CANCERCARE® CONNECT BOOKLET SERIES

TREATMENT UPDATE

# Breast Cancer

## With Highlights From the 2013 San Antonio Breast Cancer Symposium

CANCERcare®
WWW.CANCERCARE.ORG


The Cancer*Care* Connect Booklet Series offers up-to-date, easy-to-read information on the latest treatments, managing side effects and coping with cancer.

To order free copies of this booklet, please use the online order form on our website, www.cancercare.org.

---

Cancer*Care*® helps individuals and families better cope with and manage the emotional and practical challenges arising from cancer. Our services—for patients, survivors, loved ones, caregivers and the bereaved—include counseling and support groups, educational publications and workshops and financial assistance. All of our services are provided by professional oncology social workers and are offered completely free of charge. Cancer*Care* is a national nonprofit organization founded in 1944.

Cancer*Care* relies on the generosity of supporters to provide our services completely free of charge to anyone facing a cancer diagnosis. If you have found this resource helpful and wish to donate, please do so online at www.cancercare.org/donate. You may also mail a check, payable to Cancer*Care,* to Cancer*Care,* Attn: Donations, 275 Seventh Avenue, New York, NY 10001. Thank you.

---

**Cancer*Care*®**
**National Office**
**275 Seventh Avenue**
**New York, NY 10001**

**Toll-free** 800-813-HOPE (4673)
**Phone** 212-712-8400
**Fax** 212-712-8495
**Email** info@cancercare.org
**Web** www.cancercare.org

TREATMENT UPDATE

# Breast Cancer

## Table of Contents



## Editors


**Lisa A. Carey, MD**
*The Richardson and Marilyn Jacobs Preyer Distinguished Professor in Breast Cancer Research; Division Chief, Hematology and Oncology, UNC Lineberger Comprehensive Cancer Center; Physician-in-Chief, North Carolina Cancer Hospital*

**Michaela Higgins, MD, MRCPI**
*Assistant Professor of Medicine, Harvard Medical School; Attending Physician, Breast Cancer Program, Massachusetts General Hospital*

**Lisa A. Newman, MD, MPH, FACS**
*Professor of Surgery and Director, Breast Care Center, University of Michigan Comprehensive Cancer Center*

**Kathryn J. Ruddy, MD, MPH**
*Director, Cancer Survivorship, Department of Oncology, Mayo Clinic*

**Carolyn Messner, DSW, MSW**
*Director, Education and Training, CancerCare*

# *For women with breast cancer, the number of treatment options continues to grow.*

**Every year in the United States, about 233,000 women and 2,400 men are diagnosed with breast cancer.** In recent years, the number of effective treatments for breast cancer has increased. Because breast cancer is not just one disease—there are several types, each with its own unique features—doctors are able to tailor treatments. They prescribe specific medicines for specific types of breast cancer.

In this booklet, we talk about the breast cancer treatments now available and new medications in development. We also describe possible treatment side effects and how to prevent and cope with them.

# Determining Tumor Type

**Tests performed on tumor samples give valuable information that helps guide treatment decisions for breast cancer. One test your doctor may perform is a biopsy. For this test, he or she uses a hollow needle to remove a tissue sample from the tumor and examine it under a microscope. Some breast biopsies require surgery.**

Tumor samples can help doctors determine whether the tumor is non-invasive (has not spread outside the milk duct or gland, where breast tumors usually begin) or invasive (has spread outside the duct or gland into nearby breast tissue). The tumor sample also helps identify the tumor's grade, which can be a clue as to whether it is a fast-growing or slow-growing form of breast cancer.

Another important piece of information your doctor may learn from the biopsy is whether the tumor's growth is driven by hormones. This is known as the tumor's hormone receptor status. If the surface of the tumor cell has receptors (doorways) for estrogen or progesterone, cancer growth may be fueled by these female hormones. When these receptors are present, the tumor's growth can be stopped or slowed by one of several hormone therapies available. About 70 percent of breast cancers are estrogen receptor (ER)-positive. Of these cancers, about 65 percent are also progesterone receptor (PR)-positive.

About 20 percent to 25 percent of breast cancers are HER2-positive. These cancer cells have increased amounts of HER2 proteins, which are linked to their growth. HER2-positive breast cancer usually responds well to targeted treatments that block the HER2 receptor. (Targeted treatments are drugs that focus on specific cell mechanisms thought to be

important for cancer cell survival and growth. These drugs tend to cause less severe side effects than chemotherapy.)

Another 15 percent of women with breast cancer have a type called triple-negative. These tumors do not have receptors for estrogen or progesterone and do not have excess HER2 proteins. So certain drugs that work for hormone-positive or HER2-positive tumors are not effective for women with triple-negative breast cancer. However, triple-negative breast cancer often responds well to chemotherapy. Clinical trials are pointing the way to new and even better treatments for triple-negative breast cancer.

# Breast Cancer Treatments

## Surgery

In the past, surgeons thought that mastectomy (full removal of the breast) was the best way to improve the chances that the cancer would not return. But recent studies confirm that mastectomy does not reduce the chances of the tumor coming back, and that for many women, lumpectomy (removal of just the tumor with some surrounding tissue) plus radiation is equally effective. Lumpectomy also has the advantage of offering a better cosmetic result than mastectomy.

Another surgical procedure that has been used to treat breast cancer involves removing the sentinel lymph node in the underarm. (Lymph nodes filter and trap bacteria, viruses and other unwanted substances in the body, so that white blood cells called lymphocytes can then destroy them.) The sentinel lymph node is the first lymph node into which breast cancer cells spread. If the sentinel lymph node is cancer-free, chances are that other, nearby lymph nodes are also unaffected and can be left in place. That's important because removing many lymph nodes from the underarm can lead to lymphedema, a painful swelling of the arm.

