



Doctor-Approved Patient Information from ASCO®

GUIDE TO BREAST CANCER



Comprehensive cancer information from the American Society of Clinical Oncology (ASCO)

www.cancer.net

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The American Society of Clinical Oncology (ASCO) is the world's leading professional organization representing physicians of all oncology subspecialties who care for people with cancer.

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The Cancer.Net Guides to Cancer provide patients with comprehensive, peer-reviewed information based on content from Cancer.Net (www.cancer.net), ASCO's patient information website. All the information and content on Cancer.Net was developed and approved by the cancer doctors who are members of ASCO, making Cancer.Net an up-to-date and trusted resource for cancer information.

The best cancer care starts with the best cancer information. Well-informed patients are their own best advocates and invaluable partners for physicians. ASCO's patient education materials are available both in print and online to provide trusted, authoritative information for people living with cancer and those who care for and about them.

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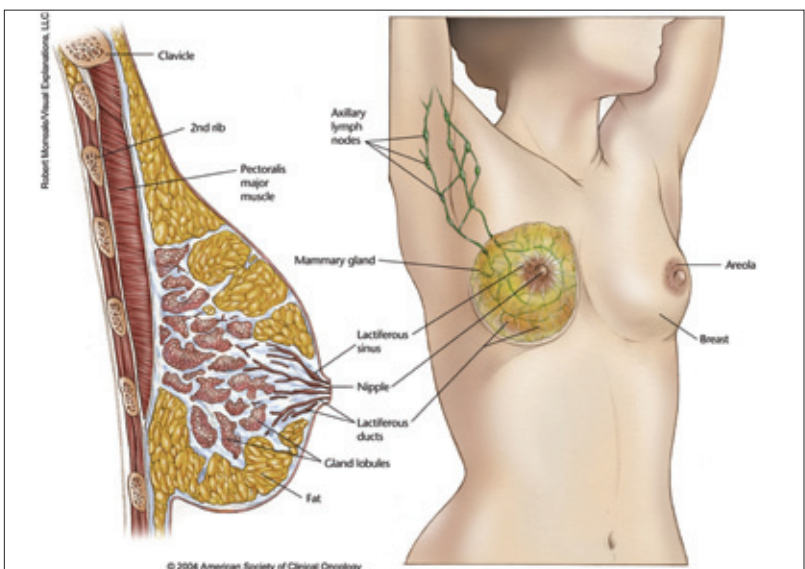
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OVERVIEW AND STATISTICS

In the United States, breast cancer is the most common cancer in women (excluding skin cancer). Men can also develop breast cancer, but male breast cancer is rare, accounting for less than 1% of all breast cancers. Cancer begins when normal cells in the breast change and grow uncontrollably, forming a mass called a tumor. A tumor can be benign (noncancerous) or malignant (cancerous, meaning it can spread to other parts of the body).

The breast is mostly made up of fatty tissue. Within this tissue is a network of lobes, which are made up of tiny, tube-like structures called lobules that contain milk glands. Tiny ducts connect the glands, lobules, and lobes, carrying the milk from the lobes to the nipple, located in the middle of the areola (darker area that surrounds the nipple). Blood and lymph vessels also run throughout the breast; blood nourishes the cells, and the lymph system drains bodily waste products. The lymph vessels connect to lymph nodes, the tiny, bean-shaped organs that help fight infection.

Breast cancer spreads when breast cancer cells move to other parts of the body through the blood vessels and/or lymph vessels. This is called metastasis. Breast cancer most commonly spreads to the regional lymph nodes. The lymph nodes can be axillary (located under the arm), cervical (located in the neck), or supraclavicular (located just above the collarbone). When it spreads further through the body, it most commonly spreads to the bones, lungs, and liver. Less commonly, breast cancer may spread to the brain. The cancer can also recur (come back after treatment) locally in the skin, in the same breast (if it was not removed as part of treatment), other tissues of the chest, or elsewhere in the body.



Anatomical and staging illustrations for many types of cancer are available at www.cancer.net.

Currently, there are more than two and a half million women living in the United States who have been diagnosed with and treated for breast cancer.

Statistics adapted from the American Cancer Society and the National Cancer Institute Surveillance Epidemiology and End Results (SEER) database.

Types of breast cancer

Most breast cancers start in the ducts or lobes. Almost 75% of all breast cancers begin in the cells lining the milk ducts and are called ductal carcinomas. Cancer that begins in the lobules is called lobular carcinoma. If the disease has spread outside of the duct and into the surrounding tissue, it is called invasive or infiltrating ductal carcinoma. If the disease has spread outside of the lobule, it is called invasive or infiltrating lobular carcinoma. Disease that has not spread is called in situ, meaning “in place.” How in situ disease grows and spreads, as well as how it is treated, depends on whether it is ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS).

Most in situ breast cancers are DCIS. Currently, oncologists recommend surgery to remove DCIS to help prevent the cancer from becoming an invasive breast cancer and spreading to other parts of the breast or the body. Radiation therapy and hormonal therapy may also be recommended for DCIS (see the Treatment section for more information).

LCIS is not considered cancer and is usually monitored by the doctor. LCIS is a risk factor for breast cancer (see the Risk Factors section for more information).

Other, less common cancers of the breast include medullary, mucinous, tubular, metaplastic, and papillary breast cancer. Inflammatory breast cancer is a faster-growing type of cancer that accounts for about 1% to 5% of all breast cancers. It may be misdiagnosed as a breast infection because there is often swelling of the breast and redness of the breast skin. Paget’s disease is a type of cancer that begins in the ducts of the nipple. The skin often appears scaly and may be itchy. Although it is usually in situ, it can also be an invasive cancer.

Find out more about basic cancer terms used in this section at www.cancer.net/dictionaryresources.

RISK FACTORS

A risk factor is anything that increases a person’s chance of developing cancer. Although risk factors can influence the development of cancer, most do not directly cause cancer. Some people with several risk factors never develop cancer, while others with no known risk factors do. However, knowing your risk factors and talking about them with your doctor may help you make more informed lifestyle and health care choices.

Many women who develop breast cancer have no obvious risk factors and no family history of breast cancer. This means that all women need to be aware of changes in their breasts and talk with their doctor about receiving regular clinical breast examinations (an examination of the breast by a physician) and mammograms (x-ray of the breast that can detect a tumor that is too small to be felt). It is likely that more than one risk factor influences the development of breast cancer.

The following factors may raise a woman's risk of developing breast cancer:

Age. The risk of developing breast cancer increases as a woman ages, with most cancers developing in women over 50.

Personal history of breast cancer. A woman who has had breast cancer in one breast has a 1% to 2% chance per year of developing a second breast cancer in her opposite breast.

Family history of breast cancer. Women who have a first-degree relative (mother, sister, daughter) diagnosed with breast cancer have an increased risk of the disease. Having more than one first-degree relative with breast cancer further increases that risk, especially if the cancer was diagnosed at a younger age, because it may be a sign of genetic changes that are inherited. Women who have a second-degree relative (aunt, niece, grandmother, granddaughter) diagnosed with breast cancer also have a higher risk of breast cancer. The father's (paternal) side of the family should also be considered equally to the mother's (maternal) side when evaluating family history. For example, you may be at higher risk if your father's sister or mother had breast cancer.

Genetic predisposition. Mutations (changes) to the breast cancer genes 1 or 2 (*BRCA1* or *BRCA2*) are associated with increased breast and ovarian cancer risk. Blood tests (genetic testing) are available to test for known mutations to these genes, but are not recommended for everyone and **only after** a person has received appropriate genetic counseling. Men may also carry these gene mutations. Breast or ovarian cancer on the paternal side of the family greatly increases the risk of having hereditary breast and ovarian cancer. Researchers estimate that *BRCA1*, *BRCA2*, and other genes linked to breast cancer risk make up 5% to 10% of all breast cancers. If a woman learns she has one of these genetic mutations, there are steps she can take to lower her risk of breast and ovarian cancers. Learn more about the genetics of breast cancer, genetic testing, and genetic counseling at www.cancer.net/genetics.

Personal history of ovarian cancer. A history of ovarian cancer can increase a woman's risk of breast cancer. Breast cancer gene mutations, such as *BRCA1* or *BRCA2*, greatly increase the risk of both ovarian and breast cancers.

Estrogen and progesterone exposure. Estrogen and progesterone are hormones in women that control the development of secondary sex characteristics (such as breast development) and pregnancy. A woman's production of estrogen and progesterone decreases at menopause. Prolonged exposure to these hormones increases breast cancer risk.

- Women who began menstruating before 11 or 12 or went through menopause after age 55 have a higher risk of breast cancer because their breast cells have been exposed to estrogen and progesterone for a longer time.
- Women who had their first pregnancy after age 35 or who have never had a full-term pregnancy have a higher risk of breast cancer. Pregnancy may protect against breast cancer because it pushes breast cells into their final phase of maturation. Breastfeeding may also help lower the risk of breast cancer.

Postmenopausal hormone replacement therapy. Recent use (within the past five years) and long-term use (several years or more) of postmenopausal (after menopause) hormone replacement therapy increases a woman's risk of breast cancer. In fact, the number of new breast cancers diagnosed has been dropping as fewer women have been taking hormone replacement therapy.

Oral contraceptives (birth control pills). Some studies suggest that oral contraceptives slightly increase the risk of breast cancer, while others have shown no link between the use of oral contraceptives to prevent pregnancy and development of breast cancer. Research on this topic is ongoing.

Race and ethnicity. Although white women are more likely to develop breast cancer, black women are more likely to die from the disease. Reasons for survival differences are unclear and probably involve both socioeconomic and biologic factors. Women of Ashkenazi Jewish heritage also have an increased risk of breast cancer because of *BRCA* mutations.

Atypical hyperplasia of the breast. This condition increases the risk of breast cancer and is characterized by abnormal, but not cancerous, cells found in a breast biopsy.

