase inhibitors**, prevent estrogen from being made in the body. As their name implies, these drugs block aromatase, a substance necessary for the production of estrogen. Examples of aromatase inhibitors include anastrozole (Arimidex), letrozole (Femara), and exemestane (Aromasin).

Another drug, called fulvestrant (Faslodex), works by binding to estrogen receptors and changing their shape. This prevents

Types of Breast Tumors

Doctors can conduct tests on breast cancer cells to find out whether they depend on hormones to grow. The results of the tests help determine what type of treatment will be most effective for metastatic breast cancer. Breast tumors may be classified as:

Estrogen-receptor positive Tumors that depend on the female hormone estrogen for their growth

Estrogen-receptor negative Tumors that do not depend on estrogen for their growth

HER2 positive Tumors that grow rapidly because they overproduce a protein called human epidermal growth factor receptor 2 (HER2)

HER2 negative Tumors that do not overproduce HER2

Progesterone-receptor negative Tumors that depend on other growth factors

Triple negative Tumors that are estrogen-receptor negative, HER2-negative, and progesterone-receptor negative

the receptors from working properly. Fulvestrant is given in monthly injections. Other drugs that interfere with estrogen's ability to fuel metastatic breast cancer growth include fluoxymesterone (Halotestin) and megestrol (Megace).

CHEMOTHERAPY

When hormonal therapy is no longer effective, or in cases when tumors are not fueled by hormones, chemotherapy is used. A large number of chemotherapies are available to treat



metastatic breast cancer. Some of the most effective and widely used drugs include capecitabine (Xeloda), which is available in pill form, a newer form of paclitaxel (Abraxane), paclitaxel (Taxol), docetaxel (Taxotere), cyclophosphamide (Cytoxan), methotrexate, fluorouracil (5-FU), carboplatin (Paraplatin), and cisplatin (Platinol-AQ). Chemotherapy can be used alone, or in combination, to shrink tumors or slow their growth and relieve symptoms. Different chemotherapies are either given one

after another, each one taken as long as it works effectively to control cancer growth, or together in combination.

The U.S. Food and Drug Administration (FDA) recently approved ixabepilone (Ixempra) for metastatic breast cancer. The drug may be used alone or in combination with capecitabine, which is more effective than capecitabine alone.

TARGETED TREATMENTS

Targeted treatments are drugs that zero in on different cancer cell mechanisms: those that promote growth and division of cancer cells and those that supply blood to tumors. Rather than killing both healthy and unhealthy cells, as chemotherapy does, targeted treatments attack cancer cells

Important Treatments for Women Whose Cancer Has Spread to the Bones

When breast cancer spreads to the bones, drugs called **bisphosphonates** play a key role in treatment. Bisphosphonates stop cells in the bone called osteoclasts from breaking down bone. These drugs strengthen bone and kill some cancer cells in the bone as well. Bisphosphonates can substantially reduce the need for radiation treatment and can decrease the risk of bone breaks.

The two bisphosphonates used to treat women with metastatic breast cancer are pamidronate (Aredia) and zoledronic acid (Zometa). Both are given **intravenously** (through a vein) at a doctor's office or at a hospital, once a month.

primarily, sparing healthy tissues and causing less severe side effects.

There are several promising targeted treatments for metastatic breast cancer:

Trastuzumab (Herceptin)

About 20 to 25 percent of women with breast cancer have what are called "**HER2-positive**" tumors. That is, their breast cancer produces too much of a substance called HER2, which promotes rapid cancer growth. HER2 resides on the surface of cancer cells, where it relays signals ordering the cells to divide and multiply. The more receptors on the cells, the more signals the cells receive to grow and multiply. HER2-positive tumors tend to be more aggressive and recur more often than tumors that don't overproduce HER2. The drug trastuzumab is used to treat HER2-positive metastatic breast cancer. When combined with chemotherapy, trastuzumab greatly improves the effectiveness of

chemotherapy and significantly improves the survival of women with HER2-positive breast cancer.

