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TREATMENT UPDATE

Breast Cancer

With Highlights from the 2015 San Antonio Breast Cancer Symposium

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TREATMENT UPDATE

Breast Cancer
With Highlights from the 2015 San Antonio Breast Cancer Symposium

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Editor

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For people coping with breast cancer, the number of treatment options continues to grow.

Each year in the United States, about 232,000 women and 2,350 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.

Although both women and men may be diagnosed with breast cancer, only about 1 percent of all cases occur in men. Because so few men have breast cancer, it is challenging for doctors to study the treatment of breast cancer in male patients separately in clinical trials. In this booklet, we refer only to women with breast cancer, but much of the information also applies to men. If you are a man affected by breast cancer, your health care team will tailor a treatment plan that best fits your situation.

In this booklet, we talk about the breast cancer treatments now available and new medicines in development. We also describe possible treatment side effects and how to prevent and cope with them, as well as how to communicate your needs to your health care team.

Biopsy Results Guide Treatment Decisions

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. Receptors are specialized proteins to which hormones and other chemical messengers in the bloodstream, like HER2, can attach and fuel the growth of cancer cells. These receptors may lie on the surface of cancer cells or within them. When hormone receptors are present, the tumor's growth can be stopped or slowed by one of several hormonal therapies available. About 75 percent to 80 percent of breast cancers are estrogen receptor (ER)-positive. Of these cancers, nearly two thirds also have receptors for the female hormone progesterone (PR-positive).

About 20 percent to 25 percent of breast cancers are HER2-positive. These cancer cells have an abundance of HER2 receptors on their surface. The attachment of HER2 to these receptors stimulates the growth of the cancer. 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 different 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 receptors on their surface. So certain drugs that work for hormone receptor-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. Studies have found that triple-negative breast cancer is twice as common in African-American women as it is in white American women, and the risk is particularly high among younger women of African descent. Clinical trials are pointing the way to new and better treatments for triple-negative breast cancer, especially for women with triple-negative breast cancer who also have a BRCA gene mutation (change).

Genomic Tests Help Determine the Need for Additional Treatment

In addition to biopsies, doctors also may order additional diagnostic tests to help choose the best treatment possible for each patient and to estimate the risk of cancer returning after treatment. One type of test that is being used more and more commonly is a genomic assay. These tests are designed to detect several genes or groups of genes in the cancerous cells. The presence of these genes can help doctors determine how likely it is that a patient with early-stage breast cancer will have her cancer return after first-line (initial) treatment. Having certain genes can also be associated with a higher likelihood of the cancer responding well to a particular drug.

Commonly used genomic assays include the Oncotype DX score, MammaPrint, and others. These tests give a quantitative estimate of benefit so that the woman and her doctor can decide whether or not it is worthwhile to use additional treatments, including chemotherapy or radiation. Women who are at low risk of cancer recurrence according to a genomic

assay may be safely spared the expense, time lost from work or family, and potential side effects of getting additional treatment to prevent their cancer from returning. Additional assays are in development, and all of these tests will continue to be studied to see how well they can predict treatment response and cancer recurrence rates in women with early-stage breast cancer.

Current 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. However, mastectomy does not completely eliminate the chances of the tumor coming back, and 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 and a shorter recovery time than mastectomy.

Surgical staging is also an important part of the treatment of breast cancer. In a staging surgery, the doctor assesses the size and microscopic patterns of the cancer cells in the breast to assess how likely the cancer is to return. The surgeon also removes one or more lymph nodes in the underarm near the affected breast to see if there are breast cancer cells hiding in them. (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.) In some cases the doctor will only remove the sentinel lymph node, which 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 may be present in the sentinel lymph node is not necessary. That is because finding such small amounts of tumor cells does not seem to affect survival.

Treatment recommendations need to be individualized, taking into consideration the biology of the cancer, the stage, and the preferences of the individual patient. All women with breast cancer who have had surgery and staging should talk with their oncologist about whether they will need further treatment. This treatment could range from more surgery to radiation plus systemic treatment (chemotherapy, hormone blockers and/or targeted treatments) or systemic treatment alone. Each of these treatments is discussed below.

Radiation

Radiation to the entire breast has been the standard of care for women who have been treated with lumpectomy. However, any form of radiation can damage healthy tissues and cause cosmetic deformities or unpleasant swelling or scars. In fact, when radiation is given in a more concentrated form to a smaller area of the breast, the cosmetic outcome may be worse than the damage caused by whole-breast radiation.

The British START trial showed that slightly higher daily doses of radiation given over as little as three to four weeks are as effective as the traditional practice of giving a higher total dose of radiation spread out over five to seven weeks, and may cause less-severe side effects. Additional benefits of the shorter treatment course include fewer visits for radiation treatments and lower out-of-pocket costs.

Several large clinical trials in Canada have since confirmed the findings of the START trial, and doctors have been encouraged

to offer the shorter treatment schedule after surgery to all eligible women age 50 and older with ER-positive breast cancer. Women with early-stage breast cancer who have had a lumpectomy should discuss their treatment options with their doctors.

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 chemotherapy 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. Diagnostic tests such as Oncotype DX and MammaPrint are now available to help identify those women with invasive ER-positive breast cancer who will likely benefit from the addition of chemotherapy to hormonal treatment (see page 9). These tests are run on a sample of the tumor that was removed during a biopsy or surgery and preserved. They often do not require another biopsy or further surgery.