In certain patients, even if routine lab tests show that there are cancer cells in the sentinel lymph nodes, removing many nearby lymph nodes is not needed. Studies confirm that these patients can be treated successfully with lumpectomy followed by radiation. Long-term studies also show that the routine lab tests used to look for cancer in the sentinel lymph node give doctors the information they need to make an effective treatment plan. Using more complex tests to search for tiny single-cell amounts of cancer that might be hiding in the sentinel lymph node is not necessary. That's because

finding such small amounts of tumor cells does not seem to affect survival.

Women with early-stage breast cancer who have had their sentinel lymph node removed should talk with their doctor about whether or not they need further treatment.

## Radiation

Radiation to the entire breast has been the standard of care for women who have been treated with lumpectomy. However, whole-breast radiation can damage healthy tissues as well as cancer cells and can create scar tissue and differences in the size and appearance of the breasts. A new study now shows that some women over age 65 who have had a lumpectomy can safely avoid radiation treatment. These women include those who had small, ER-positive breast tumors that had not spread to the lymph nodes; had successful surgery; and received hormone therapy.

The study showed that five years after surgery, there was only a slight difference in the number of women whose cancer returned, whether or not they received radiation. More than 90 percent of women in the study survived at least five years after surgery, whether or not they received radiation.

For women with more advanced-stage cancer, radiation can be used after mastectomy if the tumor was large or if cancer was found in a number of underarm lymph nodes.

## Chemotherapy

For many women, chemotherapy is an important part of treating breast cancer. It works by traveling through a patient's bloodstream to destroy cancer cells. Based on clinical trials over many years, doctors have learned how to more effectively

use these medications either alone or in combination with other treatments. They have refined the doses and schedules of these drugs so that women get the most benefit from treatment with the fewest side effects. New genetic tests of tumors help identify those women who will benefit most from chemotherapy and those who may not need it.

## Hormone Blockers

Doctors generally recommend hormonal therapy for ER- or PR-positive breast cancer. These treatments work in different ways. Some are designed to prevent estrogen or progesterone from attaching to receptors on breast cancer cells. Others are designed to reduce the amount of hormones circulating in the body that attach to estrogen or progesterone receptors. By blocking hormones, these treatments deprive tumor cells of the substances that fuel their growth.

# The Importance of Clinical Trials

**All of the advances that have been made in breast cancer treatment have been the result of clinical trials. These carefully controlled studies are the standard by which we measure the effectiveness of new treatments and their impact on patients' quality of life. Clinical trials also offer an additional treatment option. For these reasons, doctors and researchers urge people with breast cancer to take part in clinical trials.**

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

- People who take part in clinical trials often gain access to (and may be the first to benefit from) new treatments.
- Before you take part in a clinical trial, you will be fully informed about the possible risks and benefits.
- Some studies show that patients get higher quality care simply by taking part in a clinical trial, because most trials require that doctors and nurses watch patients extremely carefully, and this extra attention may be beneficial by itself.
- 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.

Tamoxifen is an estrogen-blocking treatment given to both pre- and postmenopausal women with breast cancer. Taking tamoxifen after surgery for five years reduces by half the chances of the cancer coming back. It also lowers the risk of a new breast cancer developing in the other breast. Some recent

studies show that taking tamoxifen for 10 years can be even more beneficial. For women with metastatic breast cancer, tamoxifen can stop the growth and shrink tumors. It also has been shown to reduce the chance of breast cancer in healthy women at high risk of developing the disease.

Another class of hormonal therapy is aromatase inhibitors (AIs). These medications prevent estrogen from forming in the first place by blocking aromatase, a substance that is important in making the hormone. Before menopause, a woman's ovaries make so much estrogen that AIs are not effective. (Some women with breast cancer who have not yet reached menopause choose surgery as a treatment to remove their ovaries. Your doctor can guide you in making a decision about whether this is the right step for you.)

Although estrogen is no longer produced in the ovaries after menopause, it is still made in small amounts throughout the body: in the adrenal glands (which sit on top of the kidneys and make various hormones and adrenaline) and in muscle, skin, fat and the breast itself. AIs are given to postmenopausal women to reduce the total amount of estrogen produced. Both AIs and tamoxifen are taken by mouth daily in pill form. AIs available in the United States are anastrozole (Arimidex and others), letrozole (Femara and others) and exemestane (Aromasin and others). Taking AIs for five years reduces the chance of cancer coming back in postmenopausal women. These breast cancer survivors can take an AI for five years before or after taking tamoxifen for five years.

According to a new study, anastrozole may prove to be an effective way to prevent breast cancer. For more than a decade, anastrozole has been used to treat ER-positive tumors in postmenopausal women by blocking estrogen from fueling their cancer. In this recent clinical trial, anastrozole was given

to women at high risk of developing breast cancer, based on their family history. These women had two or more blood relatives with breast cancer, a mother or sister who developed breast cancer before the age of 50 or a mother or sister who had breast cancer in both breasts.

Researchers found that the chance of developing breast cancer was reduced by 53 percent in women at high risk who were given anastrozole compared with women at high risk who were not given it. The medication also reduced the number of cancers in other parts of the body.

Anastrozole may become an alternative preventive treatment with perhaps fewer side effects than other anti-hormone drugs such as tamoxifen and raloxifene (Evista and others). Researchers plan to follow, for at least 10 years, the women who took part in the anastrozole study. This will allow doctors to know whether the benefits of anastrozole continue over time.