Lapatinib (Tykerb)

The new drug lapatinib also targets HER2. Lapatinib is unique in that it is able to get inside cancer cells and block HER2. In addition, lapatinib blocks HER1, a related substance that can also fuel the growth of some breast cancer cells along with HER2. Currently, lapatinib is used in women whose advanced breast cancer continues growing despite treatment with trastuzumab and chemotherapy. Lapatinib is given to these women along with capecitabine. The drug combination is effective at stopping cancer growth and shrinking tumors.

In addition, lapatinib and capecitabine are able to travel to brain tissue, something that most drugs for breast cancer cannot do. This combination may benefit women whose breast cancer has spread to the brain.

Bevacizumab (Avastin)

Bevacizumab works by stopping the growth of new blood vessels in tumors. Specifically, bevacizumab blocks a substance called **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. Because healthy tissues have an established blood supply, they are not affected by the drug.

Bevacizumab also helps reduce swelling and increases the ability of chemotherapy to zero in on breast cancer cells. For example, some research has shown that treatment with both bevacizumab and paclitaxel controls metastatic breast cancer growth better, and for longer periods of time, than treatment with paclitaxel alone.

Bevacizumab has been approved for treatment of colorectal cancer and non-small cell lung cancer. It is currently being tested

The Importance of Clinical Trials

There's no question that clinical trials have led to advances in cancer treatment, creating a brighter future for women with metastatic breast cancer. Clinical trials are the standard by which we measure the worth of new treatments and quality of life as women go through those treatments. For this reason, doctors and scientists urge people with cancer to take part.

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

- Often, patients who take part in clinical trials gain access to and benefit from new treatments.
- Before you participate in a trial, you will be fully informed as to the risks and benefits of the trial.
- No patient receives a placebo (or inactive pill) if there is a standard treatment available. Placebos are only used in cancer clinical trials when there is no standard treatment to which a new treatment can be compared.
- You can stop taking part in a clinical trial at any time for any reason.

in clinical trials as a possible treatment for metastatic breast cancer. Bevacizumab appears to be effective against **triple-negative breast tumors**—those that are estrogen-receptor negative, HER2-negative, and progesterone-receptor negative—as well as breast cancers that are estrogen-receptor positive and HER2-positive.

TREATMENTS ON THE HORIZON

A tremendous amount of research is under way to find out what drives triple-negative breast tumors and how best to treat them. Preliminary research suggests that carboplatin

and cisplatin, as well as bevacizumab, mentioned earlier, are effective in treating these types of breast tumors. Other standard chemotherapies may also be effective against some triple-negative breast cancers. In addition, the following drugs are currently being tested in clinical trials:

- **Trabectedin (Yondelis)** Early research has shown that trabectedin is somewhat active against triple-negative breast cancers. The drug works by altering the genetic material in cancer cells, making it more difficult for them to thrive.
- **PARP inhibitors** These new drugs now in clinical trials interfere with a cancer cell's ability to repair itself when damaged by radiation or chemotherapy, for example. PARP inhibitors may increase the effectiveness of other treatments, such as chemotherapy.
- **Notch inhibitors** This class of drugs interferes with the activities of substances in the cell that may promote the growth of triple-negative breast tumors.

Managing Side Effects

Metastatic breast cancer and the treatments for it can cause a number of side effects. A key to managing these side effects is to be aware of them and communicate with your health care team when they arise. Some common side effects include:

- **Fatigue** Feeling an extreme sense of tiredness that doesn't go away after rest can be the result of the cancer itself, treatment, **anemia** (low levels of red blood cells), or the emotional aspects of coping with cancer. If you are feeling fatigued, seek help from your health care team. Your doctor can treat anemia with medications, and oncology social workers and nurses can help you cope with the psychological concerns that can lead to fatigue.
- **Pain** Like fatigue, pain can be caused by the tumor itself, pressing on a nerve or organ, for instance, or by cancer treatments. Chemotherapy, radiation, or surgery can help

Coping With Fatigue

These tips may help you reduce your fatigue:

- Take several short naps or breaks in a comfortable chair rather than in bed.
- Take short walks or do some light exercise if possible.
- Engage in easier or shorter versions of the activities you enjoy.
- Ask your family or friends to help you with tasks you find difficult or tiring.
- Save your energy for things you find most important.

relieve pain by effectively treating the cancer.

