CANCERcare Connect®

Latest News in Breast Cancer Research

Highlights from the 2009 San Antonio Breast Cancer Symposium

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- Treatment advances in breast cancer
- Medications on the horizon
- Treatment side effects
- Breast cancer resources

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This Cancer*Care* Connect® booklet was made possible by:

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Researchers continue to make important progress in treating breast cancer.

This special edition of the Cancer*Care* Connect® booklet series presents highlights from the 2009 San Antonio Breast Cancer Symposium, which took place December 9–13 in San Antonio, Texas.

This guide includes information on advances in the treatment of breast cancer, as well as other promising treatments that researchers continue to study in clinical trials. It also provides additional resources for breast cancer support.

Please note: Some of the treatments discussed in this booklet are still in the earliest phases of research and may not be available to the general public outside of a clinical trial.

The information contained in this booklet is intended for discussion with your doctor. He or she can let you know whether these research findings affect your treatment plan, and if a clinical trial is right for you.

Early-Stage Breast Cancer

Breast cancers are categorized by stages according to their size and the extent of their spread. "Early-stage" breast cancer refers to smaller tumors that have not spread to other parts of the body beyond the breast and nearby lymph nodes such as those in the underarm.

(Lymph nodes are a linked system of small bean-shaped structures throughout the body that helps filter out and destroy bacteria and other toxic substances.)

Doctors also describe breast tumors by whether or not their growth is fueled by the female hormones estrogen and progesterone. Cancers that grow in response to these hormones are called estrogen- or progesterone-receptor positive. They are treated with medications designed to block the body's production of the hormones or their effects.

Breast tumors are also characterized by whether their growth is fueled by a gene called HER2. This gene makes a protein, also called HER2, that controls cell division. If a breast cancer cell has too much HER2—that is, if it's HER2-positive—it tends to grow more quickly. HER2-positive breast cancer can be treated with medications that block the activity of the HER2 protein.

BENEFITS OF NEWER HORMONAL TREATMENTS FOR EARLY-STAGE BREAST CANCER

Several recent studies have compared the standard hormonal treatment tamoxifen (Nolvadex and others), which blocks the effects of estrogen, with a newer type of hormonal drug called an aromatase inhibitor. Researchers wanted to find out which is more effective in women with early-stage hormone receptor-positive breast cancer.

Aromatase inhibitors, which include letrozole (Femara and others), anastrozole (Arimidex), and exemestane (Aromasin), also block estrogen but indirectly—they block a substance called aromatase that is needed for estrogen production. Aromatase inhibitors are proving to be just as effective, and in some cases even more beneficial, than tamoxifen.

Aromatase inhibitors are intended mostly for postmenopausal women. That's because before menopause, a woman's ovaries

make so much estrogen, limiting the action of aromatase doesn't make much difference.

Letrozole Versus Tamoxifen

In a clinical trial called BIG 1-98, tamoxifen was compared with letrozole. More than 8,000 postmenopausal women with hormone receptor-positive breast cancer from around the world took part in this clinical trial. Researchers found that women who received five years of letrozole treatment went longer without their cancer returning—and were less likely to have their cancer return—than those who received five years of tamoxifen treatment.

Recently, researchers updated the results of this clinical trial and found that:

- Women who were treated with letrozole tended to live longer, whether their cancer returned or not, than those treated with tamoxifen.
- The extended treatment with letrozole did a better job than tamoxifen in improving disease-free survival, which is the length of time after treatment during which a person survives with no sign of cancer.

Using these two hormonal medications in sequence—for instance, two years of letrozole followed by three years of tamoxifen or vice versa—did not appear to be more effective than five years of letrozole alone.

Exemestane Versus Tamoxifen

Exemestane is another aromatase inhibitor that has been compared with tamoxifen in women with estrogen or progesterone receptor-positive breast cancer. Recent updates of two large clinical trials looked at whether switching drugs during treatment would improve the results.

The first study, known as the TEAM clinical trial, included nearly 10,000 postmenopausal women with early-stage

breast cancer. All of the women had surgery for their hormone receptor-positive breast cancer.

After surgery, some of the women were treated with exemestane for five years. Others were treated for two to three years with tamoxifen and then were given exemestane for the rest of the five years.

Researchers found that for preventing the return of cancer, exemestane alone was just as effective as split treatment with tamoxifen and exemestane. Five years after treatment ended, about 85 percent of both groups of women still had no sign of cancer.

