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Treatment Update

Breast Cancer

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

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

Every year in the United States, approximately 230,000 women are diagnosed with breast cancer. About 2,200 men are diagnosed with breast cancer as well. In recent years, the number of effective treatments for breast cancer has increased. Doctors now know that breast cancer is not just one disease—there are several types, each with its own unique characteristics. As a result, they are able to prescribe specific treatments for the different types of breast cancer.

In this booklet, we talk about medications now available and new drugs in development. We also describe possible treatment side effects and how your medical team can help you prevent and manage them.

Determining Tumor Type

Tests performed on tumor samples give valuable information that helps guide treatment decisions for breast cancer. Your doctor may perform a biopsy and remove a tissue sample from your tumor and examine it under a microscope. Tumor samples can help doctors determine if the tumor is invasive or noninvasive (in situ). The tumor sample will also help identify your tumor's grade—whether it is a fast-growing or slow-growing form of breast cancer—as well as the tumor's hormone receptor status.

One piece of key information about breast tumors is whether they are estrogen receptor- or progesterone receptor-positive—that is, whether they depend on female hormones for their growth. Many breast cancers fall into this category. Using hormonal therapies is an effective way to treat these types of breast cancer.

About 20 percent to 25 percent of breast cancers are HER2-positive. These cancer cells have increased amounts of HER2 receptors, and this is linked to their ability to divide and grow. This type of breast cancer typically responds well to targeted treatments that block the activity of the HER2 receptor.

Another 15 percent of women with breast cancer have a type called triple-negative breast cancer. This name is derived from the fact that these tumors do not have estrogen receptors, progesterone receptors, or those for HER2. This explains why drugs that work for hormone-positive or HER2-positive tumors are not effective for women with triple-negative breast cancer. However, this kind of breast cancer usually responds to chemotherapy. And clinical trials are

pointing the way to new and even better treatments for triple-negative breast cancer.

By knowing more about breast cancer and how it is treated, you can better understand your options. This will allow you to take a more active role in your health care, as many women are doing today.

Breast Cancer Treatments

Surgery

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

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

As a result of new research published in the past several years, routinely performing extensive axillary lymph node dissection is being reconsidered, and many women are now being spared this procedure if they have only one to three involved lymph nodes and are going to receive radiation.

Chemotherapy

Chemotherapy is still a mainstay in treating breast cancer. It is administered through an injection or in pill form. Chemotherapy works by travelling through a patient's bloodstream. Based on clinical trials over many years, doctors

have learned how to more effectively use these drugs either alone or in combination. They have refined the doses and schedules of these drugs so that women get the most benefit from treatment with the fewest side effects.

Hormone Blockers

Doctors generally recommend hormonal therapy for estrogen receptor- or progesterone receptor-positive breast cancer that is either early stage or metastatic. These treatments prevent estrogen from attaching to receptors on breast cancer cells. As a result, estrogen cannot get in the cells, and tumor growth is slowed. The treatments also reduce the amount of hormones circulating in the body that attach to estrogen or progesterone receptors. By blocking hormones, the treatments deprive tumor cells of the substances they need to grow.

Tamoxifen (Nolvadex and others) is the standard estrogen-blocking treatment for premenopausal women. Tamoxifen is also effective for postmenopausal women.

Suppression of ovarian function with drugs, such as goserelin (Zoladex) and leuprolide (Lupron and others), can be an effective intervention for premenopausal women when combined with tamoxifen.

Another class of hormonal therapy is aromatase inhibitors (AIs). These medications prevent estrogen from forming in the first place by blocking aromatase, a substance that is important in producing the hormone.

AIs are approved and useful only for postmenopausal women. That's because before menopause, a woman's ovaries make so much estrogen that AIs are not effective. Some women with breast cancer who have not yet reached menopause choose to

surgically remove their ovaries. Your doctor can guide you in making a decision about whether this is the right step for you.

Although estrogen is no longer produced in the ovaries after menopause, it is still made in smaller amounts in the adrenal glands, muscle, skin, fat, and the breast itself, where aromatase plays an important role in making the hormone. So AIs are given to postmenopausal women to reduce the total amount of estrogen produced.

AIs and tamoxifen are taken by mouth daily in pill form. The AIs available in the United States are anastrozole (Arimidex and others), letrozole (Femara and others), and exemestane (Aromasin and others).

One estrogen-blocking drug, fulvestrant (Faslodex), works in a slightly different way: It attaches to estrogen receptors

and changes their shape. This prevents the receptors from working properly, which slows the growth of cancer cells. Fulvestrant is administered as an injection and is only approved for postmenopausal women with metastatic breast cancer whose tumors have not responded well to other hormonal treatments such as tamoxifen.

