

Breast Cancer Patient Guide



MY CANCER & TREATMENT

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Breast Cancer

Breast cancer is a disease in which malignant (cancer) cells form in the tissues of the breast. Both women and men can get breast cancer however, it is much more common in women. In the United States, approximately 1 in 8 women are diagnosed with breast cancer each year. After skin cancer, breast cancer is the second most common cancer for women in the U.S.

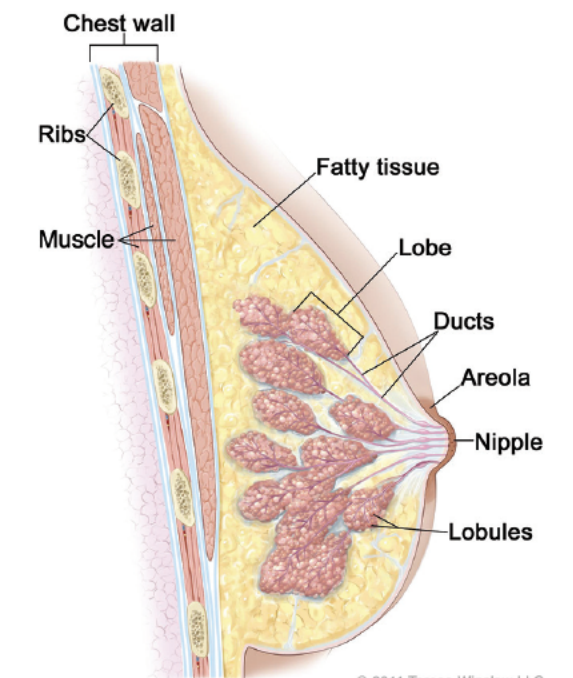
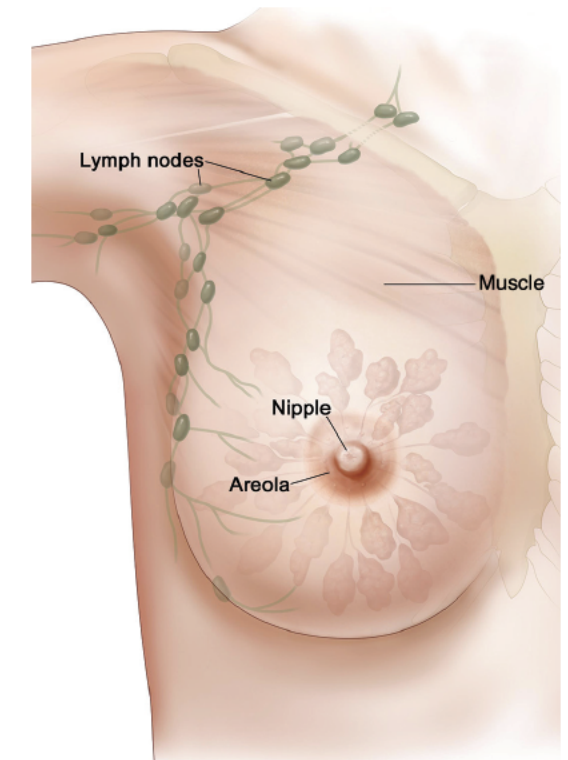
Anatomy of the Breast

The breast is made up of lobes and ducts. Each breast has 15 to 20 sections called lobes. Each lobe has many smaller sections called lobules. Lobules end in dozens of tiny bulbs that can make milk. The lobes, lobules, and bulbs are linked by thin tubes called ducts.

Each breast also has blood vessels and lymph vessels. The lymph vessels carry an almost colorless fluid called lymph. Lymph vessels carry lymph between lymph nodes. Lymph nodes are small bean-shaped structures that are found throughout the body. They filter substances in lymph and help fight infection and disease. Clusters of lymph nodes are found near the breast in the axilla (under the arm), above the collarbone, and in the chest.

The most common type of breast cancer is ductal carcinoma, which begins in the cells of the ducts. Cancer that begins in the lobes or lobules is called lobular carcinoma and is more often found in both breasts than are other types of breast cancer. Inflammatory breast cancer is an uncommon type of breast cancer in which the breast is warm, red, and swollen.

Anatomy of the Female Breast



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The nipple and areola are shown on the outside of the breast. The lymph nodes, lobes, lobules, ducts, and other parts of the inside of the breast are also shown.

Risk Factors

Anything that increases your chance of getting a disease is called a risk factor. Having a risk factor does not mean that you will get cancer; not having risk factors doesn't mean that you will not get cancer. Talk to your doctor if you think you may be at risk for breast cancer.

Risk factors for breast cancer include the following:

- A personal history of invasive breast cancer, ductal carcinoma in situ (DCIS)
- A personal history of benign (noncancer) breast disease
- A family history of breast cancer in a first-degree relative (mother, daughter, or sister)
- Breast tissue that is dense on a mammogram

Older age is the main risk factor for most cancers. The chance of getting cancer increases as you get older.

National Cancer Institute's Breast Cancer Risk Assessment Tool (www.cancer.gov/bcrisktool/) uses a woman's risk factors to estimate her risk for breast cancer during the next five years and up to age 90. This online tool is meant to be used by a health care provider. For more information on breast cancer risk, call 1-800-4-CANCER.

Breast cancer is sometimes caused by inherited gene mutations (changes). The genes in cells carry the hereditary information that is received from a person's parents. Hereditary breast cancer makes up about 5% to 10% of all breast cancer. Some mutated genes related to breast cancer are more common in certain ethnic groups.

Women who have certain gene mutations, such as a BRCA1 or BRCA2 mutation, have an increased risk of breast cancer. These women also have an increased risk of ovarian cancer, and may have an increased risk of other cancers. Men who have a mutated gene related to breast cancer also have an increased risk of breast cancer.

There are tests that can detect mutated genes. These genetic tests are sometimes done for members of families with a high risk of cancer.

- Inherited changes in the BRCA1 or BRCA2 genes or in other genes that increase the risk of breast cancer
- Exposure of breast tissue to estrogen made by the body. This may be caused by:
 - Menstruating at an early age
 - Older age at first birth or never having given birth
 - Starting menopause at a later age
- Taking hormones such as estrogen combined with progestin for symptoms of menopause
- Treatment with radiation therapy to the breast/chest
- Drinking alcohol
- Obesity

Protective Factors

The use of certain medicines and other factors decrease the risk of breast cancer. Anything that decreases your chance of getting a disease is called a protective factor.

Protective factors for breast cancer include the following:

- Taking any of the following:
 - Estrogen-only hormone therapy after a hysterectomy
 - Selective estrogen receptor modulators (SERMs)
 - Aromatase inhibitors
- Less exposure of breast tissue to estrogen made by the body. This can be a result of:
 - Early pregnancy
 - Breastfeeding
- Getting enough exercise
- Having any of the following procedures:
 - **Mastectomy:** Surgery to remove part or all of the breast to reduce the risk of cancer
 - **Oophorectomy:** Surgery to remove one or both ovaries to reduce the risk of cancer
 - **Ovarian ablation:** Treatment that stops or lowers the amount of estrogen made by the ovaries

Signs of Breast Cancer

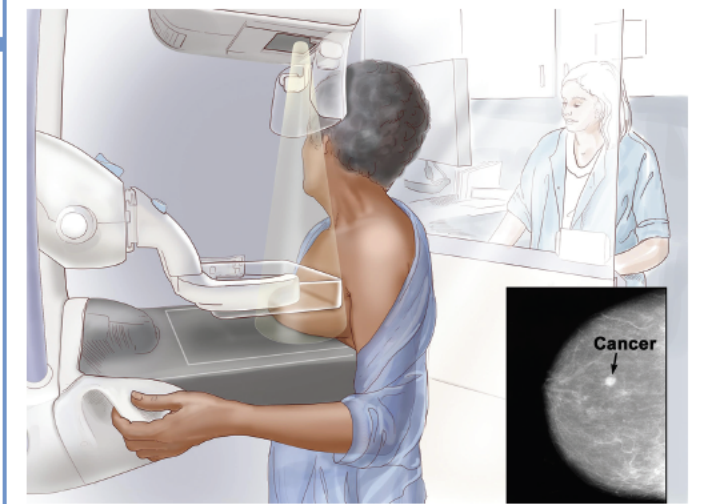
Signs of breast cancer include a lump or change in the breast. These and other signs may be caused by breast cancer or by other conditions. Check with your doctor if you have any of the following:

