TREATMENT UPDATE:

Breast Cancer With Highlights from the 2019 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, nearly 270,000 women are diagnosed with breast cancer. In recent years, the number of effective treatments for breast cancer has increased. Breast cancer is not just one disease. There are several different subtypes, each with its own unique features. Doctors are able to tailor treatments according to the characteristics of these specific subtypes.

Men can also be diagnosed with breast cancer but represent only about 1 percent of all breast cancer cases, making it challenging for doctors to conduct clinical trials on the treatment of breast cancer in male patients. 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 update, we talk about current available breast cancer treatments and new medicines in development. We also describe how to cope with possible treatment side effects and how to communicate most effectively with 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 or on the surface of cancer cells.

There are three main subtypes of breast cancer, based on the presence or absence of specific receptors:

- **Hormone receptor (HR) positive.** Cancers that have receptors for the female hormone estrogen (ER-positive) and/or progesterone (PR-positive) are considered hormone-positive. ER-positive cancers account for about 80 percent of breast cancers. Nearly two-thirds of ER-positive cancers also have receptors for progesterone (are PR-positive as well as ER-positive).
- **HER2-positive.** Cancers that are positive for human epidermal growth factor receptor 2 (HER2) have an abundance of HER2 receptor cells on their surface. HER2-positive cancers account for approximately 20 to 25 percent of breast cancers, about half of which are also hormone-positive.
- **Triple-negative.** 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.

Ultrasound

Breast ultrasound uses sound waves to examine the breast. This is another common tool in evaluating breast lumps and other abnormal findings, especially in young women who have breasts that are considered dense (have a relatively high amount of glandular tissue and fibrous connective tissue and a relatively low amount of fatty tissue).

Magnetic Resonance Imaging (MRI)

Breast MRI uses magnetic waves to evaluate breast tissue and breast abnormalities. Breast MRI is sometimes useful after a breast cancer diagnosis to look for additional findings not seen on a mammogram, to help evaluate the extent of the cancer and to help with surgical planning. For some young women at high risk of developing breast cancer (such as women with strong family histories of breast cancer and/or BRCA or other gene mutations), breast MRI is recommended as part of cancer screening.

Biopsy

Tests performed on tumor samples provide doctors with valuable information that helps guide treatment decisions. One such test is a biopsy, in which a doctor uses a needle to remove a tissue sample from the tumor so that it can be examined under a microscope. Some breast biopsies require surgery (known as an excisional biopsy).

Biopsies 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). Another important piece of information that can be learned from the biopsy is the tumor's hormone receptor status, which indicates 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 evaluates the size and microscopic patterns of 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 are part of the immune system and can be one of the first sites where cancer cells spread in cases of early breast cancer.

Genomic Tests

For certain women with early-stage breast cancer, a test called a "genomic assay" may be used. This test is designed to detect several types of genes or groups of genes in the cancerous cells. The expression profile of these genes can help doctors determine how likely it is that a woman with early-stage breast cancer will have her cancer return after completing first-line (initial) treatment. (A patient's 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.

Genomic assays provide a quantitative (numbers-based) analysis that can help women and their doctors better understand the prognosis and decide if additional treatment should be pursued. Commonly used genomic assays include the Oncotype DX score, MammaPrint and others.

Treatment Options

Treatment recommendations are individualized, taking into consideration the biology of the cancer, its stage and the woman's overall health.

Treatment for cancer that has not spread beyond the breast and lymph nodes (non-metastatic) often includes a combination of surgery, radiation and drug therapy. Treatment for cancer that has spread beyond the breast and lymph nodes (metastatic) generally focuses on drug therapy that circulates to wherever cancer cells are located, although localized treatment to specific metastatic lesions (collection of cancer cells) may sometimes be useful.

Surgery

In the past, doctors 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. For many women, lumpectomy (removal of the tumor and 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.