Another estrogen-blocking drug, fulvestrant (Faslodex), works in a slightly different way: It attaches to estrogen receptors and changes their shape. This prevents the receptors from working properly, which slows the growth of breast cancer cells. Fulvestrant is given as an injection and is only approved for postmenopausal women with metastatic breast cancer whose tumors have not responded well to other hormonal treatments such as tamoxifen.

## Targeted Treatments

Trastuzumab (Herceptin) is one example of a targeted treatment designed for women whose tumor cells are HER2-positive. Since trastuzumab was approved, many women with HER2-positive tumors are surviving much longer.

Another medication, lapatinib (Tykerb), also targets HER2. Lapatinib is able to get inside cancer cells and block HER2 signals from within. Lapatinib has been shown to be effective in women whose HER2-positive breast cancer returned, spread or continued growing despite treatment with trastuzumab and chemotherapy. When medications that target HER2-positive breast cancer such as lapatinib are given along with chemotherapy, such as capecitabine (Xeloda and others), the combination of treatments can be effective at stopping cancer growth and shrinking tumors.

For women whose breast cancer has spread to the brain, it's important to note that lapatinib and capecitabine, both taken in pill form, may be able to travel to brain tissue. Many drugs for breast cancer cannot do that.

Another effective treatment for HER2-positive metastatic breast cancer is pertuzumab (Perjeta). Given through a

vein every three weeks, pertuzumab is used as a first-line (first-time) treatment in combination with trastuzumab and docetaxel (Taxotere and others). This three-drug combination can also be used to treat earlier-stage breast cancers before surgery.

Ado-trastuzumab emtansine (Kadcyla), or T-DM1, is used to treat women with HER2-positive metastatic breast cancer who have already received treatment with trastuzumab and chemotherapy that included a taxane such as paclitaxel (Taxol and others) or docetaxel. T-DM1 combines trastuzumab with monoclonal antibodies. The antibodies zero in on HER2-positive cancer cells and deliver the trastuzumab directly to them. Not only does T-DM1 block the tumor cell growth signals, it also enlists the body's immune system to help destroy the cancer cells.

Everolimus (Afinitor) is a type of targeted treatment that helps stop cancer cells from growing by blocking a specific growth protein in the cells. Everolimus may also stop tumors from developing new blood vessels, which can help limit their growth. In treating breast cancer, this drug seems to help hormone therapy work more effectively, but it may cause increased side effects. A pill taken once a day, everolimus treats advanced hormone receptor-positive, HER2-negative breast cancer in postmenopausal women. This medication is being studied in clinical trials for use in earlier-stage breast cancer and in combination with other treatments.

# Promising New Treatment Approaches: A Report From the 2013 San Antonio Breast Cancer Symposium

**This section presents highlights from the 2013 San Antonio Breast Cancer Symposium, which took place December 10–14 in San Antonio, Texas. The information includes advances in the treatment of breast cancer as well as other promising treatments that researchers continue to study in clinical trials.**

Some of these treatments are still in the earliest phases of research and may not be available to the general public outside of a clinical trial. The information is intended for discussion with your doctor. He or she can let you know if these research findings affect your treatment plan and whether a clinical trial might be right for you.

## HER2-POSITIVE BREAST CANCER

### Combination Treatments With Trastuzumab Before and After Surgery for HER2-Positive Breast Cancer

Adding the targeted treatment trastuzumab to other treatments seems to improve outcomes in women who have HER2-positive breast cancer, according to the results of two clinical trials. The benefits were reported when the combination treatments with trastuzumab were given before and after surgery.

The first study was called the NeoALTTO trial. More than 450 women with HER2-positive breast cancer were given treatment before surgery. (Doctors call this neoadjuvant treatment, which is given to shrink or eliminate a tumor before surgery.) Approximately one-third of these women were given trastuzumab, another third were given a different targeted treatment (lapatinib) and the last third were given both trastuzumab and lapatinib. All of these women also received the chemotherapy drug paclitaxel.

Four years later, patients who had no cancer cells in the breast or underarm after neoadjuvant treatment were about 60 percent less likely to have their cancer return. Side effects such as diarrhea and changes in the levels of liver enzymes were more common in those patients who received lapatinib (alone or with trastuzumab) than in those who received trastuzumab alone.

The second study, called the BETH trial, looked at the use of chemotherapy and trastuzumab after surgery in women with

HER2-positive breast cancer. In this large clinical trial, more than 3,200 women were given either standard chemotherapy with trastuzumab—called TCH (docetaxel, carboplatin and trastuzumab)—or TCH plus bevacizumab.

About three years after treatment, the cancer had not returned in about 92 percent of both groups that received TCH treatment. There seemed to be no benefit to adding bevacizumab to TCH treatment. Researchers also found that the benefits of TCH treatment did not depend on the size of the breast tumor or whether the cancer had spread to the lymph nodes.

### *What Patients Need to Know*

Studies now suggest that treatment with trastuzumab and chemotherapy is a safe and effective way to help certain women with HER2-positive breast cancer to survive longer without their cancer returning. In fact, researchers believe that the results from the BETH study are among the best they have ever seen in the treatment of women with HER2-positive breast cancer. If doctors find no cancer cells in the breast or underarm after treatment, then the chances of long-term benefits are improved. Researchers of both studies plan to follow their patients to see whether the benefits of trastuzumab and chemotherapy continue over time.

## Less Chemotherapy for Small HER2-Positive Breast Tumors

Women who have small HER2-positive breast tumors may do well with less chemotherapy, according to two recent studies. Although further research is needed, these results suggest that, in the future, some women with small breast tumors may safely forgo longer periods of chemotherapy and its side effects.