LCIS. As explained in the Overview section, this condition describes abnormal cells found in the lobules or glands of the breast. LCIS increases the risk of developing invasive breast cancer (cancer that spreads into surrounding tissues). If LCIS is found, it may be removed to check for other changes. Talk with your doctor about the best way to monitor this condition.

Lifestyle factors. As with other types of cancer, studies continue to show that various lifestyle factors may contribute to the development of breast cancer.

- Recent studies have shown that postmenopausal women who are obese have an increased risk of breast cancer.

- Lack of exercise may increase the risk of breast cancer because exercise lowers hormone levels, alters metabolism, and boosts the immune system. Increased physical activity is associated with a decreased risk of developing breast cancer.
- Having two or more alcoholic drinks (including beer, wine, and spirits) per day raises the risk of breast cancer.

Radiation. High doses of ionizing radiation (such as from tanning booths and x-rays) may increase a woman's risk of breast cancer. However, the very small amount of radiation a woman receives during a yearly mammogram has not been linked to an increased risk of breast cancer.

Breast density. A tumor in breast tissue that is dense may be more difficult to find on a mammogram. However, researchers are also looking at whether breast density increases the risk of breast cancer.

PREVENTION

No intervention is 100% guaranteed to prevent breast cancer. However, depending on a woman's specific risk factors, there are options to reduce the risk of developing breast cancer.

- For women with *BRCA1* or *BRCA2* mutations, a prophylactic mastectomy (preventive removal of the breasts) may be considered. This appears to reduce the risk of developing breast cancer by at least 95%. These women may also consider a prophylactic salpingo-oophorectomy (preventive removal of the ovaries and fallopian tubes), which can reduce the risk of developing breast and ovarian cancers.
- Women who have a higher than normal risk of developing breast cancer may consider chemoprevention (the use of drugs to reduce breast cancer risk). Two drugs, tamoxifen (Nolvadex) and raloxifene (Evista), are approved to lower breast cancer risk. These drugs are called selective estrogen receptor modulators (SERMs). A SERM is a medication that blocks estrogen receptors in some tissues and not others. Postmenopausal women and premenopausal women may take tamoxifen, whereas raloxifene is only approved for postmenopausal women. Each drug also has different side effects. Talk with your doctor about whether you may benefit from chemoprevention for breast cancer. Other drugs are being researched to help prevent breast cancer, including aromatase inhibitors and statins. Read more about drugs to reduce breast cancer risk at www.cancer.net/whattoknow.
- Other ways to lower your risk of breast cancer include getting regular physical activity, staying at a normal weight, and limiting the amount of alcohol you drink.

Several breast cancer risk assessment tools have been developed to help a woman estimate her chance of developing breast cancer. The best studied is the Gail model (www.cancer.gov/bcrisktool). After you enter some personal and family

information, including race/ethnicity, the tool provides you with a five-year and lifetime estimate of the risk of developing invasive breast cancer. Because it only asks for information about breast cancer in first-degree family members (mother, sister) and doesn't include their age at diagnosis, the tool works best at estimating risk in women without a strong inherited breast cancer risk. For some women, other ways of determining the risk of breast cancer may be more appropriate. It's important to talk with your doctor about how to find out your risk of breast cancer.

Screening guidelines

Mammography is the best tool doctors have to screen healthy women for breast cancer, as it has been shown to lower deaths from breast cancer. Like any medical test, mammography involves risks, such as additional invasive testing and anxiety, if the test falsely shows a possible tumor; this is called a false-positive. Occasionally (up to 10% to 15% of the time), mammography may miss a cancer, called a false-negative.



Different organizations have looked at the evidence, risks, and benefits of mammography and have developed slightly different screening schedules:

- The U.S. Preventive Services Task Force (USPSTF) recommends that women aged 50 to 74 have mammography every two years. They recommend that mammography be considered in women aged 40 to 49 after evaluating the risks and benefits of this test with a physician.
- The American Cancer Society (ACS) recommends yearly mammography beginning at age 40.

All women should talk with their doctors about mammography and decide on an appropriate screening schedule. For women with a high risk of breast cancer, screening may be recommended at an earlier age or more often than the schedules listed above. Learn more about ASCO's perspective on mammography screening for breast cancer at www.cancer.net/expertsoncancernews.

The USPSTF and ACS also differ on their recommendations for clinical breast examinations. The USPSTF recommends a clinical breast examination along with mammography, and the ACS recommends a clinical breast examination every one to three years until age 40, then annually.

Finally, although breast self-examination has not been shown to lower deaths from breast cancer, it is important for women to become familiar with their breasts so that they can be aware of any changes and report these to their doctor.

Other ways to examine the breasts, such as ultrasound and magnetic resonance imaging (MRI), are not regularly used to screen for breast cancer. However, they may be helpful for evaluating women with a higher risk of breast cancer. According to the ACS, women at high risk for breast cancer (for example, women with *BRCA* gene mutations or a strong family history of breast cancer) should receive MRI screening and mammography, although not necessarily at the same time. MRI may be better than mammography and ultrasound at finding a small mass in a woman's breast, especially for women with very dense breast tissue. However, an MRI has a higher rate of false-positive test results and may result in more biopsies and other tests. In addition, an MRI does not show calcifications, a sign of in situ breast cancer (DCIS).

Ultrasound or MRI may also be used for women with a suspicious breast change in a physical examination or mammography. If there are suspicious changes during a physical examination, further testing is needed, even if the mammogram is interpreted as normal. Women are encouraged to talk with their doctor about the method of screening recommended for them and how often screening and prevention are needed.

Learn more about breast cancer screening and prevention at www.cancer.net/prevention.

SYMPTOMS AND SIGNS

Women with breast cancer may experience breast abnormalities or symptoms, but many women do not show any of these signs or symptoms when diagnosed. Many times, breast signs or symptoms can be caused by a medical condition that is not cancer. If you are concerned about a sign or symptom, please talk with your doctor.

The signs and symptoms to look for include:

- New lumps that feel like a hard knot (many women normally have lumpy breasts) or a thickening in the breast or under the arm
- Nipple tenderness, discharge (may occur suddenly, be bloody, or occur in only one breast), or physical changes (such as a nipple turned inward, a persistent sore, or a change in the size or shape of the breast)
- Skin irritation or changes, such as puckers, dimples, scaliness, or new creases
- Warm, red, swollen breasts with a rash resembling the skin of an orange (called *peau d'orange*)
- Pain in the breast (usually not a symptom of breast cancer, but it should be reported to a doctor), particularly breast pain that doesn't go away

Your doctor will ask you questions about the symptoms you are experiencing to help find out the cause of the problem, called a

diagnosis. This may include how long you've been experiencing the symptom(s) and how often.

If cancer is diagnosed, relieving symptoms and side effects remains an important part of cancer care and treatment. This may also be called symptom management, palliative care, or supportive care. Be sure to talk with your health care team about symptoms you experience, including any new symptoms or a change in symptoms.

DIAGNOSIS

Doctors use many tests to diagnose cancer and find out if it has spread. Some tests may also help the doctor decide which treatments may be the most effective. For most types of cancer, a biopsy (the removal of a small amount of tissue for examination under a microscope) is the only way to make a definitive diagnosis of cancer. If a biopsy is not possible, the doctor may suggest other tests that will help make a diagnosis.

Imaging tests may be used to find out whether the cancer has metastasized. Your doctor may consider these factors when choosing a diagnostic test:

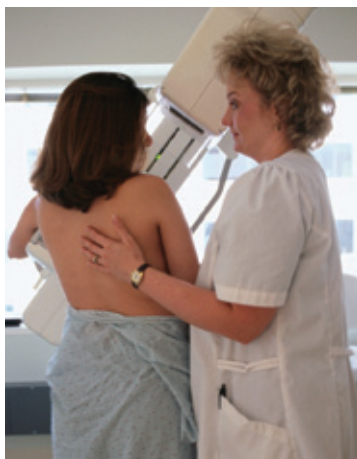
- Age and medical condition
- Type of cancer suspected
- Severity of symptoms
- Previous test results

The diagnosis of breast cancer usually begins when a woman or her doctor discovers a mass or abnormal calcification (tiny spot of calcium usually found on an x-ray) on a screening mammogram, or an abnormality in the woman's breast by clinical examination or self-examination. Several tests may be done to confirm a diagnosis of breast cancer.

The following tests may be used to diagnose breast cancer or for follow-up testing after the cancer has been diagnosed. Not every person will have all of these tests.

Imaging tests

Diagnostic mammography. Diagnostic mammography is similar to screening mammography except that more views (pictures) of the breast are taken, and it is often used when a woman is experiencing signs, such as nipple discharge or a new lump. Diagnostic mammography may also be used if something suspicious is found on a screening mammogram.



Ultrasound. An ultrasound uses high-frequency sound waves to create an image of the breast tissue. An ultrasound may distinguish between a solid mass, which may be cancer, and a fluid-filled cyst, which is usually not cancer.

MRI. An MRI uses magnetic fields, not x-rays, to produce detailed images of the body. A contrast medium (a special dye) may be injected into a patient's vein to create a clearer picture. An MRI may be used once a woman has been diagnosed with cancer to check the other breast for cancer. It may also be used for screening (see the Prevention section).

Surgical tests

Biopsy. A biopsy is the removal of a small amount of tissue for examination under a microscope. Other tests can suggest that cancer is present, but only a biopsy can make a definite diagnosis. The sample removed from the biopsy is analyzed by a pathologist (a doctor who specializes in interpreting laboratory tests and evaluating cells, tissues, and organs to diagnose disease). There are different types of biopsies, classified by the technique and/or size of needle used to collect the tissue sample.