In either a mastectomy or a lumpectomy, the surgeon often removes one or more lymph nodes in the underarm near the affected breast to see if they contain cancer cells. 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 sometimes results from the removal of lymph nodes.

Radiation

Radiation to the entire breast, usually given over 6 to 7 weeks, has been the standard of care for women who have been treated with lumpectomy. Recent trials have shown that, for some women, higher daily doses of radiation given over 3 to 5 weeks (with the same total combined dose of radiation) are as effective as the standard approach, with similar potential side effects.

There are other radiation options that can also be considered:

- Accelerated partial breast irradiation (APBI) is given only to the area of the breast that has the cancer. APBI delivers more radiation in a shorter treatment period.
- Brachytherapy uses tiny radioactive pellets, surgically inserted during a lumpectomy, to deliver a localized dose of radiation.

Some women who have undergone a mastectomy will require post-surgery radiation. Factors that increase the likelihood that radiation after a mastectomy will be required include larger tumor size and the presence of affected lymph nodes.

Drug Therapy

Drug therapy is an important treatment option for many women with breast cancer. These therapies work by traveling through the bloodstream to destroy cancer cells.

Chemotherapy

Chemotherapy can be an important part of treatment for both early stage and metastatic breast cancer. Based on clinical trials over many years, doctors have learned how to use chemotherapy more effectively, either alone or in combination with other treatments.

Doses and schedules of chemotherapy have been refined so that women get the most benefit from treatment with the fewest possible side effects.

Chemotherapy can be used before surgery (neoadjuvant) to try to shrink the tumor so the surgery can be less extensive, or after surgery (adjuvant) to try to kill any remaining cancer cells. In some cases, the use of neoadjuvant chemotherapy can also provide the doctor with information on how sensitive the cancer cells are to the treatment, which may guide further therapy. It can also be used for women whose breast cancer has metastasized.

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

- Anthracyclines, such as doxorubicin (Adriamycin) and epirubicin (Ellence)
- Cyclophosphamide (Cytoxan)
- Taxanes, such as paclitaxel (Taxol and Abraxane) and docetaxel (Taxotere)
- Carboplatin (Paraplatin) and Cisplatin (Platinol, Platinol AQ)
- Capecitabine (Xeloda)

Young women diagnosed with breast cancer who receive chemotherapy may experience a temporary or permanent menopause. For many of these women, preserving their fertility (the ability to have a child) plays a large part in their treatment decisions.

There are steps that can be taken if you are concerned about your ability to have children after treatment:

- Discuss treatment plans with all members of your health care team. The discussion should include the coverage provided by your health insurance plan.
- Consider consulting with a specialist in reproductive medicine, who can help weigh the benefits and risks of a specific treatment.
- Ask about newer options for preserving fertility, such as oocyte cryopreservation, also known as egg freezing. In this process, a woman's eggs are removed, frozen and stored for later use. Another option includes freezing fertilized eggs. You can discuss with your fertility specialist which option is best for you.

Fertility-preserving alternatives are most often used before a woman starts chemotherapy.

Hormone (Endocrine) Therapy

Doctors will often recommend hormone therapy as a treatment for early stage and metastatic ER-positive and/or PR-positive breast cancer. Hormone treatments work in different ways. Some are designed to prevent estrogen from attaching to receptors in breast cancer cells, while others are designed to reduce the level of hormones that circulate in the body. By blocking the effects of estrogen or lowering levels of estrogen, these treatments deprive tumor cells of the stimulation that fuels their growth.

The most common hormone therapies used to treat ER-positive or PR-positive breast cancer include:

- **Tamoxifen** (Soltamox, Nolvadex) is an estrogen-blocking treatment given to both pre- and postmenopausal women with breast cancer. Studies have shown that taking tamoxifen for five years following surgery reduces the chance of the cancer recurring by fifty percent. For women with cancer in one breast, tamoxifen also lowers the risk of a new tumor developing in the unaffected breast.