In the first study, researchers looked at data on patients who had small HER2-positive breast tumors that had not spread to the lymph nodes or had spread to just a few lymph nodes. Five years after treatment with chemotherapy and trastuzumab, 90 percent of the women had survived. Because this treatment was so effective, they could avoid using other HER2-targeted treatments that would cause more side effects.

In the second study, called the APT trial, more than 400 women with HER2-positive breast cancer took part. Their cancer had not spread to the lymph nodes. All of these patients were treated with the chemotherapy drug paclitaxel for 12 weeks (rather than the usual 18 weeks or longer) and trastuzumab for one year (the normal length of treatment with this drug). Nearly 90 percent of these women completed their 12 weeks of treatment.

Three-and-a-half years later, almost 99 percent of the women had survived and were cancer-free. There were few serious side effects with the 12 weeks of treatment.

### *What Patients Need to Know*

Until now, little was known about how best to treat women with small HER2-positive breast tumors. Researchers had thought that women with these smaller tumors might be at higher risk for their cancer coming back than those with HER2-negative breast tumors. The results from the APT trial suggest that many patients with HER2-positive breast tumors may do well with less chemotherapy. This means they can avoid the side effects of more chemotherapy without compromising their survival. Further studies are needed to see which women with small HER2-positive breast tumors can safely be given less chemotherapy.

## Treating HER2-Positive Breast Cancer With the PIK3CA Gene Mutation

Chemotherapy and targeted treatments given before surgery may not be effective for some patients with HER2-positive breast cancer. Breast cancer that has one or more mutations (changes) in the PIK3CA gene seems to resist the benefits of such treatment, so other options are needed.

Researchers looked at more than 500 patients with breast cancer who took part in the GeparSixto clinical trial to see whether the PIK3CA gene mutation affected their tumors' response to treatment before surgery. All of these patients received chemotherapy with paclitaxel and doxorubicin. Then, some of the women were given chemotherapy with carboplatin, and the others were not. Women who had HER2-positive breast cancer also received targeted treatment with trastuzumab and lapatinib.

HER2-positive and hormone receptor-positive breast cancers with one or more mutations in the PIK3CA gene were less likely to respond well to chemotherapy before surgery than breast cancer without this gene mutation (7 percent versus 31 percent). However, there seemed to be no difference in response to treatment with or without the PIK3CA gene mutation in women who had HER2-positive and hormone receptor-negative breast cancer (between 43 percent and 46 percent).

### *What Patients Need to Know*

Mutations in the PIK3CA gene are among the most common genetic changes in women who have breast cancer. These changes are found in about 25 percent of women who have hormone receptor-positive breast cancer and in about 20

percent of those who have HER2-positive breast cancer. These types of breast tumors tend to resist the benefits of chemotherapy and targeted treatments. Researchers will continue to search for more effective treatment options for women with these types of breast cancer.

TRIPLE-NEGATIVE BREAST CANCER

## Carboplatin Before Surgery for Triple-Negative Breast Cancer

Combining the anti-cancer drug carboplatin with standard chemotherapy or with a new drug called veliparib may be effective ways to treat women with triple-negative breast cancer. In fact, these treatments, which shrink or eliminate tumors before surgery, may change the way triple-negative breast cancer is treated in the future.

In one clinical trial, called CALGB 40603, nearly 450 women with triple-negative breast cancer took part. Some of these women received standard chemotherapy treatment, and others received standard chemotherapy treatment plus carboplatin. The standard chemotherapy drugs were paclitaxel, doxorubicin and cyclophosphamide.

Researchers found that the tumor disappeared in more patients given carboplatin than in those given standard chemotherapy alone (60 percent versus 46 percent). However, the women who received carboplatin did have more side effects such as neutropenia (low white blood cell counts) and thrombocytopenia (low levels of platelets). (White blood cells play a key role in fighting infections, and platelets help the blood to clot.)

About 70 women with triple-negative breast cancer took part in another, smaller clinical trial known as the I-SPY 2 study. Some of these women received standard chemotherapy, and the others received both carboplatin and veliparib in addition to standard chemotherapy before surgery. Veliparib belongs to a new class of drugs called PARP inhibitors. (These drugs block an enzyme that cancer cells use to repair themselves when damaged.) Again, the standard chemotherapy drugs in this study were paclitaxel, doxorubicin and cyclophosphamide.

Of the 115 patients evaluated so far, the tumor disappeared in 52 percent of those who received carboplatin plus veliparib before chemotherapy, compared with 26 percent of those who received standard chemotherapy alone. The side effects of carboplatin plus veliparib were similar to those seen with carboplatin alone in the CALGB study.

### *What Patients Need to Know*

Researchers are encouraged by the early results with these new treatments containing carboplatin for women with triple-negative breast cancer. They plan to study further the use of carboplatin before chemotherapy versus carboplatin plus veliparib before chemotherapy to find out which patients would benefit most from these treatments. Larger clinical trials with more women taking part should also show whether these promising treatments can help women with triple-negative breast cancer to survive longer without their cancer returning.

METASTATIC BREAST CANCER

## Surgery for Metastatic Breast Cancer

Breast surgery probably does not help most women with metastatic breast cancer to survive longer, according to the results of two international clinical trials. In fact, some researchers now think that many women with metastatic breast cancer may have better outcomes with newer targeted treatments.

The first clinical trial, which was performed in India, included 350 women with metastatic breast cancer whose cancer responded to chemotherapy. Some of these patients had surgery—either lumpectomy or mastectomy with removal of lymph nodes. The others did not have surgery. Both groups received hormone therapy.