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 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 about clinical trials:

- People who take part in clinical trials often gain access to and benefit from new treatments.
- Before you take part in a clinical trial, you will be fully informed about the possible risks and benefits.
- Most clinical trials are designed to test a new treatment against a standard treatment to find out whether the new treatment has any added benefit.
- You can choose to stop taking part in a clinical trial at any time for any reason.

Hormone Blockers

Doctors generally recommend hormonal therapy for ER-positive or PR-positive breast cancer. These treatments work in different ways. Some are designed to prevent estrogen or progesterone from attaching to receptors in 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 stimulation that fuels their growth.

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 tumor 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—cancer that has spread from where it started to other parts of the body—tamoxifen can stop the growth of the cancer and shrink the tumor.

Recently, tamoxifen has also been shown to reduce the chance of ER-positive breast cancer developing in healthy pre- or postmenopausal women at high risk for breast cancer. The preventive benefits of the drug extend for many years beyond when the drug is taken. However, treatment with tamoxifen slightly increases the risk of developing other cancers, including endometrial cancer. Healthy women who are at high risk for developing breast cancer should talk with their doctors about whether taking tamoxifen for breast cancer prevention is a good option for them. The doctor will consider multiple factors such as the woman's age, family history, biopsy results, and reproductive history.

Aromatase inhibitors (AIs) are another type of hormonal therapy. AIs are given to postmenopausal women with ER-positive breast cancer to help prevent the cancer returning after surgery or other treatment. In postmenopausal women,

AIs block the action of the enzyme, called an aromatase, cutting off the supply of estrogen that can stimulate tumor growth.

Three types of AIs are available in the United States: **anastrozole** (Arimidex and others), **letrozole** (Femara and others) and **exemestane** (Aromasin and others). Taking AIs for five years has helped countless postmenopausal women with ER-positive breast cancer survive longer without their cancer coming back. Most of these breast cancer survivors in clinical trials took an AI for five years after being treated with tamoxifen for five years.

However, AIs can have side effects, including joint pain, bone loss, hot flashes, and vaginal drying or itching. These side effects, which result from estrogen deprivation and are similar to those experienced by many women after menopause, can become so bothersome to patients that they stop taking AIs. In fact, studies have shown that up to one third of women with breast cancer on AIs stop taking them as directed.

Women who are taking AIs and are thinking of stopping them for any reason should talk to their oncologist first. Switching from one AI to another, taking vitamin D, exercising, acupuncture, and other approaches may lessen the side effects of AIs and help women obtain the full benefit of hormone treatment.

According to a large clinical trial that is still ongoing, anastrozole may prove to be an effective way to prevent breast cancer in women at high risk of developing the diagnosis, based on their family history. 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 those who were not given it.

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

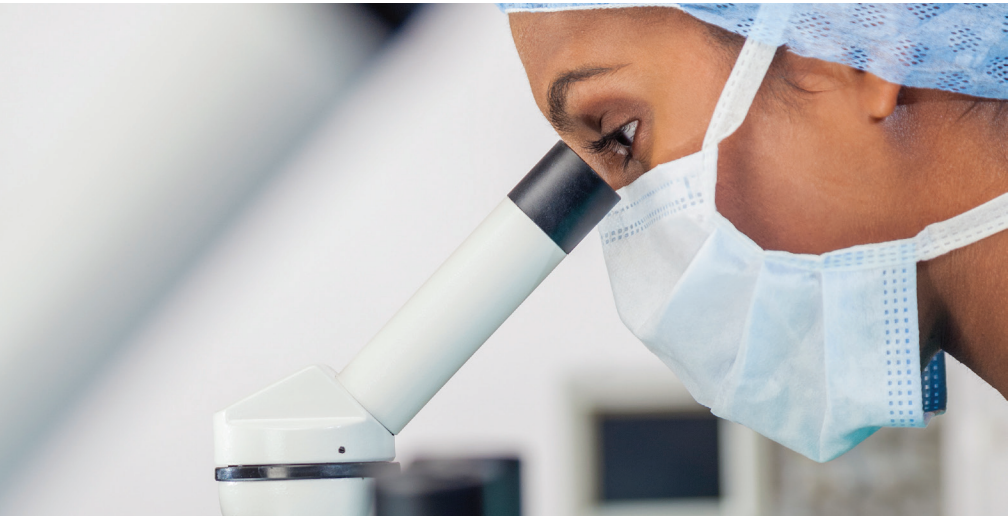
breast cancer cells. Fulvestrant is given as an injection and is approved only for postmenopausal women with metastatic breast cancer whose tumors have not responded well to other hormonal treatments such as tamoxifen.

In a recent clinical trial, women with locally advanced or metastatic breast cancer receiving fulvestrant survived significantly longer than those receiving anastrozole, which is the current standard of care. None of the women in this study had received hormone therapy before. The use of fulvestrant in women with metastatic hormone receptor-positive breast cancer is being studied further in a larger clinical trial.

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. The standard treatment for HER2-positive breast cancer is one year of trastuzumab. Trastuzumab can also be given to women whose HER2-positive breast cancer returns, even if they previously received the drug. The biggest drawback of trastuzumab treatment is that it can have negative effects on cardiac (heart) health, which can cause about 10 percent of women to have to stop taking it.

