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# Treating Recurrent Metastatic Breast Cancer

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*Learn about:*

- Current treatments
- New medications
- Coping with side effects
- Working with your health care team



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# Treating Recurrent Metastatic Breast Cancer

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# Today, women with recurrent 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 whose metastatic breast cancer returns (is recurrent) have already been treated with chemotherapy or hormonal treatments for their original breast cancer and for metastatic breast cancer. But because these treatments were not successful, the breast cancer cells either returned or continued to grow.

Fortunately, women with recurrent metastatic breast cancer now have more treatment options than ever before. Today, metastatic breast cancer is thought of as a highly treatable condition. And once a woman has a recurrence, the focus of the treatment is on maintaining a long life with as few symptoms as possible—that is, “managing” the cancer as a long-term condition.

## Treatments for Recurrent Metastatic Breast Cancer

Doctors prescribe a variety of treatments for recurrent metastatic breast cancer. The type of treatment used depends upon whether or not the tumor growth is fueled by hormones and where in the body the cancer cells have spread.

## HORMONAL THERAPY

Most breast tumors grow in response to the female hormone estrogen. In women with these types of tumors, drugs that interfere with the production of estrogen or its actions in cancer cells are often effective at treating breast cancer, slowing or stopping its growth. This includes recurrent metastatic breast cancer. These medications prevent estrogen from promoting cancer growth in one of various ways. One of the ways they work is by blocking estrogen **receptors** inside breast cancer cells. When estrogen attaches to these receptors, it fuels the growth of tumors.

One of the newest drugs, called fulvestrant (Faslodex), works by binding to estrogen receptors and changing their shape. This prevents the receptors from working properly, slowing the growth of breast tumors. Fulvestrant also reduces the number of estrogen receptors in cancer cells, which further limits the effects of estrogen in breast cancer. This medication is given in monthly injections.

Other anti-estrogen drugs, such as tamoxifen (Nolvadex and others), also block estrogen receptors in breast cancer cells. Tamoxifen can be taken in pill form.

Medications called **aromatase inhibitors** prevent estrogen from being made in tissues and organs other than the ovaries. As their name implies, these drugs inhibit aromatase, a substance needed to produce estrogen. Examples of aromatase inhibitors include anastrozole (Arimidex), letrozole (Femara), and exemestane (Aromasin). They are effective in postmenopausal women.

Other hormonal medications that interfere with estrogen's ability to promote metastatic breast cancer growth include



fluoxymesterone (Halotestin) and megestrol (Megace). Researchers are developing additional hormonal treatments to block receptors for other hormones such as progesterone that also encourage tumor growth.

## CHEMOTHERAPY

When hormonal treatment is not effective or no longer works, chemotherapy is used. A large number of such medications are available to treat recurrent metastatic breast cancer. Some of the most effective and widely used drugs include capecitabine (Xeloda), which is available in pill form, paclitaxel (Taxol and others), a newer form of paclitaxel (Abraxane), docetaxel



(Taxotere), cyclophosphamide (Cytoxan and others), methotrexate (Rheumatrex), fluorouracil (5-FU), doxorubicin (Adriamycin, Doxil, and others), vinorelbine (Navelbine and others), and gemcitabine (Gemzar). Platinum-based drugs—cisplatin (Platinol and others) and carboplatin (Paraplatin and others)—also are used, but more rarely.

Chemotherapy can be used alone or in combination with [targeted treatments](#) (discussed in the next section) to shrink tumors or slow their growth and relieve symptoms. Different chemotherapies may be

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

Ixabepilone (Ixempra) is the first new chemotherapy drug that has been approved in several years by the U. S. Food and Drug Administration (FDA) for the treatment of breast cancer. It is approved for treating women with metastatic cancer that has returned or is no longer responding to other medications.

## TARGETED TREATMENTS

Targeted treatments are drugs that zero in on different 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 primarily, sparing healthy tissues and causing less severe side effects.