Researchers found that the women who had surgery did not survive longer than those who did not. The researchers also did not seem to identify any group of patients with advanced breast cancer who might be likely to benefit from surgery.

In the second clinical trial, nearly 300 women in Turkey were treated for metastatic breast cancer. About half of these patients had surgery and then received the targeted treatment trastuzumab if they had HER2-positive tumors. The others did not have surgery.

Again, as in the first study, there did not seem to be a benefit in terms of survival for those who had surgery. Four-and-a-half years after treatment, 35 percent of those who had surgery had survived, compared with 31 percent of those who did not have surgery. However, for women with breast cancer that had spread to the bone, those who had surgery survived about seven months longer than those who did not have surgery.

### *What Patients Need to Know*

The results of these international clinical trials are making doctors lean away from the use of surgery for women with metastatic breast cancer, especially given the success of some of the new targeted treatments now available. Other clinical trials now underway in the United States will help doctors decide whether surgery is right for certain patients with metastatic breast cancer, such as those whose cancer is not responding to medication.

## Ramucirumab for HER2-Negative Metastatic Breast Cancer

A new drug called ramucirumab did not seem to stop cancer from growing in women with HER2-negative metastatic breast cancer. However, some women's breast tumors did seem to respond to treatment with ramucirumab. So researchers plan to continue to study it to find out whether certain women with advanced breast cancer might benefit.

More than 1,100 patients with HER2-negative metastatic breast cancer took part in an international clinical trial. They had not previously received chemotherapy for their metastatic cancer. Two-thirds of these women received ramucirumab plus the standard chemotherapy drug docetaxel. The other patients were given docetaxel alone. About 75 percent of the women in this study had hormone receptor-positive breast tumors.

Nearly one-and-a-half years after treatment, ramucirumab did not appear to have a significant effect on the growth of cancer. Patients who received ramucirumab plus docetaxel survived about as long as those who received docetaxel alone (about 27 months). However, the tumors did shrink in about 45 percent of the women treated with ramucirumab, compared with about 38 percent of those who did not receive this drug.

### *What Patients Need to Know*

Although researchers are always optimistic that new treatments will improve outcomes for women with metastatic breast cancer, sometimes the standard treatment remains the most effective treatment. More research is needed to figure out whether certain women with advanced breast cancer might benefit from drugs such as ramucirumab.

## Letrozole Plus Dasatinib for Metastatic Breast Cancer

In a clinical trial, adding the targeted treatment dasatinib (Sprycel) to the hormone blocker letrozole seemed to double the time it took for cancer to continue growing in women with hormone receptor-positive, HER2-negative metastatic breast cancer. In all, 120 postmenopausal women with this type of breast cancer took part. Approximately half of them received letrozole, and the others received letrozole plus dasatinib.

Researchers discovered that it took twice as long for the cancer to continue growing in the women who were treated with the combination of letrozole and dasatinib than in those who were treated with letrozole alone (20 months versus 10 months). Although the women given the combination treatment had more side effects such as fatigue, nausea and anemia (low levels of red blood cells), none of these symptoms was reported to be severe.

### *What Patients Need to Know*

Researchers are excited by these promising results with letrozole plus dasatinib. One of the ways dasatinib works is by blocking the activity of a protein called Src, which seems to be involved in the spread of breast cancer to bones. It's important to remember that this is a small study from an early stage of research. As this new combination treatment is studied further in more women with breast cancer, doctors should learn which patients are most likely to benefit. Dasatinib is currently approved by the U.S. Food and Drug Administration to treat certain types of leukemia (blood cancer); letrozole is approved to treat hormone receptor-positive breast cancer in postmenopausal women.

PREDICTING OUTCOMES

## Circulating Tumor Cells in Early-Stage Breast Cancer

One of the new ways that researchers are trying to predict how women with breast cancer will respond to treatment is by measuring circulating tumor cells (CTCs). A breast tumor can shed cancer cells into the blood, and these CTCs can be detected with a simple blood test. Doctors often use this test to track the presence of breast cancer and how well it may be responding to treatment.

A recent study showed that women with early-stage breast cancer who have no CTCs in their blood have an advantage in terms of survival and rate of tumor growth. Nearly 3,200 patients from five U.S. cancer centers were included in this study. Researchers found at least one CTC in about 20 percent of the patients. This small group of women who had at least one CTC did not survive as long as those women with no CTCs in their blood. It also took longer for the cancer to continue growing in those who did not have these tumor cells in their blood. Women with CTCs in their blood tended to have larger tumors and tumors that had spread to the lymph nodes in the underarm.

### *What Patients Need to Know*

The presence of CTCs in the blood has been used to help doctors predict outcomes in patients with metastatic breast cancer (cancer that has spread beyond the breast and lymph nodes in the underarm to other parts of the body). Now the researchers of this study believe that CTCs in the blood may

also be used to predict long-term outcomes for women with early-stage breast cancer.

## Circulating Tumor Cells in Metastatic Breast Cancer

Although measuring CTCs may help predict outcomes in some women with breast cancer, testing for CTCs in the blood may not be a good way to help doctors decide when to switch chemotherapy treatments. That is the finding of a study called the SWOG S0500 clinical trial.

More than 600 women with metastatic breast cancer who were starting chemotherapy took part in this study. They fell into three treatment groups:

- Those who had an increased number of CTCs in their blood at the start of treatment—and after 21 days of treatment—either continued on their current chemotherapy or switched to another type of chemotherapy.
- Those who had an increased number of CTCs in their blood at the start of treatment—but not after 21 days of treatment—remained on their initial chemotherapy.
- Those who did not have an increased number of CTCs in their blood continued to be tested but did not receive any further treatment.