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. On the other hand, in women who have not yet undergone breast cancer surgery, lapatinib combined with trastuzumab also may lead to a significant response without the need for adding chemotherapy.



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 having surgery.

Ado-trastuzumab emtansine (Kadcyla), or **T-DM1**, is used to treat HER2-positive metastatic breast cancer in women 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 combination of trastuzumab (T) with a chemotherapy drug (DM1). The combination is designed to block HER2 receptors on the surface of breast cancer cells to prevent HER2 from attaching to them and stimulating their growth, while delivering DM1 deep within the cells to damage their ability to multiply and to kill them. T-DM1 also alerts the body's immune (defense) system to seek out breast cancer cells and destroy them. In addition to its use in metastatic breast cancer, several ongoing trials are studying T-DM1 as an adjuvant treatment for nonmetastatic breast cancer to prevent formation of secondary tumors.

Everolimus (Afinitor) is a type of targeted treatment that works inside cancer cells to restore their sensitivity to antiestrogen therapies such as AIs. In treating breast cancer, everolimus seems to help hormone therapy work more effectively, but it may cause increased side effects. Taken once a day with exemestane, everolimus treats advanced hormone receptor-positive, HER2-negative breast cancer in postmenopausal women whose cancer has continued to grow after treatment with other AIs. Recent studies also suggest that adding everolimus to trastuzumab and paclitaxel in women with advanced HER2-positive, hormone receptor-negative breast cancer may help prevent cancer growth in this particular group of women.

Palbociclib (Ibrance) is a targeted treatment that works by stopping breast cancer cells from dividing and growing. Palbociclib can be used in combination with one of two other drugs for the treatment of locally advanced or metastatic ER-positive, HER2-negative breast cancer. It was most recently approved for use with fulvestrant in women whose disease has progressed following endocrine therapy. It was also previously given accelerated approval for use with letrozole in postmenopausal women who have not received any hormonal therapy. In addition to these approved indications, palbociclib is currently being studied as a way of boosting the effectiveness of hormonal therapies.

Promising New Treatment Approaches: A Report from the 2015 San Antonio Breast Cancer Symposium

This section presents highlights from the 2015 San Antonio Breast Cancer Symposium, which took place December 8–12 in San Antonio, Texas. The information includes new findings on a number of currently used treatments, as well as promising new treatments that researchers continue to study in clinical trials.

Some of these new 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.

Node-Positive Breast Cancer

Predicting Recurrence Risk with Genomic Assays and Metagenes

A new research study has shown that the EndoPredict clinical index provides a very good assessment of recurrence risk in women with early-stage breast cancer. This study accurately identified a low-risk group of patients who are at very low risk for recurrence and thus may be spared chemotherapy. EndoPredict uses a genomic assay that tests for a panel of eight genes, and then combines that with a score for tumor size and tumor nodal status, to come up with a single risk predictor of who is most likely to have a recurrence of breast cancer. Compared with the commonly used Oncotype DX assay, which uses a panel of 21 or 22 genes, the EndoPredict clinical index provided more accurate information, partly due to the inclusion of tumor size and nodal status. The differences

between the two tests were greatest in the lymph node-positive population. This finding is especially encouraging because node-positive patients are the population in which guidance for treatment selection is often most needed.

A second research group examined data from an older study of postmenopausal women with breast cancer that is ER-positive and lymph node-positive. The researchers were looking at molecular predictors of outcomes in patients who have been treated with either a chemotherapy regimen called CAF (cyclophosphamide, doxorubicin, and fluorouracil) plus tamoxifen or tamoxifen alone. By examining "metagenes," which are closely related gene groups, they identified five metagene signatures that define excellent prognosis for patients on tamoxifen alone, despite having node-positive cancer. In particular, they found that a three-metagene signature could actually predict chemotherapy benefit.

What Patients Need to Know

The Oncotype DX system is widely used today, and it continues to provide important information for many doctors who are making decisions about adjuvant treatment to prevent breast cancer recurrence. However, the EndoPredict scoring system may be of particular value when added to the diagnostic work-up of patients with node-positive breast cancer, to help doctors determine which patients in this group will be most likely to benefit from chemotherapy or radiation after surgery. In addition, while not yet commercially available, the finding of the metagene signatures could lead to the development of new tests that could help identify those with node-positive breast cancer who may not need to undergo additional treatment. More studies on using these metagenes as recurrence predictors are likely to be presented in the future.

Early-Stage Breast Cancer

Osteoclast Inhibitors for Prevention of Bone Metastases

Bone is the most common site of distant recurrence of breast cancer (return of breast cancer outside the breast and the

lymph node area), especially in ER-positive breast cancer. When breast cancer cells get into the bone, they stimulate osteoclasts to break down bone, and that bone breakdown helps the breast cancer cells take hold. Osteoclast inhibitors are a class of drugs that prevent bone from being broken down by these osteoclasts. In breast cancer patients, these drugs have historically been used to treat patients whose cancer has already metastasized (spread) to their bones, to reduce bone fractures caused by these bone metastases and to help with pain. Outside of the breast cancer field, osteoclast inhibitors are also used to prevent and treat osteoporosis in the general (non-cancer) population.