- A fine needle aspiration biopsy uses a small needle to remove a small sample of cells.
- A core needle biopsy uses a larger needle to remove a larger sample of tissue. This is usually the preferred biopsy technique for finding out whether an abnormality on a physical examination or an imaging test is cancer. A vacuum-assisted biopsy removes more than one large core of tissue.
- A surgical biopsy removes the largest amount of tissue. This biopsy may be incisional (removal of part of the lump) or excisional (removal of the entire lump). Because definitive surgery is best done after a cancer diagnosis has been made, a surgical biopsy is usually not the recommended way to diagnose breast cancer. Most often, non-surgical core biopsies are recommended to diagnose breast cancer to keep surgery to one operation to remove the tumor if it is cancerous.
- Image-guided biopsy is used when a distinct lump can't be felt, but an abnormality is seen with an imaging test, such as a mammogram. During this procedure, a needle is guided to the location with the help of an imaging technique, such as mammography, ultrasound, or MRI. A stereotactic biopsy is done using mammography to help guide the needle. A small metal clip may be put into the breast to mark where the biopsy sample was taken, in case the sample tissue is cancerous and more surgery is needed. An image-guided biopsy can be done using a fine needle, core, or vacuum-assisted biopsy, depending on the amount of tissue being removed.

If invasive cancer is diagnosed, surgery is needed to remove the cancer in the breast and evaluate the lymph nodes for cancer (called a sentinel lymph node biopsy; discussed in the Treatment section). The goal is to achieve clear surgical margins (no cancer

cells at the edge of the tissue removed during surgery). If there is cancer in the lymph nodes, the cancer is called lymph node-positive breast cancer (or node-positive, for short); if there is no cancer in the lymph nodes, the cancer is called lymph node-negative breast cancer (or node-negative, for short).

Additional information about lymph node evaluation can be found in the Staging section.

Testing the tissue

The pathologist tests the tissue from the biopsy and the surgery for the following to help guide treatment decisions:

Tumor features. Examination of the tumor under the microscope determines if it is invasive or in situ; ductal or lobular; the grade (how different the cancer cells look from healthy cells); and whether the cancer has spread to the lymph nodes. The margins (edges) of the tumor are also examined and their distance from the tumor is measured.

Estrogen receptor (ER) and progesterone receptor (PR) tests. Breast cancer cells with these receptors depend on the hormones estrogen and/or progesterone to grow. The presence of these receptors helps determine both the patient's prognosis (chance of recovery) and whether a type of treatment called hormonal therapy (see the Treatment section) will work. Generally, hormonal therapy works well for ER-positive or PR-positive tumors. About 75% to 80% of breast cancers have estrogen and/or progesterone receptors.

HER2 tests. There is too much of the protein called human epidermal growth factor receptor two (HER2) in about 20% to 25% of invasive breast cancers, and this is called HER2-positive cancer. The HER2 status helps determine whether a certain type of drug, such as trastuzumab (Herceptin) or lapatinib (Tykerb), might help treat the cancer.

If a person's tumor does not have ER, PR, and HER2, the tumor is called triple-negative. Triple-negative breast cancers make up about 15% of invasive breast cancers and are more common for women with *BRCA1* or *BRCA2* mutations. This subtype of breast cancer usually grows and spreads more quickly. Triple-negative breast cancer seems to be more common among black women and younger women.

Learn more about recommendations for ER, PR, and HER2 testing from ASCO and the College of American Pathologists (CAP) at www.cancer.net/whattoknow.

Testing a tumor's genes

Tests that look at the biology of the tumor are becoming more common to understand more about a woman's breast cancer. The tests below look at the genes in a tumor sample to predict the risk of cancer recurrence. They are usually done after cancer staging. A person with a higher risk of recurrence will likely

need additional treatment, while a person with a lower risk of recurrence can avoid extra treatment and its possible side effects. For more information about these tests, what they mean, and how the results might affect your treatment plan, talk with your doctor.

- Oncotype Dx is a test that evaluates 21 genes to estimate the risk of distant recurrence (return of the cancer in a place other than the breast) within 10 years for women with stage I or stage II (see the Staging section) node-negative, ER-positive breast cancer treated with hormonal therapy alone. It is mainly used to help make decisions about whether chemotherapy should be added to a person's treatment.
- Mammaprint is another, similar test using about 70 genes to predict the risk of the cancer coming back for early-stage, low-risk breast cancer. Although it is approved by the U.S. Food and Drug Administration (FDA) for estimating the risk of recurrence in early-stage breast cancer, its use is limited because of the way in which the sample of tumor must be collected and processed, which is not how cancer samples are generally handled in the United States.

Blood tests

The doctor may also need to do blood tests to learn more about the cancer.

Serum chemistry panel. This test is often done to look at blood electrolytes (minerals in your body, such as potassium and calcium) and enzymes (specialized proteins) that can be abnormal if cancer has spread. However, many noncancerous conditions can cause changes in these tests, and they are not specific to cancer.

- Alkaline phosphatase is an enzyme that can be associated with disease that has spread to the liver, bone, or bile ducts.
- Blood calcium levels can be high if cancer has spread to the bone.
- Total bilirubin count and the enzymes alanine aminotransferase (ALT) and aspartate aminotransferase (AST) evaluate liver function. High levels of any of these substances can indicate liver damage, a sign that the cancer may have spread to that organ.

Blood tumor marker tests. A serum tumor marker (also called a biomarker) is a substance found in a person's blood that can be associated with cancer. High levels of a serum tumor marker may be due to cancer or a noncancerous condition. Tumor marker testing is not usually recommended for early-stage breast cancer, but these markers may be useful to monitor recurrent or metastatic disease.

Learn more about tumor markers for breast cancer at www.cancer.net/whattoknow.

Additional tests

The doctor may recommend additional tests (depending on the woman's medical history and the results of the physical

examination) to evaluate the stage of the cancer. Read the Staging section for more information. Some of these tests may not be done until after surgery (see the Treatment section to learn more about surgery). These tests are generally only recommended for patients with more advanced stage disease.

- An x-ray is a way to create a picture of the structures inside your body, using a small amount of radiation. A chest x-ray may be used to look for cancer that has spread from the breast to the lungs.
- A bone scan may be used to look for spread to the bones. A bone scan uses a radioactive tracer to look at the inside of the bones. The tracer is injected into a patient's vein. It collects in areas of the bone and is detected by a special camera. Healthy bone appears gray to the camera, and areas of injury, such as those caused by cancer, appear dark.
- A computed tomography (CT or CAT) scan may be used to look for distant tumors. A CT scan creates a three-dimensional picture of the inside of the body with an x-ray machine. A computer combines these images into a detailed, cross-sectional view that shows any abnormalities or tumors. Sometimes, a contrast medium is injected into a patient's vein to provide better detail.
- A positron emission tomography (PET) scan may be used to determine whether the cancer has spread. A PET scan is a way to create pictures of organs and tissues inside the body. A small amount of a radioactive substance is injected into a patient's body. This substance is absorbed mainly by organs and tissues that use the most energy. Because cancer tends to use energy actively, it absorbs more of the radioactive substance. A scanner then detects this substance to produce images of the inside of the body.

After these diagnostic tests are done, your doctor will review all of the results with you. If the diagnosis is cancer, these results also help the doctor describe the cancer; this is called staging.

Learn more about the first steps to take after a diagnosis of cancer at www.cancer.net/firststeps and what to expect when having common tests, procedures, and scans at www.cancer.net/tests.

STAGING

Staging is a way of describing a cancer, such as where it is located, if or where it has spread, and whether it is affecting the functions of other organs in the body. Doctors use diagnostic tests to determine the cancer's stage, so staging may not be complete until all the tests are finished. Knowing the stage helps the doctor to decide what kind of treatment is best and can help predict a patient's prognosis. There are different stage descriptions for different types of cancer.

One tool that doctors use to describe the stage is the TNM system. This system judges three factors: the size of the tumor itself, the presence of cancer in the lymph nodes around the

tumor, and whether the tumor has spread to other parts of the body. The results are combined to determine the stage of cancer for each person. In breast cancer, there are five stages: stage 0 (zero), which is noninvasive ductal carcinoma in situ (DCIS), and stages I through IV (one through four), which are used for invasive breast cancer. The stage provides a common way of describing the cancer so doctors can work together to plan the best treatments.

TNM is an abbreviation for tumor (T), node (N), and metastasis (M). Doctors look at these three factors to determine the stage of cancer:

- How large is the primary tumor, and where is it located?
(Tumor, T)
- Has the tumor spread to the lymph nodes? **(Node, N)**
- Has the cancer metastasized to other parts of the body?
(Metastasis, M)

Tumor. Using the TNM system, the “T” plus a letter or number (0 to 4) is used to describe the size and location of the tumor. Some stages are divided into smaller groups that help describe the tumor in even more detail.

Node. The “N” in the TNM staging system stands for lymph nodes. Lymph nodes located under the arm, above and below the collarbone, and under the breastbone are called regional lymph nodes. Lymph nodes in other parts of the body are called distant lymph nodes.

If there is cancer in the lymph nodes, knowing how many lymph nodes are involved helps doctors plan treatment. The pathologist can find out the number of axillary (underarm) lymph nodes with cancer. It is not common to remove the lymph nodes above the collarbone or under the breastbone during surgery. If there may be cancer in these lymph nodes, radiation therapy will also be directed at these lymph nodes during treatment.

Distant metastasis. The “M” in the TNM system indicates whether the cancer has spread to other parts of the body.

For specific information on substages for T, N, and M, visit www.cancer.net/breast.

Cancer stage grouping

Doctors assign the stage of the cancer by combining the T, N, and M classifications.

Stage 0: Stage zero (0) describes disease that is only in the ducts and lobules of the breast tissue and has not spread to the surrounding tissue of the breast. It is also called noninvasive cancer.

Stage IA: The tumor is small, invasive, and has not spread to the lymph nodes.

Stage IB: The tumor is confined within the ducts and lobules of the breast tissue and has not spread into the surrounding tissue of the breast, or it is smaller than 20 millimeters (mm), with microscopic spread to the lymph nodes.

Stage IIA: Any one of these conditions:

- There is no evidence of a tumor in the breast, but the cancer has spread to the axillary lymph nodes but not to distant parts of the body.
- The tumor is 20 mm or smaller and has spread to the axillary lymph nodes.
- The tumor is larger than 20 mm but not larger than 50 mm and has not spread to the axillary lymph nodes.