There are several targeted treatments that show promise when used to treat recurrent metastatic breast cancer:

**Trastuzumab (Herceptin)** About 20 percent to 25 percent of women with breast cancer have what are called **HER2-positive** tumors. HER2 is a gene that makes a substance, also called HER2, which controls cell division. If a breast cancer cell has too much HER2—that is, if it's HER2-positive—it tends to grow more rapidly. 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)** A new drug, lapatinib, also targets HER2. Lapatinib is unique in that it is small enough to get inside cancer cells and block HER2 signals from that vantage point. In addition, lapatinib blocks HER1, which can also fuel the growth of some breast cancer cells. Lapatinib has been shown to be effective in women whose recurrent metastatic breast cancer continues growing despite treatment with trastuzumab and chemotherapy. Lapatinib is given to these women along with capecitabine, another oral medication. The drug combination is effective at stopping cancer growth and shrinking tumors.

In addition, capecitabine, and perhaps lapatinib, may be better 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. More study is under way with a variety of medications.

**Bevacizumab (Avastin)** Recently, the FDA approved bevacizumab, in combination with the drug paclitaxel, for women who have not received chemotherapy for metastatic HER2-negative breast cancer. This combination controls metastatic breast cancer growth better, and for longer periods, than treatment with paclitaxel alone. Bevacizumab has proven effective against a number of cancers and was previously approved as a treatment for metastatic colorectal cancer and non-small cell lung cancer. Clinical trials are now under way to study its use in a number of other cancers, including kidney, pancreatic, and ovarian.

Bevacizumab works by stopping the growth of new blood vessels in tumors. Specifically, it 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.

## TREATMENTS IN THE PIPELINE

The following medications are currently being studied in clinical trials for metastatic breast cancer:

- **Eribulin mesylate (E7389)** This medication is being studied in clinical trials in women with locally advanced or metastatic breast cancer whose tumors have continued to grow despite treatment with other chemotherapy. Eribulin mesylate also is being studied in other tumors, including non-small cell lung cancer, soft-tissue sarcoma, and prostate cancer. It works by interfering with cell mechanisms and helping to block cell growth.
- **Sunitinib (Sutent) and sorafenib (Nexavar)** These targeted oral medications are already approved for treating

## The Importance of Clinical Trials

There's no question that clinical trials have led to advances in cancer treatment, offering more promise for women with recurrent metastatic breast cancer. Clinical trials are the standard by which we measure the worth of new treatments and quality of life as patients go through those treatments. For this reason, doctors and researchers urge patients 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, 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.
- No patient receives a placebo (or look-alike medication with no active ingredient) if there is a standard treatment available. Most clinical trials are designed to test a new treatment against a standard treatment to find out whether the new treatment has any more benefit than the standard treatment.
- You can stop taking part in a clinical trial at any time for any reason.

liver, kidney, and digestive system cancers. They block the growth of new blood vessels in tumors.

- **Pazopanib** and **axitinib** In recent clinical trials these targeted treatments have shown some benefit for breast cancer patients whose tumors have returned or continued to grow after receiving multiple treatments.
- **Dasatinib (Sprycel)** This targeted treatment works by blocking the action of an abnormal protein that signals cancer cells to multiply. In so doing, it helps stop the spread of cancer cells. Dasatinib is being tested in women with recurrent metastatic breast cancer that has spread to the bones.

- **Trabectedin (Yondelis)** Early research has shown that trabectedin is somewhat active against **triple-negative breast tumors**. The drug works by altering the genetic material in cancer cells, making it more difficult for them to thrive.
- **PARP inhibitors** These new medications 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 treatments such as chemotherapy.
- **Notch inhibitors** This class of drugs blocks substances in the cell that may promote the growth of triple-negative breast tumors.

## Managing Side Effects

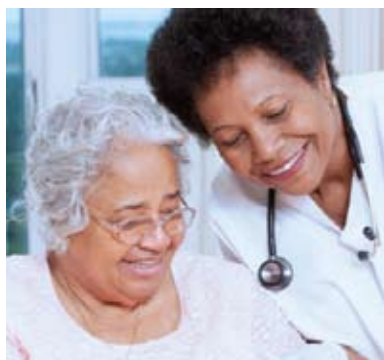
Recurrent metastatic breast cancer and its treatments can cause a number of side effects. *A key to managing these side effects is to be aware of them and to discuss them with your health care team.* Some common side effects include:

- **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 concerns raised by cancer. If your doctor doesn't ask you about fatigue, be sure to bring it up. That's the best way to find and treat the cause. Oncology social workers and nurses can help you cope with any psychological concerns that may be affecting your quality of life.
- **Pain** Pain can be caused by the tumor itself, pressing on a nerve or organ. When that is the case, chemotherapy, radiation, or surgery can be used alone or in combination to help relieve pain. Pain can also result from some cancer treatments. When that is the case, the dose or schedule of chemotherapy, for instance, may be changed. 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, including pain specialists, can help relieve pain with medications. 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 reduce the stress of pain.