The newest research question is whether osteoclast inhibitors can be used before cancer spreads to prevent breast cancer recurrences among women with early-stage breast cancer. The two main classes of osteoclast inhibitors are bisphosphonates like zoledronic acid (Zometa and others), and RANK ligand inhibitors such as denosumab (Xgeva, Prolia). The Austrian Breast Cancer Study Group 18 followed 3,425 postmenopausal women with ER-positive early stage breast cancer who were given denosumab to see if this drug could not only reduce bone fractures, but could also be used to reduce or prevent breast cancer recurrences in bone altogether. Denosumab 60 mg or a placebo was administered through a subcutaneous injection once every six months.

The authors of this study previously presented and published their finding that denosumab reduced bone fractures by about fifty percent at seven years. The new information presented in San Antonio this year was a second endpoint, which showed that at seven years of follow up, the group receiving denosumab had an 18 percent reduction in breast cancer recurrences compared with the group receiving the placebo. This supports the concept that slowing down bone turnover may make the bone a less inviting environment for breast cancer cells to take hold and grow. In this trial, there were no cases of osteonecrosis of the jaw, which is a very rare side effect of this class of drugs, and there were minimal other major side effects.

What Patients Need to Know

This new finding about denosumab adds to an existing body of research on osteoclast inhibitors. All of these findings support the theory that interfering with the destruction of the bone environment can reduce breast cancer recurrences in the bone, with very few side effects. This is only a preliminary finding, and more clinical trials will be needed to determine whether osteoclast inhibitors can safely and effectively be used to prevent bone metastases. Still, the new findings are encouraging, as osteoclast inhibitors seem to be a relatively safe group of drugs that may be able to improve outcomes in women with early-stage breast cancer.

HER2-Positive Breast Cancer

Trastuzumab as the Starting Point

Four trials were presented in San Antonio this year that showed interesting new findings in the area of HER2-positive cancers. One year of trastuzumab (Herceptin) is currently the standard treatment for this population, and the first study provided the data from ten years of follow up of one of the original trastuzumab trials. Patients either received

doxorubicin and cyclophosphamide followed by docetaxel and trastuzumab or a non-anthracycline-containing regimen of docetaxel, carboplatin, and trastuzumab. After ten years of follow up, the results show sustained and significant efficacy in the trastuzumab-containing regimens versus the non-trastuzumab containing regimens. Disease-free survival and overall survival were no different between the two regimens that contained trastuzumab. However, the regimen that contained doxorubicin had higher rates of leukemia and cardiac side effects compared with the regimen that got docetaxel, carboplatin, and trastuzumab. This study provided reassuring data that the benefits of trastuzumab hold up after ten years, and that we can alter the regimen for patients based on their cardiac risk.

Neratinib for Extended Therapy

The ExteNET trial was designed to study whether neratinib improves outcomes as adjuvant therapy. Patients with early-stage breast cancer were given the standard one-year course of trastuzumab and chemotherapy, followed by a one-year course of neratinib. The three-year disease-free survival rate with neratinib was improved by about 25 percent compared with trastuzumab alone. In the ER-positive population, the results were even more favorable. This drug is not currently FDA approved, but it is the subject of a great deal of research interest. 40 percent of patients in this trial had moderate to severe diarrhea in the first month of treatment, although in most cases the diarrhea stopped soon thereafter. Ongoing studies are looking at using preventive treatments like loperamide to avoid or reduce the diarrhea associated with neratinib. Nonetheless, it appears to be a promising drug for HER2-positive and hormone receptor-positive breast cancers.

T-DM1 for Early- and Late-Stage Cancers

Two trials focused on the drug ado-trastuzumab emtansine (Kadcyla), also known as T-DM1, which is FDA approved for HER2-positive metastatic cancer that has already been treated with trastuzumab and a taxane. The TH3RESA trial

involved women with metastatic cancer who had received more than two prior targeted therapies for advanced breast cancer, including lapatinib and a taxane. Patients were given either T-DM1 or a physician's choice of therapy. The study showed a 6.9-month improvement in overall survival with T-DM1 with few side effects. This may actually be an underestimate of the positive impact of the drug, because many of the patients who received other drugs crossed over onto the T-DM1 arm after the treatment chosen failed to produce a beneficial response.

Another T-DM1 study, the ADAPT trial, looked at prescribing T-DM1 earlier in the course of the disease, in the neoadjuvant or preparative setting. The researchers gave 12 weeks of either T-DM1 alone, T-DM1 plus endocrine therapy, or trastuzumab and endocrine therapy as a control group. The results showed that 41 percent of the patients who received just four doses of T-DM1 for those 12 weeks achieved a pathologic complete response, which compares very favorably to chemotherapy-containing regimens with pertuzumab and trastuzumab. There was also low overall toxicity. The conclusion from the study was that T-DM1 alone warrants further evaluation in early-stage breast cancer.

What Patients Need to Know

In general, smaller node-negative HER2-positive tumors may be able to be treated with a taxane and trastuzumab, while larger node-positive tumors can be treated with trastuzumab- and pertuzumab-containing regimens with chemotherapy. Extended adjuvant therapy with neratinib may provide added benefit, but this drug is not yet available outside of clinical trials, as we need more data on how best to manage the diarrhea that accompanies it. Finally, T-DM1 is available for treatment of metastatic HER2-positive cancer, and future clinical trials will bring more information about its use earlier in the course of breast cancer treatment for this population.