Stage IIB: Either of these conditions:

- The tumor is larger than 20 mm but not larger than 50 mm and has spread to one to three axillary lymph nodes.

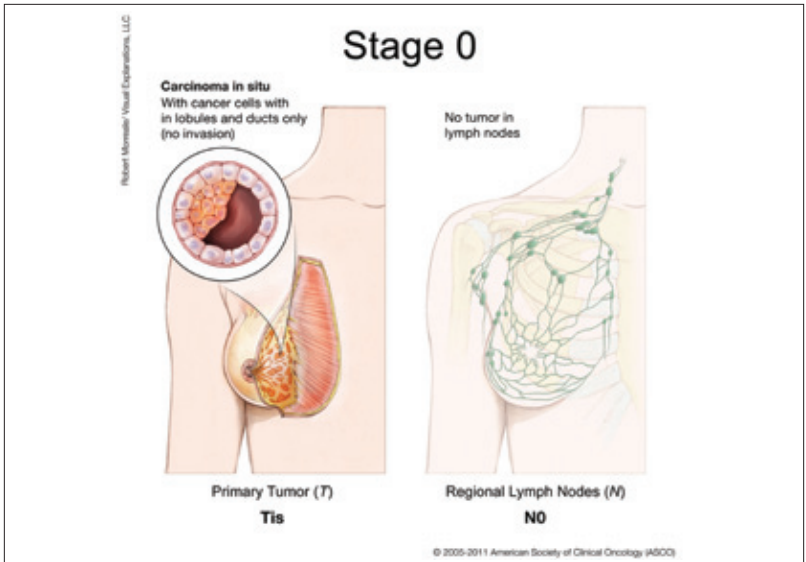


Illustration of breast cancer at stage 0.

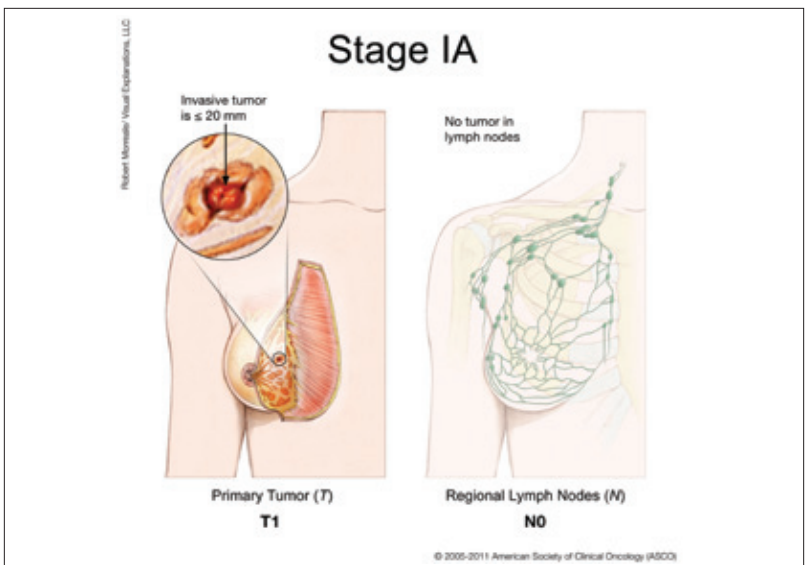


Illustration of breast cancer at stage IA.

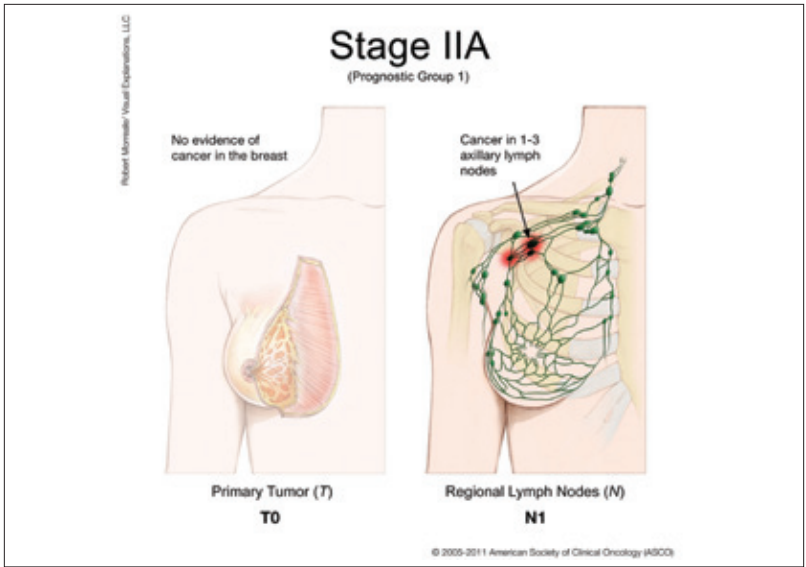


Illustration of breast cancer at stage IIA.

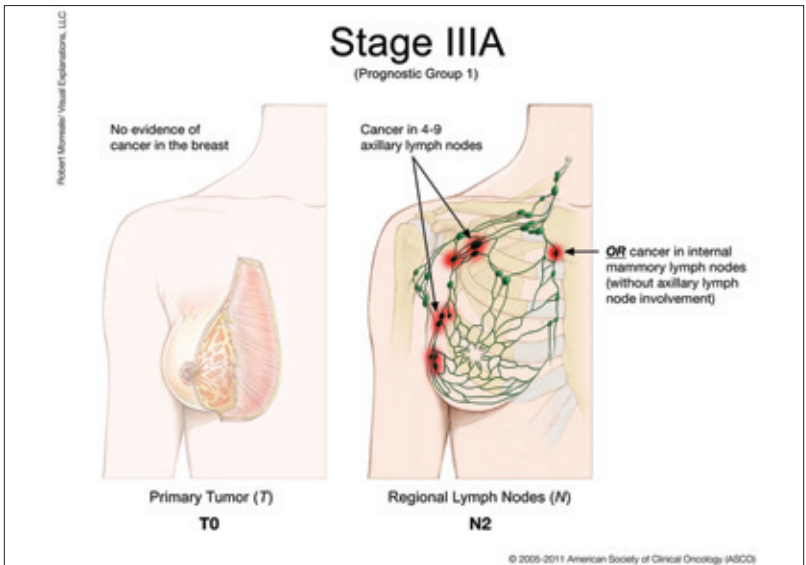


Illustration of breast cancer at stage IIIA.

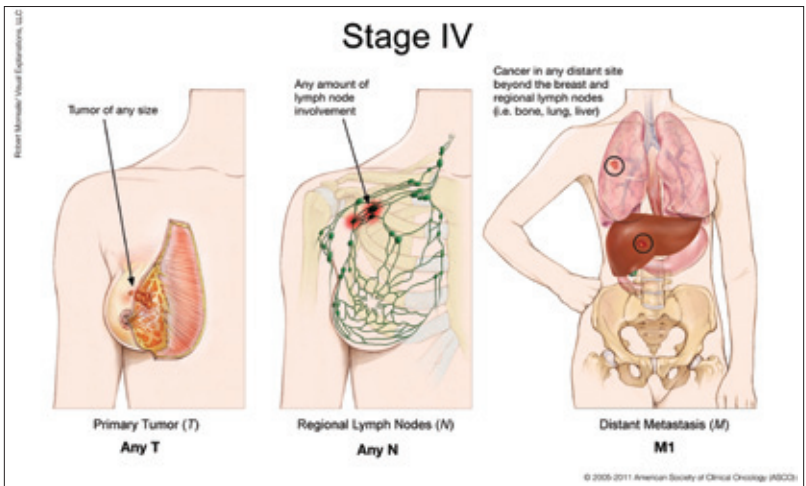


Illustration of breast cancer at stage IV.

- The tumor is larger than 50 mm but has not spread to the axillary lymph nodes.

Stage IIIA: The cancer of any size has spread to four to nine axillary lymph nodes, but not to other parts of the body. Stage IIIA may also be a tumor larger than 50 mm that has spread to one to three lymph nodes.

Stage IIIB: The tumor has spread to the chest wall or caused swelling or ulceration of the breast or is diagnosed as inflammatory breast cancer. It may or may not have spread to the lymph nodes under the arm, but it has not spread to other parts of the body.

Stage IIIC: A tumor of any size that has not spread to distant parts of the body but has spread to 10 or more axillary lymph nodes or the lymph nodes located under the collarbone, the lymph nodes under the breastbone and the axillary lymph nodes, or the lymph nodes located above the collarbone.

Stage IV (metastatic): The tumor can be any size and has spread to distant sites in the body, usually the bones, lungs or liver, or chest wall. Metastatic cancer spread is found when the cancer is first diagnosed about 5% to 6% of the time. Most commonly, metastatic breast cancer happens after a recurrence many months or years following the original cancer diagnosis and treatment.

Recurrent: Recurrent cancer is cancer that comes back after treatment. If there is a recurrence, the cancer may need to be staged again (re-staging) using the system above.

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Find additional staging information and illustrations for breast cancer at www.cancer.net/breast.

TREATMENT

This section outlines treatments that are the standard of care (the best proven treatments available) for this specific type of cancer. When making treatment plan decisions, patients are also encouraged to consider clinical trials as an option. A clinical trial is a research study to test a new treatment to evaluate whether it is safe, effective, and possibly better than standard treatment. Your doctor can help you review all treatment options. For more information, read the About Clinical Trials section.

Treatment overview

In cancer care, different types of doctors often work together to create a patient's overall treatment plan that combines different types of treatments. This is called a multidisciplinary team.

The biology and behavior of a breast cancer affects the treatment. Some tumors are small but grow fast, while others are large and grow slowly. Treatment options and recommendations depend on several factors, including:

- The stage and grade of the tumor
- The tumor's hormone receptor status (ER, PR) and HER2 status (see the Diagnosis section)
- The patient's age, general health, and preferences
- The patient's menopausal status
- The presence of known mutations in inherited breast cancer genes (*BRCA1* or *BRCA2*)

Even though the doctor will specifically tailor the treatment for each patient and the breast cancer, there are some general steps for treating breast cancer.

