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GUIDELINES
FOR PATIENTS®

2024

Invasive Breast Cancer



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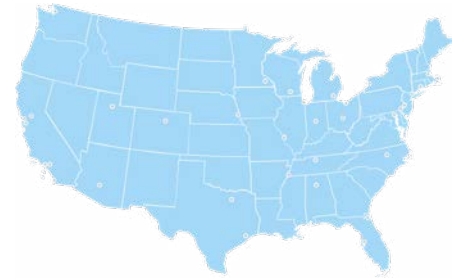
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About the NCCN Guidelines for Patients®



Did you know that top cancer centers across the United States work together to improve cancer care? This alliance of leading cancer centers is called the National Comprehensive Cancer Network® (NCCN®).



Cancer care is always changing. NCCN develops evidence-based cancer care recommendations used by health care providers worldwide. These frequently updated recommendations are the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). The NCCN Guidelines for Patients plainly explain these expert recommendations for people with cancer and caregivers.

These NCCN Guidelines for Patients are based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer, Version 1.2024 – January 25, 2024.

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NCCN Foundation seeks to support the millions of patients and their families affected by a cancer diagnosis by funding and distributing NCCN Guidelines for Patients. NCCN Foundation is also committed to advancing cancer treatment by funding the nation's promising doctors at the center of innovation in cancer research. For more details and the full library of patient and caregiver resources, visit [NCCN.org/patients](https://www.nccn.org/patients).

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Breast cancer basics

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Invasive breast cancer is cancer that has spread from the milk ducts or milk glands into the breast tissue or nearby lymph nodes.

Breast tissue contains glands that can make milk. These milk glands are called lobules. Lobules look like tiny clusters of grapes. Small tubes called ducts connect the lobules to the nipple.

The ring of darker breast skin is called the areola. The raised tip within the areola is called the nipple. The nipple-areola complex (NAC) is a term that refers to both parts.

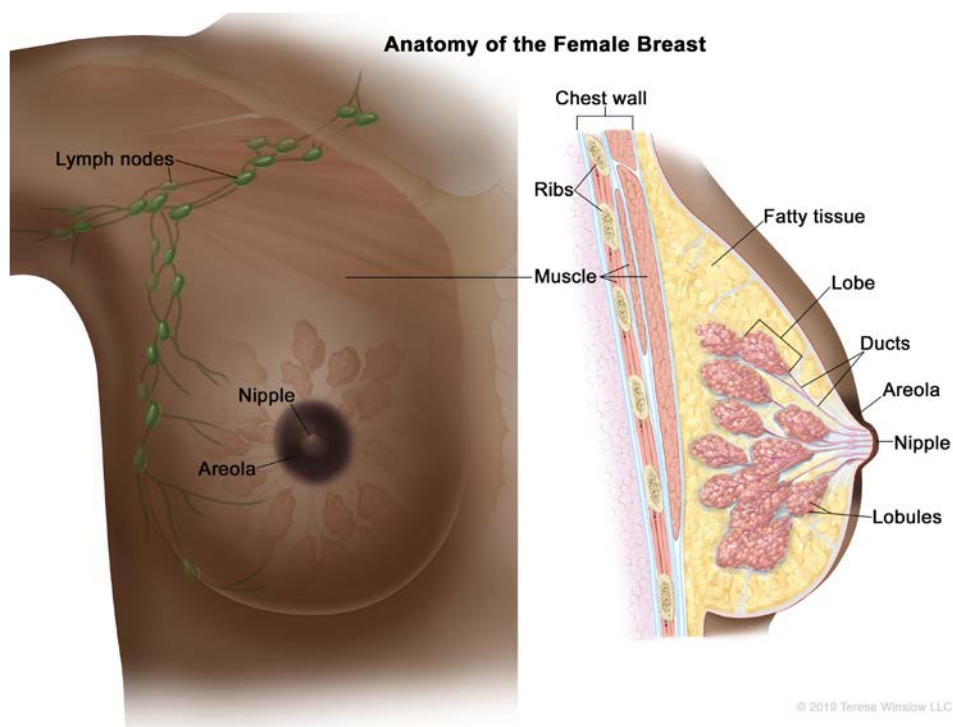
The breast

The breast is an organ and a gland found on the chest. The breast is made of milk ducts, fat, nerves, lymph and blood vessels, ligaments, and other connective tissue. Behind the breast is the pectoral (chest) muscle and ribs. Muscle and ligaments help hold the breast in place.

Lymph drains from breast tissue into lymph vessels and travels to lymph nodes near your armpit (axilla). Lymph is a clear fluid that gives cells water and food. It also helps to fight germs. Nodes near the armpit are called axillary lymph nodes (ALNs).

The breast

The breast is a glandular organ made up of milk ducts, fat, nerves, blood and lymph vessels, ligaments, and other connective tissue.



Breast cancer

Breast cancer starts in the cells of the breast. Almost all breast cancers are a subtype called carcinomas. Carcinomas are cancers that start in the cells that line the inner or outer surfaces of the body. There are different types of breast carcinoma, most of which arise in cells that make up the lining (epithelial cells) in the terminal duct lobular units (TDLUs) of the breast. The most common types are either ductal or lobular.

Anyone can develop breast cancer, including those assigned male at birth. Although there are some differences between those assigned male and those assigned female at birth, treatment is very similar for all genders.

How breast cancer spreads

Cancer cells don't behave like normal cells. Cancer cells differ from normal cells in the following ways.

Primary tumor

Over time, cancer cells form a mass called a primary tumor.

Invasive

Cancer cells can grow into surrounding tissues. Invasive breast cancer is breast cancer that has spread from the milk ducts or milk glands (lobules) into the surrounding breast tissue or nearby lymph nodes.

Metastasis

Unlike normal cells, cancer cells can spread and form tumors in other parts of the body called metastases. In this process, cancer cells break away from the first (primary) tumor and travel through blood or lymph vessels to distant sites. Once in other sites, cancer cells may form secondary tumors.

- Cancer that has spread to a nearby body part such as the axillary lymph nodes is called a local metastasis. It might be referred to as local/regional disease or locally advanced.
- Cancer that has spread to a body part far from the primary tumor is called a distant metastasis.

Breast cancer can metastasize almost anywhere but most commonly spreads to the bone (including spine), lungs, liver, brain, or distant lymph nodes. Breast cancer that has metastasized to other parts of the body is still called breast cancer.

More information on metastatic breast cancer is available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



Key points

- Anyone can develop breast cancer, but breast cancer occurs more frequently in persons assigned female at birth.
 - Inside breasts are lobules, ducts, fat, blood and lymph vessels, ligaments, and connective tissue. Lobules are structures that make breast milk. Ducts carry breast milk from the lobules to the nipple.
 - Breast cancer arises from epithelial cells (cells that make up the lining) in the terminal duct lobular units (TDLUs) of the breast.
 - Invasive breast cancer is cancer that has grown outside the ducts or lobules into surrounding tissue. Once outside the ducts or lobules, breast cancer can spread through lymph or blood to lymph nodes or other parts of the body.
- Metastatic breast cancer (MBC) has spread outside the breast and lymph nodes under the arm (axilla).

Anyone can develop breast cancer, including those assigned male at birth. Although there are some differences between those assigned male and those assigned female at birth, treatment is very similar for all genders.



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Testing for breast cancer

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Not all invasive breast cancers are the same. Treatment planning starts with testing. Your care team will want to gather information about the cancer you have. This chapter presents an overview of the tests you might receive and what to expect.

Testing takes time. It might take days or weeks for all test results to come in.

Test results

Results from biopsy and imaging studies will be used to determine your treatment plan. Treatment will be based on these findings. It is important you understand what these tests mean. Ask questions and keep copies of your test results.

Keep these things in mind:

- Choose a friend, family member, or peer who can drive you to appointments, provide meals, or offer emotional support during diagnosis and treatment.
- Bring someone with you to doctor visits, if possible.
- Write down questions and take notes during appointments. Don't be afraid to ask your care team questions. Get to know your care team and help them get to know you.
- Get copies of blood tests, imaging results, and reports about the specific type of cancer you have.

- Organize your papers. Create files for insurance forms, medical records, and test results. You can do the same on your computer.
- Keep a list of contact information for everyone on your care team. Add it to your phone. Hang the list on your refrigerator or keep it in a place where someone can access it in an emergency. Keep your primary care physician (PCP) informed of changes to this list. You are encouraged to keep your PCP in the loop. They are great partners in your care.
- In your contact list, include information on the exact type of cancer you have, as well as any treatments you've received and the date each treatment started.
- Set up a MyChart or health record account if it's available, which can help you keep track your appointments and communicate with your care team.

For possible tests, **see Guide 1.**

General health tests

Medical history

A medical history is a record of all health issues and treatments you have had in your life. Be prepared to list any illness or injury and when it happened. Bring a list of old and new medicines and any over-the-counter (OTC) medicines, herbals, or supplements you take. Some supplements interact and affect medicines that your care team may prescribe. Tell your care team about any symptoms you have. A medical history, sometimes called a health history, will help determine which treatment is best for you.

Family history

Some cancers and other diseases can run in families. Your care team will ask about the health history of family members who are blood relatives. This information is called a family history. Ask family members on both sides of your family about their health issues like heart disease, cancer, and diabetes, and at what age they were diagnosed. It's important to know the specific type of cancer, or where the cancer started, and if it is in multiple locations, and if they had genetic testing.

