TREATMENT UPDATE:

Breast Cancer With Highlights from the 2016 San Antonio Breast Cancer Symposium

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

Each year in the United States, more than 300,000 women 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, prescribing specific medicines for specific types of breast cancer.

Although men may also be diagnosed with breast cancer, only about 1 percent of all cases occur in men. Because of this, it is challenging for doctors to conduct clinical trials on the treatment of breast cancer in male patients. In this update, 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 update, we talk about the breast cancer treatments now available and new medicines in development. We also describe how to cope with possible treatment side effects, and how to communicate your needs to your health care team.

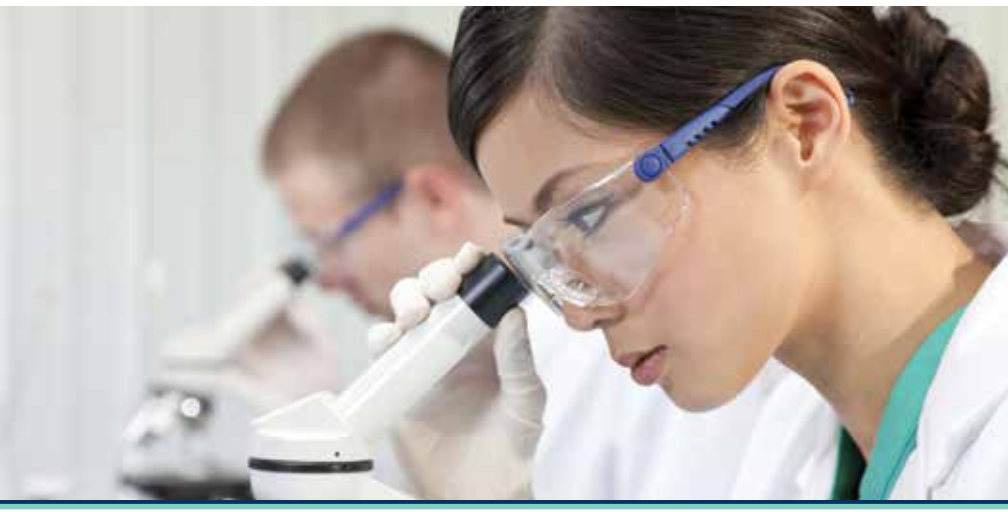
Types of Breast Cancer

Hormones and other chemical messengers in the bloodstream can attach to specialized proteins (called receptors) and fuel the growth of cancer cells. These receptors may lie within cancer cells or on the surface of those cells.

Cancers that are positive for the "estrogen receptor" (ER) account for about 65 percent of breast cancers. Nearly two thirds of ER-positive cancers also have receptors for the female hormone progesterone (are PR-positive as well as ER-positive).

Cancers that are positive for the "human epidermal growth factor receptor 2" (HER2) have an abundance of HER2 receptor cells on their surface. They are less common than ER-positive cancers, accounting for about 20 percent of cases.

Approximately 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.



Diagnostic Tests

Mammogram

A mammogram is an X-ray picture of the breast. It is often the first test used to check for breast cancer in women who have a lump or another sign of tumor growth. A mammogram is also used as a screening test in women who have no signs or symptoms of breast cancer. If the doctor sees anything suspicious, additional tests are conducted.

Biopsy

Tests performed on tumor samples provide your doctor with valuable information that helps guide treatment decisions. One such test is a biopsy, in which your doctor uses a hollow needle to remove a tissue sample from the tumor so that it can be examined 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 an indication 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 the tumor's "hormone receptor status"—whether or not the tumor's growth is driven by hormones (ER-positive, PR-positive, or HER2-positive).

Surgical Staging

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 they contain cancer cells. (Lymph nodes filter and trap bacteria, viruses, and other unwanted substances in the body, so that they can be destroyed by white blood cells called lymphocytes.)

In some cases, the surgeon will remove only the "sentinel lymph node," the first lymph node into which breast cancer cells spread. If the sentinel lymph node is cancer-free, chances are that other lymph nodes are also unaffected and can be left in place, reducing the risk of lymphedema, a painful swelling of the arm that can result from the removal of lymph nodes.

Genomic Tests

For women with early-stage breast cancer, a test called a "genomic assay" may be used. This test is 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. (The recommended first-line treatment is dependent on the type of cancer as well as other factors.) 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 provide a quantitative (numbers-based) analysis that can help the woman and her doctor decide if additional treatment, such as chemotherapy, should be pursued.

Other genomic 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 (the return of the cancer) rates in women with early-stage breast cancer.

Treatment Options

Treatment recommendations need to be individualized, taking into consideration the biology of the cancer, its stage, and the preferences of the patient.

Young women diagnosed with breast cancer often receive treatments that include radiation and chemotherapy. For many of these women, 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, and what can be covered by your insurance, 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, in which 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.

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 often offering a better cosmetic result and a shorter recovery time than mastectomy.

All women with breast cancer who have had surgery (mastectomy or lumpectomy) should talk with their oncologist about whether they will need further treatment. Post-surgical treatment options are discussed in the following sections.

Radiation

Radiation to the entire breast has been the standard of care for women who have undergone a lumpectomy. However, any form of radiation can damage healthy tissues and cause cosmetic deformities, swelling, and scarring.