Targeted Treatments

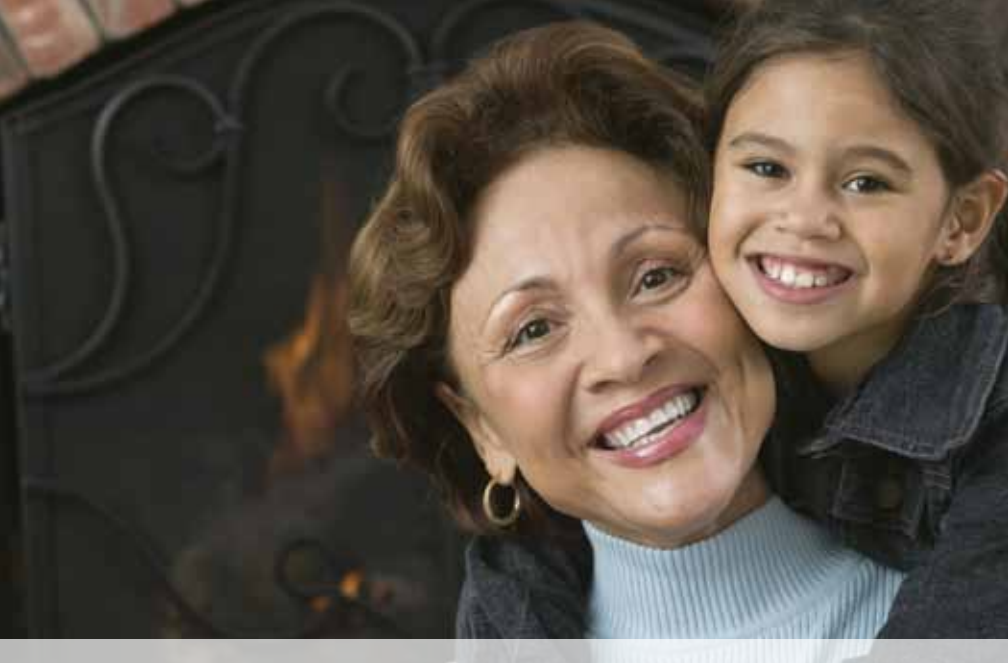
Targeted treatments are drugs that attack specific cell mechanisms thought to be important for cancer cell survival and growth. This specific targeting helps spare healthy tissues and causes less severe side effects than chemotherapy.

Tamoxifen was the first targeted therapy developed for breast cancer. Today, it is still used to treat early-stage and advanced estrogen receptor-positive breast cancer. It is also used to prevent breast cancer in women who have a high risk of developing the disease.

Trastuzumab (Herceptin) is one example of a targeted treatment designed for women whose tumor cells are HER2-positive. Since trastuzumab was approved, women with HER2-positive tumors are living significantly longer.

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

Lapatinib has been shown to be effective in women whose HER2-positive breast cancer returned, spread, or continued growing despite treatment with trastuzumab and chemotherapy. Lapatinib is given to these women along



with the chemotherapy capecitabine (Xeloda). This drug combination is effective at stopping cancer growth and shrinking tumors. Both lapatinib and capecitabine can be taken in pill form.

Capecitabine, and perhaps lapatinib, too, may be able to travel to brain tissue, something that most drugs for breast cancer cannot do. This is important for women whose breast cancer has spread to the brain.

The drug bevacizumab (Avastin) was used to treat women with advanced breast cancer but is no longer approved by the FDA to treat women with HER2-negative breast cancer that has metastasized. Patients who have been using bevacizumab for breast cancer may continue to take it. The drug, however, is still available to treat other cancers. The FDA recently approved pertuzumab (Perjeta) for women with HER2-positive metastatic breast cancer as first-line treatment in combination with trastuzumab and docetaxel (Taxotere and others).

Promising New Treatment Approaches

T-DM1 for HER2-Positive Metastatic Breast Cancer

Researchers are studying an older chemotherapy, called DM1, to treat HER2-positive breast cancer that has metastasized. They have combined DM1 with trastuzumab to create a new medication called T-DM1. Clinical trials have shown that T-DM1 can shrink, and in some cases completely destroy, breast cancer tumors.

Trial results comparing a drug combination approach with T-DM1 showed an improvement by six months in the time it takes the cancer to continue growing. Although T-DM1 is not on the market yet, it may greatly benefit patients with HER2-positive breast cancer in the future.