Guide 1 Possible tests

Medical history and physical exam

Diagnostic mammogram. Other imaging tests as needed

Biopsy with pathology review

Determine tumor status including:

- Estrogen receptor (ER) and progesterone receptor (PR) status
- HER2 status

Genetic counseling and testing if at risk for hereditary breast cancer, has triple-negative breast cancer (TNBC), or might receive olaparib

Address fertility and sexual health concerns

Pregnancy test in those of childbearing potential

Assess for distress

Physical exam

During a physical exam, your health care provider may:

- Check your temperature, blood pressure, pulse, and breathing rate
- Check your height and weight
- Listen to your lungs and heart
- Look in your eyes, ears, nose, and throat
- Feel and apply pressure to parts of your body to see if organs are of normal size, are soft or hard, or cause pain when touched.
- Examine your breasts to look for lumps, nipple discharge or bleeding, or skin changes.
- Feel for enlarged lymph nodes in your neck, underarm, and groin.

Clinical breast exam

Clinical breast exam (CBE) is a physical exam of the bare breast performed by a health care provider to check for lumps or other changes. It is done while you are seated and/or lying down. Your provider should take time to palpate (feel) the entire breast, including the armpit. A nurse or assistant might also be in the room during the exam.



Create a medical binder

A medical binder or notebook is a great way to organize all of your records in one place.

- ✓ Make copies of blood tests, imaging results, and reports about your specific type of cancer. It will be helpful when getting a second opinion.
- ✓ Choose a binder that meets your needs. Consider a zipper pocket to include a pen, small calendar, and insurance cards.
- ✓ Create folders for insurance forms, test types (blood, imaging, pathology, radiology, genetics), treatments, and procedures. Organize items in the folder by date.
- ✓ Use online patient portals to view your test results and other records. Download or print the records to add to your binder.
- ✓ Add a section for questions and to take notes.

Bring your medical binder to appointments. You never know when you might need it!

Fertility (all genders)

Treatment such as chemotherapy can affect your fertility, the ability to have children. If you think you want children in the future, ask your care team how cancer and cancer treatment might change your fertility. To preserve your fertility, you may need to take action before starting cancer treatment. Those who want to have children in the future should be referred to a fertility specialist to discuss the options before starting treatment.

Fertility preservation is all about keeping your options open, whether you know you want to have children later in life or aren't sure at the moment. Fertility and reproductive specialists can help you sort through what may be best for your situation.

More information on fertility preservation in adolescents and young adults, is available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



Changes in fertility

Treatment might cause your fertility to be temporarily or permanently impaired or interrupted. This loss of fertility is related to your age at time of diagnosis, treatment type(s), treatment dose, and treatment length. Talk to your care team about your concerns and if you are planning a pregnancy.

Preventing pregnancy during treatment

Cancer and cancer treatment can affect the ovaries and damage sperm. If you become pregnant during chemotherapy, radiation therapy, or other types of systemic therapy, serious birth defects can occur. Speak with your care team about preventing pregnancy while being treated for cancer. Hormonal birth control may or may not be recommended, so ask your doctor about options such as intrauterine devices (IUDs) and barrier methods. Types of barrier methods include condoms, diaphragms, cervical caps, and the contraceptive sponge.

Those with ovaries

Those who can become pregnant will have a pregnancy test before starting treatment. Cancer treatment can hurt the developing baby if you are or become pregnant during treatment. Therefore, birth control to prevent pregnancy during and after treatment is recommended. If you are pregnant or breastfeeding at the time of your cancer diagnosis, certain treatments will need to be avoided.

Menstruation, menses, menstrual flow, or your period may stop during treatment, but often returns within 2 years after treatment in those 35 years of age and under. It is still possible to become pregnant even though you might not have a period. Therefore, birth control is recommended during and after treatment. It is important to talk to your doctor about what methods of birth control are safe after a breast cancer diagnosis. Consult your doctor for the best time to plan a pregnancy.

Those with testicles

Cancer and cancer treatment can damage sperm. Therefore, use contraception (birth control) such as condoms to prevent pregnancy during and immediately after cancer treatment.

Blood tests

Blood tests check for signs of disease and how well organs are working. They require a sample of your blood, which is removed through a needle placed into your vein.

Alkaline phosphatase

Alkaline phosphatase (ALP) is an enzyme found in the blood. High levels of ALP can be a sign cancer has spread to the bone or liver. A bone scan might be performed if you have high levels of ALP.

Complete blood count

A complete blood count (CBC) measures the levels of red blood cells (RBCs), white blood cells (WBCs), and platelets (PLTs) in your blood. Red blood cells carry oxygen throughout your body, white blood cells fight infection, and platelets control bleeding.

Comprehensive metabolic panel

A comprehensive metabolic panel (CMP) measures 14 different substances in your blood. It is usually done on the plasma part of your blood. A CMP provides important information about how well your kidneys and liver are working, among other things.

Liver function tests

Liver function tests (LFTs) look at the health of your liver by measuring chemicals that are made or processed by the liver. Levels that are too high or low signal that the liver is not working well or that cancer has spread to the liver. It is common to see a mild increase in LFTs during chemotherapy.

Pregnancy test

Those who can become pregnant will be given a pregnancy test before treatment begins.

Imaging tests

Imaging tests take pictures of the inside of your body. Imaging tests show the primary tumor, or where the cancer started, and look for cancer in other parts of the body.

A radiologist, an expert in interpreting imaging tests, will write a report and send this report to your health care provider (HCP). It is likely that the report will be sent directly to you through your patient portal or patient access system. You should discuss these results with your HCP.

The following imaging tests are listed in alphabetical order and not in order of importance. You will not have all these tests.

Bone scan

A bone scan uses a radiotracer. A radiotracer is a substance that releases small amounts of radiation. Before the pictures are taken, the tracer will be injected into your vein. It can take a few hours for the tracer to enter your bones. However, the test is quick and painless.

A special camera will take pictures of the tracer in your bones as it moves over your body. Areas of bone damage take up more radiotracer than healthy bone and show up as bright spots on the pictures. Bone damage can be caused by cancer, cancer treatment, previous injuries, or other health issues.

Bone x-ray

An x-ray uses low-dose radiation to take one picture at a time. A tumor changes the way radiation is absorbed and will show up on the x-ray. X-rays are also good at showing bone

issues. Your care team may order x-rays if your bones hurt or were abnormal on a bone scan.

Contrast material

Contrast materials are not dyes, but substances that help make the pictures of the inside of the body clearer. The contrast is not permanent and will leave the body in your urine after the test. There is more than one type of contrast and it differs depending on the test. Tell your care team if you have had allergic reactions to contrast in the past. This is important. You might be given medicines to avoid the effects of those allergies.

CT scan

A computed tomography (CT or CAT) scan uses x-rays and computer technology to take pictures of the inside of the body. It takes many x-rays of the same body part from different angles. All the images are combined to make one detailed picture. A CT scan of your chest, abdomen, and/or pelvis might be one of the tests used to look for cancer. Intravenous (IV) contrast is often used.

Diagnostic mammogram

A mammogram is a picture of the inside of your breast. The picture is made using x-rays. A computer combines the x-rays to make detailed pictures. Mammogram results are used to plan treatment.

Diagnostic mammograms look at specific areas of your breasts, which may not be clearly seen on screening mammograms. It is used to see tumor and the size of the tumor(s). Diagnostic mammograms include extra compression in certain areas of the breast,

magnification views, or rolling the breast to image additional areas of the breast. Other diagnostic tests may include a breast MRI or ultrasound.

MRI scan

A magnetic resonance imaging (MRI) scan uses radio waves and powerful magnets to take pictures of the inside of the body. It does not use x-rays. Because of the very strong magnets used in the MRI machine, tell the technologist if you have any metal in your body. During the test, you will likely be asked to hold your breath for 10 to 20 seconds as the technician collects the images. Contrast is often used.

A closed MRI has a capsule-like design where the magnet surrounds you. An open MRI has a magnetic top and bottom, which allows for an opening on each end. Closed MRIs are more common than open MRIs, so if you have claustrophobia (a dread or fear of enclosed spaces), be sure to talk to your care team about it.

- **A breast MRI** might be used in addition to a mammogram. Contrast should be used. You will be positioned face down in the machine with your arms above your head.
- **A spine or brain MRI** can be used to detect breast cancer that has spread (metastasize) to your spine or brain. For a brain MRI, a device is placed around your head. For a spine MRI, no device is worn. Contrast should be used in an MRI.

What's the difference between a screening and diagnostic mammogram?

A mammogram is a picture of the inside of your breast made using x-rays. During a mammogram, the breast is pressed between two plates while you stand in different positions. Multiple x-rays will be taken. A computer combines the x-rays to make detailed pictures.

- **Screening mammograms** are done on a regular basis when there are no signs or symptoms of breast cancer. Results take a few days.
- **Diagnostic mammograms** are used for those who have symptoms such as a lump, pain, nipple thickening or discharge, or whose breasts have changed shape or size.
- **Diagnostic mammograms** are also used to take a closer look at an abnormal area found in a screening mammogram.
- A radiologist will evaluate the **diagnostic mammogram** while you wait so if additional testing is needed, it can be done right away.

Both types of mammograms use low-dose x-rays to examine the breast. They may use either the standard 2-dimensional (2D) digital mammogram or 3-dimensional (3D) mammogram known as tomosynthesis.

PET scan

A positron emission tomography (PET) scan uses a radioactive drug called a tracer. A tracer is a substance injected into a vein to see where cancer cells are in the body and if they are using sugar produced by your body to grow. Cancer cells show up as bright spots on PET scans. However, not all tumors will appear on a PET scan. Also, not all bright spots are cancer. It is normal for the brain, heart, kidneys, and bladder to be bright on PET. Inflammation or infection can also show up as a bright spot. When a PET scan is combined with CT, it is called a PET/CT scan.

- **An FDG PET/CT** uses a radiotracer called F-18 fluorodeoxyglucose (FDG). It is made of fluoride and a simple form of sugar called glucose. You cannot eat or drink for at least 4 hours before the scan. This scan is most helpful when other imaging results are unclear. It may help find cancer in lymph nodes and distant sites. If it clearly shows cancer in the bone, a bone scan and sodium fluoride PET/CT may not be needed. FDG-PET/CT can be done at the same time as a CT used for diagnosis.
- **A FES-PET/CT** might be used instead of FDG-PET/CT when cancer is estrogen receptor-positive (ER+). FES is a radioactive form of the hormone estrogen.
- **A sodium fluoride PET/CT** might be used instead of a bone scan. In this test, the radiotracer is made of sodium fluoride.