A British trial called START (Standardization of Breast Radiotherapy) showed that slightly higher daily doses of radiation given over as few 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.

Several large clinical trials in Canada have since confirmed the findings of the START trial, and doctors have been encouraged to discuss the shorter treatment schedule with their patients who have undergone a lumpectomy for an ER-positive tumor.

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 use chemotherapy more effectively, 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 possible side effects.

Chemotherapy can be used before surgery (neoadjuvant chemotherapy) to try to shrink the tumor so the surgery can be less extensive, or after surgery (adjuvant chemotherapy) to try to kill any remaining cancer cells. It can also be used for women whose breast cancer has metastasized (spread outside the breast and underarm area).

The most common chemotherapy drugs used to treat breast cancer include:

- Anthracyclines, such as doxorubicin (Adriamycin) and epirubicin (Ellence)
- Carboplatin (Paraplatin)
- Fluorouracil (5FU)
- Cyclophosphamide (Cytoxan)
- Taxanes, such as paclitaxel (Taxol and Abraxane) and docetaxel (Taxotere)

Hormone Therapy

Doctors generally recommend hormone therapy as a first-line treatment 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 that circulate in the body and attach to estrogen or progesterone receptors. By blocking hormones, these treatments deprive tumor cells of the stimulation that fuels their growth.

- **Tamoxifen** (Soltamox, Nolvadex) is an estrogen-blocking treatment given to both premenopausal and postmenopausal women with breast cancer. Studies have shown that taking tamoxifen for five years following surgery reduces the chance

of the cancer coming back by fifty percent. Tamoxifen also lowers the risk of a new tumor developing in the other breast.

Some recent studies show that taking tamoxifen for ten 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 been shown to reduce the chance of ER-positive breast cancer developing in healthy premenopausal or postmenopausal women who are at high risk for breast cancer. The preventive benefits of the drug extend for many years beyond when the drug is taken. However, in postmenopausal women, treatment with tamoxifen slightly increases the risk of 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 hormone 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 a certain 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 (either alone or after five years of tamoxifen) has helped many postmenopausal women with ER-positive breast cancer survive longer without their cancer coming back. Recent data suggests that taking an AI for ten years may be an effective option for some women.

- **Fulvestrant** (Faslodex), another estrogen-blocking drug, works in a slightly different way. It attaches to estrogen receptors and changes their shape, preventing 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 hormone treatments, such as tamoxifen.

Targeted Treatments

Targeted treatments focus on specific molecules and cell mechanisms thought to be important for cancer cell survival and growth, taking advantage of what researchers have learned in recent years about how cancer cells grow. Targeted treatments are meant to spare healthy tissues and cause less severe side effects than chemotherapy.

A number of targeted treatments have been developed for breast cancer:

- **Trastuzumab** (Herceptin) is the standard treatment for HER2-positive breast cancer. Typically taken for one year, trastuzumab can also be given over longer periods to women with metastatic disease.

- **Lapatinib** (Tykerb) also targets HER2-positive breast cancer. Lapatinib is able to block HER2 signals from within cancer cells. Lapatinib has been shown to be effective in women whose HER2-positive breast cancer returned, spread, or continued growing despite treatment with trastuzumab and chemotherapy.

- **Pertuzumab** (Perjeta) has been shown to be an effective treatment for HER2-positive breast cancer. Given intravenously (into a vein) every three weeks, pertuzumab is used in combination with the targeted treatment trastuzumab and the chemotherapy docetaxel (Taxotere) or paclitaxel (Taxol).

- **Ado-trastuzumab emtansine** (Kadcyla), also known as T-DM1, is a combination of trastuzumab and a chemotherapy drug. T-DM1 is used to treat HER2-positive metastatic breast cancer in women who have already received treatment with the targeted treatment trastuzumab and chemotherapy that

included a taxane such as docetaxel or paclitaxel. The trastuzumab is designed to block HER2 receptors on the surface of breast cancer cells to prevent HER2 from attaching to them and stimulating their growth. The chemotherapy is delivered deep into the cancer cells to kill them and to damage their ability to multiply; it also alerts the body's immune system to seek out breast cancer cells and destroy them.

- **Everolimus** (Afinitor) is a type of targeted treatment that works inside cancer cells to restore their sensitivity to anti-estrogen therapies such as aromatase inhibitors (AIs). In treating breast cancer, everolimus seems to help hormone therapy work more effectively, but it may cause increased side effects. Taken once each day with the AI exemestane, everolimus treats advanced hormone receptor-positive, HER2-negative breast cancer in postmenopausal women whose cancer has continued to grow after treatment with another AI.

- **Palbociclib** (Ibrance) is a targeted treatment that works by stopping breast cancer cells from dividing and growing. Palbociclib can be used in combination with letrozole or fulvestrant for the treatment of locally advanced or metastatic ER-positive, HER2-negative breast cancer.

- **Ribociclib** (Kisqali) a cyclin-dependent kinase 4/6 inhibitor, was approved by the FDA in March 2017 as an initial therapy, in combination with an aromatase inhibitor, for the treatment of postmenopausal women with HR-positive/HER2-negative advanced (metastatic) breast cancer.