As for side effects, more patients who received exemestane alone experienced pain in their muscles, bones, and joints and more bone fractures (breaks) than those who took tamoxifen followed by exemestane. But more patients who received the split treatment had hot flashes and vaginal bleeding than those who received only exemestane.

Because both treatments seem to be equally effective for women with hormone receptor-positive breast cancer, doctors may choose one over the other based on the side effects and risks in a given person, including the risk of bone thinning (osteoporosis).

In the second study, known as IES, using exemestane some time during treatment appeared to be better than taking tamoxifen alone for postmenopausal women with early-stage breast cancer.

More than 4,500 postmenopausal women took part in this study. Most of these patients (about 4,000) had estrogen receptor-positive cancer, and all had already been on tamoxifen for two to three years. Some of these women

finished five years of treatment with tamoxifen. The others switched to exemestane.

Among the women who had estrogen receptor-positive breast cancer, more of those who switched treatment survived without a return of cancer than those who did not switch. Doctors believe that this benefit occurs regardless of whether exemestane is given alone, after tamoxifen, or before tamoxifen.

How best to use these treatments requires further study.

AROMATASE INHIBITORS AND MENOPAUSAL STATUS AT DIAGNOSIS

Although aromatase inhibitors are used only for postmenopausal women, according to a recent update of a clinical trial known as MA-17, women who are premenopausal when diagnosed with breast cancer but become postmenopausal during treatment may also benefit from using the aromatase inhibitor letrozole.

A few years ago, MA-17—in which 5,000 women took part—showed that letrozole helped prevent cancer from returning in women who were treated for early-stage hormone receptor-positive breast cancer. Letrozole also seemed to improve their survival. These women received four to six years of treatment with tamoxifen after surgery and then received five more years of treatment with letrozole. Extending treatment with letrozole was very helpful in stopping their cancer from returning.

Nearly 900 women in MA-17 were premenopausal—that is, they had not yet reached menopause—when they were first diagnosed with breast cancer. All of these women went on to become postmenopausal during their initial breast cancer treatment, before receiving further treatment with letrozole.

Researchers found that five years of extended treatment with letrozole was more effective in preventing the cancer

from returning in women who had been premenopausal when they were first diagnosed than in those who had been postmenopausal at that time. They called these results very encouraging. Extended treatment with letrozole or another aromatase inhibitor may prove to be the most effective way to treat women who are *pre*menopausal when diagnosed with breast cancer but become *post*menopausal before or during treatment with tamoxifen.

TARGETED TREATMENT FOR EARLY-STAGE HER2-POSITIVE BREAST CANCER

Trastuzumab (Herceptin) is a medication that greatly improves the effectiveness of chemotherapy, helps prevent the cancer from returning, and extends the lives of women with HER2-positive breast cancer. Researchers are still learning how best to use this drug.

A recent update of a large clinical trial of trastuzumab in combination with chemotherapy sheds some more light on the benefits of trastuzumab.

Doctors recruited more than 3,000 women with HER2-positive early-stage breast cancer to take part in the BCIRG trial. Three different combination treatments were studied:

- Chemotherapy, which included doxorubicin (Adriamycin and others) and cyclophosphamide (Cytoxan and others) followed by docetaxel (Taxotere), alone
- Doxorubicin and cyclophosphamide followed by docetaxel and trastuzumab
- Docetaxel, carboplatin (Paraplatin and others), and trastuzumab

More than five years after treatment, researchers have found that the cancer has not returned in more women in the second and third groups who received trastuzumab plus chemotherapy than in those in the first group who received

chemotherapy alone. Between 81 and 84 percent of the patients who were given trastuzumab had no sign of cancer, compared with just 75 percent of those who did not receive this drug. Also, more women treated with trastuzumab were alive five years after treatment than those treated with chemotherapy alone (about 92 percent versus 87 percent).

Trastuzumab has been a major advance in the treatment of both early- and late-stage breast cancers.

Locally Advanced and Metastatic Breast Cancer

Locally advanced breast cancer is a term that refers to one of two situations: either the tumor is confined to the breast but is too large to be effectively removed or the tumor has spread (metastasized) to nearby areas outside the breast, such as the lymph nodes in the underarm, neck, or chest wall.