- A lump or thickening in or near the breast or in the underarm area
- A change in the size or shape of the breast
- A dimple or puckering in the skin of the breast
- A nipple turned inward into the breast
- Fluid, other than breast milk, from the nipple, especially if it's bloody
- Scaly, red, or swollen skin on the breast, nipple, or areola (the dark area of skin around the nipple)
- Dimples in the breast that look like the skin of an orange, called peau d'orange

Testing

Tests that examine the breasts are used to detect (find) and diagnose breast cancer. Check with your doctor if you notice any changes in your breasts. The following tests and procedures may be used:

- **Physical exam and history:** An exam of the body to check general signs of health, including checking for signs of disease, such as lumps or anything else that seems unusual. A history of the patient's health habits and past illnesses and treatments will also be taken.
- **Mammogram:** An x-ray of the breast.
- **Clinical breast exam (CBE):** An exam of the breast by a doctor or other health professional. The doctor will carefully feel the breasts and under the arms for lumps or anything else that seems unusual.
- **Ultrasound exam:** A procedure in which high-energy sound waves (ultrasound) are bounced off internal tissues or organs and make echoes. The echoes form a picture of body tissues called a sonogram. The picture can be printed to be looked at later.
- **MRI (magnetic resonance imaging):** A procedure that uses a magnet, radio waves, and a computer to make a series of detailed pictures of both breasts. This procedure is also called nuclear magnetic resonance imaging (NMRI).
- **Blood chemistry studies:** A procedure in which a blood sample is checked to measure the amounts of



Anatomy of the Female Breast

During a mammography the breast is pressed between two plates. X-rays are used to take pictures of breast tissue.

certain substances released into the blood by organs and tissues in the body. An unusual (higher or lower than normal) amount of a substance can be a sign of disease.

- **Biopsy:** The removal of cells or tissues so they can be viewed under a microscope by a pathologist to check for signs of cancer. If a lump in the breast is found, a biopsy may be done.

There are four types of biopsy used to check for breast cancer:

- **Excisional biopsy:** The removal of an entire lump of tissue
- **Incisional biopsy:** The removal of part of a lump or a sample of tissue
- **Core biopsy:** The removal of tissue using a wide needle
- **Fine-needle aspiration (FNA) biopsy:** The removal of tissue or fluid, using a thin needle

If cancer is found, tests are done to study the cancer cells. Decisions about the best treatment are based on the results of these tests. The tests give information about:

- How quickly the cancer may grow
- How likely it is that the cancer will spread through the body
- How well certain treatments might work
- How likely the cancer is to recur (come back)

Tests for breast cancer include the following:

- **An estrogen and progesterone receptor test** measure the amount of estrogen and progesterone receptors in cancer tissue. If there are more estrogen and progesterone receptors than normal, the cancer is called estrogen and/or progesterone receptor positive. This type of breast cancer may grow more quickly. The test results show whether treatment to block estrogen and progesterone may stop the cancer from growing.
- **A human epidermal growth factor type 2 receptor (HER2/neu) test** measures how many HER2/neu genes there are and how much HER2/neu protein is made in a sample of tissue. If there are more HER2/neu genes or higher levels of HER2/neu protein than normal, the cancer is called HER2/neu positive. This type of breast cancer may grow more quickly and is more likely to spread to other parts of the body. The cancer may be treated with drugs that target the HER2/neu protein, such as trastuzumab and pertuzumab.
- **Multigene tests** study samples of tissue to look at the activity of many genes at the same time. These tests may help predict whether cancer will spread to other parts of the body or recur (come back). The following multigene tests have been studied in clinical trials:
 - **Oncotype DX tests** help predict whether stage I or stage II breast cancer that is estrogen receptor positive and node negative will spread to other parts of the body. If the risk that the cancer will spread is high, chemotherapy may be given to lower the risk.
 - **MammaPrint tests** help predict whether stage I or stage II breast cancer that is node negative will spread to other parts of the body. If the risk of spreading is high, chemotherapy may be given to lower the risk.

Based on these tests, breast cancer is described as one of the following types:

- Hormone receptor positive (estrogen and/or progesterone receptor positive) or hormone receptor negative (estrogen and/or progesterone receptor negative)
- HER2/neu positive or HER2/neu negative
- Triple negative (estrogen receptor, progesterone receptor, and HER2/neu negative)

This information helps the doctor decide which treatments will work best for your cancer.

Prognosis Factors

Certain factors affect prognosis (chance of recovery) and treatment options. The prognosis and treatment options depend on the following:

- The stage of the cancer (the size of the tumor and whether it is in the breast only or has spread to lymph nodes or other places in the body)
- The type of breast cancer
- Estrogen receptor and progesterone receptor levels in the tumor tissue
- Human epidermal growth factor type 2 receptor (HER2/neu) levels in the tumor tissue
- Whether the tumor tissue is triple negative (cells that do not have estrogen receptors, progesterone receptors, or high levels of HER2/neu)
- How fast the tumor is growing
- How likely the tumor is to recur (come back)
- A woman's age, general health, and menopausal status (whether a woman is still having menstrual periods)
- Whether the cancer has just been diagnosed or has recurred (come back)

Stages of Breast Cancer Overview

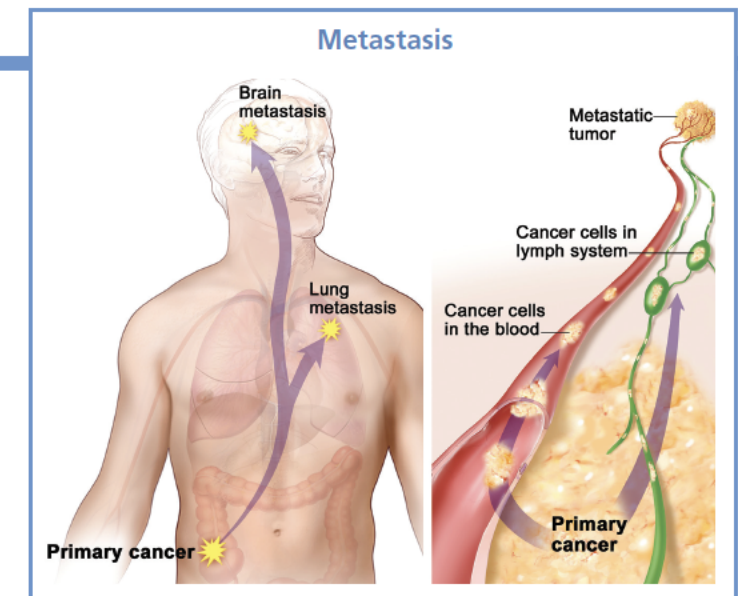
Key Points:

- After breast cancer has been diagnosed, tests are done to find out if cancer cells have spread within the breast or to other parts of the body.
- There are three ways that cancer spreads in the body.
- Cancer may spread from where it began to other parts of the body.
- The treatment of breast cancer depends partly on the stage of the disease.
- The following stages are used for breast cancer:
 - Stage 0 (carcinoma in situ)
 - Stage I
 - Stage II
 - Stage IIIA
 - Stage IIIB
 - Stage IIIC
 - Stage IV

After breast cancer has been diagnosed, tests are done to find out if cancer cells have spread within the breast or to other parts of the body. The process used to find out whether the cancer has spread within the breast or to other parts of the body is called staging. The information gathered from the staging process determines the stage of the disease. It is important to know the stage in order to plan treatment. The results of some of the tests used to diagnose breast cancer are also used to stage the disease.