Ultrasound

An ultrasound (US) uses high-energy sound waves to form pictures of the inside of the body. This is similar to the sonogram used for pregnancy. A wand-like probe (transducer) will be held and moved on your bare breast using gel. It may also be placed below your armpit. Ultrasound does not use x-rays. It is good at showing small areas of cancer that are near the skin. Sometimes, a breast ultrasound or MRI is used to guide a biopsy.

Biopsy

A biopsy is a procedure that removes a sample of tissue or fluid. The sample is sent to a lab for testing. A pathologist will examine the biopsy for cancer and write a report called a pathology report. Ask questions about your biopsy results and what it means for your treatment.

There are different types of biopsies. Some biopsies are guided using imaging, such as mammogram, ultrasound, or MRI. The primary or main tumor is biopsied first. Other tumors or tumors in different areas may also be biopsied. You may have tissue removed from the breast, lymph nodes, or both.

Types of possible biopsies include:

- **Fine-needle aspiration (FNA) or core biopsy (CB)** uses needles of different sizes to remove a sample of tissue or fluid. In a **vacuum-assisted core biopsy (VACB)**, suction is used to remove the sample with a special vacuum device.

- **Incisional biopsy** removes a small amount of tissue through a small cut in the skin or body.
- **Excisional biopsy** removes the entire abnormal area. This is not the preferred type of biopsy but may be necessary if other methods are not possible or when the biopsy results don't match the expected findings.

Before biopsies are performed, usually the area is injected with numbing medicine. A core needle biopsy (CNB) removes more than one tissue sample, but usually through the same area on the breast. The samples are small. The needle is often guided into the tumor with imaging. When mammography is used during a biopsy, it is called a stereotactic needle biopsy.

One or more clips may be placed near the breast tumor during a biopsy. The clips are small, painless, and made of metal. They will mark the site for future treatment and imaging. The clips stay in place until surgery. If the area biopsied is benign, the clip will remain in place to mark the biopsy site on future imaging. The clips cause no problems, even if they are left in place for a long time. You will be able to go through airport security and have an MRI with the clip(s) in place.

There are both physical and emotional experiences in having biopsies. You may need to rest and place an ice pack on the biopsy area after the procedure. If you are working or have other commitments, you may want to take the day off to rest.

Axillary lymph node needle biopsy

An axillary lymph node (ALN) drains lymph fluid from the breast and nearby areas. In an axillary lymph node biopsy, a sample of lymph node near the armpit (axilla) is biopsied with a needle. This is to determine if abnormal lymph nodes seen on imaging tests contain cancer cells. An ultrasound-guided fine-needle aspiration (US-FNA) or core biopsy will be used. If cancer is found, it is called node positive (node+). A marker may be placed in the node so that it can be identified later if needed.

Biopsy results

Histology is the study of the anatomy (structure) of cells, tissues, and organs under a microscope. It is used to make treatment decisions. Your pathology report will contain information about histology.

You may be recommended to have an open biopsy (surgery) to remove (excise) the tumor to confirm histology. Talk to your health care provider for more information on next steps.

Hormone receptor status

Your blood carries hormones throughout your body. A hormone is a substance made by a gland in your body. A receptor is a protein found inside or on the surface of a cell. When hormones attach (bind) to specific receptors, it causes changes within the cell.

When hormones attach to receptors inside breast cancer cells, they can cause cancer to grow. If found, these receptors may be targeted using endocrine therapy.

There are 2 types of hormone receptors:

- **Estrogen** – plays a role in breast development
- **Progesterone** – plays a role in menstrual cycle and pregnancy

Hormone receptor (HR) testing should be done on any new tumors. A biopsy sample will be used.

Immunohistochemistry

Immunohistochemistry (IHC) is a special staining process that involves adding a chemical marker to cells. These cells are then studied using a microscope. IHC can find estrogen, progesterone, and HER2 receptors in breast cancer cells. A pathologist will measure how many cells have estrogen and/or progesterone receptors and the number of receptors inside each cell.

Hormone receptor-positive

In hormone receptor-positive (HR+) breast cancer, IHC finds estrogen and/or progesterone hormone receptors. Most breast cancers are HR+.

- **Estrogen receptor (ER)** is stimulated by estrogen and provides survival and proliferation (rapid growth) signals. Cancer cells deprived of estrogen or that have their ER signal blocked with treatment may stop growing or die.
- **Progesterone receptor (PR)** binds progesterone and provides survival and proliferation signals. It is thought that PR expression also suggests the tumor is estrogen dependent.

HR+ breast cancer is treated with endocrine therapy, which blocks estrogen receptor signaling or decreases estrogen production.

Estrogen receptor-positive (ER+) breast cancer cells

- In ER+ breast cancer, testing finds estrogen hormone receptors in at least 1 out of every 100 cancer cells.
- In ER-low–positive invasive breast cancer, testing finds estrogen hormone receptors in 1 to 10 out of every 100 cancer cells.
- Endocrine therapy might not be recommended for ER-low–positive invasive breast cancer.

Hormone receptor-negative

Hormone receptor-negative (HR-) breast cancer cells do not have either estrogen or progesterone hormone receptors. These cancers are sometimes simply called hormone negative. HR- cancers often grow faster than HR+ cancers. Both the estrogen and progesterone receptors need to be negative for breast cancer to be considered HR-.

HER2 status

Human epidermal growth factor receptor 2 (HER2) is a protein involved in normal cell growth. It is found on the surface of all cells. When amounts are high, it causes cells to grow and divide. Some breast cancers have too many HER2 genes or receptors. Too many HER2s is called HER2-positive (HER2+). You might hear it called HER2 overexpression or amplification.

There are 2 tests for HER2:

- **Immunohistochemistry (IHC)** measures receptors. If the IHC score is 3+, the cancer is HER2+. If the score is 0 or 1, it is considered HER2-. If the score is 2+, further testing is needed.
- **In situ hybridization (ISH)** counts the number of copies of the *HER2* gene. This test is done mainly when the IHC score is unclear.

HER2 testing should be done on all new tumors. A tumor biopsy sample will be used. You might have more than one HER2 test.

Treatment options by cell receptor type

There are many treatments for invasive breast cancer. Which ones are right for you are based on many factors. Two important factors are the hormone receptor (HR) and HER2 status of any tumors.

- Hormone receptors include estrogen and progesterone. A tumor is considered hormone receptor-positive (HR+) if an increased number of estrogen receptors, progesterone receptors, or both are found.
- HER2 is a protein involved in normal cell growth. There might be higher amounts of HER2 in your breast cancer. If this is the case, it is called HER2-positive (HER2+) breast cancer.

Endocrine therapy stops cancer growth caused by hormones. It is a standard treatment for hormone receptor-positive (HR+) cancers. HR+ cancer can be estrogen receptor-positive (ER+) and/or progesterone receptor-positive (PR+).

HER2-targeted therapy is a standard treatment for HER2+ cancers.

Chemotherapy is often the first treatment for hormone receptor-negative (HR-) cancers.

Biomarker testing

A sample from a biopsy of your tumor may be tested to look for specific DNA (deoxyribonucleic acid) mutations/alterations, protein levels, or other molecular features. This information is used to choose the best treatment for you. It is sometimes called molecular testing or tumor profiling, tumor sequencing, gene expression profiling, or genomic testing.

Biomarker testing includes tests of genes or their products (proteins). It identifies the presence or absence of mutations and certain proteins that might suggest treatment. Proteins are written like this: BRCA. Genes are written with italics like this: *BRCA*. HER2 and hormone receptor status are part of biomarker testing. Your treatment team will recommend the best types of biomarker testing that are important for you.

Biomarker testing or mutation testing is more commonly done in metastatic breast cancer.

Tumor mutation testing

A sample of your tumor or blood may be used to see if the cancer cells have any specific DNA mutations. This is a different type of DNA testing than the genetic testing for mutations you may have inherited from your biological parents. In tumor mutation testing, only the tumor is tested and not the rest of your body. Certain mutations such as *PIK3CA* can be targeted with specific therapies.

Tumor markers

Your blood or biopsy tissue may be tested for proteins. These proteins are called tumor markers. Knowing this information can help plan treatment. Examples of some tumor markers in breast cancer include carcinoembryonic antigen (CEA), CA 15-3, and CA 27.29. An increase in the level of certain tumor markers could mean that the cancer has grown or spread (progressed). However, not everyone has elevated levels of these markers and tumor markers alone are not a reliable method of detecting breast cancer. Therefore, they are not routinely checked and depend on your individual situation.

Genetic cancer risk testing

About 1 out of 10 breast cancers are hereditary. Depending on your family history or other features of your cancer, your health care provider might refer you for hereditary genetic testing to learn more about your cancer. A genetic counselor or trained provider will speak to you about the results. Test results may be used to guide treatment planning.

Genetic testing is done using blood or saliva (spitting into a cup or a cheek swab). The goal is to look for gene mutations inherited from your biological parents called germline mutations. Some mutations can put you at risk for more than one type of cancer. You can pass these genes on to your children. Also, other blood relatives might carry these mutations. Tell your care team if there is a family history of cancer.

BRCA tests

Everyone has *BRCA* genes. Normal *BRCA* genes help to prevent tumor growth. They help fix damaged cells and help cells grow normally. *BRCA* mutations put you at risk for more than one type of cancer. Mutations in *BRCA1* or *BRCA2* increase the risk of breast, ovarian, prostate, pancreatic, and melanoma skin cancers. Mutated *BRCA* genes can also affect how well some treatments work. These tests might be repeated.

What is your family health history?