In some cases, over-the-counter pain medications such as acetaminophen or aspirin-like medications called non-steroidal anti-inflammatories (NSAIDs) can help. For many people, treatment with NSAIDs such as ibuprofen is sufficient to relieve pain.

But if over-the-counter medications don't relieve the pain, the next step is to combine an over-the-counter pain reliever with a mild **opioid**, such as codeine. If the pain becomes more severe, it's important to use more powerful opioids. There is no need for anyone to be in constant pain. It is a side effect that can and should be managed for good quality of life.

Your health care team can also recommend other techniques such as relaxation, meditation, biofeedback, hypnosis, music therapy, yoga, acupuncture, or physical therapy. All of these techniques can help enhance your treatment and reduce the stress of pain.

- **Nausea, vomiting, and other gastrointestinal symptoms** Nausea, vomiting, diarrhea, constipation, and mouth sores are all common side effects caused by chemotherapy. With proper care, all of these conditions

can be prevented or managed. If you develop any of these conditions, be sure to tell your health care team so that you can get the most effective treatment.

- **Low white blood cell counts** When you are undergoing chemotherapy, you may have low white blood cell counts, a condition called **neutropenia**. White blood cells play a key role in fighting infections. A reduced number of white blood cells increases the risk of infection. Your doctor can prescribe medications designed to help increase the white blood cell count. If you develop a fever, which is a sign of infection, it is vital that you let your health care team know immediately so that you can get proper treatment.
- **Memory lapses** Difficulty with memory or an inability to think clearly is commonly experienced by women with metastatic breast cancer. It's often referred to as "chemobrain." A number of conditions that may lead to symptoms of chemobrain can be treated effectively: low blood counts, depression, anxiety, and fatigue among them. Tell your doctor if you are having difficulty thinking clearly. Sometimes, simply changing a prescription can make a difference, since some medications make you less alert.

Working With Your Support Team

When you are diagnosed with metastatic breast cancer, you're faced with a series of new questions and choices that will have a major effect on your life, and maybe you're not sure where to turn. It's perfectly normal to feel sad, angry, afraid, or frustrated about your diagnosis. But help is available.

Your most important resources are your health care team, family members, and friends. It's essential to develop good communication with them. As breast cancer progresses, it's a good idea to discuss your treatment priorities with your team more than once. Discussions might include issues such as second opinions, acceptable side effects, and your wishes regarding end-of-life care.

In addition to your health care team and loved ones, you can turn to these resources:

Oncology social workers and nurse practitioners

are specially trained to help you find out more about your treatment options, learn how to navigate the health care system, and get the best care possible. Often, when people are coping with cancer, they need someone to talk with who can help them and their families sort through the complex emotions and issues that arise. These health care professionals

can provide emotional support, help you cope with treatment and its side effects, and guide you to resources. CancerCare® offers free counseling from professional oncology social workers on staff.



Support groups Many support groups are available for women with metastatic breast cancer. Studies have shown that these groups help improve quality of life and may improve survival in women with the disease. Support groups can reduce the feeling that you are going through cancer alone. These groups

provide reassurance, suggestions, insight—a safe haven where you can share similar concerns with your peers in a supportive environment. At CancerCare, people with cancer and their families can take part in support groups in person, online, or on the telephone.

Financial help is offered by a number of organizations, including CancerCare, to help cover such costs as transportation to treatment, child care, or help needed around the home. CancerCare can also refer you to other resources in your community that can provide assistance.

Frequently Asked Questions

Q I've been taking capecitabine (Xeloda), and it has irritated the skin of my feet so much that it is difficult to walk. What causes this side effect? Is there anything I can do to prevent it?

A As far as we can tell, as capecitabine is metabolized, a by-product of it builds up in the hands and feet, causing the inflammation and symptoms you're having. Researchers are not sure why this happens. Some clinical trials are currently under way to try to find new medications and strategies to treat the problem. For now, you can talk to your doctor about changing the dose or frequency with which you take capecitabine. For some people, lowering the dose slightly makes a tremendous difference. For others, changing the schedule of the drug from taking it for two weeks on and one week off, to one week on and then a week off can help.

Q Is there a certain amount of time that a woman with metastatic breast cancer can be on zoledronic acid (Zometa) safely?