Ovarian Suppression Combined with Tamoxifen or Aromatase Inhibitors

The estrogen produced by the ovaries can fuel tumor growth. "Ovarian suppression" uses drug therapy or surgery to stop the ovaries from producing estrogen. Some younger, premenopausal women with hormone receptor-positive breast cancer may benefit from treatment with ovarian suppression drugs, combined with tamoxifen or an aromatase inhibitor. Ovarian suppression drugs include leuprolide (Lupron) and goserelin (Zoladex).

The Importance of Clinical Trials

Clinical trials are the standard by which we measure the worth of new treatments and the quality of life of patients as they receive those treatments. For this reason, doctors and researchers urge people with 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 that you should know:

- Often, people who take part in clinical trials gain access to and benefit from new treatments.
- Before you participate in a clinical trial, you will be fully informed as to the risks and benefits of the trial, including any possible side effects.
- 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 stop taking part in a clinical trial at any time for any reason.

Promising New Treatment Approaches: A Report from the 2016 San Antonio Breast Cancer Symposium

This section presents highlights from the 2016 San Antonio Breast Cancer Symposium, which took place December 6–10 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 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.

Extending Hormone Therapy for Hormone-Positive Breast Cancer

About two-thirds of breast cancers are hormone receptor-positive and are often successfully treated with hormone therapy. The risk of recurrence, however, continues even after 20 years; therefore, researchers feel that extending hormone therapy beyond the current standard is worthy of study.

The results of three clinical trials were presented:

- For postmenopausal women with early stage hormone receptor-positive breast cancer, the Dutch DATA study looked at the possible benefit of using the aromatase inhibitor (AI)

anastrozole for either three or six years, after an initial two to three years of the estrogen-blocking tamoxifen. The results of the study—which had approximately 2,000 participants—suggest that there may some benefit to extending treatment with an aromatase inhibitor for certain patients; specifically those who have undergone prior chemotherapy and whose breast cancer is ER-positive, PR-positive, or HER2-positive.

- Another Dutch study, the phase III IDEAL trial, evaluated extending treatment with the AI letrozole after five years of hormone therapy. The study enrolled 1,824 patients between 2007 and 2011. Ten years after diagnosis, there was no observable difference in disease-free survival when comparing 2.5 years of treatment with letrozole to 5 years of treatment with letrozole, and the conclusion was that there is no general benefit to extending therapy with letrozole beyond 2.5 years. However, it is important to note that extending treatment with letrozole made a slight difference in preventing a second primary breast cancer.

- A study named NSARP B-42 evaluated the potential benefit of extending the AI letrozole for an additional five years, after five years of initial letrozole therapy treatment for early stage breast cancer. The study included approximately 4,000 women, who took either letrozole or a placebo (a look-alike containing no active ingredient) for an average of about two years following their initial treatment. The study results showed there was no statistically significant benefit of extending letrozole, in terms of either disease-free survival or overall survival.

What Patients Need to Know

Researchers and clinicians always evaluate the possible benefits and possible risks of any cancer treatment. In the case of extended hormone therapy, the benefits appear to be small and are weighed against significant side effects which can affect a woman's quality of life. There is agreement among the researchers that for most women being treated by an AI, five years of therapy is adequate; and that only the highest-risk patients should consider extending AI treatments.

Aromatase Inhibitor Effectively Added to Targeted Treatments for HER2-Positive Breast Cancer

The results of a phase II study called PERTAIN suggest that, for certain women, the addition of pertuzumab (Perjeta) to an aromatase inhibitor (AI) and trastuzumab (Herceptin) improved progression-free survival (PFS).

The PERTAIN trial enrolled 258 postmenopausal women with HER2-positive locally advanced or metastatic breast cancer. The participants were randomized to receive either a) pertuzumab with trastuzumab or b) trastuzumab alone. Both groups also received treatment with an AI. In some cases, induction chemotherapy was given prior to starting the combination of the targeted treatment(s) plus the AI.

When compared with trastuzumab plus an AI, the addition of pertuzumab to a combination of trastuzumab and an AI improved PFS by 3.09 months.

What Patients Need to Know

The most common serious AEs (grade≥3) were the same in the group treated with pertuzumab and trastuzumab plus an AI as they were in the group treated with trastuzumab alone plus an AI:

hypertension, seen in 10.2% of the pertuzumab plus trastuzumab group vs. 11.3% of the trastuzumab-only group; diarrhea (7.1% vs. 2.4% respectively), and neutropenia, an abnormally low level of white blood cells called neutrophils (3.1% vs. 6.5% respectively). The combination of pertuzumab, trastuzumab, and an AI was generally well tolerated and no new safety signals were identified.

Addition of AI to Neoadjuvant Chemotherapy Did Not Improve Results in Women with Hormone Receptor-Positive Breast Cancer

Patients whose tumors are ER-positive usually have a lower response rate to neoadjuvant (pre-surgery) chemotherapy treatment. The NSABP B-52 trial was designed to find out whether adding an aromatase inhibitor (AI) to a neoadjuvant therapy course of docetaxel, carboplatin trastuzumab, and pertuzumab (TCHP) would increase the percentage of patients who have a "pathologic complete response," meaning that they would have no residual invasive cancer detectable in the breast tissue and lymph nodes removed during surgery.

What Patients Need to Know

The study found that adding an AI (serving as estrogen deprivation) did not significantly increase or decrease the percentage of patients who experienced a pathologic complete response.