The Safety and Effectiveness of Lumpectomy for Early-Stage Breast Cancer

Lumpectomy vs. Mastectomy

Several presentations at the San Antonio Breast Cancer Symposium confirmed the safety and effectiveness of lumpectomy, sometimes called breast-conserving cancer treatment. A study of breast cancer in more than 37,000 patients from the Netherlands showed that breast cancer outcomes were somewhat better for the lumpectomy patients compared with the mastectomy patients. The authors suggested that this finding might be due to biologic differences in the women who underwent mastectomy compared to lumpectomy. It might also be related to the effects of the radiation treatment that generally accompanies lumpectomy.

A second study looked at the financial costs as well as the medical consequences of mastectomy followed by breast reconstruction versus lumpectomy for early-stage breast cancer. We know that breast reconstruction is a safe and

reasonable option for women requiring mastectomy for their breast cancer; however, this particular study confirmed that mastectomy with reconstruction is associated with a higher complication rate, which translates into a higher cost compared with the less expensive lumpectomy surgery. So this finding provides further support for lumpectomy as an effective procedure that also saves money and reduces complications.

Margin Width and Neoadjuvant Chemotherapy

A Danish study addressed the question of margin width in patients undergoing lumpectomy surgery. The margins of a breast lump are the surfaces of the tissue that is removed. After removing a lump, doctors examine the margins to decide how likely it is that any cancer cells were left behind in the breast; having "negative margins" means no cancer cells were found near the edges of the removed cells, so leftover cancer is unlikely. The researchers in this study found that women with widely negative margins did not do any better than those with narrower margins. This is reassuring because a large group of doctors recently agreed that a lumpectomy is adequate as long as the margins are negative. These findings reduce the need for patients to undergo repeat lumpectomy surgeries or even mastectomy surgery when the initial lumpectomy is shown to have narrowly negative margins.

A final study from the Breast Cancer Research Consortium confirmed that lumpectomy is also safe in women whose cancers have been treated prior to surgery with neoadjuvant (before surgery) chemotherapy. This is an important finding, as neoadjuvant treatment is becoming more and more common in breast cancer treatment.

What Patients Need to Know

These recent studies provide even more proof of what doctors have long believed, which is that lumpectomy is just as good as mastectomy in terms of breast cancer outcomes. In fact, some of these study findings suggest that lumpectomy may be an even better option than full removal of the breast, in part due to the reduced risk of cost and complications

from mastectomy and from the reconstruction of the breast that usually goes with it. Patients who receive neoadjuvant chemotherapy, as well as those who have narrow margins on their pathology report, can also rest assured that lumpectomy is a safe and effective surgical option for them.

Immune Checkpoint Inhibitors

Targeting PD-L1

One of the emerging areas of great interest in all types of breast cancer, but especially for the triple-negative type that is hardest to treat, is the role of immunotherapy. This field is focused on trying to harness the immune system to help fight cancer. Tumors are very good at hiding from the immune system, but immune checkpoint inhibitors are drugs that are designed to get around that challenge and make the cancer respond to the immune cells. Several of these drugs are in development. Some of these drugs target something called the programmed death-1 receptor (PD-1) and a related protein called PD-L1. PD-L1 is a key therapeutic target in the attempt to activate the immune response against cancer.

One anti-PD-L1 drug known as avelumab was used in a study called JAVELIN. The patients in this study had metastatic breast cancer, and about one third were triple-negative. They were given avelumab alone, without any additional chemotherapy. Generally the drug was well tolerated, and in some of the patients the tumors shrank. The researchers noticed that triple-negative patients whose tumors expressed PD-L1 seemed to have a greater likelihood of responding to this drug, so the next step is to examine that relationship more closely.

Another study, KEYNOTE, used a similar approach with a different drug, pembrolizumab. Data from this study has actually been presented previously at San Antonio regarding how often it causes tumors to shrink. What was shown this year was a different part of the study looking at women with ER-positive, HER-2 negative breast cancer, which is the most common type among women with metastatic breast cancer.

The researchers gave the drug only to women with PD-L1-positive tumors. About one in five of the patients seemed to have shrinkage of the tumor, and the tumor stopped growing for at least six months.

What Patients Need to Know

Immunotherapy is an exciting new field of research, not just for breast cancer but for many other cancer types as well; however, we are still in the early phases of these investigations. It is too early to draw definite conclusions, and more research is needed to determine when to use immune checkpoint inhibitors. Women with cancers that are positive for PD-L1 may be particularly good candidates to enroll in a clinical trial of one of these types of drugs. Your doctor can help you determine if this might be a good treatment option for you.

Triple-Negative Breast Cancer

Adding Platinum-Based Chemotherapy Drugs

Two studies presented in San Antonio looked at the addition of carboplatin, an older platinum-based chemotherapy drug, to more conventional anthracycline/taxane-based chemotherapy in the triple-negative population to see whether it can augment the cure rate in early-stage breast cancer. Researchers have reason to think that triple-negative breast cancers may be particularly sensitive to these drugs, as a few large studies have shown that adding carboplatin to conventional chemotherapy results in more patients achieving a pathologic response. However the two studies presented this year had conflicting results. The German study included about 300 patients with non-triple-negative breast cancers, which did not show much of a difference with the carboplatin overall. However, for the additional 300 patients in the triple-negative group, there was a small improvement in relapse rates with the addition of the carboplatin. Conversely, in the American Cooperative Group study, there was no significant difference with the addition of carboplatin for about 400 patients with triple-negative breast cancer.