Metastatic breast cancer is the most advanced stage of breast cancer (stage IV). At this stage, cancer cells have spread beyond the breast and nearby lymph nodes to other areas of the body, where they continue to grow and multiply. The most common parts of the body to which breast cancer spreads are the bones, lungs, and liver.

As mentioned in the section on early-stage breast cancer, breast tumors are also characterized by whether their growth is fueled by a gene called HER2 or by the hormones estrogen or progesterone.

For patients with the type of breast cancer that is fueled by estrogen or progesterone, hormonal therapy is often the first treatment of choice to control advanced breast cancer. Doctors usually switch to chemotherapy if hormone therapy no longer works for these women. Chemotherapy as a first-time treatment is also given to women with advanced or metastatic breast cancer who:

- Are candidates for breast surgery aimed at removing all the cancer
- Have breast cancer symptoms such as a lump or thickening in the breast, pain, or fatigue
- Have tumors that are not fueled by hormones

Common chemotherapies used for treating locally advanced or metastatic breast cancer include cyclophosphamide, doxorubicin, paclitaxel (Taxol and others), docetaxel, and capecitabine (Xeloda).

When used in combination with targeted treatments such as trastuzumab, these standard chemotherapy drugs can be even more effective. Rather than killing both healthy and unhealthy cells as chemotherapy does, targeted treatments attack cancer cells primarily, sparing healthy tissues and causing fewer severe side effects.

In this section, we present some of the most promising new treatments for women with locally advanced or metastatic HER2-negative and HER2-positive breast cancer. It's important to remember that many of these clinical trials are in an early stage of research and that further studies are needed to confirm their results.

FIRST-LINE TARGETED TREATMENT COMBINATIONS FOR ADVANCED HER2-NEGATIVE BREAST CANCER

Bevacizumab and Chemotherapy

Combining the chemotherapy drug docetaxel and the targeted treatment bevacizumab (Avastin) seems to be more effective than either treatment alone. This combination was tested in a later-phase clinical trial called AVADO.

Bevacizumab works by stopping the growth of new blood vessels in tumors. Specifically, it blocks a substance called vascular endothelial growth factor (VEGF). When tumor cells spread through the body, they release VEGF to create

new blood vessels. These blood vessels supply oxygen, minerals, and other nutrients to feed the tumor. Because healthy tissues have an established blood supply, they are less affected by the drug. Also, bevacizumab seems to help chemotherapy drugs to zero in on breast cancer cells.

More than 700 women with HER2-negative breast cancer that had returned or spread took part in the AVADO clinical trial. This was the first treatment these women had received for their advanced or metastatic breast cancer. Patients received either docetaxel plus bevacizumab (two different doses were tested) or docetaxel and a placebo (a look-alike pill or liquid, as in this case, containing no active ingredient).

Researchers found that women who received docetaxel plus the higher dose of bevacizumab went two months longer before their cancer started to grow again than women who received docetaxel and a placebo. And, the cancer shrank or disappeared in nearly 65 percent of patients who were treated with docetaxel and the higher dose of bevacizumab, compared with about 45 percent of those who received docetaxel and placebo.

Sorafenib and Chemotherapy

Sorafenib (Nexavar) is an approved targeted treatment for people with advanced kidney or liver cancer. The results of an early phase of research seem to show that this drug might also be an effective way to treat advanced breast cancer.

More than 200 women with HER2-negative locally advanced or metastatic breast cancer took part in the study. These women had not yet received treatment for their advanced cancer. Half of the patients were given the standard

chemotherapy paclitaxel plus sorafenib, and the others were given paclitaxel and a placebo.

Women treated with the sorafenib combination went longer from the start of treatment until their cancer continued to grow than the other women (more than eight months versus about five and a half months). The cancer shrank or disappeared after treatment in nearly 70 percent of the patients who received the paclitaxel/sorafenib combination, compared with about 55 percent of the patients who did not receive sorafenib.

Sorafenib appears to be an effective treatment for advanced breast cancer. However, it should be noted that in this study, more than half of the women who received it developed a moderate-to-severe side effect known as hand-foot skin reaction. This is a condition in which pain, swelling, numbness, tingling, or redness affect the hands or feet. It is not life-threatening, but it can severely affect a person's quality of life and ability to continue with treatment. Doctors believe that helping patients cope with this side effect may make it possible for them to continue with this effective cancer treatment.