The following tests and procedures also may be used in the staging process:

- **Sentinel lymph node biopsy:** The removal of the sentinel lymph node during surgery. The sentinel lymph node is the first lymph node to receive lymphatic drainage from a tumor and the first lymph node the cancer is likely to spread to from the tumor. A radioactive substance and/or blue dye is injected near the tumor. The substance or dye flows through the lymph ducts to the lymph nodes. The first lymph node to receive the substance or dye is removed. A pathologist views the tissue under a microscope to look for cancer cells. If cancer cells are not found, it may not be necessary to remove more lymph nodes.
- **CT scan (CAT scan):** A procedure that makes a series of detailed pictures of areas inside the body, taken from different angles. The pictures are made by a computer linked to an x-ray machine. A dye may be injected into a vein or swallowed to help the organs or tissues show up more clearly. This procedure is also called computed tomography, computerized tomography, or computerized axial tomography.
- **Bone scan:** A procedure to check if there are rapidly dividing cells, such as cancer cells, in the bone. A very small amount of radioactive material is injected into a vein and travels through the bloodstream. The radioactive material collects in the bones and is detected by a scanner.
- **PET scan (positron emission tomography scan):** A procedure to find malignant tumor cells in the body. A small amount of radioactive glucose (sugar) is injected into a vein. The PET scanner rotates around the body and makes a picture of where glucose is being used in the body. Malignant tumor cells show up brighter in the picture because they are more active and take up more glucose than normal cells do.



Possible Spreading of Cancer

There are three ways that cancer spreads in the body. Cancer can spread through tissue, the lymph system, and the blood:

- **Tissue:** The cancer spreads from where it began by growing into nearby areas.
- **Lymph system:** The cancer spreads from where it began by getting into the lymph system. The cancer travels through the lymph vessels to other parts of the body.
- **Blood:** The cancer spreads from where it began by getting into the blood. The cancer travels through the blood vessels to other parts of the body.

When cancer spreads to another part of the body, it is called **metastasis** (see image above). Cancer cells break away from where they began (the primary tumor) and travel through the lymph system or blood. The new, metastatic tumor is the same type of cancer as the primary tumor. For example, if breast cancer spreads to the lung, the cancer cells in the lung are breast cancer cells, not lung cancer cells.

Breast Cancer Stage Descriptions

This section describes the stages of breast cancer. The breast cancer stage is based on the results of tests that are done on the tumor and lymph nodes removed during surgery and on other tests.

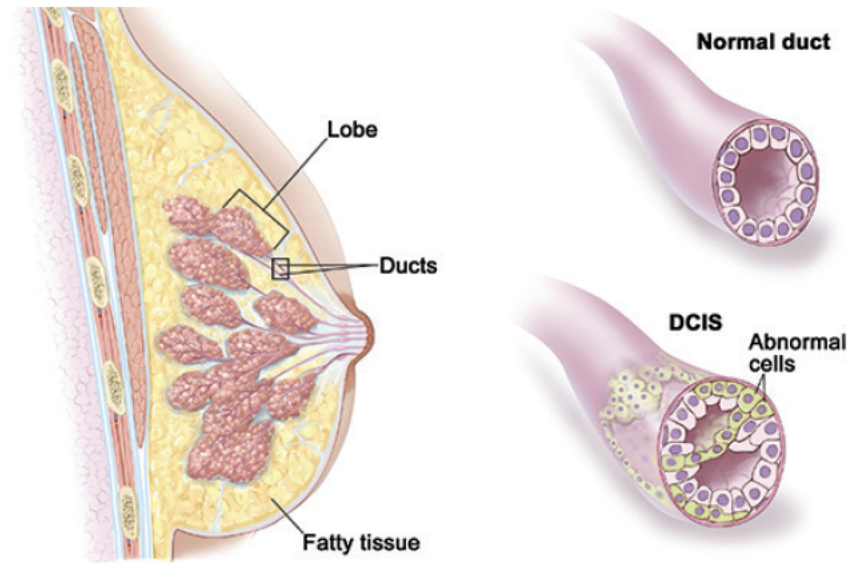
Stage 0 (Carcinoma in Situ)

There are 3 types of breast carcinoma in situ:

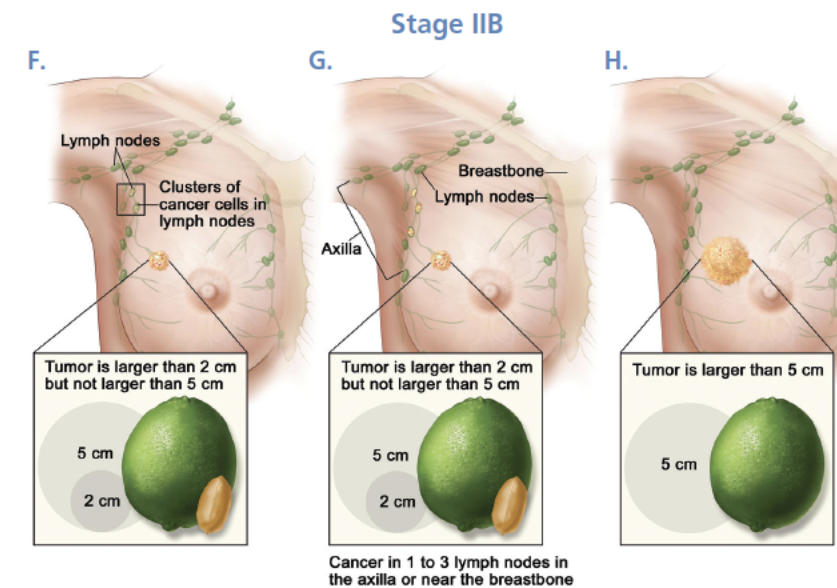
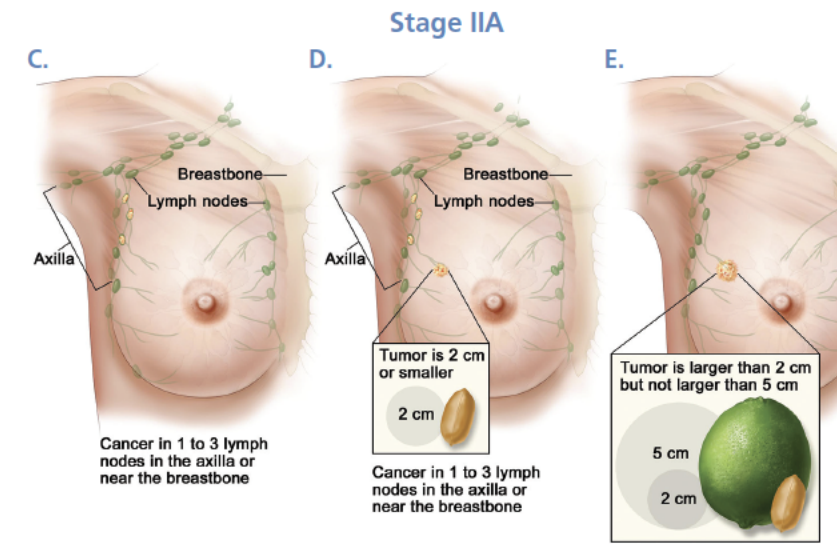
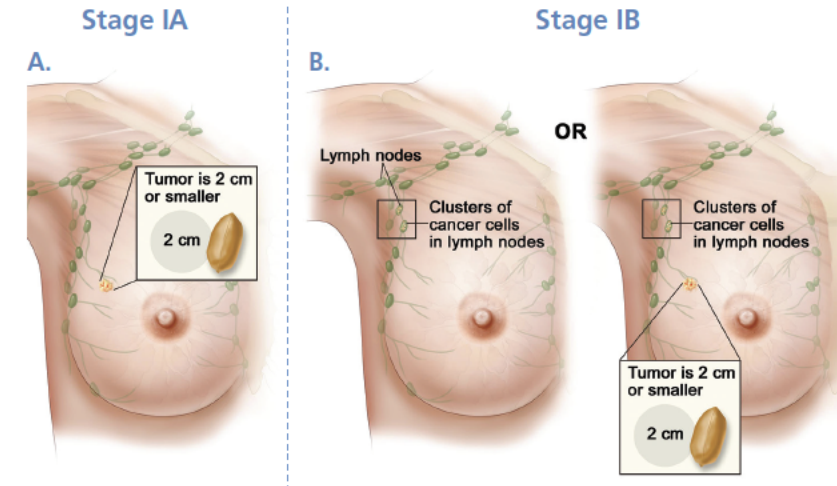
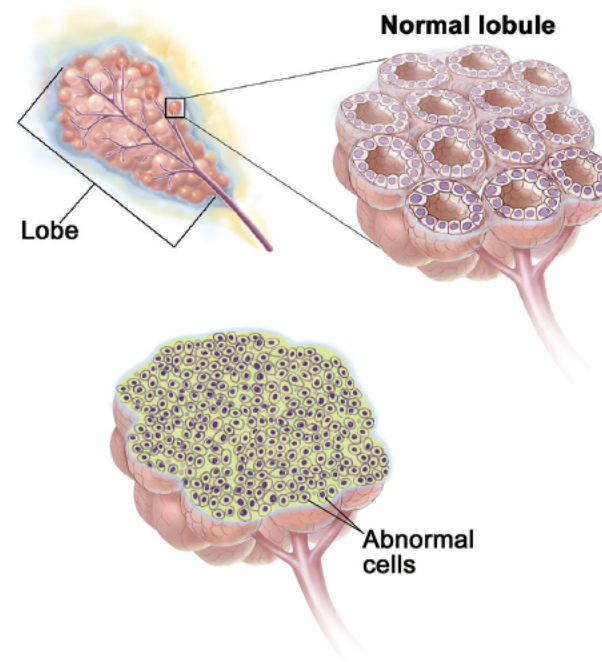
- **Ductal carcinoma in situ (DCIS)** is a noninvasive condition in which abnormal cells are found in the lining of a breast duct. The abnormal cells have not spread outside the duct to other tissues in the breast. In some cases, DCIS may become invasive cancer and spread to other tissues. At this time, there is no way to know which lesions could become invasive.
- **Paget disease** of the nipple is a condition in which abnormal cells are found in the nipple only.
- **Lobular carcinoma in situ (LCIS)** is a condition in which abnormal cells are found in the lobules of the breast. This condition seldom becomes invasive cancer.