Some cancers and other diseases run in families—those who are related to you through genes passed down from biological parent to child. This information is called a family health history. Ask blood relatives about their health issues like heart disease, cancer, and diabetes, and at what age they were diagnosed. For relatives who were diagnosed with cancer, ask them (or other relatives if they are no longer living) what type of cancer they had, if they died from the cancer, and at what age the cancer was diagnosed.

Start by asking your parents, siblings, and children. Next, talk to half-siblings, aunts and uncles, nieces and nephews, grandparents, and grandchildren.

Write down what you learn about your family history and share with your health care provider.

Some of the questions to ask include:

- ✓ How old were you when each of these diseases and health conditions was diagnosed?
- ✓ What is our family's ancestry—from what countries did our ancestors originate?

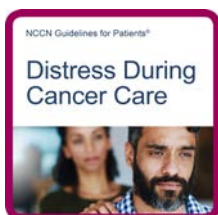
Distress screening

It is normal to have strong feelings about being diagnosed with cancer and your feelings can also change from day to day and week to week. Talk to your care team and those whom you feel most comfortable about how you are feeling. There are services and people who can help you. Support and counseling are available. Many treatment teams include mind and body therapists who can help.

Dealing with a cancer diagnosis can be stressful and may cause further distress. Distress is an unpleasant experience of a mental, physical, social, or spiritual nature. It can affect how you feel, think, and act. Distress might include feelings of sadness, fear, helplessness, worry, anger, and guilt. You may also experience depression, anxiety, and sleep issues. Your treatment team will screen your level of distress. This is part of your cancer care.

Your diagnosis of cancer may affect your family or loved ones. They may feel some degree of anxiety or depression. They can talk to the social worker and seek help, too.

More information on distress is available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



Performance status

Performance status (PS) is a person's general level of fitness and ability to perform daily tasks. Your state of general health will be rated using a PS scale called Eastern Cooperative Oncology Group (ECOG). PS is one factor taken into consideration when choosing a treatment plan. Your preferences about treatment are always important.

The ECOG PS scores range from 0 to 5.

- **PS 0** means the person is fully active.
- **PS 1** means the person is still able to perform light to moderate activity, but with some limitations.
- **PS 2** means the person is limited to the chair or bed less than half of the time and still able to care for self.
- **PS 3** means the person is limited to the chair or bed more than half of the time.
- **PS 4** means the person is totally confined to the bed or chair and completely disabled.
- **PS 5** means the person is not alive.

Good PS is usually PS 0 or PS 1.

Key points

- Tests are used to find cancer, plan treatment, and check how well treatment is working.
- You will have a physical exam, including a breast exam, to see if anything feels or looks abnormal.
- Treatment can affect your fertility, the ability to have children.
- A diagnostic bilateral mammogram includes detailed pictures of both breasts. It is different than a screening mammogram.
- During a biopsy, tissue or fluid samples are removed for testing. Samples are needed to confirm the presence of cancer and to perform cancer cell tests.
- A sample from a biopsy of your tumor will be tested for estrogen receptor (ER) status, progesterone receptor (PR) status, HER2 status, and grade (histology). This provides information about the behavior of your cancer, as well as treatments to which your cancer may respond.
- About 1 out of 10 breast cancers are hereditary. Depending on your family history or other features of your cancer, you might be referred for genetic testing, to speak with a genetic counselor, and possibly to have genetic testing.



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3

Breast cancer staging

- 25 How breast cancer is staged
- 27 TNM scores
- 29 Numbered stages
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Cancer staging is used to reflect prognosis and to guide treatment decisions. It describes the size and location of the tumor and if cancer has spread to lymph nodes, organs, or other parts of the body. It also takes into account hormone receptor (HR) and HER2 status.

How breast cancer is staged

A cancer stage is a way to describe the extent of the cancer at the time you are first diagnosed. The American Joint Committee on Cancer (AJCC) created a staging system to determine how much cancer is in your body, where it is located, and what subtype you have. This is called staging.

Based on testing, your cancer will be assigned a stage. Staging helps to predict prognosis and is needed to make treatment decisions. A prognosis is the course your cancer will likely take. AJCC is just one type of staging system.

Information gathered during staging:

- **The extent (size) of the tumor (T):** How large is the cancer? Has it grown into nearby areas?
- **The spread to nearby lymph nodes (N):** Has the cancer spread to nearby lymph nodes? If so, how many? Where?
- **The spread (metastasis) to distant sites (M):** Has the cancer spread to distant organs such as the lungs or liver?
- **Estrogen receptor (ER) status:** Does the cancer have the protein called an estrogen receptor?
- **Progesterone receptor (PR) status:** Does the cancer have the protein called a progesterone receptor?
- **Human epidermal growth factor receptor 2 (HER2) status:** Does the cancer make too much of a protein called HER2?
- **Grade of the cancer (G):** How much do the cancer cells look like normal cells?
- **Biomarker testing:** Does the cancer have any genes, proteins, markers, or mutations that might suggest treatment?

Staging is based on a combination of information to reach a final numbered stage. It takes into account what can be felt during a physical exam, what can be seen on imaging tests, and what is found during a biopsy or surgery. Often, not all information is available at the initial evaluation. More information can be gathered as treatment begins.

Staging includes:

- **Anatomic** – based on the extent of cancer as defined by tumor size (T), lymph node status (N), and distant metastasis (M).
- **Prognostic** – includes anatomic TNM plus tumor grade and the status of the biomarkers such as human epidermal growth factor receptor 2 (HER2), estrogen receptor (ER), and progesterone receptor (PR). Prognostic stage also includes the assumption that you are treated with the standard of care approaches.

Prognostic stages are divided into clinical and pathologic. Pathologic stage applies to those who have undergone surgery as the initial treatment for breast cancer. Breast cancer staging is often done twice, before and after surgery. Staging after surgery provides more

specific and accurate details about the size of the cancer and lymph node status.

Clinical stage

Clinical stage (c) is the rating given before any treatment. It is based on a physical exam, biopsy, and imaging tests. An example might look like cT1 or cN2. In breast cancer, the clinical stage is based on imaging and biopsy results. These tests are done before any treatment as part of an initial diagnosis.

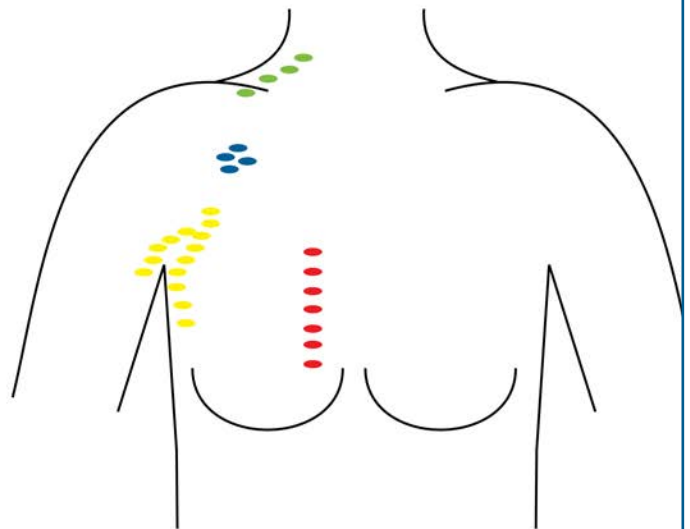
Pathologic stage

Pathologic stage (p) or surgical stage is determined by examining tissue removed during surgery. An example might be pN2. If you are given drug therapy before surgery, then the stage might add a y and look like ypT3.

Clinical staging

Clinical staging of lymph nodes is staging before surgery.

- Cancer is in axillary nodes
- Cancer is in internal mammary nodes
- Cancer is in infraclavicular nodes
- Cancer is in supraclavicular nodes



TNM scores

The tumor, node, metastasis (TNM) system is used to stage breast cancer. In this system, the letters T, N, and M describe different areas of cancer growth. Based on cancer test results, a score or number is assigned to each letter. The higher the number, the larger the tumor or the more the cancer has spread. These scores will be combined to assign the cancer a stage. A TNM example might look like this: T2N1M0 or T2, N1, M0.

- **T (tumor)** – Depth and spread of the main (primary) tumor(s) in one or both breasts
- **N (node)** – If cancer has spread to nearby (regional) lymph nodes
- **M (metastasis)** – If cancer has spread to distant parts of the body or metastasized

T = Tumor

The primary tumor size can be measured in centimeters (cm) or millimeters (mm). One inch is equal to 2.54 cm. A large pea is 1 cm (10 mm). A golf ball is 4 cm (40 mm). A tumor micrometastasis is a very small collection of cancerous cells smaller than 1 mm. It might be written as T1mi. Ipsilateral means on the same side of the body.

- **T1** Tumor is 2 cm (20 mm) or less
 - **T1mi** Tumor is micrometastasis of 1 mm or less
 - **T1a** Tumor is 1.1 mm to 5 mm
 - **T1b** Tumor is 5.1 mm to 10 mm
 - **T1c** Tumor is 10.1 mm to 20 mm
 - **T2** Tumor is 2.1 cm to 5 cm
- **T3** Tumor is more than 5 cm
- **T4** Tumor is of any size and has invaded nearby structures such as the chest wall and skin of the breast
- **T4d** Tumor is inflammatory carcinoma (inflammatory breast cancer)

More information on inflammatory breast cancer is available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



N = Regional lymph node

Lymph, a clear fluid containing cells that help fight infections and other diseases, drains through channels into lymphatic vessels. From here, lymph drains into lymph nodes. Lymph nodes work as filters to help fight infection.

Regional lymph nodes are those located near the breast in the armpit (axilla). If breast cancer spreads, it often goes first to nearby lymph nodes under the arm. It can also sometimes spread to lymph nodes near the collarbone or near the breastbone. However, it is possible for cancerous cells to travel through lymph and blood to other parts of the body without having gone to the lymph nodes first. Knowing if the cancer has spread to your lymph nodes helps doctors find the best way to treat your cancer.