  Some studies have shown that taking tamoxifen for ten years can be even more beneficial for women at higher risk of recurrence. For women with metastatic breast cancer, tamoxifen can shrink the tumor, prolong progression-free survival (the time in which the tumor does not grow) and improve overall survival.

  Tamoxifen has also been approved as chemoprevention, reducing the chance of ER-positive breast cancer developing in healthy pre- or postmenopausal women who are at high risk for breast cancer, with the preventive benefits of the drug extending for many years beyond when the drug is taken.

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 age, family history, biopsy results and reproductive history.

- **Aromatase inhibitors (AIs)**, another type of hormone therapy, are given to postmenopausal women with early-stage ER-positive breast cancer to help prevent cancer from returning after surgery. In some situations, AIs can also be used in premenopausal women, often requiring other medications to artificially induce menopause (see next section: "Ovarian Suppression"). AIs block the action of an enzyme called aromatase, cutting off the supply of estrogen (estrogen can stimulate tumor growth). AIs are also commonly used to treat metastatic breast cancer, sometimes in combination with targeted therapies. They have also shown some effectiveness in breast cancer prevention.

  The AIs primarily used to treat breast cancer are anastrozole (Arimidex), letrozole (Femara) and exemestane (Aromasin). Taking AIs for five years (either alone or after five years of tamoxifen) can help reduce recurrences in postmenopausal women with ER-positive breast cancer.

- **Fulvestrant** (Faslodex) is another estrogen-blocking drug. It works by attaching to estrogen receptors, changing their shape and preventing the receptors from working properly, which slows the growth of breast cancer cells. Fulvestrant is given as a monthly injection and is approved only for postmenopausal women with 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).

Targeted Therapy

Targeted therapy focuses 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.

A number of targeted therapies have been developed for the treatment of HER2-positive breast cancer:

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

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

- **Pertuzumab** (Perjeta) was approved by the U.S. Food and Drug Administration (FDA) in 2012 for metastatic HER2-positive breast cancer and in 2013 as a neoadjuvant treatment option for HER2-positive breast cancer when used in combination with trastuzumab and chemotherapy (docetaxel or paclitaxel). In December 2017, pertuzumab's approval was extended for use as an adjuvant treatment for HER2-positive breast cancer, also in combination with trastuzumab and chemotherapy.

- **Ado-trastuzumab emtansine** (Kadcyla), an antibody drug conjugate also known as T-DM1, is a combination of trastuzumab and a chemotherapy drug used to treat HER2-positive metastatic breast cancer. Additionally, in May 2019 the FDA approved T-DM1 for the treatment of women with early-stage HER2-positive breast cancer whose tumors do not completely respond to neoadjuvant treatments.

- **Fam-trastuzumab deruxtecan-nxki** (Enhertu), an antibody drug conjugate, was approved in December 2019 for the treatment of unresectable (inoperable) or metastatic HER2-positive breast cancer following two or more anti-HER2-based regimens.

- **Neratinib** (Nerlynx). In July 2017, the FDA approved the tyrosine kinase inhibitor neratinib as an adjuvant therapy to further reduce recurrence in women with early-stage HER2-positive breast cancer who have finished at least one year of post-surgery therapy with trastuzumab.

- **Tucatinib** (Tukysa). In April 2020, the FDA approved tucatinib, in combination with trastuzumab and the chemotherapy capecitabine, for the treatment of HER2-positive metastatic breast cancer.

Other Therapies

- **mTOR inhibitors.** Everolimus (Afinitor) is a targeted therapy that works inside cancer cells to restore their sensitivity to anti-estrogen 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 daily 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.

- **CDK4/6 inhibitors.** CDK4/6 inhibitors are designed to interrupt enzymes that promote the growth of cancer cells. The CDK4/6 inhibitors used in treating ER-positive, HER2-negative metastatic breast cancer are abemaciclib (Verzenio), palbociclib (Ibrance) and ribociclib (Kisqali). Each of these medications can be given in combination with hormone therapy. Abemaciclib can also be used as a monotherapy (a medication given alone).