PARP Inhibitors

PARP inhibitors are being studied in women who have *BRCA* mutations and in women with triple-negative breast cancer. PARP is short for poly ADP-ribose polymerase. They block a cancer cell's ability to repair itself when damaged by radiation or chemotherapy.

In the first clinical trials, when a PARP inhibitor called BSI-201 was added to chemotherapy, it improved the treatment of breast cancer and helped women live longer. The National Cancer Institute has an ongoing trial to study PARP inhibitors with chemotherapy in women with triple-negative breast cancer.

Removing a Healthy Breast: Is It Necessary?

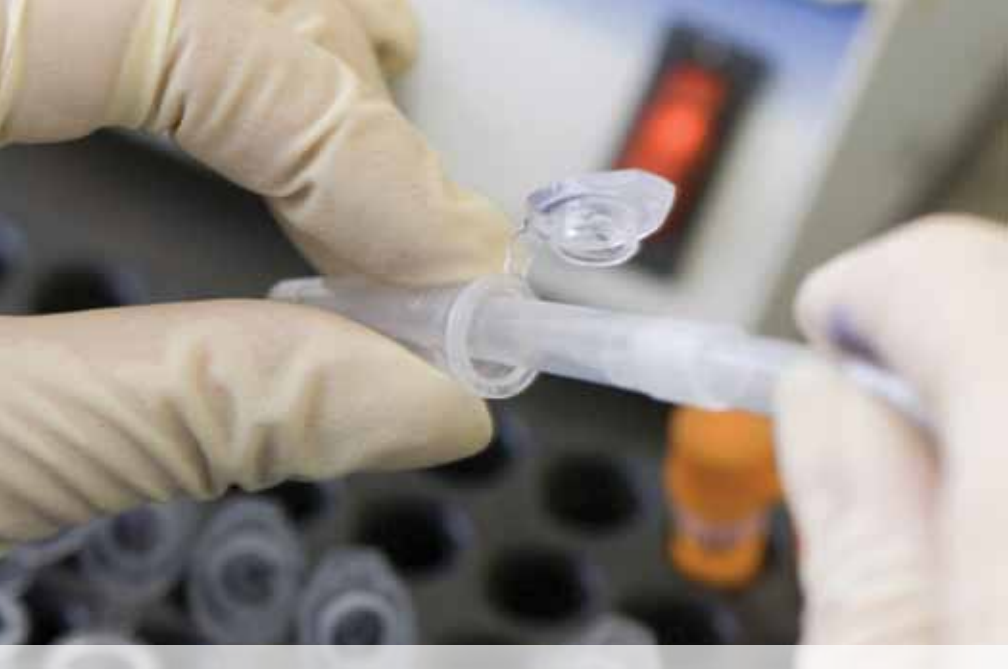
A growing number of women diagnosed with breast cancer are choosing to have their healthy breast removed along with their cancerous breast, believing the procedure will reduce their risk of developing cancer in the other breast.

According to a large study reported in the *Journal of the National Cancer Institute,* this may not be necessary. Research showed that the procedure does not make a difference in long-term survival for most women. However, researchers did find a small improvement in survival among young women with early-stage, estrogen receptor-negative breast cancer.

If removing a healthy breast is a procedure you might be considering, talk with your doctor about how the research findings may relate to you. Make sure you get all the facts you need so that you can make an informed decision that is right for you.

Personalizing Treatment

Two tests are currently approved for estimating the likelihood of deriving benefit from chemotherapy. Onco*type* DX and MammaPrint are approved for estimating the risk of recurrence in women with early-stage breast cancer. Both tests are appropriate for women with stage I or II breast cancer that is hormone receptor-positive and will be receiving hormone therapy. They work by analyzing the genes in



tumor tissue removed during surgery. If chemotherapy won't benefit some patients, these women could perhaps be spared unnecessary side effects by not using the treatment.

The National Cancer Institute is using Onco*type* DX in a clinical trial called TAILORx, which stands for Trial Assigning IndividuaLized Options for Treatment (Rx). More than 10,000 women at 900 sites in the United States and Canada will take part. These patients have been diagnosed recently with hormone receptor-positive, HER2-negative breast cancer; their cancers have not spread to the lymph nodes.

The TAILORx study will give doctors even more information about making treatment decisions. To learn more about TAILORx, talk with your doctor, call 800-4-CANCER, or visit www.cancer.gov/clinicaltrials/ECOG-PACCT-1.