Researchers found that about half of the patients started the clinical trial with an increased number of CTCs in their blood. Of the nearly 300 women who completed the study, 43 percent of them continued to have increased numbers of CTCs after the first 21 days of treatment. For women who had increased numbers of CTCs in their blood after the first chemotherapy treatment, switching to different chemotherapy did not seem to help them survive longer.

### *What Patients Need to Know*

CTCs are found in about 75 percent of patients with metastatic breast cancer. Researchers know that an increase in the number of CTCs may mean a patient's cancer is not responding to treatment; a decrease in the number of CTCs may mean the cancer is responding to treatment. So doctors had hoped that, if the first treatment was followed by an increase in CTCs, switching to a new chemotherapy would improve the chances of success—and avoid the side effects of a drug that might not be working. But that did not seem to work. However, researchers will continue to study CTCs as well as other possible indicators in the hope that they can help doctors predict which treatments will work best for women with metastatic breast cancer.

IMPROVING QUALITY OF LIFE

## Exercise for Joint Pain

Regular physical exercise seems to relieve joint pain in postmenopausal women with breast cancer who are being treated with the class of hormone therapies known as AIs (see pages 9 and 10). However, taking these effective anti-cancer drugs may cause arthritis-like symptoms that affect the muscles, bones and nerves.

In the HOPE trial, more than 720 women were given AIs. Of these patients, 121 took part in a year-long study to see whether exercise might improve their joint pain. About 60 patients exercised regularly, and the others did not. Their physical activity included 150 minutes of moderate-intensity aerobic exercise per week and supervised resistance-exercise sessions twice a week.

For those patients who exercised regularly for 12 months, pain scores decreased by 20 percent, compared with 3 percent for those who did not exercise regularly. The severity of the pain also decreased with exercise. In addition, routine exercise helped the women lose weight and improve their overall heart and lung fitness.

### *What Patients Need to Know*

Approximately 50 percent of women with breast cancer who are treated with an AI experience joint pain. This is one of the most common reasons why these women stop taking their medication. Researchers hope further studies will show that regular exercise helps women with breast cancer who are taking an AI remain on their treatment and improves their long-term outcomes.

## Bone-Strengthening Drugs for Postmenopausal Women With Early-Stage Breast Cancer

Not only do bone-strengthening bisphosphonate drugs prevent bone thinning, it now seems they may also reduce the chances of cancer recurrence (return) in postmenopausal women with early-stage breast cancer, according to the results of a new study. However, the benefits in reducing the recurrence of cancer were not seen in premenopausal women with early-stage breast cancer.

Researchers collected information on the breast cancer experience of more than 17,000 women from nearly 40 different clinical trials to learn more about the benefits of bisphosphonates. Overall, there was no major decrease in the risk of breast cancer recurrence related to the use of bisphosphonates.

But when researchers looked closely at the 10,540 postmenopausal women in the study, there was a benefit to taking bisphosphonates in terms of reducing the chance of their breast cancer returning. These benefits were seen regardless of whether the women had reached menopause naturally with age or as a result of taking medication to stop the function of their ovaries.

Furthermore, in the postmenopausal patients who were given bisphosphonates, about one-third fewer women had breast cancer spread to their bones. However, again, there appeared to be no such benefit in premenopausal women.

Bisphosphonate drugs are widely used to effectively treat osteoporosis, a condition in which bones become fragile and more likely to break. These bone-strengthening drugs include alendronate (Fosamax and others), ibandronate (Boniva and others) and zoledronic acid (Zometa and others). (See pages 33 and 35 for more information on treating bone loss.)

### *What Patients Need to Know*

Doctors have not been sure whether the use of bisphosphonates could prevent recurrence of early-stage breast cancer. The results of several clinical trials have been mixed, with some showing a benefit, and others not showing a benefit. Now, with the results of this large study, it seems that bisphosphonates may in fact prevent the spread of breast cancer to the bones in postmenopausal women and help them to survive longer. On the other hand, for premenopausal women, bisphosphonates do not seem to improve outcomes, so researchers will continue to search for better treatment options for this group of patients.

# Treatment Side Effects

**Sometimes, side effects from medications can make it challenging to cope with cancer. Side effects can even delay or stop treatment. A key to managing side effects is to be aware of them and report them to your health care team when they arise. Your health care team can help prevent and reduce the side effects of breast cancer treatment, which can include:**

**Nausea and vomiting.** With proper care, your doctor can help manage this common side effect of chemotherapy. Talk with your doctor about anti-nausea medications to ease or prevent symptoms. There are also a number of things you can do on your own:

- Rinse your mouth often to get rid of any bad taste.
- Distract yourself with music, television or other activities you enjoy.
- Wear loose-fitting clothing that doesn't bind or add stress to your body.
- Avoid strongly scented foods, which can bring on nausea.
- An hour or so after vomiting, try taking small sips of fluid or sucking on ice chips to help settle your stomach.

**Diarrhea** is defined as two or more loose stools per day. It may be caused by some types of chemotherapy or targeted treatments. Be sure to:

- Drink plenty of fluids, including Gatorade or Pedialyte. Make sure your doctor or nurse knows about the problem you are having with diarrhea.
- Choose high-protein foods such as lean meat, fish or

poultry instead of fatty foods. Eat vegetables cooked instead of raw. Ask your doctor to refer you to a registered dietitian for more information on good nutrition.

- Use anti-diarrheal medicine only if you need it. Talk with your health care team before you use any over-the-counter or prescription medicines.