  In February 2018, the FDA granted an additional approval to abemaciclib, in combination with an AI, as initial therapy for postmenopausal women with HR-positive, HER2-negative metastatic breast cancer.

  In July 2018, the FDA granted an additional approval to ribociclib, in combination with an AI, for the treatment of pre-, peri- or postmenopausal women with HR-positive/HER2-negative metastatic breast cancer. The additional approval included the use of ribociclib, in combination with fulvestrant, for the treatment of postmenopausal women with HR-positive, HER2-negative metastatic breast cancer, either as initial treatment or after disease progression while on endocrine therapy.

- **PARP inhibitors.** 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, especially those with defective DNA repair pathways, such as BRCA1/2-associated breast cancers. In January 2018, the FDA approved olaparib (Lynparza) for the treatment of women with BRCA-positive, HER2-negative metastatic breast cancer who had previously received chemotherapy. In October 2018, the PARP inhibitor talazoparib (Talzenna) was approved for the treatment of that same type of breast cancer.

- **Immunotherapy.** In March 2019, the FDA granted an accelerated approval for the immunotherapy drug atezolizumab (Tecentriq) in combination with chemotherapy for the initial treatment of women with advanced triple-negative breast cancer. This combination therapy is the first FDA-approved breast cancer treatment approach to include immunotherapy. Atezolizumab works by targeting the protein PD-L1. This protein can prevent the body's immune system from attacking tumors.

- **PIK3CA inhibitor.** In May 2019, the FDA approved alpelisib (Piqray), in combination with the endocrine therapy fulvestrant, to treat HR-positive, HER2-negative, PIK3CA-mutated metastatic breast cancer following treatment with an endocrine-based therapy.

- **Antibody-drug conjugate.** In April 2020, the FDA approved sacituzumab govitecan-hziy (Trodelvy) for the treatment of women with metastatic triple-negative breast cancer who had received at least two prior therapies.

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 individuals 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, or in combination with, 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 2019 San Antonio Breast Cancer Symposium

This section presents highlights from the 2019 San Antonio Breast Cancer Symposium, which took place December 10-14 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. They can let you know if these research findings affect your treatment plan and whether a clinical trial might be right for you.

Pembrolizumab evaluated in the treatment of triple-negative breast cancer

According to results from the KEYNOTE-522 trial, the addition of the immunotherapy pembrolizumab to neoadjuvant (pre-surgery) chemotherapy and as an adjuvant (post-surgery) therapy increased the "pathologic complete response" in patients who have triple-negative breast cancer with lymph node involvement.

Pembrolizumab works by interfering with a molecular "brake" known as PD-1 that prevents the body's immune system from attacking cancer cells.

What Patients Need to Know

A pathologic complete response is defined as the absence of residual disease in the breast and in the lymph nodes after completion of neoadjuvant treatment.

T-DM1 shows high rates of disease control in early-stage HER2-positive breast cancer

The first set of results from the ATEMPT trial showed high rates of disease control in the use of T-DM1 monotherapy for adjuvant treatment of stage I HER2-positive breast cancer. The rationale for the trial was the recognition that some stage I HER2-positive breast cancers have a sufficiently high risk of recurrence to justify adjuvant therapy, but may not require multiple chemotherapy drugs.

What Patients Need to Know

T-DM1 is a combination of the targeted therapy trastuzumab and a chemotherapy drug. It is used to treat HER2-positive metastatic breast cancer and certain cases of early-stage HER2-positive breast cancer.

FDA approval sought for margetuximab as treatment for metastatic HER2-positive breast cancer

Updated findings from the phase III SOPHIA trial found that, when compared with trastuzumab plus chemotherapy, the investigational drug margetuximab plus chemotherapy continued to show clinical benefit in patients with HER2-positive metastatic breast cancer who had received prior anti-HER2 therapies. Margetuximab is a monoclonal antibody that targets HER2-expressing tumors.

