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TREATMENT UPDATE

Breast Cancer

With Advances in the Treatment of HER2-Positive Breast Cancer and Highlights From the 2012 San Antonio Breast Cancer Symposium

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Today, there are many more options available for treating breast cancer.

Every year in the United States, about 230,000 women and 2,200 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 medications now available and new drugs in development for treating breast cancer. 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.

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—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. About 70 percent of breast cancers are estrogen receptor-positive. Of these cancers, about 60 percent are also progesterone receptor-positive. Using hormonal therapies is an effective way to treat these types of breast cancer.

About 20 percent to 25 percent of breast cancers are HER2-positive. These cancer cells have increased amounts of HER2 receptors, 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. This targeting helps spare healthy tissues and causes 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, progesterone or HER2. So 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 to chemotherapy. Clinical trials are pointing the way to new and even better treatments for triple-negative breast cancer.

Breast Cancer Treatments

Surgery

Many types of breast cancer are first treated with surgery. Studies show that the outlook for women with early-stage breast cancer is equally good whether they have a mastectomy (full removal of the breast) or a lumpectomy (removal of just the tumor with some surrounding tissue), followed by radiation. About two thirds of all women with breast cancer are diagnosed at an early stage.

Sentinel node mapping helps doctors find the first (sentinel) lymph node to which breast cancer cells would spread. (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.) If the sentinel lymph node is cancer-free, chances are that other, nearby lymph nodes are also unaffected and can be left in place. In the past, surgeons routinely cut out many lymph nodes in the underarm to find out whether the cancer had metastasized (spread). But if it's not necessary to remove those nodes, then women with breast cancer can avoid the possibility of developing lymphedema, a painful swelling of the arm.

As a result of new research published in the past several years, surgery to routinely remove many lymph nodes is being reconsidered. Many women are now being spared this procedure if they are going to receive radiation and only one to three lymph nodes contain tumor cells. For women who receive chemotherapy before surgery (called neoadjuvant therapy), there is still some debate on this question. Chemotherapy before surgery can shrink or destroy tumors. Researchers are trying to find out whether it's necessary to

remove more than just the sentinel node if tumors respond to this treatment. The answer is not yet clear, but clinical trials are ongoing.

Radiation

Doctors are also changing their thinking on how many weeks of radiation treatment women should receive after surgery for early-stage breast cancer. A recent clinical trial showed that a three-week course of radiation appears to be as effective as the standard five-week course. The shorter course of radiation was given in 15 sessions (or fractions), compared with the 25 fractions given in the standard treatment.

More than 4,400 women who had surgery for breast cancer took part in the START clinical trial in the United Kingdom. The study was designed to treat about half of the women with a higher dose of radiation in more fractions for five weeks. The others were treated with a lower dose of radiation in fewer fractions for three weeks. Nearly 10 years after treatment, it seems that the rate of the tumor returning is similar in both groups of women. Based on these study results, the shorter course of radiation after surgery is now the standard of care in the United Kingdom. Other clinical trials to confirm this finding are ongoing in the United States. Also being studied is giving the entire course of radiation in one week.

Chemotherapy

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.

Hormone Blockers

Doctors generally recommend hormonal therapy for estrogen receptor- or progesterone receptor-positive breast cancer. These treatments prevent estrogen or progesterone from attaching to receptors on breast cancer cells. The treatments also reduce the amount of hormones circulating in the body that attach to estrogen or progesterone receptors. By blocking hormones, the treatments deprive tumor cells of the substances they need to grow.

Tamoxifen (Nolvadex and others) is an estrogen-blocking treatment given to both pre- and post-menopausal women with breast cancer. Blocking the function of the ovaries with drugs such as goserelin (Zoladex) may be an effective treatment for pre-menopausal women when combined with

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 the quality of life as patients go through those treatments. They also offer an additional treatment option. For these reasons, doctors and researchers urge women 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:

- 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 all 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. But not all younger breast cancer patients need drugs to block the ovaries. The SOFT clinical trial, now under way, should shed more light on this question.