For both DCIS and early-stage invasive breast cancer, doctors generally recommend surgery to remove the tumor. To make sure that the entire tumor is removed, the surgeon will also remove a small area of normal tissue around the tumor. Although the goal of surgery is to remove all of the visible cancer, microscopic cells can be left behind, either in the breast or elsewhere.

The next step in the management of early-stage breast cancer is to lower the risk of recurrence and to get rid of any remaining cancer cells. This is called adjuvant therapy. Adjuvant therapies include radiation therapy, chemotherapy, targeted therapy, and/or hormonal therapy. The need for adjuvant therapy is determined based on an estimate of the chance of residual cancer in the breast or the body. Although adjuvant therapy lowers the risk of recurrence, it does not completely get rid of the risk.

Along with staging, other tools can help find out prognosis and help you and your doctor make decisions about adjuvant therapy. The website Adjuvant! Online (www.adjuvantonline.com) is one such tool that your doctor can access to interpret a variety of prognostic factors. This website should only be used with the interpretation of your doctor. In addition, other tests that can predict the risk of recurrence (such as Oncotype Dx and Mammprint; see the Diagnosis section) may be used to find out whether your doctor recommends adjuvant chemotherapy.

When surgery to remove the cancer is not possible, chemotherapy, targeted therapy, radiation therapy, and/or hormonal therapy may be used.

The treatment of recurrent cancer and metastatic cancer depends on how the cancer was first treated and the characteristics of the cancer (such as ER, PR, and HER2 status).

Descriptions of the most common treatment options for breast cancer are listed in the following pages. Learn more about making treatment decisions at www.cancer.net/features.

Surgery

Surgery is the removal of the tumor and surrounding tissue during an operation. Surgery is also used to evaluate the nearby axillary lymph nodes. A surgical oncologist is a doctor who specializes in treating cancer using surgery. Generally, the smaller the tumor, the more surgical options a patient has. The types of surgery include the following:

- A lumpectomy is the removal of the tumor and a small, clear (cancer-free) margin of normal tissue around the tumor. Most of the breast remains. For both DCIS and invasive cancer, follow-up radiation therapy to the remaining breast tissue is generally recommended. A lumpectomy may also be called breast-conserving surgery, a partial mastectomy, or a segmental mastectomy.
- A mastectomy is the surgical removal of the entire breast.

Lymph node removal and analysis

Lymph nodes can trap cancer cells traveling away from the original tumor before it was removed. It is important to find out whether any of the lymph nodes near the breast contain cancer.

In an axillary lymph node dissection, the surgeon removes many of the lymph nodes from under the arm, which are then examined by a pathologist for cancer cells. The actual number of lymph nodes removed varies.

Sentinel lymph node biopsy

The sentinel lymph node biopsy procedure allows for the removal of one to a few lymph nodes, saving a bigger axillary lymph node dissection procedure for patients whose sentinel lymph nodes have cancer. The smaller lymph node procedure helps patients lower the risk of lymphedema (swelling of the arm) and decreases arm mobility and range-of-motion problems.

Recent research has shown that an axillary lymph node dissection may not be needed for all women with early-stage breast cancer with small amounts of cancer in the sentinel lymph nodes. Women having a lumpectomy and radiation therapy who have smaller tumors and no more than two sentinel lymph nodes with cancer may avoid a full axillary lymph node dissection, which helps reduce the risk of side effects and does not decrease survival.

In a sentinel lymph node biopsy, the surgeon finds and removes the sentinel (first) lymph node (usually about one to three nodes) that receives drainage from the breast. The pathologist then examines it for cancer cells. To find the sentinel lymph node, the surgeon injects a dye and/or a radioactive tracer into the area of the cancer and/or around the nipple. The dye or tracer travels to the lymph nodes, arriving at the sentinel node first. The surgeon can find the node when it turns color (if the dye is used) or gives off radiation (if the tracer is used).

If the sentinel lymph node is cancer-free, research has shown that there is a good possibility that the remaining lymph nodes will also be free of cancer and no further surgery is needed. If the sentinel lymph node shows that there is cancer, then the surgeon may perform an axillary lymph node dissection to remove more lymph nodes to look for cancer, depending on the stage of the cancer and the amount of cancer in the sentinel lymph nodes.

Most patients with invasive cancer will have either a sentinel lymph node biopsy or an axillary lymph node dissection. For those with sentinel nodes with cancer, an axillary lymph node dissection is usually considered the standard procedure, although it may not be needed for some women with early-stage breast cancer. A sentinel lymph node biopsy may not be done if there is obvious evidence of cancer in the lymph nodes before any surgery. In this situation, a full axillary lymph node dissection is preferred. Normally, the lymph nodes are not evaluated for DCIS, since the risk of cancer spread is very low. However, patients diagnosed with DCIS who choose to have a mastectomy should consider a sentinel lymph node biopsy. If some invasive cancer is found with DCIS at the time of the mastectomy, which happens occasionally, the lymph nodes will then need to be evaluated. Once the breast tissue has been removed with a mastectomy, there is no way to perform a sentinel lymph node procedure, since there is no breast tissue in which to inject the dye or radioactive substance. The only option would be a full axillary lymph node dissection.

Find out more about ASCO's recommendations for sentinel lymph node biopsy at www.cancer.net/whattoknow.

Reconstructive (plastic) surgery

Women who have a mastectomy may wish to consider breast reconstruction, which is surgery to restore the breast. Reconstruction may be done with tissue from another part of the body, or with synthetic implants. A woman may be able to have this done at the same time as a mastectomy (immediate reconstruction) or at some point in the future (delayed reconstruction). In addition, reconstruction may be done after a lumpectomy to improve the look of the breast. Talk with your doctor for more information.

External breast forms (prostheses)

An external breast prosthesis or artificial breast form provides an option for women who plan to delay or not have reconstructive surgery. Breast prostheses can be made to provide a proper fit and natural appearance for each woman.

Read more about preventing lymphedema after breast cancer treatment, what to know after a mastectomy, breast reconstruction, and choosing a breast prosthesis at www.cancer.net/features.

Summary of surgical options

To summarize, surgical treatment options include the following:

- Removal of cancer in the breast: Lumpectomy (partial mastectomy) almost always followed by radiation therapy or mastectomy, with or without immediate reconstruction
- Lymph node evaluation: Sentinel lymph node biopsy and/or axillary lymph node dissection

Women are encouraged to talk with their doctors about which surgical option is right for them. More aggressive surgery (such as a mastectomy) is not always better and causes more complications. The combination of lumpectomy and radiation therapy has a



higher risk of the cancer coming back in the same breast or near the breast, but the long-term survival of women who choose lumpectomy is the same as those who have a mastectomy.

Learn more about cancer surgery at www.cancer.net/surgery and hear from an ASCO expert on breast cancer surgery options at www.cancer.net/features.

Radiation therapy

Radiation therapy is the use of high-energy x-rays or other particles to kill cancer cells. A doctor who specializes in giving radiation therapy to treat cancer is called a radiation oncologist. The most common type of radiation treatment is called external-beam radiation therapy, which is radiation given from a machine outside the body. When radiation treatment is given using small radioactive seeds or pellets, it is called internal radiation therapy or brachytherapy. A radiation therapy regimen (schedule) usually consists of a specific number of treatments given over a set period of time.

After a lumpectomy, adjuvant radiation therapy is given regularly for a set number of weeks to get rid of any remaining cancer cells near the tumor site or elsewhere in the breast. This helps lower the risk of recurrence in the breast. In fact, research has shown recurrence rates of 30% or more without radiation therapy, compared with 10% recurrence rates with radiation therapy.

Adjuvant radiation therapy is also recommended for some women after a mastectomy, depending on the size of their tumor, the number of cancerous lymph nodes under the arm, and the width of the tissue margin around the tumor removed by the surgeon.

Neoadjuvant radiation therapy is radiation therapy given before surgery to shrink a large tumor, which makes it easier to remove, although this approach is rare.

Radiation therapy can cause side effects, including fatigue, swelling of the breast, and skin changes. Rarely, a small amount of the lung can be affected by the radiation, causing pneumonitis (radiation-related swelling of the lung tissue). In the past, with older equipment and radiation therapy techniques, women treated for breast cancer on the left side of the body had a small increase in the long-term risk of heart disease. Modern techniques are now able to spare most of the heart from radiation damage. Although exposure to radiation is thought to be a risk factor for cancer after many years, fewer than one in 500 survivors will develop a different kind of cancer other than a breast cancer (usually a type of cancer called sarcoma) in the area that was treated.

Many types of radiation therapy may be available to you; talk with your doctor about the advantages and disadvantages of each option.

Radiation therapy schedule

Standard radiation therapy after a lumpectomy is external-beam radiation therapy given daily for five days per week (Monday through Friday) for six to seven weeks. This usually includes radiation therapy to the whole breast first for four-and-a-half to five weeks, followed by a more focused treatment to where the tumor was located in the breast for the remaining treatments.

This focused part of the treatment, called a boost, is standard for women with invasive breast cancer to reduce the risk of a recurrence in the breast. Women with DCIS may also receive the boost. For women with a low risk of recurrence, though, the boost may be optional. It is important to discuss this treatment approach with your doctor.

If there is cancer in the underarm lymph nodes, radiation therapy may also be given to the lymph nodes in the neck or underarm near the breast or chest wall. Usually, patients who have a mastectomy do not require radiation therapy. However, for patients with large cancers, several cancerous lymph nodes, or cancer that has grown into the skin or chest wall, the doctors may still recommend radiation therapy after a mastectomy. This is given to the chest wall for five days (Monday through Friday) for five to six weeks.