What Patients Need to Know

Based on these trial results, the drug developer has submitted a license application to the FDA, seeking approval for margetuximab in combination with chemotherapy for the treatment of patients with metastatic HER2-positive breast cancer.

Analysis of ctDNA may guide treatment decisions in triple-negative breast cancer

Many women with early-stage triple-negative breast cancer will undergo neoadjuvant treatment to reduce tumor size. Investigators collected blood samples from women who had residual disease after neoadjuvant treatment to examine mutations in their "circulating tumor DNA" (tiny bits of DNA shed by cancer cells).

What Patients Need to Know

The investigators will use this information to further evaluate whether circulating tumor DNA (ctDNA) could be used to guide treatment decisions in women with early-stage triple-negative breast cancer.

Adding immunotherapy to chemotherapy in treatment of triple-negative breast cancer studied in ongoing trial

Preliminary results from the phase III NeoTRIPaPDL1 Michelangelo study showed that adding the immunotherapy atezolizumab to the chemotherapy combination of carboplatin and nab-aclitaxel did not significantly increase the "pathologic complete response" (absence of detectable cancer) in patients with early high-risk and locally advanced triple-negative breast cancer.

The trial is ongoing, and has the primary aim of determining the 5-year event-free survival (EFS) rates of the combination of atezolizumab plus carboplatin and nab-paclitaxel.

What Patients Need to Know

The combination of chemotherapy used in this study did not include anthracyclines. Other studies including anthracyclines have shown different results.

Immunotherapy maintenance may improve outcomes in triple-negative breast cancer

According to an exploratory analysis from the phase II SAFIR02-IMMUNO trial, patients with triple-negative breast cancer may benefit from the immunotherapy durvalumab given as maintenance therapy, as compared with chemotherapy.

What Patients Need to Know

The analysis also indicated that durvalumab as a maintenance therapy may also benefit patients with certain subtypes of breast cancer in which with the protein PD-L1 is "overexpressed" (too high), which can prevent the body's immune system from attacking cancer cells.

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.

Managing Digestive Tract Symptoms

Nausea and vomiting

- Avoid food with strong odors as well as overly sweet, greasy, fried or highly seasoned food.
- Eat meals that are chilled, 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 that provide electrolytes. 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, contact a member of your health care team.
- Choose foods that contain soluble fiber, like beans, oat cereals and flaxseed, and high-pectin foods such as peaches, apples, oranges, bananas and apricots.
- Avoid foods high in refined sugar and those sweetened with sugar alcohols such as sorbitol and mannitol.

Loss of appetite

- Eating small meals throughout the day is an easy way to take in more protein and calories, which will help maintain your weight. 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.
- 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.
- If you are struggling to maintain your appetite, talk to your health care team about whether appetite-building medication could be right for you.

Managing 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 during the day.
- Take 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.

There are also prescription medications that may help, such as modafinil. Your health care team can provide guidance on whether medication is the right approach for your individual circumstances.

Managing Pain

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 it is safe and to make sure it will not interfere with your treatment. 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

Hormone therapies and chemotherapy can cause bone loss, which increases the risk of osteoporosis (a condition in which bones become weak and brittle). Talk with your health care team about how exercise and changes in your diet may help keep your bones healthy, and 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. Currently, 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. There are several medications that potentially help decrease hot flashes. Talk to your doctor to determine if medication is an option for you.

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 your specific triggers. That may mean regular exercise, using relaxation techniques and changing your diet.
- Dress in layers so that you can remove clothing if needed.
- Keep ice water handy to help you cool off.
- Avoid synthetic materials, especially at nighttime. Wear pajamas and use sheets made of cotton instead.
- Take a cool shower before going to bed.

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 is a type of massage that 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. If vaginal dryness persists, talk to your doctor about whether a prescription medicine is right for you. These medicines include hormone creams and suppositories (medicines inserted into the vagina). 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. They can include the following:

- **Hair loss.** Depending on the treatment, hair loss may start anywhere from one to three weeks after the first chemotherapy session. If you choose to wear a wig, consider buying one before you lose much hair so you feel more prepared and so you can match 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. 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.