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. AIs benefit post-menopausal women; 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 post-menopausal women to reduce the total amount of estrogen produced. 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).

One 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 post-menopausal 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 living much longer.

Another medication, lapatinib (Tykerb), also targets HER2. Lapatinib is able to get inside cancer cells and block HER2 signals from within. In addition, lapatinib blocks HER1, which can also increase the growth of some breast cancer cells.

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 treatments that target HER2-positive breast cancer (such as lapatinib) are given along with chemotherapy (such as capecitabine [Xeloda]), the combination is 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. Most drugs for breast cancer cannot do that.

Lapatinib has also been used with trastuzumab before surgery. Together, they are a powerful combination, although they tend to cause side effects. In clinical trials, researchers are studying the combination of two or more such anti-HER2 treatments before surgery or for women with breast cancer that has spread. Clinical trials are also studying whether pairing these types of drugs with hormone treatments can benefit women with HER2-positive breast cancer.

Another effective treatment for HER2-positive metastatic breast cancer is pertuzumab (Perjeta). It is approved by the U.S. Food and Drug Administration (FDA) as a first-line

(first-time) treatment in combination with trastuzumab and docetaxel (Taxotere and others).

Ado-trastuzumab emtansine (Kadcyla), or T-DM1, was recently approved by the FDA. It 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 is a new kind of treatment that combines trastuzumab with monoclonal antibodies. The antibodies zero in on 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 destroy the cancer cells.

T-DM1 was approved based on the positive results of the EMILIA clinical trial, in which nearly 1,000 women with advanced or metastatic breast cancer took part. Women who received T-DM1 in the study lived longer than those who had standard treatment with lapatinib and capecitabine (30.9 months versus 25.1 months). They also lived longer without their cancer growing (9.6 months versus 6.4 months).

Promising New Treatment Approaches: A Report From the 2012 San Antonio Breast Cancer Symposium

This section presents highlights from the 2012 San Antonio Breast Cancer Symposium, which took place December 4–8 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.

ESTROGEN RECEPTOR-POSITIVE BREAST CANCER

Benefits of Extending Tamoxifen Treatment in Early-Stage Breast Cancer

Women with early-stage breast cancer who have already received five years of tamoxifen treatment may live longer without their cancer returning if they continue on tamoxifen for another five years. The greatest benefit of the additional treatment was seen 10 to 14 years after the women were first diagnosed.

Nearly 7,000 women with early-stage estrogen receptor-positive breast cancer took part in the international ATLAS

trial. All of these women received five years of tamoxifen treatment. Half of them stopped taking tamoxifen after five years, and the others continued tamoxifen for another five years. When the women were evaluated eight years later, the cancer returned in fewer women who were given the extended tamoxifen treatment than in those who stopped treatment at five years.

As time went on, researchers found that more women who continued treatment with tamoxifen were still alive compared with those who stopped treatment at five years.

What Patients Need to Know

The results of the ATLAS trial received a lot of media attention. It's an important study, with many years of data. The findings are very good news for women with estrogen

receptor-positive breast cancer, especially younger women already being treated with tamoxifen. Tamoxifen remains the standard of care for pre-menopausal women with estrogen receptor-positive breast cancer. However, post-menopausal women may be better treated with aromatase inhibitors (discussed earlier). There are some side effects associated with the use of tamoxifen, such as a higher risk of blood clots, hot flashes, night sweats and insomnia (sleeplessness).

As with all medical treatments, the benefits and risks of tamoxifen treatment must be weighed for each woman to be sure it is the right choice for her.

Letrozole for Invasive Estrogen Receptor-Positive Breast Cancer

Women who have invasive estrogen receptor-positive breast cancer seem to benefit more from letrozole than from tamoxifen, according to findings from the BIG 1-98 trial. This

type of breast cancer, which begins in the milk-producing glands of the breast, spreads to surrounding breast tissue. If not treated early, invasive breast cancer can spread to other parts of the body.