What Patients Need to Know

At the moment, whether or not carboplatin is helpful in the triple-negative population is still an open question. More studies will be conducted to determine the usefulness of carboplatin as an addition to standard chemotherapy for this type of breast cancer. This will be an important question to answer, because effective treatments for the triple-negative cancer type are especially needed.

Residual Breast Cancer after Neoadjuvant Chemotherapy

Capecitabine to Improve Survival

This was a Japanese study on HER2-negative patients with residual (left over) breast cancer after receiving neoadjuvant chemotherapy. There were 910 patients, half of whom received additional chemotherapy with capecitabine (Xeloda), a drug often used in metastatic cancer. The other half did not receive the study drug but received standard adjuvant chemotherapy. The capecitabine improved survival rates, but it was also associated with significant toxicity, including low white blood cell counts, diarrhea, and hand-foot syndrome (redness, pain, and swelling on the palms and soles) that caused up to 25 percent of patients to stop taking it.

What Patients Need to Know

Similar studies in the past did not find that capecitabine made a major difference in patients with cancer remaining after neoadjuvant chemotherapy, so more research will be needed to confirm the findings of this study. Because women with residual breast cancer are at greater risk of relapse, doctors are likely to keep studying this drug to determine whether capecitabine can improve survival rates in this group.

Hormone Blockers for ER-Positive Breast Cancer

Anastrozole vs. Tamoxifen for DCIS

DCIS (ductal carcinoma in situ) is a type of breast cancer that is not invasive. After surgical removal of the tumor, DCIS is often treated with hormone blockers both to prevent recurrence and to prevent a tumor in the other breast or a second invasive cancer. The study IBIS-II compared two types of hormone blockers for the treatment of DCIS. This was a large study, with 2,800 postmenopausal women between ages 40 and 70 who were given either tamoxifen or anastrozole after undergoing surgery. The two drugs appeared to be equally effective at preventing the recurrence of non-invasive disease and in preventing the development of invasive breast cancer. Those results suggest that it is very important to consider the side effects of each drug when choosing between tamoxifen and an AI. As seen in other studies, tamoxifen is more likely to cause uterine cancer and blood clots than AIs, so that risk may be particularly important for patients who have a family history of these conditions or who are at increased risk for either. Hot flashes are also slightly worse in patients taking tamoxifen. On the other hand, the women in

this study who took anastrozole experienced bone fractures, as well as joint and muscle pain and high cholesterol. So the risks of these side effects need to be considered when choosing the best hormone blocker medication for an individual patient.

Another study, NSABP B-35, previously looked at these same drugs in a similar setting and concluded that anastrozole was more effective than tamoxifen. But this year in San Antonio, those researchers presented some of the symptom data from that study. They also found that hot flashes were more commonly reported in the women who took tamoxifen, whereas joint pains and vaginal dryness were more problematic with anastrozole. Interestingly, in the NSABP B-35 study, women younger than 60 had more trouble with side effects, such as hot flashes, vaginal dryness, and weight gain.

What Patients Need to Know

These studies taken together emphasize that the side effect profiles of different types of hormone blockers can be very important when making decisions between therapies that have similar efficacy. Women who have increased risks for blood clots or high cholesterol because of their personal or family medical history may make different choices than women who have an especially difficult time coping with hot flashes or joint pain. In choosing a hormone blocker, it is important that each patient has a discussion with her doctor about which side effects may make one drug preferable to another in her particular situation.

Advanced ER-Positive Breast Cancer

Fulvestrant Plus Buparlisib

Patients in the BELLE-2 study had postmenopausal metastatic breast cancer that was ER-positive and HER2-negative, and their tumors had progressed either while taking an aromatase inhibitor or soon afterwards. Participants received either fulvestrant alone or fulvestrant with a targeted therapy called buparlisib. Fulvestrant is chemically related to tamoxifen and

has been proven effective to control metastatic breast cancer. Buparlisib, on the other hand, is an experimental drug that is under study in a variety of settings. This drug inhibits a protein called PI-3-kinase, which is of particular importance in ER-positive breast cancer. The results showed a significantly longer control of metastatic breast cancer with the addition of buparlisib, but only in patients whose circulating tumor DNA (genetic material floating in their bloodstream) had a PI-3-kinase mutation. Those whose tumor DNA did not carry that mutation did not seem to receive any benefit from buparlisib.

What Patients Need to Know

This is a very encouraging study that suggests that buparlisib may have a place in breast cancer treatment for the subgroup of patients who carry this particular type of genetic mutation. Findings like these support the use of personalized medicine, which aims to tailor therapies to the individual genetic make-up of each person's unique type of cancer.

Breast Cancer Survivorship

Risks of Radiation and Long-Term Emotional Health

Many patients with breast cancer may worry that the radiation treatment they receive to the chest can cause additional cancer. A study looking at the side effects of radiation showed that the risk of lung cancer from radiation for breast cancer is only present in smokers. Patients who do not smoke do not seem to have an increased risk of lung cancer after radiation for breast cancer—or if there is an increased risk, it is less than 1 percent.

Another issue that many doctors and patients worry about is the long-term emotional health of women who go through breast cancer treatment. In a Korean study, breast cancer survivors who were at least two years beyond their initial diagnosis were surveyed and compared to matched healthy women who have never had cancer. Interestingly, psychosocial health was found to be better in the cancer survivors than in the women who had not had cancer.