Prognostic information provided by genomic testing in women with early stage breast cancer

Using the dataset of more than 800 patients from the prior TransATAC study, investigators retrospectively evaluated and compared the performance of four "multigene expression profiles" (genomic tests). The purpose of these profiles is to provide prognostic information related to recurrence for postmenopausal women with node-negative, hormone receptor-positive, ER2-negative early stage breast cancer.

The study found that Prosigna provided the most accurate prognostic information of the four multigene expression profiles tested, as measured by the "likelihood ratio," a statistical measure of the probability that a test result is correct. The study also found that, among the four profiles, Prosigna provided the most accurate differentiation between low and high risk patients.

What Patients Need to Know

The results supported the conclusions of the 2016 evidence-based ASCO guidelines that multi-gene expression signatures provide clinical value for the selection of low risk patients who may be spared adjuvant chemotherapy. Those guidelines gave a strong recommendation to Prosigna, equivalent to the strong recommendation given to the similar Oncotype Dx test.

Mutations in the Estrogen Receptor Gene Facilitate Spread of Tumors

According to findings from lab experiments with mice, mutations in the estrogen receptor gene (ESR1) facilitate the metastasis (spread) of tumors. ESR1 mutations are common in metastatic breast tumors following hormone therapy, but their role in metastasis has been unclear.

ESR1 mutations are a known mechanism of acquired hormone resistance, but this is the first evidence that ESR1 mutations also enhance tumor progression and metastatic behavior.

What Patients Need to Know

ESR1 mutations are potential new predictive markers for metastatic breast cancer and may influence decisions about treatment with hormone therapy.

In BRCA Positive Breast Cancer, PARP Inhibitors Show Some Limited Benefit

PARP is a type of enzyme that helps repair DNA. In cancer treatment, PARP inhibitors are used to prevent cancer cells from repairing their damaged DNA; this prevention can cause the cancer cells to die. PARP inhibitors have shown promise in patients with BRCA-positive breast cancer and those with triple negative breast cancer.

The BROCADE trial, a randomized phase II study, compared chemotherapy (carboplatin/paclitaxel) alone with the combination of chemotherapy and the PARP inhibitor veliparib in BRCA 1 and 2-positive breast cancer patients whose cancers had recurred locally or had metastasized.

What Patients Need to Know

The results of the study showed that patients who received veliparib with the chemotherapy had longer progression free survival (PFS), overall survival, and overall response rates, but the results were not statistically significant. However, the study results were promising enough to justify continuing a larger phase III trial of velparib in combination with chemotherapy.

A positive result of the BROCADE trial was that the patients receiving the combined therapy did not have significantly more side effects than those receiving chemotherapy alone.

BRCA Mutations Studied in the Treatment of Triple Negative Breast Cancer

Previous results from the Triple Negative Breast Cancer Trial (TNT) had shown that women with triple negative breast cancer (TNBC) with BRCA gene mutations were more likely to benefit from treatment with the platinum-based chemotherapy carboplatin than from the standard chemotherapy drug docetaxel.

A new TNT analysis asked whether patients whose tumors contained "silenced" or "methylated" BRCA genes at the time of diagnosis were also more likely to benefit from carboplatin. The analysis showed that this was not the case; patients with tumors with BRCA1 methylation or mRNA silencing actually had a higher response when treated with docetaxel than with carboplatin.

What Patients Need to Know

The latest results from the TNT do not support testing for BRCA1 methylation or mRNA silencing to guide treatment in metastatic TNBC.

Interruption of Endocrine Therapy to Permit Pregnancy

Breast cancer in young women can occur before the completion of reproductive plans.

A study called Pregnancy Outcome and Safety of Interrupting Therapy for Women with Endocrine Responsive Breast Cancer (POSITIVE) is currently in progress. The goal of the study is to investigate if a temporary interruption of endocrine (hormone) therapy, with the goal to permit pregnancy, is associated with a higher risk of breast cancer recurrence. The study also aims to evaluate different specific indicators related to fertility, pregnancy, and breast cancer biology in young women.

Study participants must have received adjuvant (post-surgery) endocrine therapy (tamoxifen alone or ovarian suppression plus tamoxifen or AI) for between 18 and 30 months in treatment of early breast cancer.

What Patients Need to Know

A psycho-oncological companion study on fertility concerns, psychological well-being, and decisional conflicts will be conducted in interested Study Centers.

Treatment of Older Women with Breast Cancer

Key findings from several studies that focused on the treatment of older women with breast cancer were presented, including:

- The side effects of the targeted treatment palbociclib are not increased when given to women age 65 or older.
- Due to a generally lower risk of recurrence, older women with hormone-sensitive, node-negative breast cancer can at times be spared radiation after a lumpectomy.
- Regardless of the age of the patient, surgery (prior to other treatments) is needed for optimal results.

What Patients Need to Know

Researchers continue to study how to best treat breast cancer in older women.