- **N0** means no cancer is in the regional lymph nodes. Isolated tumor cells (ITCs) may be present. These are malignant cell clusters no larger than 0.2 mm.
- **N1mi** means micrometastases (approximately 200 cells, larger than 0.2 mm, but not larger than 2.0 mm) are found in lymph nodes.
- **N1, N2, N3** means regional lymph node metastases are found. The higher the number, the more lymph nodes that have metastases.

M = Metastasis

Cancer that has spread to distant parts of the body is shown as M1. This is metastatic breast cancer (MBC). The most common sites for metastasis are bone and lung.

- **M0** means no evidence of distant metastasis.
- **M1** means distant metastasis is found. This is metastatic breast cancer.

Grade

Grade describes how abnormal the tumor cells look under a microscope (called histology). Higher-grade cancers tend to grow and spread faster than lower-grade cancers. GX means the grade can't be determined, followed by G1, G2, and G3. G3 is the highest grade for breast cancers.

- **GX** – Grade cannot be determined
- **G1** – Low
- **G2** – Intermediate
- **G3** – High

Numbered stages

Numbered stages are based on TNM scores and receptor (hormone and HER2) status. Stages range from stage 0 to stage 4, with 4 being the most advanced. They might be written as stage 0, stage I, stage II, stage III, and stage IV.

- **Stage 0 is noninvasive** – Noninvasive breast cancer is rated stage 0. Ductal carcinoma in situ (DCIS) is found only in the ducts (Tis). It has not spread to the surrounding breast tissue, lymph nodes (N0), or distant sites (M0).
- **Stages 1, 2, and 3 are invasive** – Invasive breast cancer is rated stage 1, 2, or 3. It has grown outside the ducts, lobules, or breast skin. Cancer might be in the axillary lymph nodes.
- **Stage 4 is metastatic** – In stage 4 breast cancer, cancer has spread to distant sites. It can develop from earlier stages. Sometimes, the first diagnosis is stage 4 metastatic breast cancer (called *de novo*).

Key points

- Staging helps to predict prognosis and is needed to make treatment decisions. A prognosis is the course your cancer will likely take.
- The tumor, node, metastasis (TNM) system is used to stage breast cancer.
- Breast cancer is often staged twice, before and after surgery.
- Clinical stage (c) is the rating given before any treatment. It is written as cTNM.
- Pathologic stage (p) or surgical stage is determined by examining tissue removed during surgery. It is written as pTNM.
- Grade describes how abnormal the tumor cells look under a microscope (called histology).
- Regional lymph nodes are found near the breast.

4

Treating breast cancer

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There is more than one treatment for breast cancer. This chapter describes treatment options and what to expect. Together, you and your care team will choose a treatment plan that is best for you.

Care team

Treating breast cancer takes a team approach. Treatment decisions should involve a multidisciplinary team (MDT).

An MDT is a team of health care and psychosocial care professionals from different professional backgrounds who have knowledge (expertise) and experience in your type of cancer. This team is united in planning and implementing your treatment. Ask who will coordinate your care.

Some members of your care team will be with you throughout cancer treatment, while others will only be there for parts of it. Get to know your care team and help them get to know you.

Depending on your diagnosis, the care team might include the following specialists:

- **Oncologists** specialize in diagnosing and treating cancer. Types of oncologists include medical, radiation, and surgical oncologists.
- **Reconstructive (plastic) surgeon** performs oncoplastic (breast cancer

surgery) reductions, balancing procedures, and breast reconstruction.

- **Oncology nurses** provide your hands-on care, like giving systemic therapy, managing your care, answering questions, and helping you cope with side effects.
- **Oncology pharmacists** are experts in knowing how to use medicines to treat cancer and to manage symptoms and side effects.
- **Palliative care specialists** concentrate on preventing and alleviating suffering and improving quality of life.
- **Nutritionists and dietitians** can provide guidance on what foods are most suitable for your condition.
- **Occupational therapist** helps people with the tasks of daily living.
- **Physical therapist** helps people move with greater comfort and ease.
- **Certified lymphedema therapist** gives a type of massage called manual lymph drainage.
- **Psychologists and psychiatrists** are mental health experts who can help manage issues such as depression, anxiety, or other mental health conditions that can affect how you think and feel.
- **Social workers** help people solve and cope with problems in their everyday lives. Clinical social workers also diagnose and treat mental, behavioral, and emotional issues. The anxiety a person feels when diagnosed with cancer might be managed by a social worker in some cancer centers. They, or other designated professionals, can help

navigate the complexities of financial and insurance stresses.

- **Spiritual care specialists** identify and support those with spiritual distress or unmet spiritual needs.
- **Smoking cessation specialists** can provide medication and counseling for those who would like to stop using tobacco or nicotine products.
- **Research team** helps to collect research data and coordinate care if you are in a clinical trial. Clinical trials help bring new therapies to patients and advance the treatment for everyone. Consider asking your care team about access to clinical trials.



You know your body better than anyone

Help your care team understand:

- ✓ How you feel
- ✓ What you need
- ✓ What is working and what is not

Keep a list of names and contact information for each member of your team. This will make it easier for you and anyone involved in your care to know whom to contact with questions or concerns.

Get to know your care team and help them get to know you.

Treatment overview

Invasive breast cancer is treatable. Treatment can be local, systemic, or usually a combination of both.

Local therapy focuses on the breast, chest wall, and lymph node area. It includes:

- Surgery (lumpectomy, mastectomy, and lymph node surgery)
- Radiation therapy

Systemic therapy works throughout the body. It includes:

- Chemotherapy
- HER2-targeted therapy
- Inhibitors or other targeted therapies
- Immunotherapy
- Endocrine therapy

Surgery

Surgery is an operation or procedure to remove cancer from the body. Surgery is the main or primary treatment for invasive breast cancer. This is only one part of a treatment plan. When preparing for surgery, seek the opinion of an experienced surgeon. The surgeon should be an expert in performing your type of surgery. Hospitals that perform many surgeries often have better results. You can ask for a referral to a hospital or cancer center that has experience in treating your type of cancer.

Systemic (drug) therapy might be used before surgery to shrink the tumor or reduce the amount of cancer (called cancer burden).

- **Preoperative or neoadjuvant therapy** is systemic treatment before surgery.
- **Postoperative or adjuvant therapy** is systemic treatment after surgery.

Goal of surgery

The goal of surgery or tumor resection is to remove all the cancer. To do so, the tumor is removed along with a rim of normal-looking tissue around its edge called the surgical margin.

The surgical margin may look normal during surgery, but cancerous cells may be found when viewed under a microscope by a pathologist. In a clear or negative margin (R0), no cancer cells are found in the tissue around the edge of the tumor. In a positive margin, cancer cells are found in normal-looking tissue around the tumor.

After surgery, you may receive treatment such as radiation to kill any remaining cancer cells. You might have a wound drain to prevent fluid from collecting in the body after surgery. These drains are usually removed a few days after surgery.

Lumpectomy

Lumpectomy is the removal of abnormal cells or tumor. It does not remove the whole breast. A lumpectomy is also called breast-conserving therapy or breast-conserving surgery (BCS). In a lumpectomy, the surgeon aims to remove the tumor with a small rim of healthy tissue around it, called a negative, or clear surgical margin. Having a negative surgical margin will decrease the chance that cancer may return in that area of the breast. You may need more than one surgery to achieve negative margins and ensure all the cancer was removed. A lumpectomy is usually followed by radiation therapy to part of or the whole breast.

The breast might not look the same after a lumpectomy. Speak to your surgeon about how a lumpectomy might affect the look and shape

of your breast, and any concerns you have. You can also seek the opinion of a plastic (reconstructive) surgeon.

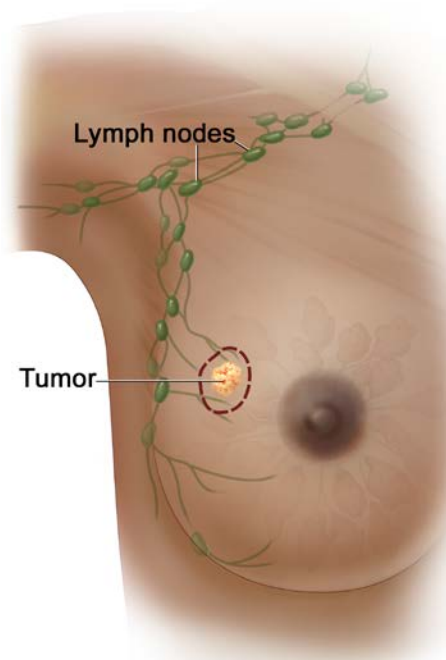
Breastfeeding or chestfeeding

Breastfeeding or chestfeeding following a lumpectomy may be possible. However, after treatments, the breast may produce less milk than before, or none. Breastfeeding/chestfeeding is not recommended during active treatment or within 6 months of completing certain types of endocrine therapy.

Breast-conserving surgery

The dotted line shows where the tumor is removed. Lumpectomy is the removal of abnormal cells or tumor and not the whole breast. It is also called a partial mastectomy, breast-conserving therapy, or breast-conserving surgery (BCS).

Breast-conserving Surgery



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Mastectomy

A mastectomy is surgery to remove all of the breast. Underarm sentinel lymph nodes might be removed. Before removing the breast, the surgeon may do a sentinel lymph node biopsy (SLNB). Sentinel lymph nodes are the first lymph nodes cancer cells are likely to have spread from the primary tumor.