- **Nerve damage.** Some women being treated with chemotherapy experience nerve damage with symptoms that may include difficulty picking up objects or buttoning clothing, problems maintaining 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. If you are coping with this side effect, take extra care when handling hot, sharp or dangerous objects. You should 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 infection. Your doctor can prescribe medication designed to help increase white blood cell counts. If you develop a fever (a sign of infection), let your health care team know immediately so that you can get proper treatment.

- **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 using "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 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 area, as this could indicate an infection. Infections can be treated with an oral antibiotic or topical antibiotic cream.

Targeted Therapy and Hormone Therapy

Targeted therapy 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 specific type of therapy and include hot flashes (seen more with tamoxifen) and joint pain (seen more with aromatase inhibitors).

Immunotherapy

Immunotherapy travels through the bloodstream, helping to prompt what is called an "immune response." Because immunotherapy can attack healthy cells as well as cancer cells, certain side effects may be experienced.

Atezolizumab is currently the only immunotherapy approved by the FDA for the treatment of breast cancer. Common side effects include digestive tract symptoms, fatigue, shortness of breath, elevated blood pressure and joint pain.

Communicating With Your Health Care Team

As you manage your breast 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 get to know the members of your health care team, including doctors, nurses, dietitians, 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.

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 you bring 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. You can also ask the person who accompanies you to take notes for you, either in your journal or on a tablet or smartphone.

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 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 specialist as needed.

Remember, there is no such thing as over-communication.

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 navigate 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, composed 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.

Notes

Frequently Asked Questions

Q: What do "tumor grade" and "pathological stage" mean?

A: Tumor grade is a way of classifying tumors based on how closely the cancer cells resemble normal cells. This can be determined based on an examination of tumor tissue removed during a biopsy or at the time of surgery. Using a microscope, a pathologist rates the grade as 1, 2 or 3, which is an indication of whether the breast cancer is slow-growing, growing at a moderate pace or fast-growing.

Pathological stage describes the extent of the cancer within the body and is based on a pathologist's study of the tumor tissue and any lymph nodes removed during surgery. The most widely used staging system, TNM, assesses the size of the tumor in the breast (T), the number and location of lymph nodes with cancer (N) and whether the cancer has spread beyond the breast and neighboring lymph nodes (M). Starting in 2018, the TNM system added the additional measures of tumor grade, estrogen receptor status, progesterone receptor status and HER2 status.

Q: My doctor suggested I see a genetic counselor. Why?

A: Genetic counseling can help women make informed decisions about genetic testing. In a genetic counseling session for breast cancer, the counselor will typically collect a detailed family and medical history and discuss genetic mutations, such as those in BRCA1 and BRCA2 genes, which can increase the chance of developing breast cancer.

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 molecular markers. Women with triple-negative breast cancer 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: 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 women, the presence or absence of tumor markers may help guide treatment options.

Q: What is a treatment summary and why is important?

A: A treatment summary is a document that you create and keep in your possession.Maintaining your own records allows you and your family members to have instant access to the specifics of your breast cancer diagnosis and treatment. A treatment summary should include:

- Your name and date of birth
- Date of diagnosis
- Prescribed therapy/therapies, including dates started and stopped and dosages when appropriate
- Dates and types of post-diagnosis testing, and the results of these tests
- Other medications 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 what else they suggest be included. Take your treatment summary with you when you visit any doctor, not just your oncologist.

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

Medicine Assistance Tool
www.medicineassistancetool.org

CLINICAL TRIALS WEBSITES

EmergingMed
www.emergingmed.com

National Cancer Institute
www.cancer.gov

Supported by an educational grant from Daiichi Sankyo, Inc.

CANCERcare®

Help and Hope

WWW.CANCERCARE.ORG

800-813-HOPE (4673)