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Advances in the Treatment of Breast Cancer

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Learn about:

- The latest breast cancer treatments
- Personalized medicine
- Working with your health care team
- Managing treatment side effects



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Advances in the Treatment of Breast Cancer

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The information in this booklet is based on the CancerCare Connect® Education Workshop "Advances in the Treatment of Breast Cancer." This workshop was conducted by CancerCare in partnership with AdvancedBC.org, American Cancer Society, American Pain Foundation, American Society of Clinical Oncology, Association of Clinicians for the Underserved, Association of Oncology Social Work, Black Women's Health Imperative, Bone and Cancer Foundation, Breast Cancer Alliance, Breast Cancer Network of Strength, The Breast Cancer Research Foundation, Cancer Patient Education Network, Cancer Support Community, Education Network to Advance Cancer Clinical Trials, Intercultural Cancer Council, Joe's House—A Lodging Guide for Cancer Patients, Latinas Contra Cancer, Linda Creed Breast Cancer Foundation, Living Beyond Breast Cancer, Men Against Breast Cancer, Multinational Association of Supportive Care in Cancer, National Black Leadership Initiative on Cancer, National Center for Frontier Communities, National Coalition for Cancer Survivorship, National Family Caregivers Association, Redes en Accion: The National Latino Cancer Research Network, Research Advocacy Network, The Sister Study, Tigerlily Foundation, Vital Options International & The Group Room, The Witness Project, and Young Survival Coalition.

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This CancerCare Connect booklet was made possible by
Amgen, AstraZeneca, and sanofi-aventis U.S. LLC.

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

Every year in the United States, approximately 192,000 women are diagnosed with breast cancer. In recent years, the number of effective treatments available has increased. That is because doctors now understand much more about breast cancer. They know that it is not just one disease—there are several types of breast cancer, each with its own unique characteristics. Today, doctors are able to prescribe specific treatments for the different types of breast cancer.

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 of breast cancers are HER2-positive. These cancer cells have increased amounts of HER2 receptors. These receptors act as doorways that allow a substance, also called HER2, into the cells, where it encourages tumor growth. These types of breast cancer tend to respond well to targeted treatments that block the activity of the HER2 receptor.

Another 15 percent to 20 percent of women with breast cancer have a type called triple-negative breast cancer. This type of breast cancer is both estrogen receptor-negative and



progesterone receptor-negative, as well as HER2-negative. So, generally, the drugs that work for hormone-positive or HER2-positive tumors are not effective for women with triple-negative breast cancer. However, this kind of 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. In this booklet, we talk about medications now available and new drugs in development. We also describe possible side effects and how your medical team can help you prevent and manage them.

Breast Cancer Treatments

SURGERY

One of the biggest advances in breast cancer treatment is improved 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.

Another important step forward is sentinel node mapping. This term refers to finding the first (or sentinel) lymph node in the underarm into which breast cancer cells would travel. If the sentinel 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.

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 most premenopausal women. Tamoxifen is also effective for postmenopausal women.



When combined with tamoxifen, other estrogen-blocking drugs such as goserelin (Zoladex) and leuprolide (Lupron and others) are also effective. These medications are sometimes given to premenopausal women to block the estrogen produced in the ovaries.

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 for postmenopausal women. That's because before menopause, a woman's ovaries make so much estrogen, AIs are not effective. Although estrogen is no longer produced in the ovaries after menopause, it is still made in smaller amounts in the adrenal glands, where aromatase plays an important role in making the hormone. So AIs are given to postmenopausal women to block that source of estrogen.

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

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.

One of the newer estrogen-blocking drugs, 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 often effective in postmenopausal women with metastatic breast cancer whose tumors have not responded well to other hormonal treatments.

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.

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 newer 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, and 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.

Another targeted treatment used with chemotherapy is bevacizumab (Avastin). It has been approved by the U. S. Food and Drug Administration (FDA) to treat women with HER2-negative breast cancer that has metastasized.

Bevacizumab works by stopping the growth of new blood vessels in tumors. It blocks a substance called vascular endothelial growth factor (VEGF). When tumor cells spread through the body, they release VEGF to create new blood vessels. These blood vessels supply oxygen, minerals, and other nutrients to feed the tumor. Because healthy tissues have an established blood supply, they are less affected by the drug.