Ductal Carcinoma in Situ (DCIS)

Abnormal cells are found in the lining of a breast duct.



Lobular Carcinoma in Situ (LCIS)



Stage I

In stage I, cancer has formed. Stage I is divided into stages IA and IB.

- In stage IA (image A), the tumor is 2 centimeters or smaller and has not spread outside the breast.
- In stage IB (image B), small clusters of breast cancer cells (between 0.2 – 2 millimeters) are found in the lymph nodes and either:
 - no tumor is found in the breast; or
 - tumor is 2 centimeters or smaller

Stage II

Stage II is divided into stages IIA and IIB.

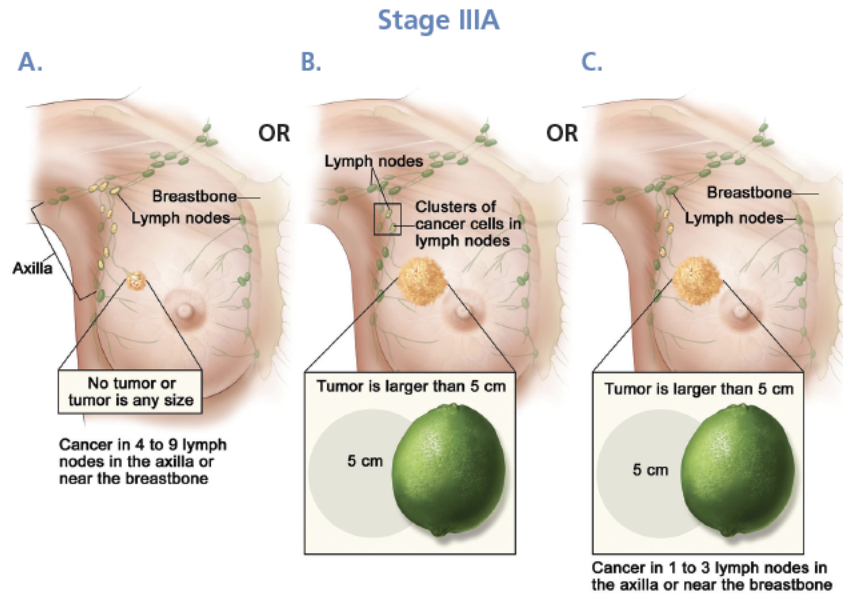
- In stage IIA:
 - no tumor is found in the breast or the tumor is 2 centimeters or smaller (image C). Cancer (larger than 2 mm) is found in 1 – 3 axillary lymph nodes or in the lymph nodes near the breastbone (found during a sentinel lymph node biopsy) (image D); or
 - the tumor is between 2 – 5 centimeters. Cancer has not spread to the lymph nodes (image E).
- In stage IIB the tumor is:
 - between 2 – 5 centimeters. Small clusters of breast cancer cells (between 0.2 – 2 millimeters) are found in the lymph nodes (image F); or
 - the tumor is between 2 – 5 centimeters. Cancer has spread to 1 – 3 axillary lymph nodes or to the lymph nodes near the breastbone (found during a sentinel lymph node biopsy) (image G); or
 - larger than 5 centimeters. Cancer has not spread to the lymph nodes (image H).

Stage III

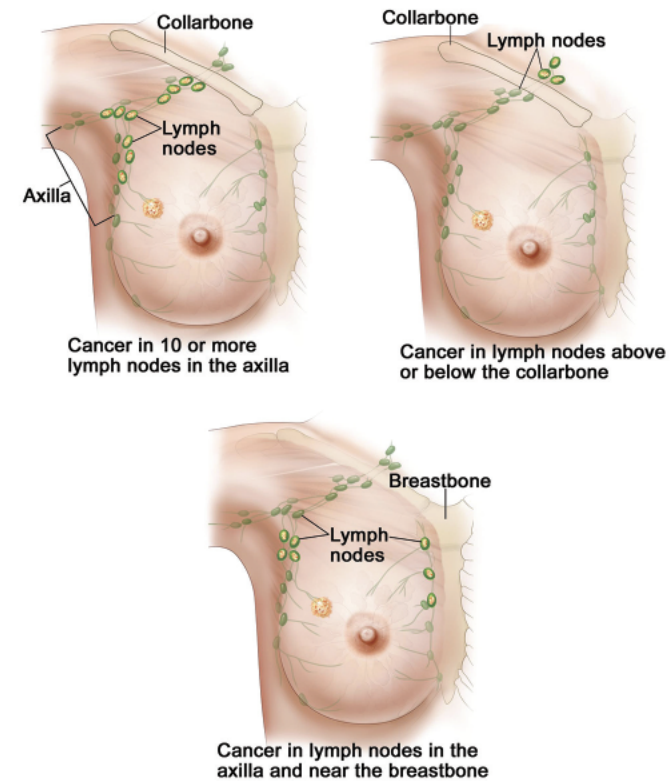
Stage III is divided into stages IIIA and IIIB.

• In stage IIIA:

- no tumor is found in the breast or the tumor may be any size. Cancer is found in 4 – 9 axillary lymph nodes or in the lymph nodes near the breastbone (found during imaging tests or a physical exam) (image A); **or**
- the tumor is larger than 5 centimeters. Small clusters of breast cancer cells (between 0.2 – 2 millimeters) are found in the lymph nodes (image B); **or**
- the tumor is larger than 5 centimeters. Cancer has spread to 1 – 3 axillary lymph nodes or to the lymph nodes near the breastbone (found during a sentinel lymph node biopsy) (image C).