Quality of Life Issues

Key findings from several studies that focused on quality of life issues were presented, including:

- A study of over 600 patients conducted from 2005 through 2016 showed no increased risk of lymphedema (swelling of the arm after lymph node removal) when chemotherapy was administered intravenously (into a vein) on the arm where the node removal took place.
- Taxane-based chemotherapies have been associated with permanent nerve damage, which can cause numbness, pain, and tingling in hands and feet. The results of a small study suggested that patients who wore compression gloves during the administration of the chemotherapy had fewer sensory and motor symptoms after the treatment session.
- A study of the effect of acupuncture to treat existing taxane-induced nerve damage in women with stage 1 to stage 3 breast cancer showed that intervention with 18 sessions of acupuncture over an 8-week period resulted in a significant lessening of nerve damage symptoms.
- Approximately 60 percent of women treated with the targeted therapy everolimus develop mouth sores. A study showed that the use of a steroid mouth rinse (4 times each day for 12 weeks) beginning from the start of treatment reduced the expected rate of mouth sores by about fifty percent.

What Patients Need to Know

There are ongoing studies on quality of life issues for women being treated for breast cancer; some of which will result in ways to help women better cope with treatment side effects.

Concerns about Medication Linked to Non-Adherence

A study of 224 women currently taking an aromatase inhibitor (AI) set out to identify the association between concerns about the medication ("concern beliefs") and adherence to the therapy ("necessity beliefs").

Significantly higher concern beliefs were found among women who were experiencing pain or other side effects from the AI therapy, had depression of any severity, or previously stopped therapy with another AI. The women with higher concern beliefs were at a statistically significant higher risk of not staying on the AI therapy for the recommended five to ten years.

What Patients Need to Know

Non-adherence (lack of persistence) to the full course of AI therapy can increase the risk of breast cancer recurrence. Women who are experiencing side effects or have any concerns about potential side effects should stay in close contact with their health care team.

Treatment Side Effects

All cancer treatments can cause side effects. It's important that you report any side effects that you experience to your health care team so they can help you manage them. Report them right away—don't wait for your next appointment. Doing so will improve your quality of life and allow you to stick with your treatment plan. It's important to remember that not all patients experience all side effects, and patients may experience side effects not listed here.

There are certain side effects that may occur across different treatment approaches. Following are tips and guidance for managing these side effects.

Digestive Tract Symptoms

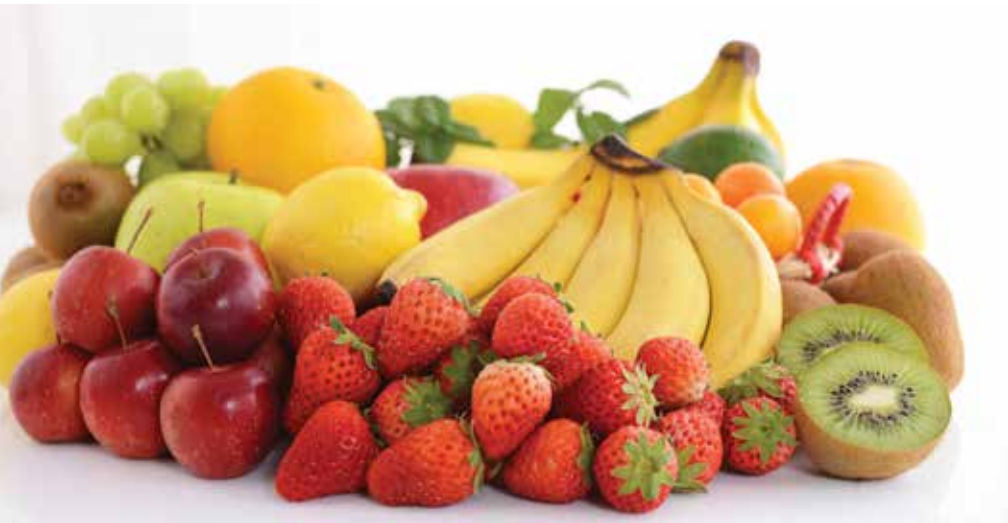
Nausea and vomiting

- Avoid food with strong odors, as well as overly sweet, greasy, fried, or highly seasoned food.
- Eat meals cold or at room temperature, which often makes food more easily tolerated.
- Nibble on dry crackers or toast. These bland foods are easy on the stomach.
- Having something in your stomach when you take medication may help ease nausea.

Diarrhea

- Drink plenty of water. Ask your doctor about using drinks such as Gatorade which provide electrolytes as well as liquid. Electrolytes are body salts that must stay in balance for cells to work properly.

- Over-the-counter medicines such as loperamide (Imodium A-D and others) and prescription drugs are available for diarrhea but should be used only if necessary. If the diarrhea is bad enough that you need medicine, discuss it with your doctor or nurse.
- Choose foods that contain soluble fiber—for example beans, oat cereals, oranges, and flaxseeds. High-pectin foods such as peaches, apples, oranges, grapefruit, bananas, and apricots can also help to avoid diarrhea.
- Avoid food high in refined sugar and those sweetened with sugar alcohols such as sorbitol and mannitol. Look for this low-calorie sweetener on food labels; the names of this type of sweetener usually end with the letters "ol."
- Low fat food choices are less likely to cause diarrhea than fatty, greasy, or fried foods. The fats you eat should come from healthy sources, such as olive oil, canola oil, avocado, olives, nuts, and seeds.
- Limit or avoid lactose, especially if you are lactose-intolerant. There are plant-based milk alternatives you can try, such as soy or rice milk. If lactose is an essential part of your diet, there are dairy products with added lactase (which breaks down lactose) and dietary lactase supplements.