CHEMOTHERAPY

Chemotherapy is still a mainstay in treating breast cancer. 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 these drugs are given in so that women with breast cancer get the most benefit from treatment with the fewest side effects.

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. The results seem promising because the women who took part in the clinical trials had received an average of seven previous treatments for their metastatic cancer. Another bonus: T-DM1 does not cause hair loss, as standard chemotherapy does.

PARP INHIBITORS FOR TRIPLE-NEGATIVE BREAST CANCER

There are few targeted treatment options available for women with triple-negative breast cancer. But that may soon change, thanks to a new class of medications now being studied in clinical trials. These new drugs are called PARP inhibitors. 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. This combination will be studied in a larger clinical trial to confirm the results. Doctors hope to know more within a year.

PERSONALIZING TREATMENT

Most women with breast cancer are hormone receptor-positive but HER2-negative. For these women, doctors have been trying to answer the question of when chemotherapy should be given with hormonal therapy.

A new test called *Oncotype DX* is helping to answer this question. *Oncotype DX* can help predict which women probably won't benefit from further treatment with chemotherapy for early-stage breast cancer that has not spread to the lymph nodes. If the treatment won't benefit

them, these women could perhaps be spared unnecessary side effects by not using the treatment.

Many doctors have based their treatment plans on the results of the Oncotype DX Recurrence Score, or RS. Each tumor has its own RS, which helps indicate benefit from chemotherapy as well as risk of having a recurrence within 10 years.

Oncotype DX may also be helpful in deciding on the best treatment for women who have breast cancer that has already spread to the lymph nodes.

The National Cancer Institute is using Oncotype 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 1-800-4-CANCER, or visit www.cancer.gov/clinicaltrials/ECOG-PACCT-1.

It Takes a Team

Treating breast cancer requires a multidisciplinary approach, one that involves many types of specialists: medical, surgical, and radiation oncologists; oncology nurses; pain management experts; registered dietitians; genetic counselors; and oncology social workers. To ensure the best possible outcome, all of these experts need to communicate with each other, the patient, and her family.

In working with this 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?

- **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.



- **What about fertility (the ability to have a baby)?**

Younger women who want to start a family or add to it might wish to ask about egg harvesting or techniques that protect the ovaries' ability to produce eggs.

Managing Treatment Side Effects

Your health care team can help prevent and reduce the side effects of breast cancer treatment. Some patients worry that if they complain about side effects, their doctor will focus less on treatment. That is not true. Doctors know that maintaining a good quality of life is an important part of your treatment. 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.

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. Diet and light exercise can also help you cope with fatigue. Oncology social workers and nurses can help you cope with the emotional or practical concerns that can lead to 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, it is vital that you let your health care team know immediately so that you can get proper treatment.

Memory lapses Difficulty with memory or an inability to think clearly is commonly experienced by women with breast cancer. It's often referred to as "chemobrain." Tell your doctor if you are having a problem remembering things or thinking clearly after receiving chemotherapy. Sometimes, simply changing a prescription can make a difference, since some medications make you less alert. For more information, see the Frequently Asked Questions section on page 13.

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.

Although women with breast cancer are at a higher risk of developing a second, unrelated cancer in the breast, it is more likely to be caught at an early, more curable stage. That's because women who have already had breast cancer are screened more often. So changes in their health are spotted sooner.

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.

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. Researchers are comparing zoledronic acid to a new drug called denosumab (Prolia). Recently approved by the

FDA for the treatment of osteoporosis in postmenopausal women, denosumab seems to do a better job than zoledronic acid of delaying or preventing bone-related side effects in patients with cancer. Denosumab is better



tolerated by patients and causes fewer kidney problems. It belongs to a new class of drugs called RANK ligand inhibitors.

Talk with your doctor about which drugs may be available to you 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, have a frank discussion with your doctor about ways to cope.

CancerCare® Can Help

If you or a loved one has been diagnosed with breast cancer, contact CancerCare. We are a national nonprofit organization that provides free professional support 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 learn more, call us at 1-800-813-HOPE (4673) or visit www.cancercares.org.

Frequently Asked Questions

Q How long can you take Arimidex? My doctor says five years, but I know some clinical trials have gone as long as nine years.