Types of mastectomies include the following:

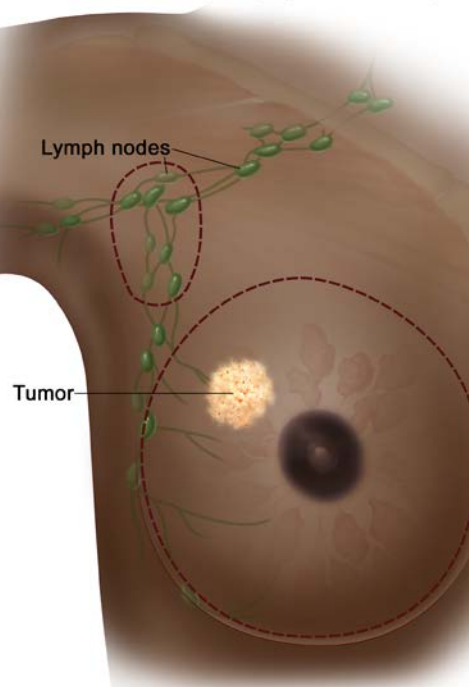
- **A total mastectomy or simple mastectomy** is a surgery that removes the whole breast with an aesthetic flat skin closure.
- **A skin-sparing mastectomy** removes the breast but not all the skin, in order to have breast reconstruction that might include flaps and/or implants.
- **Nipple-sparing mastectomy** preserves the nipple-areola complex (NAC) as well as all the skin. Not everyone is a candidate for nipple-sparing mastectomy based upon location of cancer, breast size, and breast ptosis (degree of drooping).

Breast reconstruction is an option after a mastectomy. It might be done at the same time as mastectomy (immediate) or at some time following the completion of cancer treatment (delayed). Breast reconstruction is most commonly done in stages. If you are considering breast reconstruction surgery, it requires collaboration between a breast surgeon and a reconstructive (plastic) surgeon.

Total (simple) mastectomy

The dotted line shows where the entire breast is removed. Some lymph nodes under the arm may also be removed. Clinical staging of lymph nodes is staging before surgery.

Total (Simple) Mastectomy



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Lymph node surgery

Sentinel lymph node biopsy

Sentinel lymph node biopsy (SLNB or SNB) is done during a lumpectomy or mastectomy to determine if any cancer cells have traveled to the lymph nodes. The lymph nodes removed are called the sentinel nodes.

A sentinel lymph node (SLN) is the first lymph node or nodes that cancer cells are most likely to spread to from a primary tumor. Often, there is more than one sentinel lymph node. Just because these nodes are removed, it does not mean that they test positive for cancer.

To find the sentinel lymph nodes, a dye is injected into the breast. It may be a radioactive material, blue dye, or other tracer. The tracer travels through the lymph channels in the breast to the lymph nodes in the armpit. This helps the surgeon find which of the lymph nodes are the sentinel lymph nodes. The lymph nodes containing the tracer are removed and tested by a pathologist.

Axillary lymph node dissection

Axillary lymph node dissection (ALND) is surgery to remove axillary lymph nodes. This is performed after an axillary lymph node biopsy or SLNB shows cancer in the lymph nodes (called node positive). Then, an ALND will remove any other lymph nodes that contain cancer. Removing lymph nodes can cause lymphedema and other health issues.

If the axillary nodes are removed with the breast, it is called a modified radical mastectomy.

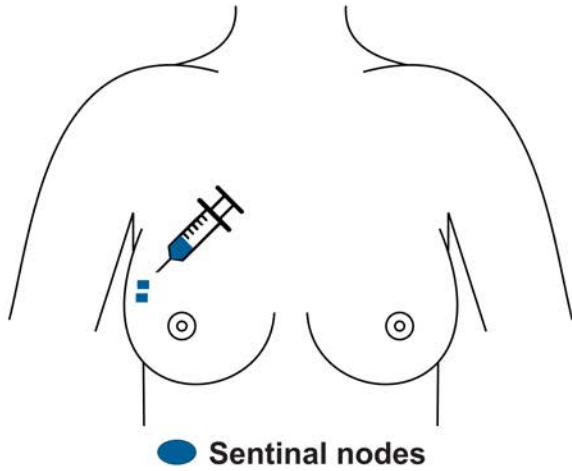
There are 3 levels of axillary lymph nodes:

- **Level I** – nodes located below the lower edge of the chest muscle
- **Level II** – nodes located underneath the chest muscle
- **Level III** – nodes located above the chest muscle near the collarbone

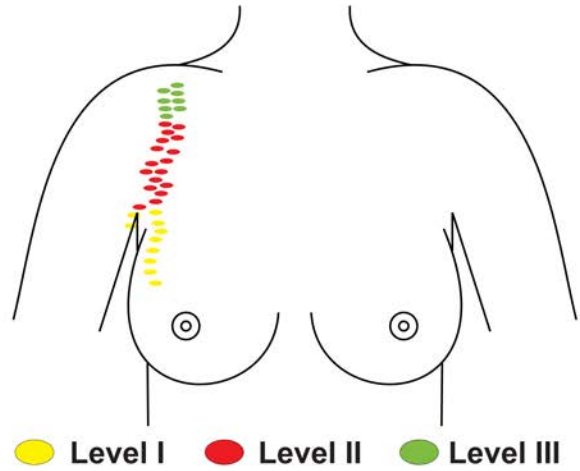
An ALND usually removes level I and II axillary lymph nodes. For more information about the timing of biopsies, talk with your care team.

Lymph node surgery

Sentinel lymph node biopsy

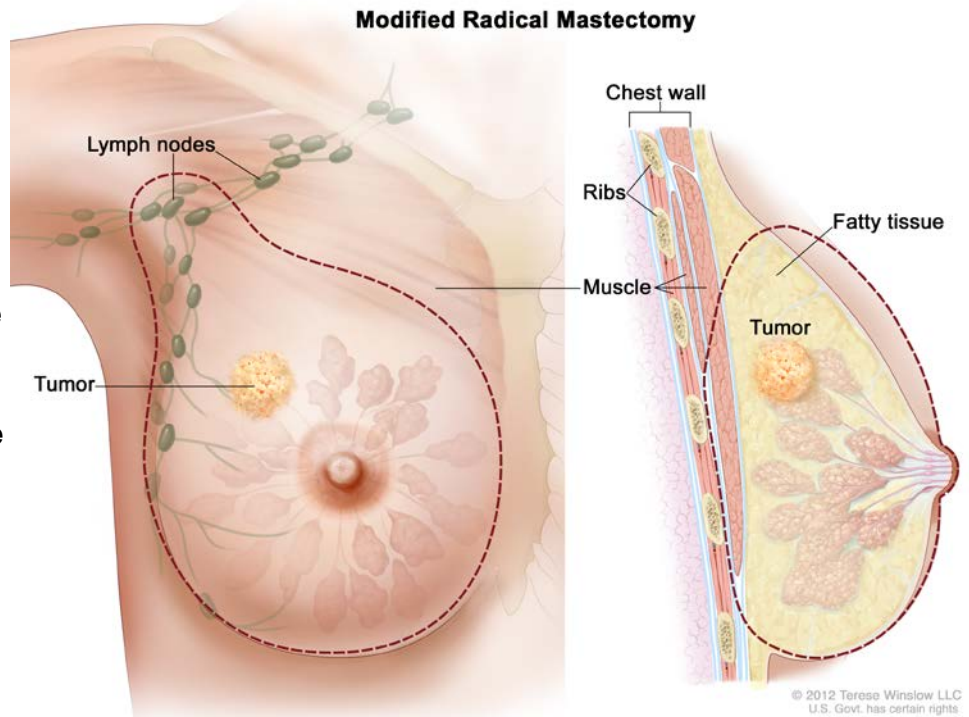


Axillary lymph node dissection



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.



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Radiation therapy

Radiation therapy (RT) uses high-energy radiation from x-rays (photons), protons, and other sources to kill cancer cells and shrink tumors. Radiation therapy can be given alone or before or after surgery to treat or slow the growth of cancer. Sometimes, radiation is given with certain systemic (drug) therapies. It may be used as supportive care to help ease pain or discomfort caused by cancer. Most types of radiation include several short treatment sessions that are given once daily over a few days to weeks. Ask your care team which radiation option(s) are best for you and what side effects to expect.

The following are types of radiation therapy used to treat breast cancer:

- **Whole breast radiation therapy (WBRT)** is used to treat the entire breast. Sometimes, additional treatments may be given to the tumor area. This is called a boost.
- **Partial breast irradiation (PBI)** is used to treat only the tumor area of the breast. Accelerated partial breast irradiation (APBI) is radiation given over a shorter period of time.
- **Lymph node radiation therapy** is used to treat the lymph nodes. It is also called regional nodal irradiation (RNI).

Radiation may be given to the breast and chest wall, infraclavicular region (below the collarbone), supraclavicular area (above the collarbone), lymph nodes found inside the

breast (intramammary), behind the ribcage (internal mammary), or axillary bed (armpit).

External beam radiation therapy

External beam radiation therapy (EBRT) uses a machine outside of the body called a linear accelerator to aim radiation at the whole breast (WBRT), only the tumor area of the breast (PBI), and lymph nodes (RNI).

Internal radiation

Internal radiation (brachytherapy) involves placing one or more small tubes into the tumor area of the breast. A small radioactive seed travels into the tube(s) and delivers radiation to the tumor area of the breast from inside the body. This type of radiation is used only for PBI.

Systemic therapy

There are many treatment options. Many factors play a role in how the cancer will respond to treatment. It is important to have regular talks with your care team about your goals for treatment and your treatment plan.

For systemic therapy examples, **see Guide 2.**

Did you know?

Chemotherapy, targeted therapy, immunotherapy, and endocrine therapy are types of systemic therapy.