Loss of appetite

- To help maintain your weight, eat small meals throughout the day. That's an easy way to take in more protein and calories. Try to include protein in every meal.
- To keep from feeling full early, avoid liquids with meals or take only small sips (unless you need liquids to help swallow). Drink most of your liquids between meals.
- Be as physically active as you can. Sometimes, taking a short walk an hour or so before meals can help you feel hungry.
- Keep high-calorie, high-protein snacks on hand such as hard-boiled eggs, peanut butter, cheese, ice cream, granola bars, liquid nutritional supplements, puddings, nuts, canned tuna, or trail mix.
- Eat your favorite foods any time of the day. For example, if you like breakfast foods, eat them for dinner.
- If you are struggling to maintain your appetite, talk to your health care team about whether appetite-building medication could be right for you.

Fatigue

Fatigue (extreme tiredness not helped by sleep) is one of the most common side effects of many cancer treatments. If you are taking a medication, your doctor may lower the dose of the drug, as long as it does not make the treatment less effective. If you are experiencing fatigue, talk to your doctor about whether taking a smaller dose is right for you.

There are a number of other tips for reducing fatigue:

- Take several short naps or breaks.
- Take short walks or do some light exercise, if possible.
- Try easier or shorter versions of the activities you enjoy.

- Ask your family or friends to help you with tasks you find difficult or tiring.
- Save your energy for things you find most important.

Fatigue can be a symptom of other illnesses, such as anemia, diabetes, thyroid problems, heart disease, rheumatoid arthritis, and depression. So be sure to ask your doctor if he or she thinks any of these conditions may be contributing to your fatigue.

Also, it could be very valuable to talk to an oncology social worker or oncology nurse. These professionals can also help you manage fatigue. They can work with you to manage any emotional or practical concerns that may be causing symptoms and help you find ways to cope.

Pain

To help your doctor prescribe the best medication, it's useful to give an accurate report of your pain. Keep a journal that includes information on:

- Where the pain occurs.
- When the pain occurs.
- How long it lasts.
- How strong it is on a scale of 1 to 10, with 1 being the least amount of pain and 10 the most intense.
- What makes the pain feel better and what makes it feel more intense.

There are a number of options for pain relief, including prescription and over-the-counter medications. It's important to talk to a member of your health care team before taking any over-the counter medication, to determine if they are safe and will not interfere with your treatments. Many pain medications can lead

to constipation, which may make your pain worse. Your doctor can prescribe medications that help to avoid constipation.

Physical therapy, acupuncture, and massage may also be of help in managing your pain. Consult with a member of your health care team before beginning any of these activities.

Bone Loss

Both hormone therapies and chemotherapy can cause bone loss, which increases a woman's risk for osteoporosis (a condition in which bones become weak and brittle, leading to a higher risk of fracture). 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:

- Bisphosphonates such as zoledronic acid (Zometa and others) slow the process by which bone wears away and breaks down. These medications belong to a class 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). Like bisphosphonates, RANK ligand inhibitors are a type of osteoclast inhibitor.

Hot Flashes

Breast cancer treatments can lead to menopausal symptoms, such as hot flashes and night sweats. If you are experiencing these side effects, speak with your health care team about ways to cope with them. The following tips may also help:

- Identify the triggers for your hot flashes. For many women, hot flashes can be triggered by stress, a hot shower, caffeine, or spicy foods.
- Change your lifestyle habits to cope with the triggers. That may mean regular exercise, using relaxation techniques, and/or changing your diet.
- Dress in layers and keep ice water handy to cool yourself off.
- Avoid synthetic materials, especially at nighttime; wear pajamas and use sheets made of cotton instead.
- Take a cool shower before going to bed.
- Try a mild medication such as acetaminophen (Tylenol and others).

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, a condition in which the body's lymphatic fluid is unable to circulate properly. The lymphatic fluid builds up in soft tissues (usually in an arm or a leg), causing painful swelling. 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.

Here are some things you can do to ease the discomfort of lymphedema:

- Get help for your symptoms as soon as possible. Contact your health care team at the first sign of lymphedema symptoms. If left untreated, the swelling can get worse and may cause permanent damage.
- Consider undergoing manual lymph drainage (MLD). This type of massage helps move the fluid from where it has 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 lymphedema exercises, taught and monitored by a physical therapist.
- Wear a compression sleeve. This can help drain the lymphatic fluid. It's important to always wear a compression garment when flying, even on short flights.
- 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.

Vaginal Dryness

Treatments for breast cancer can lead to vaginal dryness and a lowered sex drive. Use of a personal lubricant (such as Astroglide) and/or a moisturizer (such as Replens) can often help. 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 each other.

If vaginal dryness persists, talk to your doctor about whether prescription medicines designed to treat the condition are right for you, such as hormone creams or suppositories (medicines inserted into the vagina). Your health care team can also provide advice on regaining the desire for sex.You may wish to ask for a referral to a health care professional who specializes in these issues.

Treatment-Specific Side Effects

Chemotherapy

The side effects specific to chemotherapy depend on the type and dose of drugs given and the length of time they are used, and can include the following:

- **Hair loss.** 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 the end of treatment. It may have a different texture or color, but these changes are usually temporary.