SECOND-LINE TARGETED TREATMENT COMBINATIONS FOR ADVANCED HER2-NEGATIVE BREAST CANCER

As discussed in the previous section, combining the targeted treatment bevacizumab with chemotherapy has been shown to be an effective first-line (first-time) treatment for metastatic breast cancer. New research shows that this approach appears to be an effective second-line (secondary) treatment as well.

More than 680 women with HER2-negative metastatic breast cancer took part in the clinical trial known as RIBBON-2. For all of the women in the study, their first-line chemotherapy either did not work to control the cancer or stopped working.

Two-thirds of the women were treated with chemotherapy

(such as paclitaxel, docetaxel, gemcitabine [Gemzar], or capecitabine) plus bevacizumab. The others were treated with chemotherapy plus a placebo. None of the women had ever received bevacizumab.

It took longer for the cancer to continue growing in the women who received bevacizumab than in those who did not (more than seven months versus five months). Fifteen months after treatment, the tumor had shrunk or disappeared in nearly 40 percent of the patients treated with the bevacizumab combination, compared with 30 percent of patients treated with chemotherapy alone.

This is the first clinical trial in a later stage of research to show that bevacizumab is an effective second-line treatment for metastatic breast cancer. However, this drug has not yet been shown to increase survival for women with metastatic breast cancer. Researchers hope that future updates on the patients in this study may show that it does.

NEW TREATMENT OPTIONS FOR TRIPLE-NEGATIVE BREAST CANCER

Recent research shows that newer targeted drugs, called PARP and Notch inhibitors, may become effective ways to treat triple-negative breast cancer.

Triple-negative breast tumors are made up of cancer cells that are estrogen receptor-negative, progesterone receptor-negative, and HER2-negative. Approximately 15 percent of all breast cancers are triple-negative. These tumors tend to grow more quickly and are usually larger than other types of breast tumors.

PARP Inhibitors

PARP inhibitors are quickly becoming one of the most exciting developments in breast cancer research. PARP is short for poly ADP-ribose polymerase. These new drugs block a cancer cell's ability to repair itself when damaged by

radiation or chemotherapy. PARP inhibitors may make these other treatments more effective.

Recently, more than 160 women took part in two small clinical trials that tested a PARP inhibitor called BSI-201 in combination with chemotherapy. All of these patients had metastatic triple-negative breast cancer. Half of the women received a chemotherapy combination of gemcitabine and carboplatin. The others received the same two drugs plus BSI-201.

The tumor shrank or disappeared in nearly 50 percent of the patients who received BSI-201, compared with 16 percent of those who did not. The women who received BSI-201 also went longer before their cancer continued to grow than the women who did not take the drug (about seven months versus three months).

In addition, BSI-201 also seemed to lengthen the lives of the women who received it.

Although the results with BSI-201 are encouraging, it should be noted that PARP inhibitors are still in a very early stage of development. It is hoped that the results of ongoing and future studies will show doctors how these new drugs can best be used to treat breast cancer and whether they are effective for other types of cancer as well.

Notch Inhibitors

Another new class of drugs for advanced breast cancer is Notch inhibitors. These drugs work in an entirely different way than standard treatments of breast cancer. Although these drugs are still in the early stages of research, doctors are enthusiastic about their potential.

Breast cancer stem cells make up about one percent of all cells in a breast tumor. Sometimes called the mother cells of a breast tumor, they create other stem cells as well as regular cancer cells to replace the ones destroyed by chemotherapy.

Although current treatments are effective ways to destroy

regular cancer cells and shrink tumors, many are not as good at destroying breast cancer stem cells. When stem cells are left behind after treatment, they can re-grow—and may be the reason why breast cancer comes back or resists treatment.

That's where Notch inhibitors could be effective. They block a chain of cell activities called the "Notch pathway" that control breast cancer stem cells. Researchers believe that using Notch inhibitors along with targeted treatment or chemotherapy may be a powerful way to treat breast cancer and prevent it from coming back.

One Notch inhibitor, called MK0752, has been studied in 35 women with advanced breast cancer who were being treated with docetaxel. Before treatment, doctors removed some of the cancer cells to count the breast cancer stem cells. After treatment with MK0752 and docetaxel, there were many fewer breast cancer stem cells.

Researchers believe that the Notch inhibitor weakened or destroyed these breast cancer stem cells. The decrease in the number of these stem cells was seen after the first cycle of treatment with MK0752 and docetaxel and continued after other cycles of treatment.