Stage IIIC



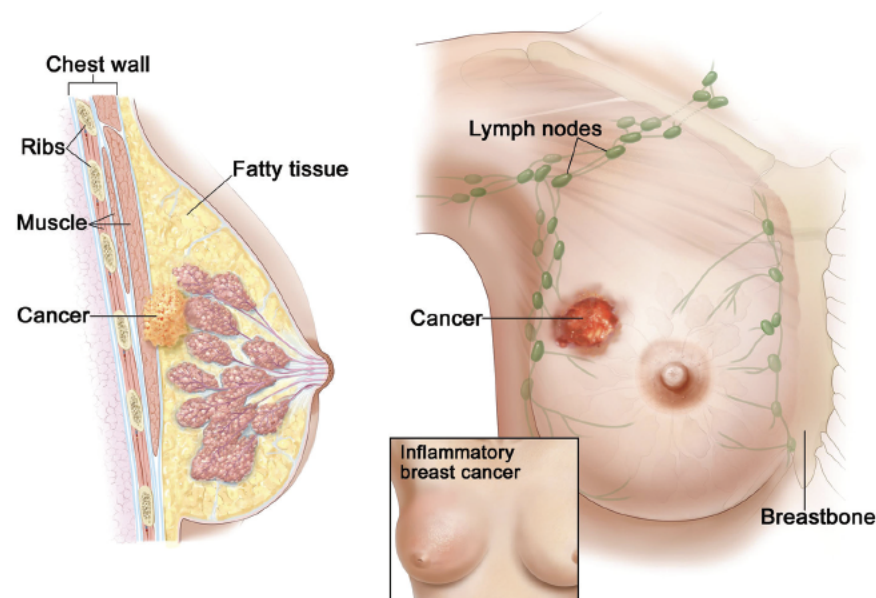
- In stage IIIC no tumor is found in the breast or the tumor may be any size. Cancer may have spread to the skin of the breast and caused swelling or an ulcer and/or has spread to the chest wall. Also, cancer has spread to:
 - 10 or more axillary lymph nodes; **or**
 - lymph nodes above or below the collarbone; **or**
 - axillary lymph nodes and lymph nodes near the breastbone.

• In stage IIIB the tumor may be any size and cancer has spread to the chest wall and/or to the skin of the breast and caused swelling or an ulcer. Also, cancer may have spread to:

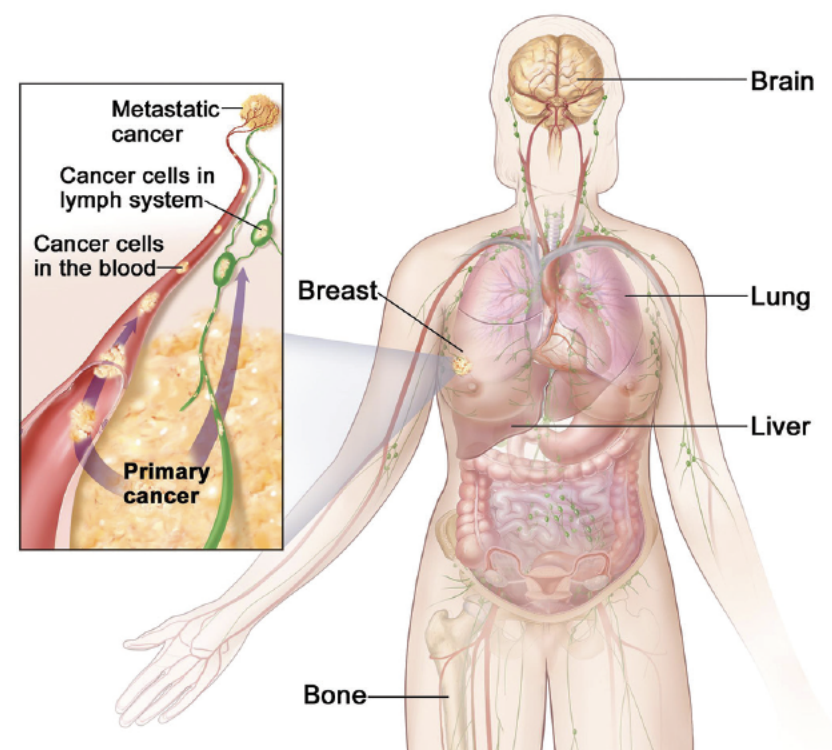
- up to 9 axillary lymph nodes; **or**
- the lymph nodes near the breastbone.

Cancer that has spread to the skin of the breast may also be inflammatory breast cancer.

Stage IIIB



Stage IV



Stage IV

In stage IV, cancer has spread to other organs of the body, most often the bones, lungs, liver, or brain.

Inflammatory Breast Cancer



Inflammatory breast cancer of the left breast showing peau d'orange and inverted nipple.

Inflammatory Breast Cancer

In inflammatory breast cancer, cancer has spread to the skin of the breast and the breast looks red and swollen and feels warm. The redness and warmth occur because the cancer cells block the lymph vessels in the skin. The skin of the breast may also show the dimpled appearance called *peau d'orange* (like the skin of an orange). There may not be any lumps in the breast that can be felt. Inflammatory breast cancer may occur in stage IIIB, stage IIIC, or stage IV.

Recurrent Breast Cancer

Recurrent breast cancer is cancer that has recurred (come back) after it has been treated. The cancer may come back in the breast, in the skin of the breast, in the chest wall, or in nearby lymph nodes.

Treatment Options

There are different types of treatment for patients with breast cancer. Some treatments are standard (the currently used treatment), and some are being tested in clinical trials. A treatment clinical trial is a research study meant to help improve current treatments or obtain information on new treatments for patients with cancer. When clinical trials show that a new treatment is better than the standard treatment, the new treatment may become the standard treatment. Patients may want to think about taking part in a clinical trial. Some clinical trials are open only to patients who have not started treatment.

Five types of standard treatment are used:

- Surgery
- Radiation therapy
- Chemotherapy
- Hormone therapy
- Targeted therapy

SURGERY

Most patients with breast cancer have surgery to remove the cancer.

Sentinel lymph node biopsy is the removal of the sentinel lymph node during surgery. The sentinel lymph node is the first lymph node to receive lymphatic drainage from a tumor. It is the first lymph node where the cancer is likely to spread. A radioactive substance and/or blue dye is injected near the tumor. The substance or dye flows through the lymph ducts to the lymph nodes. The first lymph node to receive the substance or dye is removed. A pathologist views the tissue under a microscope to look for cancer cells. After the sentinel lymph node biopsy, the surgeon removes the tumor using breast-conserving surgery or mastectomy. If cancer cells were not found in the sentinel lymph node, it may not be necessary to remove more lymph nodes. If cancer cells were found, more lymph nodes will be removed through a separate incision. This is called a lymph node dissection.

Types of surgery include the following:

- **Breast-conserving surgery** is an operation to remove the cancer and some normal tissue around it, but not the breast itself (see image A on the next page). Part of the chest wall lining may also be removed if the cancer is near it. This type of surgery may also be called lumpectomy, partial mastectomy, segmental mastectomy, quadrantectomy, or breast-sparing surgery.