**Mouth sores** inside the mouth and on the lining of the throat and digestive tract can result from radiation and some types of chemotherapy. Called mucositis, this side effect can be serious. Once treatment ends, the mouth sores do disappear. But before they fade, it's important that you work closely with your health care team to manage this side effect. A few things you can do on your own:

- Soothe mouth pain with ice chips or ice pops, over-the-counter pain relievers or Gelclair, a prescription oral gel designed to coat and protect sensitive areas in the mouth.

- Take care of your mouth and keep it clean. If toothpaste irritates your mouth, use a mixture of one-half teaspoon of salt with four cups of water instead.
- Gargle with one quart of plain water, one-half teaspoon of salt and one-half teaspoon of baking soda.
- Drink plenty of fluids.

**Constipation** is defined as fewer than three bowel movements a week (although fewer than four or five may be a reduced number for some people). Prescription pain medicines may be the biggest cause of constipation for women with breast cancer. Talk with your doctor about using over-the-counter stool softeners or gentle stimulating laxatives. The best thing to do is to prevent constipation. Among the steps you can take yourself:

- Eat plenty of dietary fiber—grains, beans and vegetables such as cauliflower or broccoli.
- Drink plenty of fluids.
- Make light exercise a part of your everyday schedule.

**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 medication and, if needed, blood transfusions.
- Consult with a registered dietitian about changing your diet.
- Do light exercises, whenever possible. Moderate activity such as walking can help you feel better and increase your energy.

**Memory lapses.** After chemotherapy, some people have difficulty concentrating or thinking clearly. If you experience what is often called chemobrain, ask your doctor about seeing a neuropsychologist. Studies show that feeling tired or anxious even before treatment may make it more challenging to focus. Treating such symptoms before chemotherapy may improve mental function during treatment.

There are a number of things you can do to cope with these symptoms. Many of these techniques are used every day by people who want to increase the power of their typical aging brain:

- Keep a diary or a log to track how your memory lapses affect your daily routine.
- Make lists. Carry a pad with you and write down the things you need to do.
- Organize your environment. Keep things in familiar places so you'll remember where you put them. To help stay focused, work, read and do your thinking in an uncluttered, peaceful environment.
- Repeat information aloud after someone gives it to you. Spoken cues give your memory an extra boost.
- Keep your mind active. Do crossword puzzles and word games, or go to a lecture on a subject that interests you.
- Exercise, eat well and get plenty of rest and sleep to help keep your memory working at its best.

**Low white blood cell counts.** Chemotherapy may lead to low white blood cell counts, a condition called neutropenia. White blood cells play a key role in fighting infections. A reduced number of these cells increases your risk of infection. Your doctor can prescribe medication designed to help increase white blood cell counts. If you develop a fever, which is a sign

of infection, let your health care team know immediately so you can get proper treatment.

**Bone loss.** Both hormonal therapies and chemotherapy can cause bone loss, which increases a woman's risk for osteoporosis—thinning bones that are more likely to break. When cancer spreads to the bone, it can also weaken bone and lead to fractures. Talk with your health care team about how exercise and changes in your diet may help keep your bones healthy.

It's also important to talk to your doctor about the medications available for bone health. There are three different classes of drugs, and each acts differently:

- Bisphosphonates such as zoledronic acid slow the process by which bone wears away and breaks down.
- RANK ligand inhibitors block a factor in bone development known as RANK ligand, which stimulates cells that break bone down. By blocking RANK ligand,

# Your Support Team

**When you are diagnosed with breast cancer, you're faced with a series of choices that will have a major effect on your life. Your health care team, family members and friends will likely be an invaluable source of support at this time. You can also turn to these resources:**

**Oncology social workers** provide emotional support for people with breast cancer and their loved ones. These professionals can help you cope with the challenges of a breast cancer diagnosis and guide you to resources. Cancer*Care*® offers free counseling from professional oncology social workers who understand the challenges faced by people with cancer and their caregivers. We can work with you one-on-one to develop strategies for coping with treatment and its side effects.

Oncology social workers can also help you communicate with your doctor and other members of your medical care team about the health care issues that are important to you.

**Support groups** provide a caring environment in which you can share your concerns with others in similar circumstances. Support group members come together to help one another, providing insights and suggestions on ways to cope. At Cancer*Care,* people with breast cancer and their families can participate in support groups in person, online or on the telephone.

**Financial help** is offered by a number of organizations to help with cancer-related expenses such as transportation to treatment, child care or home care.

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

these drugs increase bone density and strength. So far, the only drug approved in this class is denosumab (Xgeva), which has been shown to be less toxic and cause fewer kidney problems than zoledronic acid.

- SERMs (selective estrogen receptor modulators) are believed to slow the breakdown and removal of old bone. Examples of SERMs are raloxifene, tamoxifen and toremifene (Fareston).

**Hot flashes.** Breast cancer treatments can lead to menopausal symptoms such as hot flashes and night sweats. They also can lead to vaginal dryness and a lowered sex drive. If you are experiencing these side effects, speak with your doctor about ways to cope with them. There are a number of things you can do:

- Identify the triggers for hot flashes. For many women, stress, a hot shower, caffeine or spicy foods set off a hot flash.
- Change your lifestyle habits to cope with the triggers. That may mean doing exercise, using relaxation techniques or changing your diet.
- Dress in layers and keep ice water handy. Wear pajamas and use sheets made of cotton rather than synthetic material.
- Take a cool shower before going to bed.
- Try a mild medication such as acetaminophen (Tylenol and others).
- For vaginal dryness, try using lubricants and moisturizers such as Astroglide, K-Y or Replens. Talk to your doctor about whether other prescription medicines are safe to use (such as hormone creams or suppositories—

medicines inserted into the vagina). Your health care team can also advise you on regaining the desire for sex. (You may wish to ask for a referral to a health care professional who specializes in these issues.) It's important to keep an open dialog with your intimate partner. Vaginal dryness can make sexual intercourse uncomfortable, but together you can find other ways to please one another.