Although these results are promising, it's important to remember that research on Notch inhibitors is just getting started. Further studies will help doctors learn whether Notch inhibitors can become a safe and effective way to treat breast cancer.

TARGETED TREATMENT COMBINATIONS FOR HER2-POSITIVE BREAST CANCER

Trastuzumab Plus Lapatinib

Combining two targeted treatments—trastuzumab and lapatinib (Tykerb)—appears to benefit women with metastatic breast cancer more than either drug alone. These

results are from a recent update of a late-stage clinical trial.

Lapatinib has been studied in women with HER2-positive breast cancer when the cancer continues to grow despite treatment with trastuzumab and chemotherapy.

Lapatinib and trastuzumab both target the HER2 protein, but in different ways. For instance, trastuzumab seems to attach to the HER2 protein to block its activity. Lapatinib appears to go inside the cell to block HER2 signals from there. Both methods work to block HER2 and tumor growth.

Nearly 300 women with HER2-positive metastatic breast cancer took part in the clinical trial. Half of them were treated with lapatinib alone, and the others were treated with both lapatinib and trastuzumab. These patients had received an average of three previous treatments, including trastuzumab, for their metastatic breast cancer.

The combination of these two drugs helped women with HER2-positive metastatic breast cancer to live longer than those who received lapatinib alone (14 months versus nine and a half months). A year after treatment, more than 55 percent of the women treated with lapatinib and trastuzumab had survived, compared with about 40 percent of the women treated with just lapatinib.

This is the first time any drug or drug combination that targets HER2-positive breast cancer has shown a survival advantage in women who had received so many previous treatments for their metastatic breast cancer. Clinical trials of this “double blockade” approach to halting the growth of HER2-positive tumors are being conducted in women with early-stage breast cancer as well.

Sequential Versus Concurrent Treatment

In an update of a large clinical trial that included more than 3,000 women with HER2-positive breast cancer, researchers compared sequential treatment (chemotherapy followed by trastuzumab) with concurrent treatment (chemotherapy, followed by chemotherapy plus trastuzumab, and then trastuzumab alone). They found that cancer returned less often in the women who used concurrent treatment.

The sequential treatment consisted of two standard chemotherapy drugs (doxorubicin and cyclophosphamide), followed by 12 weeks of paclitaxel, and then 52 weeks of trastuzumab. Concurrent treatment was the same two chemotherapy drugs, followed by 12 weeks of paclitaxel and trastuzumab together, and then another 40 weeks of trastuzumab.

Eighty-four percent of the women given concurrent treatment survived with no sign of cancer, compared with 80 percent of those given sequential treatment. Based on these results, many researchers now believe that concurrent treatment with chemotherapy and trastuzumab should be recommended for women with HER2-postive breast cancer.

Trastuzumab Plus DM1

Another potential new treatment for women with metastatic HER2-positive breast cancer is called T-DM1. Results from a recent clinical trial show that this drug can eliminate or shrink tumors.

T-DM1 combines two approaches in one medicine: the targeted drug trastuzumab with a chemotherapy called DM1. This combination blocks the growth of cancer cells and causes less severe side effects than does chemotherapy alone.

More than 100 women with advanced HER2-positive breast cancer took part in this clinical trial, which is in an early stage of research. All of these patients had received an average

of seven previous treatments for their metastatic cancer, including doxorubicin, trastuzumab, and lapatinib. Even with these treatments, their cancer had continued to grow.

About eight months after treatment with T-DM1, the tumor disappeared or shrank by at least half in more than 30 percent of these women. The cancer neither grew nor shrank for at least six months in another 10 percent of all of these patients.

Researchers called these early results remarkable, especially in women who had already received so many treatments for their advanced cancer. Later-stage clinical trials of T-DM1 in similar groups of women are ongoing. This combination treatment also is likely to be studied in women with early-stage breast cancer.

Trastuzumab Plus Ridaforolimus

In a small clinical trial, combining trastuzumab with a new drug called ridaforolimus has successfully shrunk tumors in women with HER2-positive metastatic breast cancer.

Ridaforolimus belongs to a class of drugs called mTOR inhibitors. These drugs work by blocking a protein called mTOR, which acts as a master switch in cancer cells, turning on processes related to cancer growth. Blocking this protein interferes with the growth and reproduction of cancer cells.