Treatment Side Effects

Sometimes, side effects from medications can make people coping with cancer feel worse. Maintaining a good quality of life is an important part of your treatment because it will enable you to finish taking your medication. A key to managing side effects is to be aware of them and communicate with your health care team when they arise. Your health care team can help prevent and reduce the side effects of breast cancer treatment. Some common side effects include:

Nausea, vomiting, and other digestive system symptoms
Nausea, vomiting, diarrhea, constipation, and mouth sores are all common side effects caused by chemotherapy. With proper care, these conditions can be prevented or managed. If you develop any of them, be sure to tell your health care team so that you can get the most effective treatment.

Fatigue Feeling an extreme sense of tiredness that doesn't go away after rest can be the result of the cancer itself, treatment, anemia (low levels of red blood cells), or the emotional aspects of coping with cancer. If you are feeling fatigued, seek help from your health care team. Your doctor can treat anemia with medications and, if needed, blood transfusions. Changes to your diet and light exercise can also help you cope. Moderate activity, such as walking, can help you feel better and increase your energy. If treatment side effects leave you unable to eat, you may experience an increase in fatigue because your body does not have the energy that it needs. Consult with your health care team for more information on ways to manage fatigue.

Low white blood cell counts When you are undergoing chemotherapy, you may have low white blood cell counts, a condition called neutropenia. White blood cells play a key role in fighting infections. A reduced number of these cells increases your risk of infection. Your doctor can prescribe medications 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 People undergoing treatment for breast cancer often have some difficulty with memory or are unable to think clearly at times. This is commonly referred to as "chemobrain." Tell your doctor if you are having a problem remembering things or thinking clearly after receiving chemotherapy. Your doctor may be able to refer you to experts who can help you cope. Keep a diary or a log to track

how your memory lapses are affecting your daily routine and bring it with you to your doctor's appointments.

Bone loss Both hormonal therapies and chemotherapy can cause bone loss, increasing a woman's risk for osteoporosis. And when cancer spreads to the bone, it can also weaken bone and lead to fractures. One drug used for bone complications in women with metastatic breast cancer is zoledronic acid (Zometa). This medication slows the process by which bone wears away and breaks down.

The FDA approved a new bone-modifying drug called denosumab (Xgeva) after studies found that denosumab may be better than zoledronic acid in delaying or preventing bone-related side effects in patients with cancer. Denosumab is less toxic and causes fewer kidney problems in patients than zoledronic acid. It belongs to a class of drugs called RANK ligand inhibitors.

Ask your doctor which drugs may be available to help manage your bone health. Also, talk with your health care team about how exercise and changes in your diet may help.

Hot flashes Breast cancer treatments can lead to menopausal symptoms such as hot flashes and night sweats. They can also lead to vaginal dryness and a lowered sex drive. If you are experiencing these side effects, speak with your doctor about ways to cope with them.

Communicating With Your Health Care Team

In working with your team of specialists, it's important that you feel comfortable talking about any topic related to your diagnosis and treatment. Some questions to ask include:

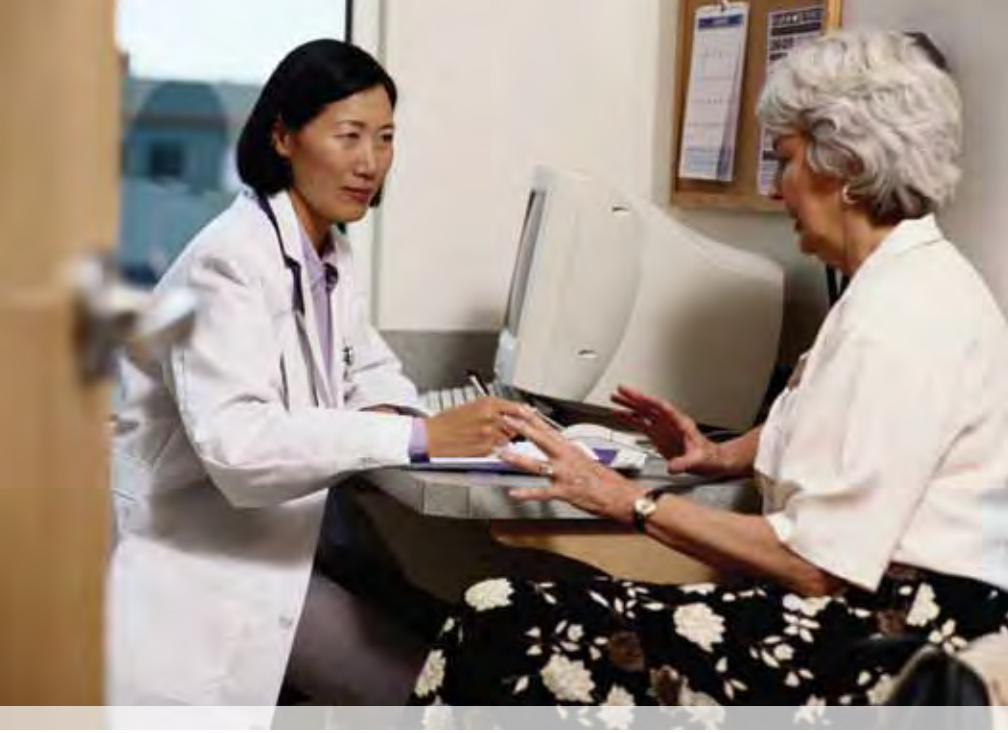
What are the goals of treatment? For example, if chemotherapy and surgery are recommended, what are the pros and cons of chemotherapy before surgery versus after surgery?