A Most large clinical trials with the drug have only followed women for about two years, so we don't have enough information yet on the impact of taking the drug for longer periods. But, in general, most women continue using the drug for more than two years. Of course, throughout treatment, it's important to make decisions based on how the cancer is progressing. For example, if cancer has spread to the liver and it is life-threatening, then it might not make sense to continue with zoledronic acid if the bone disease is not causing any problems.

Q I read something about pamidronate (Aredia) causing breakdown of the jaw bone. I haven't taken the drug for about five years, but I'm wondering if there are possible jaw problems I should be aware of.

A Data have shown that women who take pamidronate and zoledronic acid are at risk of jaw breakdown, though the risk is very low. About half of women who develop the problem do so after a tooth extraction. In general, for people with cancer it's important that their oncologist and dentist work together before, during, and even after treatment to make sure they are getting the best care possible, as dental concerns can arise.

Q How effective is trastuzumab (Herceptin) in treating breast cancer recurrence? Should lapatinib (Tykerb) only be used after trastuzumab, or can it be used instead of trastuzumab?

A If the tumor is HER2 positive, then adding a targeted treatment like trastuzumab at the time of recurrence can be very beneficial. If the cancer recurs while a woman is being treated with trastuzumab, then doctors usually favor switching to another drug, such as lapatinib. Currently, the FDA has approved lapatinib for use in women who have already been treated with chemotherapy and trastuzumab. However, doctors are excited about reports from ongoing clinical trials in which lapatinib is used earlier in treatment, before a tumor has been treated with trastuzumab. A large international clinical trial comparing the two drugs as first treatment for recurrent breast cancer is currently under way. Until the results come in, we're fortunate to have the options of restarting trastuzumab after a period off of it or adding lapatinib to the treatment plan.

Glossary

anemia An abnormally low level of red blood cells that can lead to fatigue, shortness of breath, and other symptoms.

aromatase inhibitors Drugs that interfere with the production of estrogen by blocking the substance aromatase.

bisphosphonates A group of drugs that helps prevent loss of calcium from bone, reduce bone pain, strengthen bone, and reduce risk of fractures. They are often used to treat cancer that has spread to bone.

HER2 positive Tumors that grow rapidly because they overproduce a substance called human epidermal growth factor receptor 2 (HER2).

intravenously Delivered through a blood vein.

lymph nodes Structures throughout the body that help filter and destroy bacteria and other toxic substances.

lymph vessels A series of vessels that connect the small, bean-shaped collections of cells called lymph nodes.

metastatic breast cancer Breast cancer that has spread beyond the breast and lymph nodes in the armpit to another part of the body.

neutropenia A low white blood cell count that can increase risk of infection. Neutropenia is a complication of chemotherapy experienced by some patients.

opioids Drugs used to treat severe pain.

receptors On each cell's surface, receptors serve as doorways for specific substances that enter the cell and encourage it to grow and divide.

targeted treatments Treatments that attack cancer cells primarily, sparing normal, healthy tissues. Targeted treatments tend to cause fewer side effects than conventional chemotherapy.

triple-negative breast tumors Tumors that are estrogen-receptor negative, HER2-negative, and progesterone-receptor negative.

vascular endothelial growth factor (VEGF) A substance that plays a critical role in promoting the growth of new blood vessels that feed tumors.

Resources

CancerCare

1-800-813-HOPE (4673)

www.cancercares.org

American Cancer Society

1-800-227-2345

www.cancer.org

People Living With Cancer

(Patient website of the American Society of Clinical Oncology)

www.plwc.org

Cancer Patient Education Network

www.cancerpatienteducation.org

National Coalition for Cancer Survivorship

1-877-622-7937

www.canceradvocacy.org

National Cancer Institute

Cancer Information Service

1-800-422-6237

www.cancer.gov

The Wellness Community

1-888-793-9355

www.thewellnesscommunity.org

Y-ME National Breast Cancer Organization

1-800-221-2141

www.y-me.org

To find out about clinical trials:

Coalition of Cancer Cooperative Groups

www.CancerTrialsHelp.org

National Cancer Institute

www.cancer.gov/clinicaltrials



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