What Patients Need to Know

The findings about lung cancer risk are very reassuring, given that radiation is an important and highly effective treatment option for breast cancer. This is particularly true as more and more patients move away from full mastectomy and toward breast-conserving surgeries like lumpectomy, because lumpectomy is generally accompanied by radiation to treat any remaining cancer cells. The results of the emotional and psychosocial health study speak to the fact that some survivors undertake health-promoting behaviors and actually experience positive emotional changes after breast cancer, particularly after the acute toxicities of chemotherapy and radiation resolve. It is comforting to know that once the most intense treatment period is over, breast cancer survivors may be happier and mentally healthier than ever.

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 may 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.

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, fruits and vegetables such as cauliflower or broccoli.
- Drink plenty of fluids.
- Make light exercise a part of your everyday schedule.

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 tissues 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.

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 they are 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.

Hair loss is often one of the more frustrating aspects of chemotherapy. When hair falls out, it can affect a woman's self-image and quality of life. Depending on the treatment, hair loss may start anywhere from one to three weeks after the first chemotherapy session. Hair usually starts to grow back after you are finished with treatment. It may have a different texture or color, but these changes are normally temporary.

Many women who lose their hair after chemotherapy choose to wear some kind of head covering, whether it's a scarf, turban, hat, or wig. Some insurance plans cover part of the cost of these head coverings. If you choose to wear a wig, consider buying one before all of your hair falls out. This way, you will have a good match to your own hair color. Having a wig ahead of time also will help you feel more prepared. You can have your wig professionally fitted and styled by a full-service wig salon. Some salons specialize in hair loss from chemotherapy.

Nerve damage. Some women on chemotherapy or targeted treatments experience numbness or tingling in their hands and feet—what doctors call peripheral neuropathy. Other symptoms of nerve damage include difficulty picking up objects or buttoning clothing, problems maintaining your balance, difficulty walking and hearing loss. These symptoms can become worse over time. It's important to tell your doctor as soon as possible if you experience these types of side effects. He or she may want to adjust some of your medicines

or chemotherapy and may want to see if there is another reason for the problem that can be treated.

Often, nerve damage due to cancer treatment is temporary; it will usually get better, but it can take time. If you are coping with this side effect, take extra care when handling hot, sharp, or dangerous objects. Also, use handrails on stairs and in the tub or shower.

Lymphedema. Women with breast cancer who have undergone lymph-node removal and/or radiation as part of their treatment are at risk for developing lymphedema. Lymphedema is a painful swelling that happens when your body's lymphatic fluid is unable to circulate properly and builds up in your soft tissues instead. It usually occurs in an arm or leg. Here are some things you can do:

- Get help for your symptoms as soon as possible. In addition to swelling of the affected limb, the most common problems associated with lymphedema are pain, hardening of the skin and loss of mobility. If left untreated, the swelling can get worse and may cause permanent damage.

- Consider undergoing manual lymph drainage, or MLD. This type of massage helps move the fluid out from where it is settled. Afterward, the affected limb is wrapped in low-stretch bandages that are padded with foam or gauze.
- Learn exercises that can help prevent swelling due to fluid build-up. Your health care team can refer you to a program of special exercises that are taught and monitored by a physical therapist.
- Wear a compression sleeve. This can help drain the lymph fluid. It's important to wear a compression garment when flying, even on short flights.
- Always treat scratches, cuts, and insect bites by cleaning the area and applying an antibiotic ointment. If you notice swelling or redness, contact your health care team immediately. Bring your own nail-care supplies when you have a manicure, and ask them not to cut your cuticles.
- Wear gloves when gardening or removing hot items from the oven or stove.
- Be kind to your body. Carrying heavy packages, luggage, or shoulder bags puts stress on your affected limb and could cause additional swelling and pain.

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.

Memory lapses. After chemotherapy, some people have difficulty concentrating or thinking clearly. If you experience what is often called chemobrain, speak with your health care team. Studies show that feeling tired or anxious even before treatment may make it more challenging to focus afterward. 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 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.

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 (Zometa and others) slow the process by which bone wears away and breaks down. This class belongs to a group of drugs called osteoclast inhibitors.

- 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, Prolia), which has been shown to be less toxic and cause fewer kidney problems than zoledronic acid. Like bisphosphonates, RANK ligand inhibitors are a type of osteoclast inhibitor.
- SERMs (selective estrogen receptor modulators) are believed to slow the breakdown and removal of old bone. Examples of SERMs are raloxifene (Evista and others), 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 health care team 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 can 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 to cool yourself off. 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 a personal lubricant or moisturizer such as Astroglide, K-Y or Replens.

- If vaginal dryness persists, 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 also can 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 dialogue 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 treatments that include 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 doctors and nurses, it's important that you feel comfortable talking about any topic related to your diagnosis and treatment. Here are some tips:

Prioritize your questions and concerns. It may not be possible to get to every item on your list, so write down your questions before each visit and place them in order of their importance. Make sure whoever accompanies you agrees on which questions need to be answered.

Keep in mind that you are a consumer of health care. Seek out doctors who have experience treating breast cancer. Make sure that your doctors are available to you based on your schedule and location—and that the cost of seeing them is not prohibitive. Take ownership of your own health care, and be active and engaged in the process of getting the care you need.

Think about how you prefer to communicate. Do you want the "big picture," or do you need to know all the details? Do you want to be an equal partner with your doctors in making treatment decisions, or do you want to be well informed but leave the decisions to them? Tell your oncologist how much you want to know and your preferences.