- **Weakened bones** Many women with recurrent metastatic breast cancer that has spread to the bones are given

medications known as **bisphosphonates**, which stop bone cells called osteoclasts from breaking down the bone. These drugs strengthen bone and can substantially reduce the need for radiation treatment and can decrease the risk of fractures. The



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

- **Nausea, vomiting, and other digestive tract symptoms** As with other side effects of cancer treatment, nausea, vomiting, diarrhea, constipation, and mouth sores can affect your quality of life. But there are many effective treatments that can prevent or ease these symptoms.
- **Low white blood cell counts** When you are undergoing chemotherapy, your white blood cell count may go down, 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 such as filgrastim (Neupogen) and pegfilgrastim (Neulasta) to help increase the white blood cell count. If you develop a fever, which is a sign of infection, it's important that you tell your health care team immediately so that you can get proper treatment.

- **Memory lapses** Difficulty with memory or an inability to think clearly are commonly experienced by women with recurrent metastatic breast cancer. These symptoms often are referred to as “chemobrain.” A number of conditions that may lead to chemobrain can be treated effectively, including low blood cell counts, depression, anxiety, and fatigue. Because some medications can make you less alert, simply changing a prescription may make a difference. There also are a number of practical tips that your health care team can suggest to help you cope with changes in memory or thinking, such as being aware of distractions and breaking tasks into smaller, more manageable parts.

## Coping with Recurrent Metastatic Breast Cancer

When metastatic breast cancer recurs, you're faced with a new series of questions and concerns. The choices you make about treatment will have a major effect on you and your family. It may be difficult to know whether the choices you are making are the right ones. Learning to deal with uncertainty is probably the most difficult part of coping with recurrent metastatic breast cancer. The following tips can help:

- **Get a second opinion.** It's always a good idea to get a second opinion, so that you have as much information as possible to help you make treatment decisions. Second opinions add to the information you have from your health care team and can give you a new perspective. You should also feel free to review your care periodically with your doctor. You may wish to include a discussion about treatment side effects and any concerns you may have about quality of life.

- **Focus on wellness.** Eat well, stay as physically active as possible, and do whatever else you can to stay as healthy as possible during treatment.
- **Find ways to help you relax.** Take time to do the things that relax you, such as reading, listening to music, meditating, practicing yoga, or simply resting during the day.
- **Ask for help.** Turn to your health care team, your family and your friends for help. Remember that it's not a sign of weakness to need extra emotional support or practical help at this time.
- **If pain management is an issue, get help.** Having pain under control can make a huge difference in your quality of life.
- **Express your feelings.** It's normal to experience a wide range of emotions at this time, including sadness, anger, frustration, and fear. Many people find it helpful to talk about these feelings with a family member, friend, or member of the health care team. CancerCare® provides free individual counseling from professional oncology social workers who can help you find ways to cope with difficult emotions and practical challenges raised by cancer.
- **Consider a support group.** Studies have shown that support groups can improve quality of life and reduce feelings of isolation in women with recurrent metastatic breast cancer. They offer reassurance, education, and a sense of community. CancerCare offers free face-to-face, telephone, and online support groups led by professional oncology social workers.



To learn more about how CancerCare can help you cope with recurrent metastatic breast cancer, call us at 1-800-813-HOPE (4673) or visit [www.cancercare.org](http://www.cancercare.org).

# Frequently Asked Questions

**Q** I've been taking a maintenance dose of Herceptin for three years. Is there a point at which I could consider coming off the drug?

**A** There is no hard-and-fast rule. It's really a decision made between the patient and her health care team. Some women choose to go off all therapy after three years on trastuzumab (Herceptin) if there is no evidence that the cancer is growing. These women are monitored closely with scans and blood tests and can restart the medication at any time. If a woman taking trastuzumab still has an actively growing tumor, another option is to switch to a different HER2-targeted treatment such as lapatinib (Tykerb) or to add chemotherapy to trastuzumab.

**Q** If a woman with HER2-positive cancer has tried standard treatments (trastuzumab and lapatinib) and they no longer work, are there any other treatment options?