Twenty-two women took part in this study. In all of these patients, the cancer no longer responded to treatment with trastuzumab. The tumor shrank by at least half in two of the first 14 women evaluated.

More women with HER2-positive metastatic breast cancer

are joining this study, which is still in progress. Ridaforolimus is also being studied as a possible treatment for bone cancer.

HORMONE THERAPY FOR ADVANCED HORMONE RECEPTOR-POSITIVE BREAST CANCER

Postmenopausal women who have metastatic hormone receptor-positive breast cancer that has recurred or grown after treatment with chemotherapy are often treated with fulvestrant (Faslodex). The standard dose of this drug is 250 milligrams (mg) a month. However, doubling this dose may be even more effective in treating these women without increasing side effects, according to a recent clinical trial.

Estrogen receptor-positive cells depend on estrogen for their growth. So they can be treated effectively with anti-estrogen hormonal treatment, such as fulvestrant. The U.S. Food and Drug Administration (FDA) has approved fulvestrant for treating postmenopausal women with hormone receptor-positive metastatic breast cancer that has returned or grown after treatment with tamoxifen or other hormonal treatments.

More than 730 women took part in a late stage of research called the CONFIRM clinical trial. This aptly named study was designed to confirm the results of two other major clinical trials: the NEWEST and FIRST trials. All of these postmenopausal women had metastatic estrogen receptor-positive breast cancer that had returned or grown after hormonal treatment.

The women were divided into two groups. One group received the standard dose of fulvestrant (250 mg a month). The other group received a higher dose of fulvestrant (500 mg a month).

From the time treatment started, it took longer for the tumor to continue growing in patients given the higher dose of fulvestrant than in those given the standard dose (six-and-a-

half months versus five-and-a-half months). There appeared to be no increase in side effects with the higher dose.

Although researchers do not yet know whether these results will lengthen the lives of these women, they believe this is a good possibility. However, they hope to know for sure when further results of this clinical trial are available in the middle of 2011. Researchers also hope to learn which women with advanced breast cancer may benefit most from higher doses of fulvestrant.

Personalizing Treatment

In a new approach to treating breast cancer, doctors are moving away from "one-size-fits-all" treatments. Today, researchers are trying to determine the best approach for each patient based on her tumor's genes, or genetic makeup.

Every cell in the body contains approximately 30,000 genes. These genes create a blueprint for the human body and its functions. In the same way, the cells of each type of breast cancer have a different pattern of genes.

As doctors learn more about these patterns, they are finding ways to predict how some patients will respond to certain treatments. This kind of information is helpful for doctors as they make decisions about what treatments to recommend.

PREDICTING RECURRENCE OF BREAST CANCER WITH GENETIC TESTING

Based on the results of a test called the Onco*type* DX breast cancer assay, many physicians are changing their treatment plans. Using the test, they can now predict which women with estrogen receptor-positive breast cancer are not likely to benefit from chemotherapy. As a result, these women can be spared unnecessary side effects by not using a treatment that would probably not work for them.

Two recent studies have focused on the Onco*type* DX test. This test uses modern laboratory techniques to remove the genetic information, or DNA, from a tumor and evaluate 21 genes in the DNA. These are the genes that can predict benefit from chemotherapy. This test is also a powerful predictor of whether cancer will spread from one part of the body to another in women receiving hormonal treatment with tamoxifen or anastrozole.

In the first study, 160 doctors were surveyed regarding their treatment plans for 160 women with estrogen receptor-positive breast cancer. Nearly 70 percent of these women had cancer that had spread to one lymph node.

Before the test, chemotherapy plus hormonal therapy was planned for nearly 90 women (more than 50 percent). After the test, the recommended treatment was changed to hormonal therapy alone in 48 women (35 percent). The genetic test helped doctors spare these women from receiving chemotherapy and having to endure its side effects. Instead, the doctors could focus their treatment efforts on hormonal therapy, which could be more beneficial for this group.

ONCO*TYPE* DX HELPS PLAN TREATMENT FOR BREAST CANCER THAT HAS SPREAD

A recent study shows that Onco*type* DX may also be helpful in deciding on the best treatment for women who have breast cancer that has spread to the lymph nodes.