Guide 2

Systemic therapy examples

Chemotherapy examples	<ul style="list-style-type: none"> • Capecitabine (Xeloda) • Carboplatin • Cisplatin • Cyclophosphamide • Docetaxel (Taxotere) 	<ul style="list-style-type: none"> • Doxorubicin (Adriamycin) • Fluorouracil • Methotrexate • Paclitaxel
HER2-targeting therapy (antibody, inhibitor, and conjugate) examples	<ul style="list-style-type: none"> • Trastuzumab (Herceptin) or trastuzumab substitutes (biosimilars) such as Kanjinti, Ogivri, Herzuma, Ontruzant, and Trazimera • Ado-trastuzumab emtansine (T-DM1) (Kadcyla) • Fam-trastuzumab deruxtecan-nxki (Enhertu) 	<ul style="list-style-type: none"> • Pertuzumab (Perjeta) • Neratinib (Nerlynx) • Tucatinib (Tukysa) • Phesgo as a substitute for combination therapy of trastuzumab with pertuzumab
Immunotherapy	<ul style="list-style-type: none"> • Pembrolizumab (Keytruda) 	
PARP inhibitors	<ul style="list-style-type: none"> • Olaparib (Lynparza) and talazoparib (Talzenna) 	
CD4/6 inhibitors	<ul style="list-style-type: none"> • Abemaciclib (Verzenio), palbociclib (Ibrance), and ribociclib (Kisqali) 	
Endocrine therapy	<ul style="list-style-type: none"> • Endocrine therapy can be found in Guide 3. 	

Chemotherapy

Chemotherapy kills fast-dividing cells throughout the body, including cancer cells and some normal cells. More than one chemotherapy may be used to treat invasive breast cancer. When only one drug is used, it's called a single agent. A combination or multi-agent regimen is the use of two or more chemotherapy drugs.

Some chemotherapy drugs are liquids that are infused into a vein or injected under the skin with a needle. Other chemotherapy drugs may be given as a pill that is swallowed.

Some examples of chemotherapy drugs include the following:

- **Anthracyclines** include doxorubicin and epirubicin.
- **Taxanes** include docetaxel, paclitaxel, and albumin-bound paclitaxel.

- **Anti-metabolites** include capecitabine, fluorouracil, gemcitabine, and methotrexate.

Most chemotherapy is given in cycles of treatment days followed by days of rest. This allows the body to recover before the next cycle. Cycles vary in length depending on which drugs are used. The number of treatment days per cycle and the total number of cycles given also vary.

Antibody drug conjugates

An antibody drug conjugate (ADC) delivers cell-specific chemotherapy. It attaches to a protein found on the outside of the cancer cell, then enters the cell. Once inside the cell, chemotherapy is released. Ado-trastuzumab emtansine (Kadcyla) and fam-trastuzumab deruxtecan-nxki (Enhertu) attach to HER2. Sacituzumab govitecan-hziy (Trodelvy) attaches to Trop-2.

Standard of care is the best-known way to treat a particular disease based on past clinical trials. There may be more than one treatment regimen that is considered standard of care. Ask your care team what treatment options are available and if a clinical trial might be right for you.



HER2-targeted therapy

HER2 is a protein involved in normal cell growth. There might be higher amounts of HER2 in your breast cancer. If this is the case, it is called HER2-positive (HER2+) breast cancer. HER2-targeted therapy is drug therapy that treats HER2+ breast cancer. Some HER2-targeted therapy is given with chemotherapy. However, it might be used alone or in combination with endocrine therapy.

HER2-targeted therapies include:

- **HER2 antibodies** prevent HER2 growth signals from outside the cell. They also increase the attack of immune cells on cancer cells.
- **HER2 inhibitors** stop HER2 growth signals from within the cell.
- **HER2 conjugates or HER2 antibody drug conjugates (ADCs)** deliver cell-specific chemotherapy. They attach directly to HER2s then enter the cell. Once inside, chemotherapy is released.

Your heart will be monitored before and during treatment with HER2-targeted therapy. Tests will measure the left ventricular ejection fraction (LVEF), the amount of blood pumping from the left side of the heart.

Other targeted therapies

PARP inhibitors

Cancer cells often become damaged. PARP is a cell protein that repairs cancer cells and allows them to survive. Blocking PARP can cause cancer cells to die. Olaparib (Lynparza) and talazoparib (Talzenna) are PARP inhibitors.

CDK4/6 inhibitors

Cyclin-dependent kinase (CDK) is a cell protein that helps cells grow and divide. For hormone receptor-positive (HR+), HER2-negative cancer, taking a CDK4/6 inhibitor with endocrine therapy may help control cancer longer and improve survival. With all CDK4/6 regimens, those who are premenopausal must also receive ovarian ablation or suppression. CDK4/6 inhibitors include abemaciclib (Verzenio), palbociclib (Ibrance), and ribociclib (Kisqali).

Immunotherapy

Immunotherapy is a type of systemic treatment that increases or turns on the activity of your immune system. By doing so, it improves your body's ability to find and destroy cancer cells. Immunotherapy can be given alone or with other types of treatment. Pembrolizumab (Keytruda) may be given with chemotherapy for early-stage triple-negative breast cancer.

Endocrine therapy

Hormones may cause breast cancer to grow. Endocrine therapy will stop your body from making hormones or it will block what hormones do in the body. This can help to reduce the risk of cancer returning. **See Guide 3.**

The endocrine system is made up of organs and tissues that produce hormones. Hormones are natural chemicals released into the bloodstream.

There are 4 hormones that might be targeted in endocrine therapy:

- **Estrogen** is made mainly by the ovaries, but also made by other tissues in the body such as fat tissue.
- **Progesterone** is made mainly by the ovaries.
- **Luteinizing hormone-releasing hormone (LHRH)** is made by a part of the brain called the hypothalamus. It tells the ovaries to make estrogen and progesterone and testicles to make testosterone. LHRH is also called gonadotropin-releasing hormone (GnRH).

Guide 3

Endocrine therapy types

Bilateral oophorectomy	Surgery to remove both ovaries.
Ovarian ablation	Radiation to permanently stop the ovaries from making hormones.
Ovarian or testosterone suppression	Drugs to temporarily stop the ovaries or testicles from making hormones such as LHRH and GnRH.
Aromatase inhibitors (AIs)	Drugs to stop a type of hormone called androgen from changing into estrogen by interfering with an enzyme called aromatase. Nonsteroidal AIs include anastrozole (Arimidex) and letrozole (Femara). Exemestane (Aromasin) is a steroidal AI.
Estrogen receptor (ER) modulators	<ul style="list-style-type: none"> • Selective estrogen receptor modulators (SERMs) block estrogen from attaching to hormone receptors. Tamoxifen and toremifene (Fareston) are SERMs. • Selective estrogen receptor degraders (SERDs) block and destroy estrogen receptors. Fulvestrant (Faslodex) and elacestrant (Orserdu) are SERDs.
Hormones	Hormone examples include ethinyl estradiol, fluoxymesterone, and megestrol acetate (Megace).

- **Androgen** is made by the adrenal glands, testicles, and ovaries.

Endocrine therapy is sometimes called hormone therapy. It is not the same as hormone replacement therapy (HRT) used for menopause.

Types of endocrine therapy that might be used for invasive breast cancer:

- **Aromatase inhibitors (AIs)** stop a type of hormone called androgen from changing into estrogen by interfering with an enzyme called aromatase. They do not affect estrogen made by the ovaries. Nonsteroidal aromatase inhibitors include anastrozole (Arimidex) and letrozole (Femara). Exemestane (Aromasin) is a steroidal aromatase inhibitor.
- **Estrogen receptor (ER) modulators** or anti-estrogens prevent hormones from binding to receptors.
- **Selective estrogen receptor modulators (SERMs)** block estrogen from attaching to hormone receptors. They include tamoxifen and toremifene (Fareston).
- **Selective estrogen receptor degraders (SERDs)** block and destroy estrogen receptors. Fulvestrant (Faslodex) and elacestrant (Orserdu) are SERDs.
- **Gonadotropin-releasing hormone (GnRH) agonists** might be used to suppress ovarian hormone or testosterone production.

Endocrine therapy will suppress the production of hormones and affect one's ability to become pregnant during treatment. Those who want to have children in the future should be referred to a fertility specialist before starting endocrine therapy.

Testosterone

For those assigned male at birth whose bodies continue to make testosterone, endocrine therapy includes tamoxifen or an aromatase inhibitor with testosterone-suppressing therapy.

Premenopause

If you have menstrual periods and still have a uterus, you are in premenopause. In premenopause, the ovaries are the main source of estrogen and progesterone. Menstrual periods may stop during treatment and for up to 2 years after treatment, but often return in those 35 years of age and under.

- Tamoxifen is the endocrine treatment option for those in premenopause. Ovarian suppression or ablation is frequently considered for higher-risk ER+ breast cancers.

Menopause

In menopause, the ovaries permanently stop producing hormones and menstrual periods stop. Estrogen and progesterone levels are low, but the adrenal glands, liver, and body fat continue to make small amounts of estrogen. If you don't have periods, a test using a blood sample may be used to confirm your status.

Cancer treatment can cause temporary menopause. If you stopped having periods due to removal of your uterus (hysterectomy) but you still have your ovaries, then you should have your menopausal status confirmed with a blood test. If both ovaries have been removed (with or without your uterus), you are in menopause.

- Tamoxifen or an aromatase inhibitor is the endocrine treatment for those in menopause. Aromatase inhibitors include anastrozole (Arimidex), exemestane (Aromasin), and letrozole (Femara).

Bone-strengthening therapy

Medicines that target the bones may be given to help relieve bone pain or reduce the risk of bone problems. Some medicines work by slowing or stopping bone breakdown, while others help increase bone thickness.

When breast cancer spreads to distant sites, it may metastasize in your bones. This puts your bones at risk for injury and disease. Such problems include bone loss (osteoporosis), fractures, bone pain, and squeezing (compression) of the spinal cord. Some treatments for breast cancer, like aromatase inhibitors or GnRH agonists, can cause bone loss, which puts you at an increased risk for fractures.