**A** Currently, several other drugs that target HER2 are being studied in clinical trials. For example, when combined with trastuzumab, a new medication called pertuzumab (Omnitarg) has been shown to slow the growth of tumors that no longer respond to treatment with trastuzumab alone. Another new drug currently being studied is T-DM1, which combines trastuzumab with a strong anti-cancer medication called DM1.

T-DM1 appears to slow the growth of recurrent metastatic breast cancer that no longer responds to trastuzumab alone.

In addition, women who have already received trastuzumab and lapatinib may respond to treatment with the targeted drug bevacizumab (Avastin) or to a chemotherapy or combination that is different from the ones they've tried before.

**Q** I developed a heart condition related to treatment with chemotherapy and trastuzumab, so I've stopped using all medications. Is there anything else I can do to treat my recurrent metastatic breast cancer?

**A** We know that trastuzumab can cause heart problems, particularly in women who have already been treated with chemotherapy. Once these treatments are stopped, some of the damage to the heart may be reversed. If your heart function returns to normal, treatment with lapatinib is often an option. In any case, it is vital that your oncologist communicate with a cardiologist to design the best treatment plan for you. These two specialists should work together to coordinate your care. It also may be a good time to consider getting a second opinion about your cancer treatment.

# Glossary

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

**aromatase inhibitors** Drugs that interfere with the production of estrogen in postmenopausal women by blocking the substance known as aromatase. Aromatase is used by tissues and organs other than the ovaries to produce estrogen. Estrogen stimulates the growth of breast cancer cells.

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

**HER2-positive** HER2 is a gene that makes a substance, also called HER2, which controls cell division. If a breast cancer cell has too much HER2—that is, if it's HER2-positive—it tends to grow more rapidly.

**intravenous** Delivered through a blood vein.

**lymph nodes** Small, bean-shaped structures that act as filtering stations to remove waste and fluids and help fight infection. When invaded by cancer cells, lymph nodes are a point from which tumors can spread throughout the body.

**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 the risk of infection. Neutropenia is a complication of chemotherapy experienced by some patients.

**receptors** Receptors serve as doors for specific substances (in this case, in cancer cells) that encourage them to grow and divide.

**targeted treatments** Treatments that attack cancer cells primarily, sparing normal, healthy tissues. Targeted treatments tend to cause less severe side effects than standard chemotherapy.

**triple-negative breast tumors** Tumors that are estrogen-receptor negative, HER2-negative, and progesterone-receptor negative. These tumors tend to be more aggressive and are likely to recur.

**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

Services: 1-800-813-HOPE (4673)  
[www.cancercares.org](http://www.cancercares.org)

## AdvancedBC.org

[www.advancedbc.org](http://www.advancedbc.org)

## American Cancer Society

1-800-227-2345  
[www.cancer.org](http://www.cancer.org)

## Breast Cancer Network of Strength

1-800-221-2141  
[www.networkofstrength.org](http://www.networkofstrength.org)

## Breast Cancer Research Foundation

1-866-346-3228  
[www.bcrfcure.org](http://www.bcrfcure.org)

## Cancer.Net

(Patient information from the American Society of Clinical Oncology)  
[www.cancer.net](http://www.cancer.net)

## Living Beyond Breast Cancer

1-888-753-5222  
[www.lbbc.org](http://www.lbbc.org)

## Men Against Breast Cancer

1-866-547-6222  
[www.menagainstbreastcancer.org](http://www.menagainstbreastcancer.org)

## Metastatic Breast Cancer Network

1-888-500-0370  
[www.mbcnetwork.org](http://www.mbcnetwork.org)

## National Coalition for Cancer Survivorship

1-888-650-9127  
[www.canceradvocacy.org](http://www.canceradvocacy.org)

## National Cancer Institute Cancer Information Service

1-800-422-6237  
[www.cancer.gov](http://www.cancer.gov)

## The Wellness Community

1-888-793-9355  
[www.thewellnesscommunity.org](http://www.thewellnesscommunity.org)

## *To find out about clinical trials:*

Coalition of National Cancer Cooperative Groups  
[www.CancerTrialsHelp.org](http://www.CancerTrialsHelp.org)

National Cancer Institute  
[www.cancer.gov/clinicaltrials](http://www.cancer.gov/clinicaltrials)



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- Education and practical help
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