Researchers used Onco*type* DX to see which women with estrogen receptor-positive breast cancer that had spread to the lymph nodes would benefit from chemotherapy. More than 350 women took part in the clinical trial. Nearly 150 of them received treatment with the hormonal drug tamoxifen. The others were treated with chemotherapy (cyclophosphamide, doxorubicin, and fluorouracil) followed by tamoxifen.

According to the results of the Onco*type* DX test, 40 percent of the women were at lower risk of recurrence (return of their cancer) based on the genetic makeup of the breast cancer. Five years after treatment, women in this group did not seem to benefit from chemotherapy over tamoxifen alone. However, chemotherapy did appear to benefit women whose tumors were found to be in the high-risk group based on Onco*type* DX testing. Women with a high-risk score lived longer when treated with chemotherapy plus tamoxifen, compared with those treated with tamoxifen only (73 percent versus 54 percent).

These results must be confirmed in further studies.

Treatment Side Effects

Breast cancer and its treatments can cause a number of side effects. The key to managing these side effects, if they arise, is to be aware of them and to communicate with the members of your health care team. In that way, they can help you manage side effects so you can maintain the best possible quality of life during and after treatment.

NEW DRUG MAY OUTPERFORM STANDARD TREATMENT FOR BONE-RELATED SIDE EFFECTS

In a clinical trial, denosumab, which belongs to a new class of drugs called RANK ligand inhibitors, seemed to do a better job of delaying or preventing bone-related side effects than the standard drug zoledronic acid (Zometa).

RANK ligand is a protein that plays a major part in the way bone is formed and destroyed. By blocking the effects of RANK ligand, denosumab protects bone from breaking down, making it stronger.

Doctors know that it is very important to check the bones of women with breast cancer during and after treatment. There are two good reasons for this.

First, many breast cancer treatments can cause side effects in the bones. These side effects can increase a person's chances of developing osteoporosis.

Second, when breast cancer spreads to other parts of the body, the bone is often one of the first places it goes. When that happens, bones become weaker, often breaking, without any apparent injury. Cancer in the bone may require radiation or surgery. And cancer that has spread to the bone (bone metastases) can cause pain.

More than 2,000 women with breast cancer that had spread to their bones took part in a clinical trial to study denosumab. Half of the patients were given denosumab in a shot beneath the skin. The others were given zoledronic acid intravenously (through a vein).

Nearly three years after treatment, bone side effects occurred in about 30 percent of those who received denosumab, compared with 37 percent of those who received zoledronic acid.

Denosumab also seemed to be better tolerated than zoledronic acid. Flu-like symptoms occurred in 10 percent of the women who received denosumab, compared with about 27 percent of those treated with zoledronic acid. There were also fewer kidney problems with denosumab. This means there may be less of a need to keep close track of how the kidneys are working with denosumab, which is necessary with zoledronic acid.

Denosumab has not yet been approved by the FDA. However, doctors believe it probably will be approved first

for treating osteoporosis and then, perhaps later in 2010, for treating cancer that has spread to the bones.

SEVERE BONE CONDITION LINKED TO TREATMENT PROVES TO BE RARE

For people with cancer, bisphosphonates such as etidronate (Didronel and others), pamidronate (Aredia and others), alendronate (Fosamax and others), risedronate (Actonel and others), and zoledronic acid help prevent the loss of calcium from bone, reduce bone pain, strengthen bone, and reduce the risk of bone fractures (breaks). The drugs are also used by people with osteoporosis to slow or prevent further bone loss.

In recent years, researchers started to think that bisphosphonates given to cancer patients might increase the chances of developing ONJ, a rare but potentially serious side effect causing bone loss in the jaw that is difficult to treat. This assumption was based on a small study.

However, now researchers have performed a large study of this condition in more than 3,500 women who were treated for breast cancer. They say that the risk of ONJ is actually one percent, not the 16 percent previously reported.

The recent study included women with locally recurrent or metastatic breast cancer from three large clinical trials who received treatment with bevacizumab combined with chemotherapy and had taken bisphosphonates. Researchers say this is the largest-ever study of ONJ in women receiving bevacizumab for advanced breast cancer.

Even though ONJ appears to be rare, women with breast cancer who are being treated with bisphosphonates should remember that good dental and oral hygiene is very important to prevent ONJ. These women also should have regular dental examinations and avoid dental procedures that involve cutting the gums in the mouth.