Nearly 5,000 post-menopausal women with early estrogen receptor-positive breast cancer were evaluated. Some of these women received letrozole, and the others received tamoxifen. More than eight years after the women started treatment with these drugs, researchers found that those who had taken letrozole for five years lived longer than those who had taken tamoxifen for the same amount of time.

In addition, patients who had a subtype of invasive estrogen receptor-positive breast cancer called lobular luminal B carcinoma seemed to benefit the most from treatment with letrozole. These women lived longer without the cancer continuing to grow.

What Patients Need to Know

Studies such as the BIG 1-98 trial shed more light on the most effective treatment for women with certain types of estrogen receptor-positive breast cancer. For women who have the less aggressive luminal A estrogen receptor-positive breast cancer, there was little difference between treatment with letrozole and treatment with tamoxifen. However, for women with the more aggressive luminal B estrogen receptor-positive breast cancer, letrozole seems to be much more effective than tamoxifen in reducing the chance of cancer coming back.

Further studies on the different types of estrogen receptor-positive breast cancer will help doctors select the treatment with the best chance of success for each patient.

Combination Treatment With Letrozole and PD-0332991 for Estrogen Receptor-Positive Breast Cancer

The combination of letrozole and a new drug called PD-0332991 seems to be a promising treatment for women with estrogen receptor-positive breast cancer, according to the results of a recent clinical trial. PD-0332991, the first in a new class of drugs called cyclin-dependent kinase inhibitors, works by blocking cancer cells at a certain stage in their growth.

In this study, 165 women with advanced estrogen receptor-positive/HER2-negative breast cancer were treated with letrozole alone or letrozole plus PD-0332991 at the time their cancer returned. In the patients evaluated so far, it took the cancer much longer to grow in those who received the combination treatment than in those who received letrozole alone (26.1 months versus 7.5 months). Furthermore, the cancer either shrank or did not continue to grow in 70 percent of the women who were on letrozole and PD-0332991, compared with 44 percent of those on letrozole alone.

What Patients Need to Know

Researchers are encouraged by these unprecedented responses to letrozole and PD-0332991 in women with advanced estrogen receptor-positive/HER2-negative breast cancer. This is an early look at a new treatment approach that combines a targeted drug and hormone therapy, and it may prove to be an effective way to treat women with this type of breast cancer. However, it is important to remember that these results are from a very early stage of research. Larger ongoing trials should show whether these benefits continue over time.

Higher Dose of Fulvestrant More Effective in Metastatic Estrogen Receptor-Positive Breast Cancer

For women who have locally advanced or metastatic estrogen receptor-positive breast cancer, higher doses of fulvestrant (500 milligrams) can help them live longer than lower doses (250 milligrams). Based on these updated results from the CONFIRM trial, the FDA changed the approved dose of fulvestrant for these patients to 500 milligrams.

Nearly 750 women with locally advanced or metastatic estrogen receptor-positive breast cancer that no longer responded to other hormone treatments took part in this study. (Locally advanced cancer has spread from where it started to nearby tissue or lymph nodes.) Half of these women received the higher dose of fulvestrant, and the others received the lower dose. The women on the higher dose lived about four months longer than those on the lower

dose (26.4 months versus 22.3 months). Overall, there were no major differences in the frequency of side effects between the two treatments.

What Patients Need to Know

A few years ago, the early results from the CONFIRM trial showed that the higher dose of fulvestrant was more effective than the lower dose in stopping the growth of metastatic estrogen receptor-positive breast cancer. Now, with the final results of this study, we know that the higher dose of fulvestrant can also extend the lives of these women. Researchers now recommend that doctors use the higher dose of fulvestrant for treating women with locally advanced or metastatic estrogen receptor-positive breast cancer.