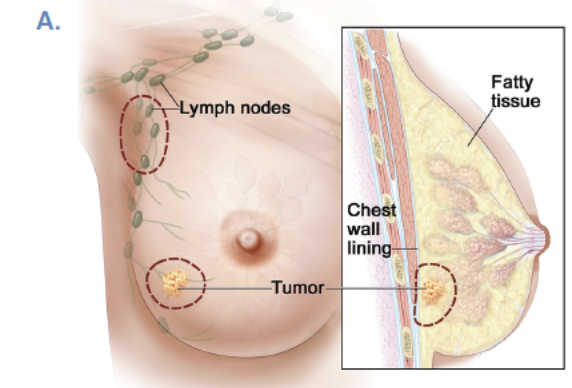
- **Total mastectomy** (also called a simple mastectomy): Surgery to remove the whole breast that has cancer (image B). Some of the lymph nodes under the arm may be removed and checked for cancer. This may be done at the same time as the breast surgery or after. This is done through a separate incision.
- **Modified radical mastectomy:** Surgery to remove the whole breast that has cancer, many of the lymph nodes under the arm, the lining over the chest muscles, and sometimes, part of the chest wall muscles (image B).

Chemotherapy may be given before surgery to remove the tumor. When given before surgery, chemotherapy will shrink the tumor and reduce the amount of tissue that needs to be removed during surgery. Treatment given before surgery is called preoperative therapy or neoadjuvant therapy.

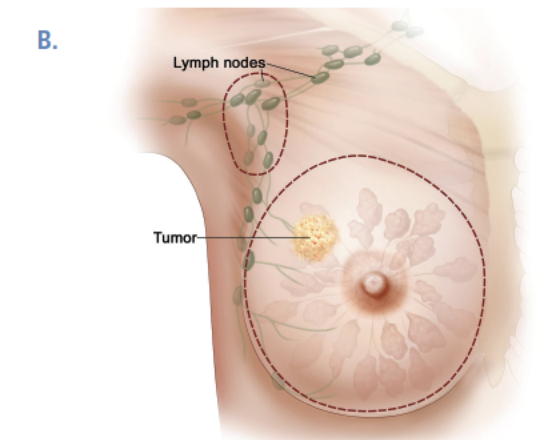
Even if the doctor removes all the cancer that can be seen at the time of the surgery, some patients may be given radiation therapy, chemotherapy, or hormone therapy after surgery, to kill any cancer cells that are left. Treatment given after the surgery, to lower the risk that the cancer will come back, is called postoperative therapy or adjuvant therapy.

If a patient is going to have a mastectomy, breast reconstruction (surgery to rebuild a breast's shape after a mastectomy) may be considered. Breast reconstruction may be done at the time of the mastectomy or at some time after. The reconstructed breast may be made with the patient's own nonbreast tissue or by using implants filled with saline or silicone gel. Before the decision to get an implant is made, patients can call the Food and Drug Administration's (FDA) Center for Devices and Radiologic Health at 1-888-INFO-FDA (1-888-463-6332) or visit the FDA website for more information on breast implants.

Breast-conserving Surgery

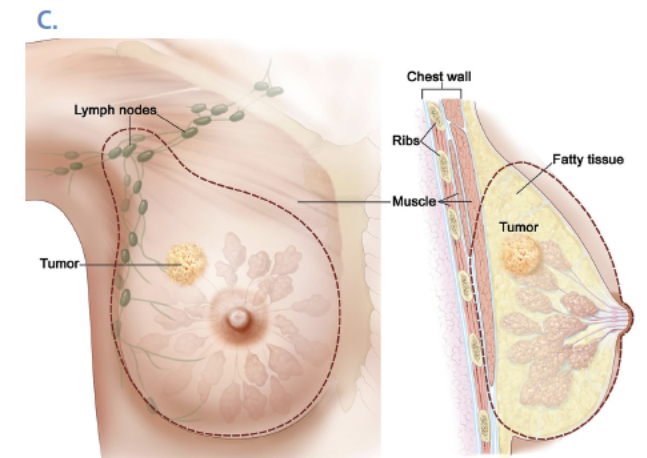


Total (Simple) Mastectomy



The dotted line shows where the entire breast is removed. Some lymph nodes under the arm may also be removed.

Modified Radical Mastectomy



The dotted line shows where the entire breast and some lymph nodes are removed. Part of the chest wall muscle may also be removed.

How Does Radiation Therapy Work?

Radiation therapy works by making small breaks in the DNA inside cells. These breaks keep cancer cells from growing and dividing and cause them to die. Nearby normal cells can also be affected by radiation, but most recover and go back to working the way they should. Unlike chemotherapy, which usually exposes the whole body to cancer-fighting drugs, radiation therapy is usually a local treatment. In most cases, it's aimed at and affects only the part of the body being treated. Radiation treatment is planned to damage cancer cells, with as little harm as possible to nearby healthy cells.



RADIATION THERAPY

Radiation therapy uses high-energy x-rays or other types of radiation to kill cancer cells or keep them from growing. There are two types of radiation therapy:

- **External radiation therapy** uses a machine outside the body to send radiation toward the cancer.
- **Internal radiation therapy** uses a radioactive substance sealed in needles, seeds, wires, or catheters that are placed directly into or near the cancer.

The way the radiation therapy is given depends on the type and stage of the cancer being treated. External radiation therapy is used to treat breast cancer. Internal radiation therapy with strontium-89 (a radionuclide) is used to relieve bone pain caused by breast cancer that has spread to the bones. Strontium-89 is injected into a vein and travels to the surface of the bones. Radiation is released and kills cancer cells in the bones.

CHEMOTHERAPY

Chemotherapy treatment uses drugs to stop the growth of cancer cells, either by killing the cells or by stopping them from dividing. When chemotherapy is taken by mouth or injected into a vein or muscle, the drugs enter the bloodstream and can reach cancer cells throughout the body (systemic chemotherapy). When chemotherapy is placed directly into the cerebrospinal fluid, an organ, or a body cavity such as the abdomen, the drugs mainly affect cancer cells in those areas (regional chemotherapy).

The way the chemotherapy is given depends on the type and stage of the cancer being treated. Systemic chemotherapy is used in the treatment of breast cancer.

HORMONE THERAPY

Hormone therapy is a cancer treatment that removes hormones or blocks their action and stops cancer cells from growing. Hormones are substances made by glands in the body and circulated in the bloodstream. Some hormones can cause certain cancers to grow. If tests show that the cancer cells have places where hormones can attach (receptors), drugs, surgery, or radiation therapy is used to reduce the production of hormones or block them from working. The hormone estrogen, which makes some breast cancers grow, is made mainly by the ovaries. Treatment to stop the ovaries from making estrogen is called ovarian ablation.

Hormone therapy with tamoxifen is often given to patients with early localized breast cancer that can be removed by surgery and those with metastatic breast cancer (cancer that has spread to other parts of the body). Hormone therapy with tamoxifen or estrogens can act on cells all over the body and may increase the chance of developing endometrial cancer. Women taking tamoxifen should have a pelvic exam every year to look for any signs of cancer. Any vaginal bleeding, other than menstrual bleeding, should be reported to a doctor as soon as possible.

Hormone therapy with a luteinizing hormone-releasing hormone (LHRH) agonist is given to some premenopausal women who have just been diagnosed with hormone receptor positive breast cancer. LHRH agonists decrease the body's estrogen and progesterone.

Hormone therapy with an aromatase inhibitor is given to some postmenopausal women who have hormone receptor positive breast cancer. Aromatase inhibitors

decrease the body's estrogen by blocking an enzyme called aromatase from turning androgen into estrogen. Anastrozole, letrozole, and exemestane are types of aromatase inhibitors.

For the treatment of early localized breast cancer that can be removed by surgery, certain aromatase inhibitors may be used as adjuvant therapy instead of tamoxifen or after 2 to 3 years of tamoxifen use. For the treatment of metastatic breast cancer, aromatase inhibitors are being tested in clinical trials to compare them to hormone therapy with tamoxifen.

Other types of hormone therapy include megestrol acetate or anti-estrogen therapy such as fulvestrant.

TARGETED THERAPY

Targeted therapy is a type of treatment that uses drugs or other substances to identify and attack specific cancer cells without harming normal cells. Monoclonal antibodies, tyrosine kinase inhibitors, cyclin-dependent kinase inhibitors, mammalian target of rapamycin (mTOR) inhibitors, and PARP inhibitors are types of targeted therapies used in the treatment of breast cancer.