What are the possible side effects of treatment? Talk with members of your health care team about how to manage and prevent treatment side effects to improve your quality of life.

Is the standard of care right for me? Or should I consider entering a clinical trial?

Who do you recommend if I want to get a second opinion? No member of the team should mind that an individual seeks a second opinion if she desires one. Often, second opinions offer more insight into the recommendations of your health care team.

Should I consider a genetic test? In families where there is a clear genetic pattern of breast cancer, genetic testing should be discussed at the time of diagnosis. The results could affect treatment decisions and may provide important information for other family members. Some people don't know enough details about their family history to see a genetic pattern of breast cancer. But even if you don't know how many relatives had cancer and at what age, certain hereditary backgrounds



can provide a clue. For example, women of Jewish descent are more likely to be carriers of the *BRCA1* or *BRCA2* breast cancer genes. If you were diagnosed with breast cancer before the age of 45, your doctor may recommend genetic testing, even without a family history. The National Comprehensive Cancer Network recently updated its guidelines to recommend genetic testing for women under the age of 65 who have been diagnosed with triple-negative breast cancer. To learn more about genetic testing, speak with your health care provider.

What about fertility (the ability to have a baby)? Younger women who want to start a family or expand their family should speak with their oncologist to discuss how treatment may affect fertility before they begin treatment. They may also wish to ask for an urgent referral to a reproductive endocrinologist or fertility specialist to discuss options for fertility preservation.

Cancer*Care* Can Help

If you or a loved one has been diagnosed with breast cancer, contact Cancer*Care*. We are a national nonprofit organization that provides free professional services to anyone affected by cancer. Our services are provided by oncology social workers and include individual counseling, support groups, education, financial assistance, and referrals to resources in your community.

To learn more, call us at 800-813-HOPE (4673) or visit www.cancercare.org.

Frequently Asked Questions

Q. How can I know if chemotherapy is the right treatment option for me?

A. When you meet with your medical oncologist to discuss treatment options, you may want to ask about testing to see whether or not you should receive chemotherapy. Tests such as Onco*type* DX or MammaPrint can be performed on your tumor at the time of surgery or after surgery. The tests are not helpful to patients who have already finished their treatments, and they do not affect recommendations about tamoxifen or hormone therapy use. However, they do help doctors and patients decide whether or not to treat the tumor with chemotherapy.

Q. Are there any specific targeted therapies being developed for triple-negative breast cancer?

A. Currently, chemotherapy is the first line of treatment for women with triple-negative breast cancer. There are no targeted therapies for triple-negative breast cancer, but it is an active area of research. There are clinical trials currently under way to investigate treatment options for women with triple-negative breast cancer. Patients with triple-negative breast cancer may want to discuss with their doctor about participating in a clinical trial.

Q. Are the side effects of aromatase inhibitors different from those of chemotherapy?

A. Aromatase inhibitors are a new class of drugs that block the majority of estrogen production. Common side effects from these drugs include joint stiffness, vaginal dryness, hot flashes, and fatigue. Other side effects include bone thinning, bone fractures, hair thinning, difficulty sleeping, and night sweats. Talk with your doctor to learn more about the side effects and ways to help manage and prevent them.

Resources

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

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

Cancer.Net
www.cancer.net

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

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

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

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

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

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

TO FIND OUT ABOUT CLINICAL TRIALS:

Coalition of Cancer Cooperative Groups
www.CancerTrialsHelp.org

National Institutes of Health
www.cancer.gov/clinicaltrials

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