21-Gene Recurrence Score Predicts Response to Treatment in Estrogen Receptor-Positive Breast Cancer

The 21-gene recurrence score (RS) can help doctors predict whose estrogen receptor-positive breast cancer is likely to return and who is likely to benefit from certain types of chemotherapy. These findings come from a trial known as NSABP B-28. The RS is based on a commercially available genetic test that analyzes 21 genes within a breast tumor.

This study included more than 1,000 women with estrogen receptor-positive breast cancer. Some of the women received doxorubicin and cyclophosphamide (AC). Others received AC followed by paclitaxel. Approximately one third of the patients had a low RS, one third had an intermediate RS and one third had a high RS.

For women with a low RS, there was no difference in outcome

regardless of the treatment received. However, adding paclitaxel to AC seemed to be of most benefit to those with an intermediate or high RS.

What Patients Need to Know

When they know the RS beforehand, doctors have a better chance of choosing the most effective treatment for a given patient with estrogen receptor-positive breast cancer. Armed with this genetic information, both doctors and patients can make more informed decisions about different breast cancer treatment options. More aggressive chemotherapy may not be necessary for women who are unlikely to have a recurrence, or return, of their breast cancer. These women can be safely spared the side effects of such treatment without affecting their outcomes.

HER2-POSITIVE BREAST CANCER

Long-term Benefits of Trastuzumab and Chemotherapy for Early HER2-Positive Breast Cancer

Adding trastuzumab to chemotherapy may help women with HER2-positive breast cancer live longer, according to the final reports of two major clinical trials. More than 4,000 women took part in these studies. Half of them received a combination of trastuzumab, doxorubicin, cyclophosphamide and paclitaxel. The others received the same treatment but without trastuzumab.

Approximately eight-and-a-half years after treatment, more women treated with trastuzumab were still alive than were those who did not receive the drug (84 percent versus 75 percent). More women treated with trastuzumab were living

without a return of their cancer than were the other women (74 percent versus 62 percent). In other words, the chance of the cancer returning was reduced by 40 percent in those who received treatment with trastuzumab.

What Patients Need to Know

When it was approved by the FDA 15 years ago, trastuzumab was one of the most important advances in the treatment of breast cancer in decades. Doctors are very pleased with these long-term results showing that the lifesaving benefits of trastuzumab for women with HER2-positive breast cancer continue to hold up over time. Not only is it effective in treating advanced breast cancer but also newly diagnosed breast cancer as well.

One Year of Trastuzumab Still the Standard for Early HER2-Positive Breast Cancer

One year of treatment with trastuzumab remains the standard of care for women with early HER2-positive breast cancer, according to the recent results of two different studies—the European HERA and the French PHARE clinical trials.

In the HERA study, more than 3,000 women with early HER2-positive breast cancer received trastuzumab for either one year or two years. Trastuzumab was given to these women after they had completed their initial treatment (surgery, chemotherapy or radiation). Researchers found that the second year of trastuzumab treatment was no more effective than one year of treatment at stopping the cancer from returning or helping these women live longer.

In the PHARE study, more than 3,300 women with early HER2-positive breast cancer were given trastuzumab for either six months or 12 months. These patients already had surgery and received at least four cycles of chemotherapy. Four years after treatment with trastuzumab, there was no sign that cancer returned in 85 percent of those treated for six months. In those treated for 12 months, there was no sign of a return of the cancer in 88 percent. There did not appear to be a benefit to taking the drug for six months rather than 12 months.

What Patients Need to Know

For now, one year of trastuzumab after surgery remains the standard of care for women with HER2-positive breast cancer. The first report from the HERA clinical trial and the early results from the PHARE clinical trial do not clearly show that longer or shorter treatment with trastuzumab is better than one year. However, several studies continue to look at the length of trastuzumab treatment to be sure that one year is

the most effective approach with the fewest side effects for women with this type of breast cancer.

Pertuzumab, Trastuzumab and Docetaxel for Metastatic HER2-Positive Breast Cancer

A recent clinical trial has shown that adding the new drug pertuzumab to trastuzumab plus docetaxel (PTD) helps women with metastatic HER2-positive breast cancer live longer than the two-drug combination alone.