**Infertility.** Young women with breast cancer generally receive rigorous treatment, including radiation and chemotherapy after lumpectomy. Many of these women may not have started or finished expanding their families, so preserving their fertility (ability to conceive a child) plays a large part in their treatment decisions. If you are concerned about your ability to have children after treatment, you can take these steps:

- Discuss treatment plans with all members of your health care team.
- Consider consulting with a specialist in reproductive medicine, who can help weigh the benefits and risks of a given treatment.
- Ask about newer options for preserving fertility such as oocyte cryopreservation—where a woman's eggs can be removed, frozen and stored for later use. Some fertility-preserving alternatives may be used before a woman starts chemotherapy.

# Communicating With Your Health Care Team

**In working with your team of specialists, it's important that you feel comfortable talking about any topic related to your diagnosis and treatment. Some questions to ask your health care team include:**

**What are the goals of treatment?** For example, if both chemotherapy and surgery are recommended, what are the pros and cons of receiving chemotherapy before surgery versus after surgery?

**What are the possible side effects of treatment?** Talk with members of your health care team about how to manage and prevent treatment side effects to improve your quality of life. Ask them: Is the standard of care right for me? Should I

consider enrolling in a clinical trial? Who do you recommend if I want to get a second opinion? No member of the team should mind that an individual seeks a second opinion if she desires one. Often, second opinions offer more insight into the recommendations of your health care team.

**Should I consider a genetic test?** In families where there is a clear genetic pattern of breast cancer, genetic testing should be discussed at the time of diagnosis. This includes families where there are a number of women affected by breast or ovarian cancer at young ages. The results could affect treatment decisions and may provide important information for other family members.

Some people don't know enough details about their family history to see a genetic pattern of breast cancer. But even if you don't know how many relatives had cancer and at what age, certain hereditary backgrounds can provide a clue. For example, women of Ashkenazi Jewish descent are more likely to carry mutations (changes) in the BRCA1 gene or BRCA2 gene that may place them at higher risk for breast cancer.

If you were diagnosed with breast cancer before the age of 50, your doctor may recommend genetic testing, even without a family history. To learn more about genetic testing, talk with your doctor.

**What about fertility?** Before beginning treatment, younger women who want to start a family or expand their family should speak with their doctor to discuss how treatment may affect fertility. They may also wish to ask for a referral to a reproductive endocrinologist or fertility specialist to discuss options for fertility preservation. (See page 36 for more information on preserving fertility.)

# Frequently Asked Questions

**Q. Is there any evidence that staying on aromatase inhibitors longer than five years or switching drugs after five years and continuing with a second course of treatment is beneficial in reducing the risk for a return of breast cancer?**

A. Currently, there is no evidence that more than five years of taking aromatase inhibitors in early-stage breast cancer is beneficial. But ongoing clinical trials are studying the effect of using these medications for longer periods. With tamoxifen, studies have shown that taking the drug for 10 years rather than five appears to more effectively reduce the recurrence (return) of breast cancer and increase survival somewhat. So, researchers want to explore the potential benefits and side effects of longer use of aromatase inhibitors. Although researchers do not have enough information on the effect of switching from an aromatase inhibitor to tamoxifen, they do know that after taking tamoxifen for five years, switching to an aromatase inhibitor can be beneficial. Future clinical trials will shed more light on the long-term effects of aromatase inhibitors in breast cancer survivors.

**Q. Is there a blood test that checks for complete remission (a decrease in or disappearance of signs and symptoms of cancer) of breast cancer?**

A. Doctors sometimes use a tumor marker called CA15-3 to monitor metastatic breast cancer. (Markers are substances found in tissue, blood or other body fluids that may be a sign of cancer.) But CA15-3 is of limited use because

it doesn't accurately reflect the status of cancer in all patients. However, a blood test that tells us whether cancer cells have disappeared from the body is something we continue to look for.

Two promising techniques, still being studied in clinical trials, may be useful in the near future. One is the detection of circulating tumor cells (see pages 23 to 26). The other is the detection of the DNA (genetic material) of circulating tumor cells, or ctDNA.

# Resources

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

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

**Cancer.Net**
Patient information from the American Society of Clinical Oncology
888-651-3038
www.cancer.net

**Cancer Support Community**
888-793-9355
www.cancersupportcommunity.org

**Living Beyond Breast Cancer**
855-807-6386
www.lbbc.org

**National Cancer Institute**
800-422-6237
www.cancer.gov

**Susan G. Komen for the Cure**
877-465-6636
www.komen.org

**Triple Negative Breast Cancer Foundation**
877-880-8622
www.tnbcfoundation.org

## CLINICAL TRIALS WEBSITES

**Coalition of Cancer Cooperative Groups**
877-227-8451
www.CancerTrialsHelp.org

**EmergingMed**
877-601-8601
www.emergingmed.com

**National Cancer Institute**
www.cancer.gov/clinicaltrials

This booklet has been made possible by educational donations provided by Amgen; Celgene; Genentech, A Member of the Roche Group; and Novartis Oncology; and a contribution from Lilly USA, LLC.

CANCERcare®

*for Help and Hope, visit or call:*

**WWW.CANCERCARE.ORG**

**800-813-HOPE (4673)**