Resources

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

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

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

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

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

Breast Cancer Network of Strength
1-800-221-2141
www.networkofstrength.org

Living Beyond Breast Cancer
1-888-753-5222
www.lbbc.org

Susan G. Komen for the Cure
1-877-465-6636
www.komen.org

To find out about clinical trials:

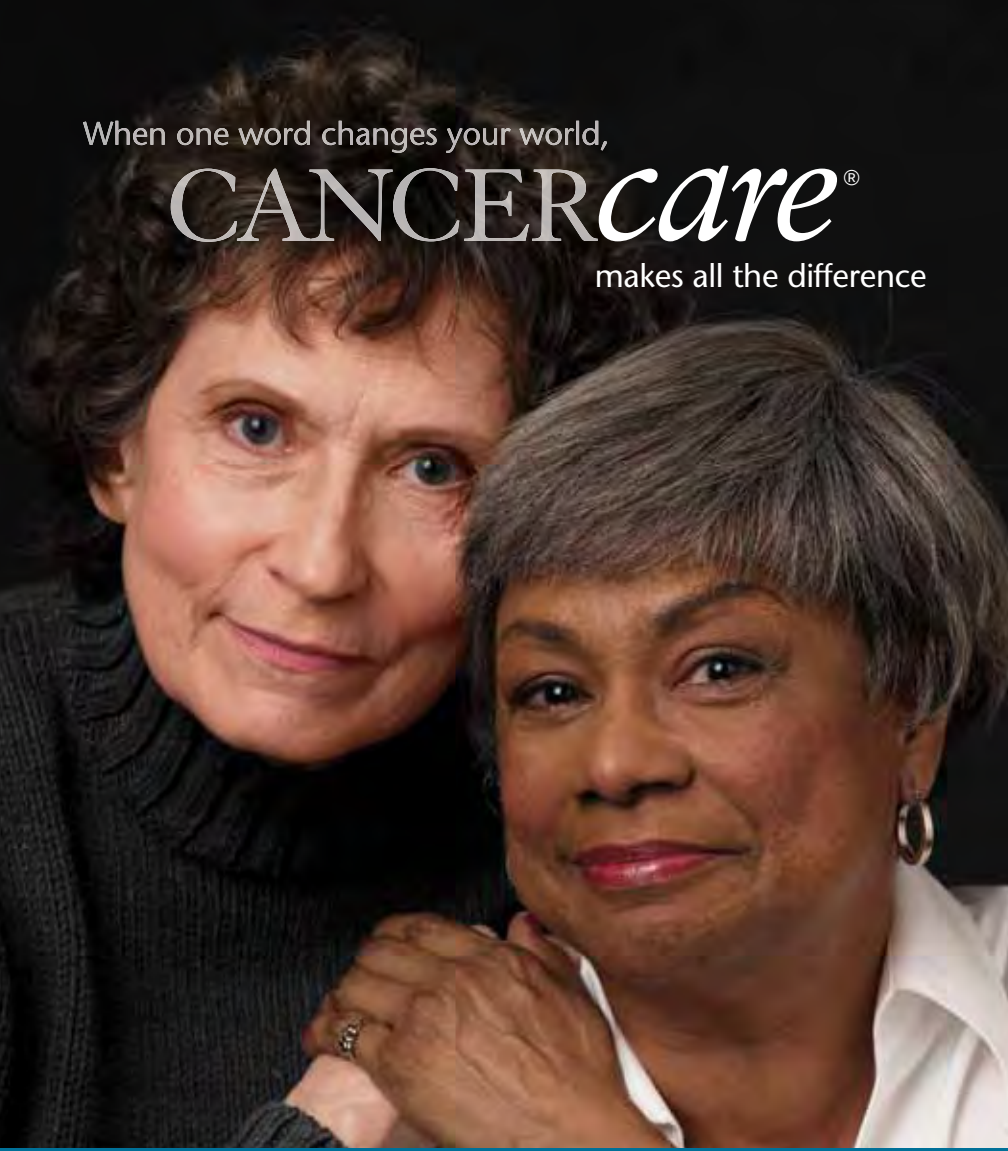
Coalition of Cancer Cooperative Groups
www.CancerTrialsHelp.org

National Cancer Institute
www.cancer.gov/clinicaltrials

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

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

This booklet was edited and produced by Elsevier Oncology.



With Cancer*Care*, the difference comes from:

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

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

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Help and Hope

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