In the CLEOPATRA study, more than 800 women with metastatic HER2-positive breast cancer were treated with the three-drug combination or with just trastuzumab and docetaxel. Approximately three years later, 66 percent of the women who received PTD were still alive, compared with 50 percent of those who received trastuzumab and docetaxel without pertuzumab. It took longer for the cancer to continue growing in the PTD group than in the two-drug group (18.5 months versus 12.4 months).

Researchers found that women whose cancer cells had a genetic mutation (change) in an important cell mechanism called the PI3 kinase pathway may be less likely to respond to treatment with pertuzumab.

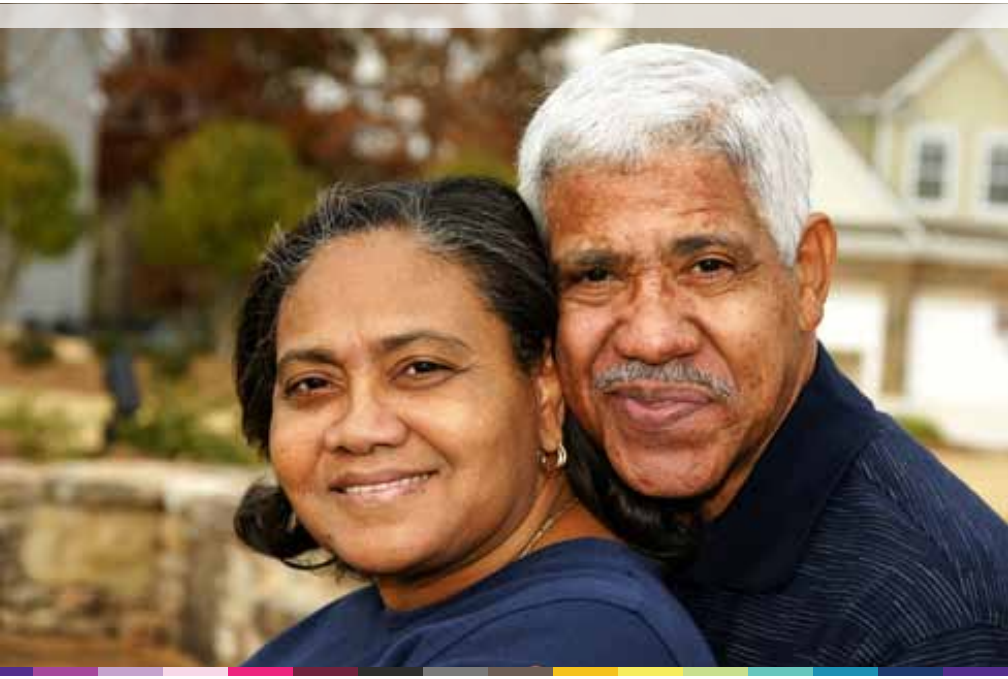
What Patients Need to Know

Researchers now believe that the combination of targeted treatments such as pertuzumab and trastuzumab and the chemotherapy drug docetaxel should be considered the standard of care for women with HER2-positive metastatic breast cancer. As a result of the CLEOPATRA study, pertuzumab has been approved by the FDA for treating this type of breast cancer. Researchers are studying combinations of drugs that target both HER2 and the PI3 kinase pathway.

Adding Bevacizumab Does Not Increase the Benefit of Chemotherapy for Triple-Negative Breast Cancer

Combining chemotherapy and the targeted drug bevacizumab (Avastin) did not offer an added benefit for women with triple-negative breast cancer. In a large study known as the BEATRICE clinical trial, bevacizumab did not help these women live longer without their cancer continuing to grow.