There has been growing interest in newer radiation regimens to shorten the length of treatment from six to seven weeks to periods of three to four weeks. In one method (called hypofractionated radiation therapy), a higher daily dose is given to the whole breast so that the overall length of treatment is shortened to three to four weeks. This can also be combined with a higher dose given to where the tumor was in the breast either during or after the whole breast radiation treatments. Clinical trials from Canada and the United Kingdom have shown that these shorter schedules are similarly safe and control the cancer as well as longer radiation treatment schedules

in patients with node-negative breast cancer. These shorter schedules may become more accepted in the United States and are one way to improve the convenience and time required to complete a course of radiation (see also partial breast irradiation below).

Partial breast irradiation

Partial breast irradiation (PBI) is radiation therapy that is given directly to the tumor area, usually after a lumpectomy, instead of the entire breast, as is usually done with standard radiation therapy. Targeting the radiation to the tumor area more directly usually shortens the amount of time that patients need to receive radiation therapy. However, only some patients may be eligible for PBI. Although early results have been promising, PBI is still being studied. It is the subject of a large, nationwide clinical trial, and the results on the safety and effectiveness compared with standard radiation therapy are not yet ready. This study will help find out which patients and tumors are the best candidates for PBI.

PBI can be done with standard external-beam radiation therapy that is focused on where the tumor was removed and not the entire breast. Or, PBI may be done using brachytherapy. Brachytherapy is the implantation of small radioactive pellets, placed in or near the site of the breast tumor, or in plastic catheters placed temporarily in the breast. Most types of breast brachytherapy involve short treatment times, ranging from one dose to one week.

Intensity-modulated radiation therapy

Intensity-modulated radiation therapy (IMRT) is a more advanced way to give external-beam radiation therapy to the breast. The intensity of the radiation directed at the breast is varied to target the tumor more precisely, spread the radiation more evenly throughout the breast, and avoid damaging healthy tissue more than is possible with traditional radiation treatment. IMRT may reduce the dose to nearby organs, such as the heart and lung, and reduce the risks of some immediate side effects, such as peeling of the skin during treatment. This can be especially important for women with medium to large breasts who are at greater risk for side effects, such as peeling and burns, compared with women with smaller breasts. IMRT also may help to reduce long-term effects on the breast tissue that were common with older radiation techniques, such as hardness, swelling, or discoloration.

Despite the short-term benefits seen with IMRT, many insurance providers are requiring longer-term data on this therapy and may not cover IMRT. It is important to check with your health insurance company before treatment begins to be sure it is covered.

Adjuvant radiation therapy concerns for older patients and/or those with small tumors

Recent studies have looked at the consequences of using no

radiation therapy for women age 70 or older or for those women with a small tumor size. Overall, these studies show that radiation therapy reduces the risk of breast cancer recurrence in the same breast, compared with no radiation therapy, but does not affect overall survival. Guidelines from the National Comprehensive Cancer Network (NCCN) continue to recommend radiation therapy as the standard option after lumpectomy. However, they also indicate that women with special personal or tumor features (such as being age 70 or older and having other medical conditions that could limit life expectancy within five years, a small tumor, no evidence of cancer in the lymph nodes or surgical margins, and an ER-positive cancer) could reasonably choose not to have radiation therapy and use hormonal therapy (see below) alone after lumpectomy, if they are willing to accept a modest increase in the risk rate of local recurrence.

Learn more about radiation therapy at www.cancer.net/radiationtherapy.

Chemotherapy

Chemotherapy is the use of drugs to kill cancer cells, usually by stopping the cancer cells' ability to grow and divide. Systemic chemotherapy is delivered through the bloodstream to reach cancer cells throughout the body. Chemotherapy is prescribed by a medical oncologist, a doctor who specializes in treating cancer with medication.



Chemotherapy may be given on many different schedules depending on what worked best in clinical trials for that specific type of chemotherapy. An adjuvant chemotherapy regimen (schedule) consists of a specific treatment schedule of drugs given at repeating intervals for a set period of time. It may be given once a week, once every two weeks (also called dose-dense), once every three weeks, or even once every four weeks.

Chemotherapy may be given intravenously (injected into a vein) or occasionally orally (by mouth). It is usually given in cycles. Chemotherapy may be given before surgery to shrink a large tumor and reduce the risk of recurrence, or given after surgery to reduce the risk of recurrence. Chemotherapy is also commonly given at the time of a metastatic breast cancer recurrence.

The side effects of chemotherapy depend on the individual and the drug and the dose used, but they can include fatigue, hair loss, risk of infection, nausea and vomiting, loss of appetite, and diarrhea. These side effects usually go away

once treatment is finished. Rarely, long-term side effects may occur, such as heart damage, nerve damage, or secondary cancers, but studies have shown that these side effects do not shorten a woman's life.

A patient may receive one drug at a time or combinations of different drugs at the same time. Research has shown that combinations of certain drugs are sometimes more effective than single drugs for adjuvant treatment. The following drugs or combinations of drugs may be used as adjuvant therapy to treat breast cancer:

- Cyclophosphamide (Clafen, Cytoxan, Neosar)
- Methotrexate (multiple brand names)
- Fluorouracil (5-FU, Adrucil)
- Doxorubicin (Adriamycin)
- Epirubicin (Ellence)
- Paclitaxel (Taxol)
- Docetaxel (Docefrez, Taxotere)
- CMF (cyclophosphamide, methotrexate, and 5-FU)
- CAF (cyclophosphamide, doxorubicin, and 5-FU)
- CEF (cyclophosphamide, epirubicin, and 5-FU)
- EC (epirubicin and cyclophosphamide)
- AC (doxorubicin and cyclophosphamide)
- TAC (docetaxel, doxorubicin, and cyclophosphamide)
- AC followed by T (doxorubicin and cyclophosphamide, followed by paclitaxel or docetaxel)
- TC (docetaxel and cyclophosphamide)

Trastuzumab (Herceptin), a HER2 targeted therapy (see the Targeted therapy section), may also be given with chemotherapy as an adjuvant treatment for HER2-positive breast cancer.

In addition to the drugs and combinations of drugs listed above, the following drugs may be used to treat recurrent or metastatic breast cancer, either individually or in combination:

- Vinorelbine (Navelbine)
- Capecitabine (Xeloda)
- Protein-bound paclitaxel (Abraxane)
- Pegylated liposomal doxorubicin (DOXIL, Dox-SL, Evacet, LipoDox)
- Gemcitabine (Gemzar)
- Carboplatin (Paraplat, Paraplatin)
- Cisplatin (Platinol)
- Ixabepilone (Ixempra)
- Eribulin (Halaven)

Trastuzumab and lapatinib are HER2-targeted therapies that may be given with chemotherapy for HER2-positive metastatic breast cancer. Bevacizumab (Avastin), a blood vessel blocking drug (called anti-angiogenic), is another targeted therapy that has been used in combination with chemotherapy for the treatment of metastatic breast cancer. (See the Targeted therapy section.)

Learn more about chemotherapy and preparing for treatment at www.cancer.net/chemotherapy. The medications used to treat cancer are continually being evaluated. Talking with your doctor, oncology nurse, or pharmacist is often the best way to learn about the medications prescribed for you, their purpose, and their potential side effects or interactions with other medications. Learn more about your prescriptions by using searchable drug databases at www.cancer.net/druginforesources.

Targeted therapy

Targeted therapy is a treatment that targets the cancer's specific genes, proteins, or the tissue environment that contributes to cancer growth and survival. This type of treatment blocks the growth and spread of cancer cells while limiting damage to normal cells, usually leading to fewer side effects than other cancer medications.

Recent studies show that not all tumors have the same targets. To find the most effective treatment, your doctor may run tests to identify the genes, proteins, and other factors in your tumor. As a result, doctors can better match each patient with the most effective treatment whenever possible. In addition, many research studies are taking place now to find out more about specific molecular targets and new treatments directed at them.

Currently, the two main types of targeted therapies approved to treat breast cancer are targeted to the HER2 molecule and the blood vessels in the area of the tumor (called anti-angiogenesis therapy). Targeted therapy is also used to treat bone metastasis.

HER2 targeted therapy

- Trastuzumab is approved for both the treatment of advanced breast cancer and as an adjuvant therapy for early-stage breast cancer for HER2-positive tumors. At this time, one year of trastuzumab is recommended for early-stage breast cancer. For metastatic cancer, trastuzumab is given as long as it is still working. Patients receiving trastuzumab have a small (2% to 5%) risk of heart problems, and this risk is increased if a patient has other risk factors for heart disease. These heart problems do not always go away, but they are usually treatable with medication.
- Lapatinib is commonly used in women with HER2-positive breast cancer when trastuzumab no longer works. The combination of lapatinib and capecitabine is approved to treat women with advanced or metastatic HER2-positive breast cancer when chemotherapy and trastuzumab have already been used. The combination of lapatinib and letrozole (Femara) is also approved for treatment of metastatic HER2-positive and ER-positive cancer. Lapatinib is being studied for early-stage breast cancer, as well.

Anti-angiogenesis therapy

Anti-angiogenesis therapy is focused on stopping angiogenesis, which is the process of making new blood vessels. Because a tumor needs the nutrients found in blood vessels to grow and

spread, the goal of anti-angiogenesis therapies is to “starve” the tumor.

An anti-angiogenic drug called bevacizumab has been used to treat metastatic or recurrent breast cancer for many years. It has also been combined with paclitaxel for women whose breast cancer has spread. Because bevacizumab may not work well for all tumors, the FDA has stopped recommending it as a treatment for breast cancer until more research can show the benefit. Talk with your doctor for more information. Learn more about anti-angiogenic drugs at www.cancer.net/features.