A Clinical trials now under way are looking at longer-term hormonal therapy—usually tamoxifen followed by an aromatase inhibitor, such as Arimidex (anastrozole). Some studies include five years of treatment with tamoxifen followed by five years of an aromatase inhibitor. Others include two to three years of tamoxifen followed by two to three years of an aromatase inhibitor. One ongoing study is looking at using aromatase inhibitors for 10 years versus five years. But until the studies are complete, five years on an aromatase inhibitor remains the standard practice.

Q I'm experiencing both chemobrain and peripheral neuropathy. What can be done to help ease these symptoms?

A There are still a lot of unknowns about chemobrain. Doctors don't know whether the thinking and memory difficulties that some women experience during or after treatment are caused by chemotherapy, by hormonal therapy, or by conditions such as depression or fatigue, which can develop when you are going through cancer. Most likely, it is caused by a combination of all these things. Research is ongoing in this area.

Chemobrain seems to improve in most women within two years after treatment, but that's not the case for everyone. Some women continue having problems with memory and thinking for a much longer time. Ask your doctor to

refer you to a neuropsychologist for testing. He or she will help you judge how serious the problem is and may also provide you with ways to cope. Some medications, such as methylphenidate (Ritalin and others), have been shown to help.

Some practical tips for improving your memory and ability to concentrate include:

- Making lists and keeping them in a prominent place.
- Always leaving car and house keys in the same spot. Some women paste a red tag on their keys to make them more visible.
- Practicing meditation or other relaxation techniques, which can help you regain a sense of calm. They also seem to improve memory recall.
- Doing mentally stimulating activities such as crossword and jigsaw puzzles.

Peripheral neuropathy, or nerve damage in the hands and feet, tends to improve over time. But it can be painful, so you should talk with your doctor about seeing a neurologist, a specialist in nervous system disorders and pain management. Some doctors prescribe gabapentin (Neurontin and others) or other similar drugs that are designed to control seizures. These medications may also reduce hot flashes and ease sleeplessness. Certain types of antidepressants can also help relieve the symptoms of neuropathy.

Q What are the newest advances in radiation treatment for breast cancer?

A Generally, after lumpectomy (removal of a breast tumor, sparing the breast), most women have between five and six weeks of radiation treatment, five days a week, Monday through Friday. However, studies done in Canada, Europe,

and the United States now show that this treatment can be shorter (three weeks) with slightly higher doses of radiation.

Especially after the removal of small tumors, some research shows that the radiation can be done on only part of the breast rather than the entire breast.

There is also a different way to deliver this treatment: by implanting radioactive “seeds” directly into the breast. For certain patients, this approach can be very effective. Talk with your doctor to find out whether this treatment is right for you.

Q Can techniques such as relaxation exercises, acupuncture, yoga, or meditation help women with breast cancer?

A A number of studies have shown that these techniques do benefit patients with breast and other types of cancer.

They seem to improve a person’s overall sense of well-being and help many women tolerate treatments with fewer side effects. For example, acupuncture appears to reduce chemotherapy-caused nausea in some people and may even ease peripheral neuropathy.

Such findings have received so much attention that many medical centers have established complementary (sometimes called “integrative”) medicine departments. Complementary medicine is combined with all the advances in medical management of these side effects for the most benefit.

Resources

CancerCare

1-800-813-HOPE (4673)

www.cancercares.org

American Cancer Society

1-800-227-2345

www.cancer.org

Cancer.Net

Patient information from the American Society of Clinical Oncology

www.cancer.net

Cancer Support Community

1-888-793-9355

www.cancersupportcommunity.org

National Cancer Institute

1-800-422-6237

www.cancer.gov

National Library of Medicine (MedlinePlus)

www.medlineplus.gov

Breast Cancer Network of Strength

1-800-221-2141

www.networkofstrength.org

Living Beyond Breast Cancer

1-888-753-5222

www.lbbc.org

Susan G. Komen for the Cure

1-877-465-6636

www.komen.org

Triple Negative Breast Cancer Foundation

1-877-880-8622

www.tnbcfoundation.org

To find out about clinical trials:

Coalition of Cancer Cooperative Groups

www.CancerTrialsHelp.org

National Cancer Institute

www.cancer.gov/clinicaltrials



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This booklet was edited and produced by Elsevier Oncology.

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