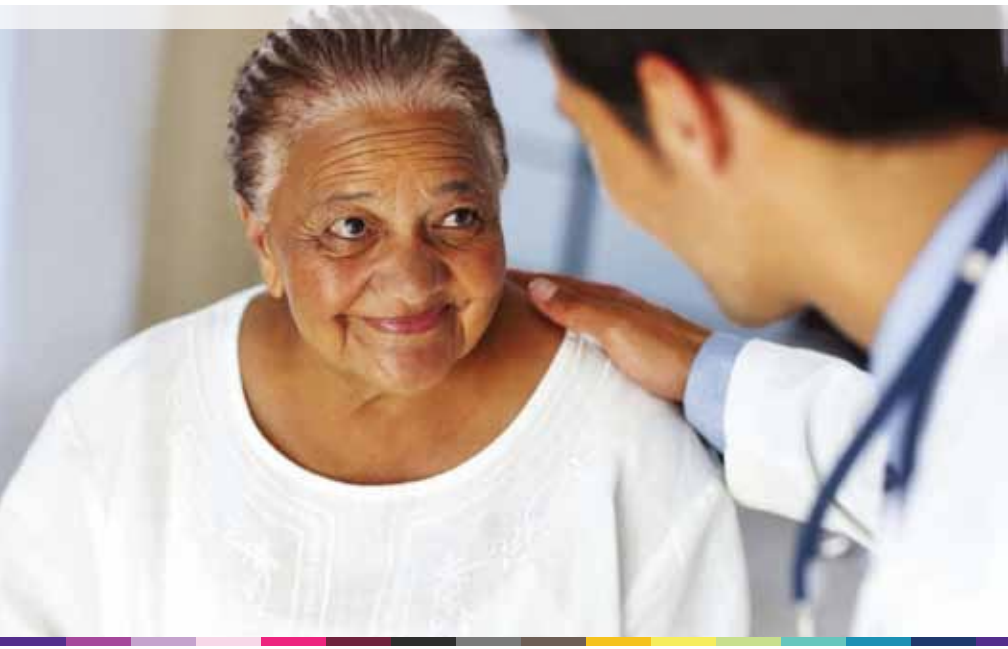
More than 2,500 patients with triple-negative breast cancer took part in this international study. After surgery, about half of these women received chemotherapy alone, and the others received chemotherapy plus bevacizumab for one year. Nearly



three years after this treatment, the cancer had not continued to grow in approximately 83 percent of both groups of patients. Although it is still too soon to tell, the addition of bevacizumab did not seem to help patients live longer. More women taking the bevacizumab combination treatment developed high blood pressure and blood clots than those on chemotherapy alone, causing many of them to stop their treatment early.

What Patients Need to Know

The final results of the BEATRICE trial are not yet available. But so far, it seems that adding bevacizumab to chemotherapy is no more effective than standard chemotherapy alone and causes more side effects. At this time, researchers do not support the use of this combination treatment for women with triple-negative breast cancer. However, other trials with bevacizumab are currently in progress or recently completed. Once the results of all of these studies are compared, researchers should have a much



better idea of whether bevacizumab has a place in the treatment of this type of breast cancer. In the meantime, clinical trials on a number of other targeted treatments for triple-negative breast cancer are ongoing.

Bevacizumab is a targeted treatment that blocks a tumor's ability to grow new blood vessels. Without its blood vessels, tumors are "starved" of the nutrients they need to grow and divide. This drug has been approved by the FDA for treating colorectal, kidney and lung cancers.

RECURRENT AND METASTATIC BREAST CANCER

Eribulin for Metastatic Breast Cancer

Eribulin (Halaven) may prove to be as effective as capecitabine, a type of chemotherapy, in treating women with metastatic breast cancer. Once used as a later treatment for women with this type of cancer, eribulin is now showing promise as an earlier treatment option.

More than 1,100 women with metastatic breast cancer took part in a recent clinical trial comparing eribulin with capecitabine. Nearly 85 percent of these patients received one of these drugs as part of their first or second treatment. The time it took for the cancer to continue growing was about the same for both drugs. Women in both treatment groups lived about the same length of time (between 14.5 months and 15.9 months).