Monoclonal antibody therapy uses antibodies made in the laboratory, from a single type of immune system cell. These antibodies can identify substances on cancer cells or normal substances that may help cancer cells grow. The antibodies attach to the substances and kill the cancer cells, block their growth, or keep them from spreading. Monoclonal antibodies are given by infusion and may be used alone or to carry drugs, toxins, or radioactive material directly to cancer cells. Monoclonal antibodies may be used in combination with chemotherapy as adjuvant therapy. Types of monoclonal antibody therapy include:

- **Trastuzumab** is a monoclonal antibody that blocks the effects of the growth factor protein HER2, which sends growth signals to breast cancer cells. It may be used with other therapies to treat HER2 positive breast cancer.
- **Pertuzumab** is a monoclonal antibody that may be combined with trastuzumab and chemotherapy to treat breast cancer. It may be used to treat certain patients with HER2 positive breast cancer that has metastasized (spread to other parts of the body). It may also be used as neoadjuvant therapy in certain patients with early stage HER2 positive breast cancer.

- **Pado-trastuzumab emtansine** is a monoclonal antibody linked to an anticancer drug. This is called an antibody-drug conjugate. It is used to treat HER2 positive breast cancer that has spread or recurred (come back).

Tyrosine kinase inhibitors are targeted therapy drugs that block signals needed for tumors to grow. Tyrosine kinase inhibitors may be used with other anticancer drugs as adjuvant therapy. Tyrosine kinase inhibitors include the following:

- **Lapatinib** blocks the effects of the HER2 protein and other proteins inside tumor cells. It may be used with other drugs to treat patients with HER2 positive breast cancer that has progressed after treatment with trastuzumab.
- **Neratinib** blocks the effects of the HER2 protein and other proteins inside tumor cells. It may be used to treat patients with early stage HER2 positive breast cancer after treatment with trastuzumab.

Cyclin-dependent kinase inhibitors are targeted therapy drugs that block proteins called cyclin-dependent kinases, which cause the growth of cancer cells. Cyclin-dependent kinase inhibitors include the following:

- **Palbociclib** is a cyclin-dependent kinase inhibitor used with the drug letrozole to treat breast cancer that is estrogen receptor positive and HER2 negative and has spread to other parts of the body. It is used in postmenopausal women whose cancer has not been treated with hormone therapy. Palbociclib may also be used with fulvestrant in women whose disease has gotten worse after treatment with hormone therapy.
- **Ribociclib** is a cyclin-dependent kinase inhibitor used with letrozole to treat breast cancer that is hormone receptor positive and HER2 negative and has come back or spread to other parts of the body. It is used in postmenopausal women whose cancer has not been treated with hormone therapy.
- **Abemaciclib** is used to treat hormone receptor positive and HER2 negative breast cancer that is advanced or has spread to other parts of the body. It may be used alone or with other drugs to treat breast cancer that has gotten worse after other treatments.

Mammalian target of rapamycin (mTOR) inhibitors block a protein called mTOR, which may keep cancer cells from growing and prevent the growth of new blood vessels that tumors need to grow. mTOR inhibitors include:

- **Everolimus** is an mTOR inhibitor used in postmenopausal women with advanced hormone receptor positive breast cancer that is also HER2 negative and has not gotten better with other treatment.

PARP inhibitors are a type of targeted therapy that block DNA repair and may cause cancer cells to die. PARP inhibitor therapy is being studied for the treatment of patients with triple negative breast cancer or tumors with BRCA1 or BRCA2 mutations.

SIDE EFFECTS

Treatment for breast cancer may cause immediate side effects as well as those that continue or appear months or years after treatment has ended (late effects).

Side effects of chemotherapy may include:

- Bleeding
- Anemia
- Infections that are more serious
- Fatigue
- Loss of memory or clarity
- Pain and changes to nerves
- Swelling
- Nausea, vomiting, diarrhea, and constipation
- Dry mouth, mouth sores, or swelling in the mouth
- Appetite changes and weight loss
- Changes to skin, nails and hair loss

Late effects of radiation therapy are not common, but may include:

- Inflammation of the lung after radiation therapy to the breast, especially when chemotherapy is given at the same time.
- Arm lymphedema, especially when radiation therapy is given after lymph node dissection.
- In women younger than 45 years who receive radiation therapy to the chest wall after mastectomy, there may be a higher risk of developing breast cancer in the other breast.

Late effects of chemotherapy depend on the drugs used, but may include:

- Heart failure
- Blood clots
- Premature menopause
- Second cancer, such as leukemia

Late effects of targeted therapy with trastuzumab, lapatinib, or pertuzumab may include:

- Heart problems such as heart failure

Clinical Trials

Patients may want to think about taking part in a clinical trial. For some patients, participating in a clinical trial may be the best treatment choice. Clinical trials are part of the cancer research process. Clinical trials are done to find out if new cancer treatments are safe and effective or better than the standard treatment.

Many of today's standard treatments for cancer are based on earlier clinical trials. Patients who take part in a clinical trial may receive the standard treatment or be among the first to receive a new treatment.

Patients who take part in clinical trials also help improve the way cancer will be treated in the future. Even when clinical trials do not lead to effective new treatments, they often answer important questions and help move research forward.

Patients can enter clinical trials before, during, or after starting their cancer treatment.

Some clinical trials only include patients who have not yet received treatment. Other trials test treatments for patients whose cancer has not gotten better. There are also clinical trials that test new ways to stop cancer from recurring (coming back) or reduce the side effects of cancer treatment.

Clinical trials are taking place in many parts of the country. General information about clinical trials is available from the NCI website (www.cancer.gov/about-cancer/treatment/clinical-trials).

Follow-up Tests May Be Needed

Some of the tests that were done to diagnose the cancer or to find out the stage of the cancer may be repeated. Some tests will be repeated in order to see how well the treatment is working. Decisions about whether to continue, change, or stop treatment may be based on the results of these tests.

Some of the tests will continue to be done from time to time after treatment has ended. The results of these tests can show if your condition has changed or if the cancer has recurred (come back). These tests are sometimes called follow-up tests or check-ups.



Treatment Options for Breast Cancer

This section will cover treatment options for the following:

- Early, localized, or operable breast cancer
- Locally advanced or inflammatory breast cancer
- Locoregional recurrent breast cancer
- Metastatic breast cancer
- Ductal carcinoma in situ (DCIS)

EARLY, LOCALIZED, OR OPERABLE BREAST CANCER TREATMENT OPTIONS

Treatment may include the following:

Surgery

- Breast-conserving surgery and sentinel lymph node biopsy. If cancer is found in the lymph nodes, a lymph node dissection may be done.
- Modified radical mastectomy. Breast reconstruction surgery may also be done.

Postoperative radiation therapy

For women who had breast-conserving surgery, radiation therapy is given to the whole breast to lessen the chance the cancer will come back. Radiation therapy may also be given to lymph nodes in the area.

For women who had a modified radical mastectomy, radiation therapy may be given to lessen the chance the cancer will come back if any of the following are true:

- Cancer was found in 4 or more lymph nodes.
- Cancer had spread to tissue around the lymph nodes.

- The tumor was large.
- There is tumor close to or remaining in the tissue near the edges of where the tumor was removed.

Postoperative systemic therapy

Systemic therapy is the use of drugs that can enter the bloodstream and reach cancer cells throughout the body. Postoperative systemic therapy is given to lessen the chance the cancer will come back after surgery to remove the tumor.