Teach your oncologist to work with you. Oncologists may be experts in diagnosing and treating cancer, but they are not mind readers. However, they will listen and work with you in a way that best meets your needs if you let them know what they are. You and your doctor should learn from each other.

Make the conversation about you, and share with your health care team what matters most to you. Increasingly, we are facing choices and trade-offs, where something has to go to achieve a more important goal. For example, if you are a young woman recently diagnosed with a hormone-sensitive breast cancer, your oncologist may recommend a treatment

that blocks the function of your ovaries. This means you will spend at least five years managing the symptoms of early menopause. Though temporary, those symptoms will affect your quality of life. It's important to partner with your health care team to explore all of these options.

Tell your oncologist what you worry about. For instance, it could be the cost of your medicine, the difficulty of taking time off from work for treatment, or the effect fatigue is having on your social life. Your health care team is there to help you. The most important thing is to try to establish a relationship that thrives on open communication.

Create a survivorship care plan with your oncology team. Survivorship care plans are documents that summarize for you and your primary care providers the details of the cancer diagnosis, what types of treatments were received, and what you should expect in the years to come regarding symptoms to watch for, visit frequency, follow-up tests and imaging, and other things to consider as a breast cancer survivor. This document is an important vehicle for communication between the oncology team, the patient, and the patient's primary care providers.

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 also can 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. Cancer*Care*'s professional oncology social workers work with you one-on-one to develop strategies for coping with treatment and its side effects.

Oncology social workers also 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*, people with 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.

Frequently Asked Questions

Q. How is triple-negative breast cancer diagnosed?

A. The triple-negative status, meaning the absence of the three major molecular markers, is generally diagnosed at the initial biopsy. For many women this is done with a core needle biopsy, in which tissue is extracted through a special biopsy needle and then analyzed under the microscope. The pathology doctors apply particular stains to the biopsy material on the microscope slide and then evaluate the tissue to determine whether the tumor expresses hormone receptor markers or HER2 markers. Patients who have surgical biopsies may have those markers tested again on the surgical specimens, and occasionally some specimens may need to undergo more sophisticated testing of their genetic content to evaluate these markers. However, for the most part, a triple-negative cancer can be diagnosed with just the initial biopsy.

Q. If denosumab has been linked to an 18 percent reduction in breast cancer recurrence, is it being prescribed now for indications besides osteoporosis? Can women without bone loss take it to prevent breast cancer recurrence?

A. The data reported this year on reduced breast cancer recurrence in the bone is very interesting, and it is consistent with data from other trials that have looked at not only RANK ligand inhibitors like denosumab, but also other osteoclast inhibitors such as bisphosphonates.

The dilemma for prescribers is that denosumab is only indicated for osteopenia and osteoporosis, which are both degrees of bone loss. It is not currently indicated for women with normal bone health to reduce the risk of breast cancer recurrence. Unless the FDA approves the use of the drug for that indication, third-party insurance companies are unlikely to pay for the drug for women with normal bone density who want to use it to reduce their cancer recurrence risk. Clinical trials often move faster than actual practice. For now, your best chance of accessing denosumab for the prevention of breast cancer recurrence is to enroll in a clinical trial.

Q. What is the latest information on the management of lymphedema?

A. Lymphedema is one of the most difficult complications of breast cancer treatment, and doctors are working on both management and prevention strategies. Most often lymphedema occurs in women who have undergone a full surgical removal of the underarm lymph nodes. Fortunately, today many women are diagnosed with node-negative breast

cancer by having a minimally invasive procedure called a sentinel lymph node biopsy, in which only the most important lymph node is removed, thus dramatically reducing the risk of lymphedema.

Nonetheless, some women do still require full axillary lymph node dissection, and researchers are working to identify strategies—such as a procedure called reverse axillary mapping—to allow for more refined dissection of the lymph nodes that could reduce the risk of lymphedema. Right now these strategies are still being studied.

For those women who do develop lymphedema, plastic surgeons are developing new microvascular surgery strategies that allow them to improve the lymphatic drainage of the arm, resulting in some improvement in cases of severe lymphedema.

Finally, there are some studies that suggest that weight management and exercise may be helpful for managing lymphedema. Because data suggest that exercise and weight management may help prevent breast cancer recurrence as well, breast cancer survivors are encouraged to exercise both for lymphedema management and for general health and reduction of recurrence risk.

It is important to work with your health care team to address lymphedema and other survivorship issues. You can also call Cancer*Care* with any questions having to do with emotional or social coping with your cancer or practical issues that you may be confronting. Cancer*Care*'s HopeLine number is 800-813-4673. No one needs to feel alone in coping with breast cancer. We want you to know that you are now part of the support world of Cancer*Care*. We have a large staff of oncology social workers, and we are help to help with any practical and emotional challenges.

Resources

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

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

Cancer.Net
888-651-3038
www.cancer.net

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

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

National Comprehensive Cancer Network
215-690-0300
www.nccn.org/patients

BreastCancer.org
610-642-6550
www.breastcancer.org

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

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
215-789-3600
www.CancerTrialsHelp.org

EmergingMed
877-601-8601
www.emergingmed.com

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

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for Help and Hope, visit or call:

WWW.CANCERCARE.ORG
800-813-HOPE (4673)