Anti-osteoclast targeted therapy (drugs that block bone destruction)

- Bisphosphonates are drugs that block the cells that cause bone destruction (osteoclasts). Bisphosphonates are commonly used in relatively low doses to prevent and treat osteoporosis (thinning of the bones). In patients with breast cancer that has spread to bone, higher doses of bisphosphonates have been shown to reduce the complications of cancer in the bone, including bone fractures and pain. Pamidronate (Aredia) and zoledronic acid (Zometa) are two intravenous bisphosphonates used to treat breast cancer bone metastasis. Recent studies have suggested that these drugs may also be able to reduce breast cancer recurrences when given in the adjuvant setting, although more data are needed.
- Denosumab (Xgeva) is another osteoclast-targeted therapy called a RANK ligand inhibitor. Recent studies have shown that these drugs may be effective for treating breast cancer bone metastases.

Learn more about drugs that block bone destruction for breast cancer at www.cancer.net/whattoknow and find out more about targeted treatments at www.cancer.net/targetedtreatments.

Hormonal therapy

Hormonal therapy helps manage a tumor that tests positive for either estrogen or progesterone receptors in both early-stage and metastatic cancer. This type of tumor uses hormones to fuel its growth. Blocking the hormones usually slows the growth of the tumor. If a tumor is hormone receptor-positive (ER-positive or PR-positive; see the Diagnosis section), then adjuvant hormonal treatment may be used alone or after chemotherapy.

Tamoxifen is a drug that blocks estrogen from binding to breast cancer cells. It is effective for reducing the risk of recurrence in the breast that had cancer, the risk of developing cancer in the other breast, and the risk of distant recurrence. It is also approved to reduce the risk of breast cancer in women at high risk for developing the disease and for reducing local recurrence in DCIS.

Tamoxifen is a pill that is taken daily by mouth. The side effects of tamoxifen include hot flashes; vaginal dryness, discharge or bleeding; a small increased risk of uterine (endometrial) cancer

and uterine sarcoma; and an increase in the risk of blood clots. However, tamoxifen improves bone health and cholesterol levels and can be effective for both premenopausal and postmenopausal women.

An aromatase inhibitor (AI) decreases the amount of estrogen in postmenopausal women by blocking the aromatase enzyme, which is needed to make estrogen. These drugs include anastrozole (Arimidex), exemestane (Aromasin), and letrozole (Femara). All of the AIs are pills taken daily by mouth. The side effects of AIs may include muscle and joint pain, hot flashes, vaginal dryness, an increased risk of osteoporosis and fractures (broken bones), and increases in cholesterol. Clinical trials show that all three AI drugs work equally well and have similar side effects. However, these drugs are not appropriate for women who have not gone through menopause.

Women who have gone through menopause and are prescribed hormonal therapy have several options: take tamoxifen or an AI for five years, begin treatment with tamoxifen for two to three years and then switch to an AI for the rest of the five-year period, or take tamoxifen for five years then switch to an AI for what is called extended therapy.

Suppressing ovarian function, or ovarian ablation, may be another option for women with ER-positive breast cancer who have not yet been through menopause and who are not healthy enough for other treatments or who choose not to have other treatments. This can be done temporarily with drugs called luteinizing hormone-releasing hormone (LHRH) analogues. Goserelin (Zoladex) and leuprolide (Lupron, Viadur) are injection drugs that can suppress the ovaries for one to three months. Surgical removal of the ovaries (oophorectomy) or radiation of the ovaries, which are permanent forms of ovarian suppression, may also be considered.

Tamoxifen and the aromatase inhibitors are also commonly used to treat metastatic recurrences. In addition, fulvestrant (Faslodex) is a hormonal therapy approved for patients with metastatic cancer. Fulvestrant is in a class called selective estrogen receptor downregulators (SERDs). Unlike the other oral hormonal therapies used to treat breast cancer, fulvestrant is given monthly by intramuscular injection. Its side effects include menopausal symptoms, such as hot flashes and vaginal dryness.

Learn more about hormonal therapy at www.cancer.net/whattoknow and ovarian ablation at www.cancer.net/expertsoncancernews.

Recurrent breast cancer

Once your treatment is complete and there is a remission (absence of cancer symptoms; also called “no evidence of disease” or NED), talk with your doctor about the possibility of the cancer returning. Many survivors feel worried or anxious that the cancer will come back.

If the cancer does return after the original treatment, it is called recurrent cancer. It may come back in the same place (called a local recurrence), in the chest wall (regional recurrence), or in another place, including distant organs such as the lungs, liver, and bones (distant recurrence). A local or regional recurrence is frequently considered controllable with further treatment. A metastatic (distant) recurrence is generally considered incurable, but is frequently treatable. Some patients live years after a metastatic recurrence of breast cancer (see the section on metastatic breast cancer).

Generally, a recurrence is detected when a person has symptoms. These symptoms depend on where the cancer has recurred and may include:

- A lump under the arm or along the chest wall
- Bone pain or fractures, a possible sign of bone metastases
- Headaches or seizures, a possible sign of brain metastases
- Chronic coughing or trouble breathing, possible symptoms of lung metastases
- Abdominal pain or jaundice (yellow skin and eyes), which may be associated with liver metastases

Other symptoms may be related to the location of metastasis and may include changes in vision, changes in energy levels, feeling ill, or extreme fatigue. A biopsy of the recurrent tumor is often recommended to be certain of the diagnosis and to check for ER, PR, and HER2 status, because this may have changed from the time of the original diagnosis.

If a woman has a recurrence, a cycle of testing will begin again to learn as much as possible about the recurrence. After testing is done, you and your doctor will talk about your treatment options. Often the treatment plan will include the therapies described above (such as surgery, radiation therapy, chemotherapy, targeted therapy, and hormonal therapy) but may be used in a different combination or given at a different pace. Your doctor may also suggest clinical trials that are studying new ways to treat this type of recurrent cancer.

The treatment of recurrent breast cancer depends on the previous treatment(s), the time since the original diagnosis, and the characteristics of the tumor (such as ER, PR, and HER2 status).

- For women with a local recurrence within the breast after initial treatment with lumpectomy and adjuvant radiation therapy, the treatment is mastectomy. Usually the cancer is completely removed with this treatment.
- For women with a local or regional recurrence of the chest wall after an initial mastectomy, surgical removal of the recurrence followed by radiation therapy to the chest wall and lymph nodes is the recommended treatment, unless radiation therapy has already been given (radiation therapy cannot usually be given at full dose to the same area more than once).

Women with recurrent breast cancer often experience emotions such as disbelief or fear. Patients are encouraged to talk with their health care team about these feelings and ask about support services to help them cope.

Learn more about coping with the fear of a cancer recurrence at www.cancer.net/coping.

Metastatic breast cancer

If cancer has spread to another location in the body or come back in another distant location, it is called metastatic cancer or recurrent metastatic cancer.

Patients with this diagnosis are encouraged to talk with doctors who are experienced in treating this stage of cancer, because there can be different opinions about the best treatment plan. Consider seeking a second opinion before starting treatment, so you are comfortable with the treatment plan chosen. This discussion may include clinical trials studying new treatments.

Your health care team may recommend a treatment plan that includes a combination of total-body therapies, such as chemotherapy, hormonal therapy, and targeted therapies. Radiation therapy and surgery may be used in certain situations for women with a distant metastatic recurrence. Radiation therapy is often used to treat painful bone metastases.

In addition to treatment to slow, stop, or eliminate the cancer (also called disease-directed treatment), an important part of cancer care is relieving a person's symptoms and side effects. It includes supporting the patient with his or her physical, emotional, and social needs, an approach called palliative or supportive care. People often receive disease-directed therapy and treatment to ease symptoms at the same time.

If disease-directed treatment is not successful, this may also be called advanced cancer. This diagnosis is stressful, and it may be difficult to discuss. However, it is important to have open and honest conversations with your doctor and health care team to express your feelings, preferences, and concerns. The health care team is there to help, and many team members have special skills, experience, and knowledge to support patients and their families. Learn more about advanced cancer care planning at www.cancer.net/advancedcancer.

Find out more about common terms used during cancer treatment at www.cancer.net/dictionaryresources.

ABOUT CLINICAL TRIALS

Doctors and scientists are always looking for better ways to treat patients with breast cancer. To make scientific advances, doctors create research studies involving people, called clinical trials.

Many clinical trials are focused on new treatments, evaluating whether a new treatment is safe, effective, and possibly better than the current (standard) treatment. These types of studies evaluate new drugs, different combinations of existing treatments, new approaches to radiation therapy or surgery, and new methods of treatment. Patients who participate in clinical trials are often among the first to receive new treatments before they are widely available. However, there is no guarantee that the new treatment will be safe, effective, or better than a standard treatment.

There are also clinical trials that study new ways to ease symptoms and side effects during treatment and manage the late effects that may occur after treatment. Talk with your doctor about clinical trials regarding side effects. In addition, there are ongoing studies about ways to prevent the disease.

Patients decide to participate in clinical trials for many reasons. For some patients, a clinical trial is the best treatment option available. Because standard treatments are not perfect, patients are often willing to face the added uncertainty of a clinical trial in the hope of a better result. Other patients volunteer for clinical trials because they know that these studies are the only way to make progress in treating breast cancer. Even if they do not benefit directly from the clinical trial, their participation may benefit future patients with breast cancer. For example, the use of dose-dense chemotherapy (giving the drugs more frequently than the traditional three-week intervals) and the addition of trastuzumab for early-stage breast cancer were tested and confirmed in a clinical trial.

Sometimes people have concerns that, by participating in a clinical trial, they may receive no treatment by being given a placebo or a “sugar pill.” The use of placebos in cancer clinical trials is rare. When a placebo is used in a study, it is done with the full knowledge of the participants.

To join a clinical trial, patients must participate in a process known as informed consent. During informed consent, the doctor should list all of the patient’s options, so that the person understands the standard treatment, and how the new treatment differs from the standard treatment. The doctor must also list all of the risks of the new treatment, which may or may not be different from the risks of standard treatment. Finally, the doctor must explain what will be required of each patient to participate in the clinical trial, including the number of doctor visits, tests, and the schedule of treatment. The coverage of clinical trial costs differs by state. In some programs, expenses associated with participating in the research, such as transportation, childcare, meals, and accommodations are reimbursed. It’s important to talk with the research team and your insurance company to learn about how the treatment in a clinical trial will be covered.