What Patients Need to Know

Researchers found that eribulin is no better than capecitabine in the earlier treatment of women with metastatic breast cancer. However, it still seems to be an effective alternative. Eribulin will be studied further to help doctors figure

out exactly where it fits in the treatment of women with metastatic breast cancer. Perhaps in the future, researchers will know who may benefit most from treatment with this relatively new drug.

Bevacizumab Does Not Add Benefit to Hormone Therapy in Metastatic Breast Cancer

Adding bevacizumab to hormone treatment does not appear to benefit women with metastatic breast cancer. Nearly 400 women with advanced breast cancer that had responded to hormone therapy took part in this Spanish-German clinical trial. Half of the patients received one of two hormone treatments: letrozole or fulvestrant. The others received one of these hormone treatments plus bevacizumab.

Compared with hormone treatment alone, adding bevacizumab did not significantly lengthen the time it took for the cancer to continue growing. Women in both groups lived an average of three-and-a-half years with treatment. Those who received bevacizumab had more side effects than those who did not, such as fatigue, high blood pressure and a risk of bleeding.

What Patients Need to Know

In terms of stopping the cancer from continuing to grow in women with metastatic breast cancer, bevacizumab did help a little bit. But researchers did not believe this small benefit made up for the added side effects of this drug. So they do not think this treatment approach is helpful for women with this type of breast cancer. Studies such as this one can help spare women unnecessary treatment. Because bevacizumab is an effective treatment for other cancers, it will be the subject of future clinical trials.

Ixabepilone Plus Dasatinib Shows Promise in Metastatic Breast Cancer

The combination of two newer drugs—ixabepilone (Ixempra) and dasatinib (Sprycel)—has shown promise in the treatment of women with metastatic breast cancer that no longer responds to other treatments. Ixabepilone has been approved by the FDA for treating metastatic breast cancer, alone or in combination with capecitabine. Dasatinib is an approved treatment for people with chronic myeloid leukemia, a blood cancer.

Fifty women with resistant metastatic breast cancer received ixabepilone plus dasatinib. Of the 47 patients evaluated so far, the cancer shrank or did not continue growing in about one quarter of them. On average, the cancer did not continue growing for six months in these women. In terms of side effects, approximately half of the patients reported fatigue, diarrhea and nausea.

What Patients Need to Know

Ixabepilone and dasatinib seem to complement each other. Researchers are pleased with these very early findings and plan to study this combination treatment further. In future clinical trials, the combination may be compared with established treatments to find out just how much it benefits women with metastatic breast cancer.

Carboplatin, Nab-paclitaxel and Bevacizumab Encouraging in Metastatic Breast Cancer

Combining carboplatin, nab-paclitaxel (Abraxane) and bevacizumab may prove to be an effective combination for women with metastatic breast cancer, according to the results

of a small clinical trial. Carboplatin is a standard anti-cancer drug, and nab-paclitaxel is an "albumin-bound" form of the standard drug paclitaxel. (Binding paclitaxel to the protein albumin seems to make it easier to concentrate the drug in the tumor.)

Thirty women who had not already received chemotherapy for their metastatic cancer took part in the study. Seventy-five percent of them had estrogen receptor-positive breast cancer. All of them were given the three-drug combination. The cancer shrank or did not continue to grow in nearly 97 percent of the patients. However, 75 percent of all patients developed a side effect known as neutropenia—a low level of white blood cells, which help the body fight infection.

What Patients Need to Know

Researchers are encouraged by these positive early results with carboplatin, nab-paclitaxel and bevacizumab. The drugs seem to work well together to target metastatic breast cancer. Many think that the best way to use this promising approach may be earlier in the treatment process, before other options have been tried. Future studies will help doctors find the best way to use this trio of drugs to help women with advanced breast cancer.

Chemotherapy After the Return of Cancer May Benefit Some Women With Breast Cancer

For women who have had surgery to remove a tumor that returned, chemotherapy may help some of them live longer. These benefits were seen only in those women whose new tumors were estrogen receptor-negative and not estrogen receptor-positive.