Many women who lose their hair during chemotherapy treatments choose to wear a head covering, whether it's a scarf, turban, hat, or wig. Some insurance plans may cover part of the cost of these head coverings. If you choose to wear a wig, consider buying one before you lose much hair so that you feel more prepared, and so that you will have a good match to your own hair color. You can have your wig professionally fitted and styled by a full-service wig salon; look for a salon in your community that specializes in hair loss resulting from chemotherapy.

- **Nerve damage.** Some women on chemotherapy or targeted treatments experience nerve damage; the symptoms may include difficulty picking up objects or buttoning clothing, problems maintaining your balance, difficulty walking, and hearing loss. Peripheral neuropathy is a form of nerve damage that may cause numbness or tingling in the hands and feet. Often, nerve damage due to cancer treatments 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.

- **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, and a reduced number of these cells increases the risk of infection. Your doctor can prescribe medication designed to help increase white blood cell counts. If you develop a fever, which is a sign of infection, let your health care team know immediately so that you can get proper treatment.

- **Memory lapses.** After chemotherapy, some people have difficulty concentrating or thinking clearly. If you experience any of these symptoms, speak with your health care team. There are a number of things you can do to help you cope, including:
  - ✓ Keep a diary or a log to track how your memory lapses affect your daily routine.
  - ✓ Make lists. Carry a pad, smart phone, or tablet with you and note 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, you should work, read and do your thinking in an uncluttered, peaceful environment.
  - ✓ Repeat information you're given aloud. This can help 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. This helps to keep your memory working at its best.

- **Mouth sores (mucositis)** are also a side effect of chemotherapy. Your doctor may recommend treatments such as:
  - ✓ Coating agents. These medications coat the entire lining of your mouth, forming a film to protect the sores and minimize pain.
  - ✓ Topical painkillers. These are medications that can be applied directly to your mouth sores.
  - ✓ Over-the-counter treatments. These include rinsing with baking soda or salt water, or "magic mouthwash," a term given to a solution to treat mouth sores. Magic mouthwash usually contains at least three of these ingredients: an antibiotic, an antihistamine or local anesthetic, an antifungal, a corticosteroid, and/or an antacid.

Chemotherapy can also cause changes in the way food and liquids taste, including causing an unpleasant metallic taste in the mouth. Many people find that switching to plastic utensils helps. It may also help to avoid eating or drinking anything that comes in a can, and to use enamel-coated pots and pans for food preparation.

Radiation Therapy

Changes to the skin are the most common side effects of radiation therapy; those changes can include dryness, swelling, peeling, redness, and blistering. If a reaction occurs, contact your health care team so the appropriate treatment can be prescribed. It's especially important to contact your health care team if there is any open skin or painful areas, as this could indicate an infection. Infections can be treated with an oral antibiotic or topical antibiotic cream.

Targeted Treatments and Hormone Therapy

Targeted treatment drugs and hormone therapy don't have the same effect on the body as do chemotherapy drugs, but they can still cause side effects.

Side effects of certain targeted therapies can include diarrhea, liver problems (such as hepatitis and elevated liver enzymes), problems with blood clotting and wound healing, and high blood pressure. Nerve damage, as outlined in the Chemotherapy Side Effects section, may also occur.

The side effects of hormone therapy are dependent on the type of therapy and include hot flashes (seen more with tamoxifen) and joint pain (seen more with aromatase inhibitors).

The Importance of Treatment Summaries

A treatment summary, sometimes called a "shadow chart," is a document you create and which remains in your possession. Maintaining your own records allows you and your family members instant access to the specifics of your diagnosis and treatment. A treatment summary should include:

- Your name and date of birth.
- Date of diagnosis.
- Name, affiliation, and contact information of the doctor who gave the diagnosis.
- Prescribed therapy/therapies; include dates started and stopped, and dosages when appropriate.
- Dates and types of post-diagnosis testing, and the results.
- Other medication and supplements you are taking.
- Names, affiliations, and contact information of all members of your health care team.

Talk to your doctor or a member of your health care team about your intention to create a treatment summary, and ask them what else they suggest be included. Take your treatment summary with you when you visit any doctor, not just your oncologist.

Communicating With Your Health Care Team

As you manage your bladder cancer, it's important to remember that you are a consumer of health care. The best way to make decisions about health care is to educate yourself about your diagnosis and the members of your health care team, including nurses, social workers and patient navigators.

In addition to creating a treatment summary, here are some tips for improving communication with your health care team:

Start a health care journal. Having a health care journal or notebook will allow you to keep all of your health information in one place. You may want to write down the names and contact information of the members of your health care team, as well as any questions for your doctor. Keep a diary of your daily experiences with cancer and treatment. You can separate your journal or notebook into different sections to help keep it organized.

Prepare a list of questions. Before your next medical appointment, write down your questions and concerns. Because your doctor may have limited time, you should ask your most important questions first, and be as specific and brief as possible.

Bring someone with you to your appointments. Even if you have a journal and a prepared list of questions or concerns, it's always helpful to have support when you go to your appointments. The person who accompanies you can serve as a second set of ears. He or she may also think of questions to ask your doctor or remember details about your symptoms or treatment that you may have forgotten.