Patients who participate in a clinical trial may stop participating at any time for any personal or medical reason. This may include that the new treatment is not working or there are serious side effects. It is important that patients participating in a clinical trial talk with their doctor and researchers about who will be providing their treatment and care during the clinical trial, after the clinical trial ends, and/or if the patient chooses to leave the clinical trial before it ends.

Learn more about clinical trials, including patient safety, phases of a clinical trial, deciding to participate in a clinical trial, questions to ask the research team, and links to find cancer clinical trials at www.cancer.net/clinicaltrials.

For specific topics being studied for breast cancer, learn more in the Current Research section at www.cancer.net/breast.

SIDE EFFECTS

Cancer and its treatment can cause a variety of side effects. However, doctors have made major strides in recent years in reducing pain, nausea and vomiting, infection, fatigue, and other physical side effects of cancer treatments. Many treatments used today are less intensive but equally effective as or more effective than treatments used in the past. Doctors and nurses also have many ways to provide relief to patients when such side effects occur.

Fear of treatment side effects is common after a diagnosis of cancer, but it may be helpful to know that preventing and controlling side effects is a major focus of your health care team. Before treatment begins, talk with your doctor about possible side effects of the specific treatments you will be receiving. The specific side effects that can occur depend on a variety of factors, including the type of cancer, its location, the individual treatment plan (including the length and dosage of treatment), and your overall health. Common side effects for each treatment option are described in detail within the Treatment section.

Ask your doctor which side effects are most likely to happen (and which are not), which need to be reported right away, when side effects are likely to occur, and how they will be addressed by the health care team. Also, be sure to communicate with the doctor and nurses about side effects you experience during and after treatment. Care of a patient's symptoms and side effects is an important part of a person's overall treatment plan; this is called palliative or supportive care. It helps people with cancer at any stage of illness be as comfortable as possible. Learn more about the most common side effects of cancer and different treatments, along with ways to prevent or control them at www.cancer.net/sideeffects.

Be sure to talk with your doctor about the level of caregiving you may need during treatment and recovery, as family members and friends often play an important role in the care

of a person with breast cancer. Learn more about caregiving at www.cancer.net/caregiving.

In addition to physical side effects, you may experience psychosocial (emotional and social) effects and sexual health concerns. For many patients, a diagnosis of breast cancer is stressful and can bring difficult emotions. Patients and their families are encouraged to share their feelings with a member of their health care team, who can help with coping strategies. Learn more about the importance of addressing such needs, including concerns about managing the cost of your cancer care at www.cancer.net/patientcare and www.cancer.net/managingcostofcare.

A side effect that occurs more than five years after treatment is called a late effect. Treatment of late effects is an important part of survivorship care. Learn more about late effects or long-term side effects by reading the After Treatment section or talking with your doctor.

AFTER TREATMENT

After treatment for breast cancer ends, talk with your doctor about developing a follow-up care plan. This plan may include regular physical examinations and/or medical tests to monitor your recovery for the coming months and years. ASCO's recommendations for breast cancer follow-up care include regular physical examinations and mammograms, among other recommendations. In addition, ASCO offers cancer treatment summaries and a survivorship care plan at www.cancer.net/treatmentsummaries to help keep track of the breast cancer treatment you received and develop a follow-up care plan once treatment ends. In some instances, patients may be seen at survivorship clinics that specialize in the post-treatment needs of people with cancer.

Learn more about ASCO's recommendations for breast cancer follow-up care, including regular physical examinations and mammograms, among other recommendations at www.cancer.net/whattoknow.

As explained in the Treatment section, breast cancer can come back in the breast or other areas of the body. The symptoms of a cancer recurrence include a new lump in the breast, under the arm, or along the chest wall; bone pain or fractures; headaches or seizures; chronic coughing or trouble breathing; extreme fatigue; and/or feeling ill. Talk with your doctor if you have any of these or other symptoms. The possibility of recurrence is a common concern among cancer survivors; learn more about coping with the fear of recurrence at www.cancer.net/features.

After surgery (mastectomy or lumpectomy) to treat breast cancer, the breast may be scarred and may have a different shape or size than before surgery. Or, the area around the

surgical site may become hardened. If lymph nodes were removed as part of the surgery or affected during treatment, lymphedema (swelling of the hand and/or arm) may occur, and this is a life-long risk for patients. Read more about what to expect after a mastectomy, preventing lymphedema after breast cancer treatment, breast reconstruction, and choosing a breast prosthesis at www.cancer.net/features.

Some patients experience breathlessness, a dry cough, and/or chest pain two to three months after finishing radiation therapy because the treatment can cause swelling and fibrosis (hardening or thickening) of the lungs. These symptoms are usually temporary. Talk with your doctor if you develop any new symptoms after radiation therapy or if the side effects are not going away.

Patients who received trastuzumab or certain types of chemotherapy called anthracyclines may be at risk of heart problems. Talk with your doctor about the best ways to check for heart problems.

Women taking tamoxifen should have yearly pelvic exams, because this drug can increase the risk of uterine cancer. Tell your doctor or nurse if you notice any abnormal vaginal bleeding or other new symptoms. Women who are taking an aromatase inhibitor, such as anastrozole, exemestane, or letrozole, should have a bone density test before they start treatment and as recommended by their doctor, as these drugs may cause some bone weakness or bone loss.

In addition, women recovering from breast cancer have other symptoms that may persist after treatment. However, these can often be managed. For example, drugs can help manage neuropathy (gabapentin [Horizant, Neurontin], pregabalin [Lyrica]), menopausal symptoms (antidepressants, clonidine [Catapres]), and joint pain. Learn about ways of coping with cancer-related fatigue, a drop in cognitive function (sometimes called “chemo brain”), and other late effects of cancer treatment at www.cancer.net/sideeffects.

Women recovering from breast cancer are encouraged to follow established guidelines for good health, such as maintaining a healthy weight, not smoking, eating a balanced diet, and having recommended cancer screening tests. Talk with your doctor to develop a plan that is best for your needs. Moderate physical activity can help rebuild your strength and energy level and may lower the risk of cancer recurrence. Your doctor can help you create a safe exercise plan based upon your needs, physical abilities, and fitness level.

Many breast cancer survivors need time to adapt to the “new normal.” Treatment for breast cancer may cause physical or emotional changes that affect how you view yourself.

Learn more about what comes next after cancer treatment and the next steps to take in survivorship, including making positive lifestyle changes at www.cancer.net/survivors and www.cancer.net/features.

Find out more about common terms used after cancer treatment is complete at www.cancer.net/dictionaryresources.

QUESTIONS TO ASK THE DOCTOR

Talking often with the doctor is important to make informed decisions about your health care. These suggested questions are a starting point to help you learn more about your cancer care and treatment. You are also encouraged to ask additional questions that are important to you.

- What type of breast cancer do I have?
- What is the grade and stage of this disease? What does this mean?
- Can you explain my pathology report (laboratory test results) to me?
- What is the hormone status of my tumor? What does this mean?
- What is my HER2 status? What does this mean?
- What is a sentinel lymph node biopsy? What are the benefits and risks? Would you recommend it for me?
- Has the cancer spread to my lymph nodes or anywhere else in my body?
- Would you explain my treatment options?
- What is the goal of each treatment?
- Am I candidate for a lumpectomy?
- Do I need a mastectomy? If so, would you recommend an immediate breast reconstruction (plastic surgery)? What are the advantages and disadvantages to this?
- What clinical trials are available to me?
- What is the expected timeline for each treatment option?
- What are the potential side effects of this treatment? What can be done to ease these?
- How will this treatment affect my daily life? Will I be able to work, exercise, and perform my usual activities?
- If I'm worried about managing the costs related to my cancer care, who can help me with these concerns? Who can help me understand what aspects of my care are covered by my insurance?
- Who will help coordinate my treatment and follow-up care?
- Could this treatment affect my fertility (ability to have children in the future)?
- Where can I find emotional support for me and my family?
- Whom do I call for questions or problems?
- Is there anything else I should be asking?

Additional questions to ask your doctors can be found at www.cancer.net/breast.

Patient Information Resources

Find organizations that offer information for breast cancer at www.cancer.net/support.

Dear Friend,

From the instant that the word *cancer* is spoken, life's major and minor chords are played differently.

At the Conquer Cancer Foundation of the American Society of Clinical Oncology (formerly known as The ASCO Cancer Foundation), we are well acquainted with the human cost of cancer. We feel great responsibility to be there for all who have been touched by cancer. We're working toward conquering this disease, and we're doing all we can to ensure that high-quality information and treatment are accessible to all.

One way we're doing this is by supporting education and information for patients and physicians worldwide through Cancer.Net, ASCO's award-winning patient information website. We also support patient information materials found in physicians' offices nationwide. And we hold public forums that distill scientific findings from ASCO's Annual Meeting for patients, families, and others from a non-clinical background.

As part of our mission, we will also continue to support breakthrough research in every aspect of patients' lives—from prevention through diagnosis, treatment, survivorship, and end-of-life care.

And we will continue to support work toward ensuring that more people have access to high-quality cancer care by working to eliminate health disparities in the United States and by offering professional development opportunities for physicians internationally.

We are committed to strengthening our partnerships with visionary organizations dedicated to working on behalf of all people with cancer and with generous individuals who contribute their time, talent, and resources to fuel our shared passions.

If you are a current supporter of the Conquer Cancer Foundation, ***thank you!***

If you have not partnered with the Conquer Cancer Foundation before, join us today in building ***a world free from the fear of cancer.***

Warmest Regards,

Nancy R. Daly, MS, MPH
Executive Director
Conquer Cancer Foundation *of the American Society of
Clinical Oncology*

P.S. To make a gift online and be part of our ambitious future, visit **ConquerCancerFoundation.org**.



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For more information about ASCO's patient information resources,
call toll-free 888-651-3038 or e-mail contactus@cancer.net.

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