These results come from a clinical trial called the CALOR study, which took place over many years in many centers around the world. More than 160 women took part. Eighty-five of them received chemotherapy for their new tumor, and the others did not. (Doctors in the clinical trial were allowed to select the type of chemotherapy used.)

Nearly five years later, the tumor had not continued to grow in 69 percent of those on chemotherapy, compared with 57 percent of those who were not on chemotherapy. Treatment with chemotherapy also helped women live longer: Five years later, 88 percent of those who were treated with chemotherapy were still alive, compared with 76 percent of those who did not receive chemotherapy.

What Patients Need to Know

This important study offers the first evidence that giving chemotherapy for a return of cancer to the breast can help women live longer. For years, researchers have debated whether to give chemotherapy to women who had a tumor recurrence. Now, as a result of the CALOR clinical trial, they know that some women whose tumors come back can be helped with chemotherapy.

Studies such as this one help both doctors and patients with breast cancer recurrence make the best decisions about further treatment. Not everyone benefits from chemotherapy, and those who are unlikely to benefit can be spared the unnecessary side effects of treatment.

Treatment Side Effects

Sometimes, side effects from medications can make it difficult 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 soothe mouth sores.

- 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.
- 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. The steps you can take yourself include:

- 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 that you can get proper treatment.

Bone loss. Both hormonal therapies and chemotherapy can cause bone loss. The loss increases a woman's risk for osteoporosis—thinning bones that are more likely to break (fracture). 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 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 (Zometa) 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, 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), which are believed to slow the breakdown and removal of old bone. Examples of SERMs are raloxifene (Evista), 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 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 contained in a glycerin tablet that, when inserted into the vagina, melt at body temperature). 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.

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 Jewish descent are more likely to be carriers of the *BRCA1* or *BRCA2* breast cancer gene.

If you were diagnosed with breast cancer before the age of 50, your doctor may recommend genetic testing, even without a family history. The National Comprehensive Cancer Network guidelines recommend genetic testing for women under the age of 65 who have been diagnosed with triple-negative breast cancer. To learn more about genetic testing, talk with your doctor.

What about fertility (the ability to have a baby)? 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.

Your Support Team

When you are diagnosed with 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 oncology social workers on staff, who understand the challenges faced by patients. We can work with you one-on-one to develop strategies for coping with treatment and its side effects. Oncology social workers can 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,* women with breast 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 to cover 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.

Frequently Asked Questions

Q. If you have been on an aromatase inhibitor and it stops working, can you go back on it at a later time?

A. Usually, not, because once the cancer grows in spite of a drug, we assume that the tumors will continue to resist this treatment. But since there are quite a few aromatase inhibitors (which block the production of estrogen), we sometimes try a different one if the first drug has stopped working. For example, if letrozole (Femara and others) is no longer working, we may try exemestane (Aromasin and others). There are always other combinations of drugs to try as well, which you should discuss with your doctor. He or she may recommend using a different aromatase inhibitor with a type of drug called an mTOR inhibitor, such as everolimus (Afinitor).

Q. For women with metastatic breast cancer who have tried many treatments, are there clinical trials with the new kinase inhibitors?

A. There absolutely are trials going on for these women who have received several treatments. In the next few years, we are going to see a lot of data from clinical trials on these types of drugs. It's important to talk with your doctor about entering a clinical trial. Online, you can explore what is available, but your health care team will need to help you enter a trial. Often, these studies are conducted in community cancer clinics, which makes it convenient for many people. See the resource list on the facing page for more information on finding a clinical trial.

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
888-753-5222
www.lbbc.org

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

National Library of Medicine (MedlinePlus)
www.medlineplus.gov

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

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

TO FIND OUT ABOUT CLINICAL TRIALS:

Coalition of Cancer Cooperative Groups
www.CancerTrialsHelp.org

National Institutes of Health
www.cancer.gov/clinicaltrials

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WWW.CANCERCARE.ORG

800-813-HOPE (4673)