Write down your doctor's answers. Taking notes will help you remember your doctor's responses, advice and instructions. If you cannot write down the answers, ask the person who accompanies you to do that for you. If you have a mobile device, ask if you can use it to take notes. Writing notes will help you review the information later.

Record your visit if your doctor allows it. Recording the conversation with your doctor gives you a chance to hear specific information again or share it with family members or friends.

Incorporate other health care professionals into your team. Your medical oncologist is an essential member of your health care team, but there are other health care professionals who can help you manage your diagnosis and treatment:

- Your primary care physician should be kept updated about your breast cancer treatment and any test results.
- Your local pharmacist is a great source of knowledge about the medications you are taking; have all of your prescriptions filled at the same pharmacy to avoid the possibility of harmful drug interactions.
- Make sure your oncologist knows of any other medical conditions you have, or any pain you are experiencing, so that they can consult with your primary care physician or your specialist as needed.

Remember, there is no such thing as over-communication. Your health care team wants to know about how you're feeling overall, which includes your level of pain, your energy level, your appetite, and your mood and spirits.

Cancer*Care*'s Free Support Services and Programs

It can be very difficult to receive a diagnosis of breast cancer, and adjusting to the necessary changes in your life can be challenging.

Cancer*Care* can help. We are a national nonprofit organization providing free, professional services to anyone affected by cancer. Our licensed oncology social workers can provide support and education, help in navigating the complicated health care system, and provide information on support groups and other resources.

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

You will likely also build your own personal support network, comprised of family and friends. In doing so, it's best to take some time to think about the people in your life and how they are best suited to help. Match the task to their strengths—ask a family member who loves to shop to pick up something for you at the store; ask a friend who's a good listener to come over for a chat.

Frequently Asked Questions

Q. How is triple negative breast cancer diagnosed and treated?

A. Triple negative breast cancer tumors do not have "molecular markers"; they have neither receptors for estrogen or progesterone nor excess HER2 receptors on their surface. This type of breast cancer is generally diagnosed at the initial biopsy. Tissue is extracted through a special needle and analyzed under a microscope. The pathologist applies specific stains to the biopsy material on the microscope slide and evaluates the tissue sample to determine whether the tumor expresses any of the molecular markers. Patients who have subsequent surgical biopsies may have the surgical specimens tested again for the markers, and occasionally some specimens may need to undergo more sophisticated testing of their genetic content.

Some drugs that work for hormone receptor-positive tumors are not effective for women with triple negative breast cancer. However, triple negative breast cancer often responds well to chemotherapy. Clinical trials are pointing the way to new and better treatments for triple negative breast cancer, especially for women with this type of cancer who also have a BRCA gene mutation.

Q: Are there any drugs available for the treatment of lymphedema?

A: Lymphedema, a painful swelling of the arms or legs caused by a buildup of lymphatic fluid, affects many women being treated for breast cancer. It is an area of ongoing research and concern. There are no medications for lymphedema currently approved by the FDA, but there is hope for progress, and there is a clinical trial

underway for a gene therapy designed to repair damage to the lymphatic system. If you are experiencing lymphedema, talk to your health care team immediately and discuss steps you can take to manage your symptoms.

Q: What is a tumor marker?

A: Tumor markers are proteins manufactured by tumors and shed into the blood. They can be measured through a blood test, and some oncologists find the measurements useful in assessing the success of treatment in women with advanced (metastatic) breast cancer. In those same women, the presence or absence of tumor markers may help guide treatment options.

Q: I've heard about hand-foot syndrome. What is it and what can I do to prevent it?

A: Hand-foot syndrome (HFS) is a side effect of some types of chemotherapy and other medicines used in the treatment of breast cancer. Symptoms can include numbness, tingling, burning, itching, redness, swelling, and discomfort. In severe cases, there can be cracked or peeling skin, blisters or sores, and intense pain.

The risk of HFS can be lessened by following these tips during the week after each chemotherapy treatment:

- Avoid prolonged heat exposure on hands and feet.
- Avoid using hand tools and kitchen knives. The squeezing or chopping motions can cause excessive pressure and increase symptoms.
- Stay off your feet as much as possible if you are starting to notice symptoms; this may require taking a break from exercising.
- Talk to your health care team about using a 10% urea cream; a study has found that it may be helpful in preventing HFS.

It's important to talk to your health care team if HFS occurs. Your doctor may want to adjust your drug dose or change your treatment schedule until your symptoms improve. He or she may also prescribe corticosteroids to reduce inflammation, or suggest that you take an over-the-counter pain reliever.

Additionally, these tips may help ease the discomfort of HFS:

- Keep your hands and feet moist by using mild skin creams. Pat the lotion into your skin; don't rub, as rubbing can cause irritation. (Also, pat your skin dry after you shower—don't rub.)
- Elevate your hands and feet and apply ice packs to help cool the sensation of burning.
- Wear loose, well-ventilated shoes.
- Stay away from harsh chemicals.

Notes

Resources

CancerCare®
800-813-HOPE (800-813-4673)
www.cancercare.org

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

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

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

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

National Coalition for Cancer Survivorship
877-622-7937
www.canceradvocacy.org

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

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

Susan G. Komen
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
www.cancertrialshelp.org

EmergingMed
www.emergingmed.com

National Cancer Institute
www.cancer.gov

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