Postoperative systemic therapy is given depending on whether:

- The tumor is hormone receptor negative or positive
- The tumor is HER2/neu negative or positive
- The tumor is hormone receptor negative and HER2/neu negative (triple negative)
- The size of the tumor

In premenopausal women with hormone receptor positive tumors, no more treatment may be needed or postoperative therapy may include:

- Tamoxifen therapy with or without chemotherapy.
- Tamoxifen therapy and treatment to stop or lessen how much estrogen is made by the ovaries. Drug therapy, surgery to remove the ovaries, or radiation therapy to the ovaries may be used.
- Aromatase inhibitor therapy and treatment to stop or lessen how much estrogen is made by the ovaries. Drug therapy, surgery to remove the ovaries, or radiation therapy to the ovaries may be used.

In postmenopausal women with hormone receptor positive tumors, no more treatment may be needed or postoperative therapy may include the following:

- Aromatase inhibitor therapy with or without chemotherapy
- Tamoxifen followed by aromatase inhibitor therapy, with or without chemotherapy

In women with hormone receptor negative tumors, no more treatment may be needed or postoperative therapy may include chemotherapy.

In women with HER2/neu negative tumors, postoperative therapy may include chemotherapy.

In women with small, HER2/neu positive tumors, and no cancer in the lymph nodes, no more treatment may be needed. If there is cancer in the lymph nodes, or the tumor is large, postoperative therapy may include the following:

- Chemotherapy and targeted therapy (trastuzumab)
- Hormone therapy, such as tamoxifen or aromatase inhibitor therapy, for tumors that are also hormone receptor positive

In women with small, hormone receptor negative and HER2/neu negative tumors (triple negative) and no cancer in the lymph nodes, no more treatment may be needed. If there is cancer in the lymph nodes or the tumor is large, postoperative therapy may include these treatments:

- Chemotherapy
- Radiation therapy
- A clinical trial of a new chemotherapy regimen
- A clinical trial of PARP inhibitor therapy

Preoperative systemic therapy

Systemic therapy is the use of drugs that can enter the bloodstream and reach cancer cells throughout the body. Preoperative systemic therapy is given to shrink the tumor before surgery.

In postmenopausal women with hormone receptor positive tumors, preoperative therapy may include:

- Chemotherapy
- Hormone therapy, such as tamoxifen or aromatase inhibitor therapy, for women who cannot have chemotherapy

In premenopausal women with hormone receptor positive tumors, preoperative therapy may include a clinical trial of hormone therapy, such as tamoxifen or aromatase inhibitor therapy.

In women with HER2/neu positive tumors, preoperative therapy may include the following:

- Chemotherapy and targeted therapy (trastuzumab)
- Targeted therapy (pertuzumab)

In women with HER2/neu negative tumors or triple negative tumors, preoperative therapy may include chemotherapy.

LOCALLY ADVANCED OR INFLAMMATORY BREAST CANCER TREATMENT OPTIONS

Treatment of locally advanced or inflammatory breast cancer is a combination of therapies that may include:

- Surgery (breast-conserving surgery or total mastectomy) with lymph node dissection
- Chemotherapy before and/or after surgery
- Radiation therapy after surgery
- Hormone therapy after surgery for tumors that are estrogen receptor positive or estrogen receptor unknown
- Clinical trials testing new anticancer drugs, new drug combinations, and new ways of giving treatment

Check the list of NCI-supported cancer clinical trials online that are now accepting patients with stage IIIB, IIIC, or IV breast cancer and inflammatory breast cancer. For more specific results, refine the search by using other search features, such as the location of the trial, the name of the drug, etc. Talk with your doctor about clinical trials. General information about clinical trials is available at www.cancer.gov/about-cancer/treatment/clinical-trials.

LOCOREGIONAL RECURRENT BREAST CANCER TREATMENT OPTIONS

Treatment of locoregional recurrent breast cancer (cancer that has come back after treatment in the breast, in the chest wall, or in nearby lymph nodes), may include:

- Chemotherapy
- Hormone therapy for tumors that are hormone receptor positive
- Radiation therapy
- Surgery

- Targeted therapy (trastuzumab)
- A clinical trial of a new treatment

Check the list of NCI-supported cancer clinical trials that are now accepting patients with recurrent breast cancer. Talk with your doctor about clinical trials that may be right for you.

METASTATIC BREAST CANCER TREATMENT OPTIONS

Treatment options for metastatic breast cancer may include the following:

Hormone Therapy

In postmenopausal women who have just been diagnosed with metastatic breast cancer that is hormone receptor positive or if the hormone receptor status is not known, treatment may include:

- Tamoxifen therapy
- Aromatase inhibitor therapy such as anastrozole, letrozole, or exemestane (sometimes cyclin-dependent kinase inhibitor therapy (palbociclib) is also given)

In premenopausal women who have just been diagnosed with metastatic breast cancer that is hormone receptor positive, treatment may include Tamoxifen, an LHRH agonist, or both.

In women whose tumors are hormone receptor positive or hormone receptor unknown, with spread to the bone or soft tissue only, and who have been treated with tamoxifen, treatment may include:

- Aromatase inhibitor therapy
- Other hormone therapy such as megestrol acetate, estrogen or androgen therapy, or anti-estrogen therapy such as fulvestrant

Targeted Therapy

In women with metastatic breast cancer that is hormone receptor positive and has not responded to other treatments, options may include targeted therapy such as:

- Trastuzumab, lapatinib, pertuzumab, or mTOR inhibitors
- Antibody-drug conjugate therapy with ado-trastuzumab emtansine
- Cyclin-dependent kinase inhibitor therapy (palbociclib) combined with letrozole

In women with metastatic breast cancer that is HER2/neu positive, treatment may include targeted therapy such as trastuzumab, pertuzumab, ado-trastuzumab emtansine, or lapatinib.

Chemotherapy

In women with metastatic breast cancer that is hormone receptor negative, has not responded to hormone therapy, has spread to other organs or has caused symptoms, treatment may include chemotherapy.

Surgery

Surgical treatment for metastatic breast cancer may include:

- Total mastectomy for women with open or painful breast lesions. Radiation therapy may be given after surgery.
- Surgery to remove cancer that has spread to the brain or spine. Radiation therapy may be given after surgery.
- Surgery to remove cancer that has spread to the lung.
- Surgery to repair or help support weak or broken bones. Radiation therapy may be given after surgery.
- Surgery to remove fluid that has collected around the lungs or heart.

Radiation Therapy

- Radiation therapy to the bones, brain, spinal cord, breast, or chest wall to relieve symptoms and improve quality of life.
- Strontium-89 (a radionuclide) to relieve pain from cancer that has spread to bones throughout the body.

Other treatment options

Other treatment options for metastatic breast cancer include the following:

- Drug therapy with bisphosphonates or denosumab to reduce bone disease and pain when cancer has spread to the bone
- A clinical trial of high-dose chemotherapy with stem cell transplant
- Clinical trials testing new anticancer drugs, new drug combinations, and new ways of giving treatment

Check the list of NCI-supported cancer clinical trials that are now accepting patients with metastatic cancer. For more specific results, refine the search by using other search features, such as the location of the trial, the type of treatment, or the name of the drug. Talk with your doctor about clinical trials that may be right for you. General information about clinical trials is available from the NCI website (www.cancer.gov/about-cancer/treatment/clinical-trials).

DUCTAL CARCINOMA IN SITU (DCIS) TREATMENT OPTIONS

Treatment of ductal carcinoma in situ may include:

- Breast-conserving surgery and radiation therapy, with or without tamoxifen.
- Total mastectomy with or without tamoxifen. Radiation therapy may also be given.

Check the list of NCI-supported cancer clinical trials that are now accepting patients with ductal breast carcinoma in situ.

For more information and related links visit: https://www.cancer.gov/types/breast/patient/breast-treatment-pdq#link/_515

Resource: PDQ® Adult Treatment Editorial Board. PDQ Breast Cancer Treatment. Bethesda, MD: National Cancer Institute. Updated <06/26/2017>. Available at: <https://www.cancer.gov/types/breast/patient/breast-treatment-pdq>. Accessed <06/23/2017>. [PMID: 26389406]

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