Drugs used to prevent bone loss and fractures:

- Oral bisphosphonates
- Zoledronic acid (Zometa)
- Pamidronate (Aredia)

- Denosumab (Prolia)

You will be screened for bone weakness (osteoporosis) using a bone mineral density test. This measures how much calcium and other minerals are in your bones. It is also called a dual-energy x-ray absorptiometry (DEXA) scan and is painless. Bone mineral density tests look for osteoporosis and help predict your risk for bone fractures.

A baseline DEXA scan is recommended before starting endocrine therapy.

Zoledronic acid, pamidronate, and denosumab

Zoledronic acid, pamidronate, and denosumab are used to prevent bone loss (osteoporosis) and fractures. You might have blood tests to monitor kidney function, calcium levels, and magnesium levels. A calcium and vitamin D supplement will be recommended by your doctor.

Let your dentist know if you are taking any of these medicines. Also, ask your care team how these medicines might affect your teeth and jaw. Osteonecrosis, or bone tissue death of the jaw, is a rare but serious side effect. Tell your care team about any planned trips to the dentist and surgeries or dental procedures that might also affect the jawbone. It will be important to take care of your teeth and to see a dentist before starting treatment with any of these drugs.

Clinical trials

A clinical trial is a type of medical research study. After being developed and tested in a laboratory, potential new ways of treating cancer need to be studied in people. If found to be safe and effective in a clinical trial, a drug, device, or treatment approach may be approved by the U.S. Food and Drug Administration (FDA).

Everyone with cancer should carefully consider all of the treatment options available for their cancer type, including standard treatments and clinical trials. Talk to your doctor about whether a clinical trial may make sense for you.

Phases

Most cancer clinical trials focus on treatment. Treatment trials are done in phases.

- **Phase 1 trials** study the dose, safety, and side effects of an investigational drug or treatment approach. They also look for early signs that the drug or approach is helpful.
- **Phase 2 trials** study how well the drug or approach works against a specific type of cancer.
- **Phase 3 trials** test the drug or approach against a standard treatment. If the results are good, it may be approved by the FDA.
- **Phase 4 trials** study the long-term safety and benefit of an FDA-approved treatment.



Finding a clinical trial

In the United States

NCCN Cancer Centers

[NCCN.org/cancercenters](https://www.nccn.org/cancercenters)

The National Cancer Institute (NCI)

[cancer.gov/about-cancer/treatment/clinical-trials/search](https://www.cancer.gov/about-cancer/treatment/clinical-trials/search)

Worldwide

The U.S. National Library of Medicine (NLM)

clinicaltrials.gov/

Need help finding a clinical trial?

NCI's Cancer Information Service (CIS)

1.800.4.CANCER (1.800.422.6237)

[cancer.gov/contact](https://www.cancer.gov/contact)

Who can enroll?

Every clinical trial has rules for joining, called eligibility criteria. The rules may be about age, cancer type and stage, treatment history, or general health. These requirements ensure that participants are alike in specific ways and that the trial is as safe as possible for the participants.

Informed consent

Clinical trials are managed by a group of experts called a research team. The research team will review the study with you in detail, including its purpose and the risks and benefits of joining. All of this information is also provided in an informed consent form. Read the form carefully and ask questions before signing it. Take time to discuss with family, friends, or others whom you trust. Keep in mind that you can leave and seek treatment outside of the clinical trial at any time.

Start the conversation

Don't wait for your doctor to bring up clinical trials. Start the conversation and learn about all of your treatment options. If you find a study that you may be eligible for, ask your treatment team if you meet the requirements. If you have already started standard treatment you may not be eligible for certain clinical trials. Try not to be discouraged if you cannot join. New clinical trials are always becoming available.

Frequently asked questions

There are many myths and misconceptions surrounding clinical trials. The possible benefits and risks are not well understood by many with cancer.

Will I get a placebo?

Placebos (inactive versions of real medicines) are almost never used alone in cancer clinical trials. It is common to receive either a placebo with a standard treatment, or a new drug with a standard treatment. You will be informed, verbally and in writing, if a placebo is part of a clinical trial before you enroll.

Do I have to pay to be in a clinical trial?

Rarely. It depends on the study, your health insurance, and the state in which you live. Your treatment team and the research team can help determine if you are responsible for any costs.

Supportive care

Supportive care will be specific to your needs. Supportive care is health care given to prevent, reduce, and relieve suffering, and to improve quality of life. Supportive care might include pain relief, palliative care, emotional or spiritual support, financial aid, or family counseling. Tell your care team how you are feeling and about any side effects so they can be managed. Supportive care, best supportive care, and palliative care often mean the same thing.

It is very important to take care of yourself by eating well, drinking plenty of fluids, exercising, and doing things that make you feel energized.

Side effects

All cancer treatments can cause unwanted health issues called side effects. Side effects depend on many factors. These factors include the drug type and dose, length of treatment, and the person. Some side effects may be harmful to your health. Others may just be unpleasant.

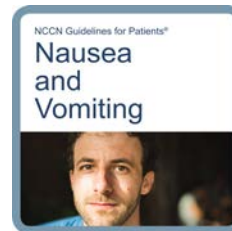
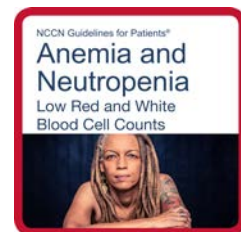
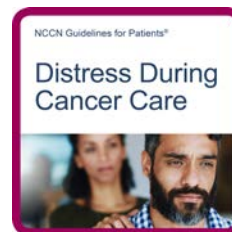
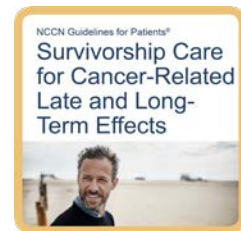
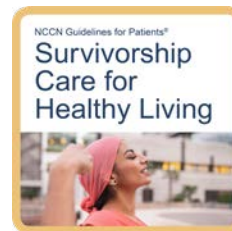
Ask for a complete list of side effects of your treatments. Also, tell your treatment team about any new or worsening symptoms. There may be ways to help you feel better. There are also ways to prevent some side effects.

Late effects

Late effects are side effects that occur months or years after a disease is diagnosed or after treatment has ended. Late effects may be caused by cancer or cancer treatment. They may include physical, mental, and social problems, and second cancers. The sooner

Supportive care resources

More information on supportive care is available at: [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



late effects are treated the better. Ask your care team about what late effects could occur. This will help you know what to look for.

Blood clots

Cancer or cancer treatment can cause blood clots to form. This can block blood flow and oxygen in the body. Blood clots can break loose and travel to other parts of the body causing stroke or other health issues. Venous thromboembolism (VTE) refers to blood clots in the veins.

Bone health

Breast cancer may spread to your bones. Some breast cancer treatments may also weaken your bones. Both can put your bones at increased risk for injury and disease. Such problems include bone fractures, bone pain, and squeezing (compression) of the spinal cord. High levels of calcium in the blood, called hypercalcemia, may also occur.

Medicine may be given to help relieve bone pain and reduce the risk of other bone problems. Some medicines work by slowing or stopping bone breakdown, while others help increase bone thickness. It is recommended that you take calcium and vitamin D with these bone health medicines. Talk to your care team first.

Diarrhea

Diarrhea is frequent and watery bowel movements. Your care team will tell you how to manage diarrhea. It is important to drink lots of fluids.

Keep a pain diary

A pain diary is a written record that helps you keep track of when you have pain, how bad it is, what causes it, and what makes it better or worse. Use a pain diary to discuss your pain with your care team. You might be referred to a specialist for pain management.

Include in your pain diary:

- ✓ The time and dose of all medicines
- ✓ When pain starts and ends or lessens
- ✓ Where you feel pain
- ✓ A description of your pain. Is it throbbing, sharp, tingling, shooting, or burning? Is it constant, or does it come and go?
- ✓ Does the pain change at different times of day? When?
- ✓ Does the pain get worse before or after meals? Does certain food or drink make it better?
- ✓ Does the pain get better or worse with activity? What kind of activity?
- ✓ Does the pain keep you from falling asleep at night? Does pain wake you up in the night?
- ✓ A rating of your pain from 0 (no pain) to 10 (worst pain you have ever felt)
- ✓ Does pain get in the way of you doing the things you enjoy?

Difficulty eating and loss of appetite

Sometimes side effects from surgery, cancer, or other treatments might cause you to feel not hungry or sick to your stomach (nauseated). Healthy eating is important during treatment. It includes eating a balanced diet, eating the right amount of food, and drinking enough fluids. A registered dietitian who is an expert in nutrition and food can help. Speak to your care team if you have trouble eating or maintaining your weight.

Distress

Depression, anxiety, and sleeping issues are common and are a normal part of cancer diagnosis. Talk to your care team and with those whom you feel most comfortable about how you are feeling. There are services, people, and medicine that can help you. Support and counseling services are available.

Fatigue

Fatigue is extreme tiredness and inability to function due to lack of energy. Fatigue may be caused by cancer or it may be a side effect of treatment. Let your care team know how you are feeling and if fatigue is getting in the way of doing the things you enjoy. Eating a balanced diet, exercise, yoga, acupuncture, and massage therapy can help. You might be referred to a nutritionist or dietitian to help with fatigue.

Hair loss

Chemotherapy may cause hair loss (alopecia) all over your body — not just on your scalp. Some chemotherapy drugs are more likely than others to cause hair loss. Dosage might also affect the amount of hair loss. Most of the time, hair loss from chemotherapy is temporary. Hair often regrows 3 to 6 months after treatment ends. Your hair may be a different shade or texture. Scalp cooling (or scalp hypothermia) might help lessen hair loss in those receiving certain types of chemotherapy.

Low blood cell counts

Some cancer treatments can cause low blood cell counts.

- **Anemia** is a condition where your body does not have enough healthy blood cells, resulting in less oxygen being carried to your cells. You might tire easily if you are anemic.
- **Neutropenia** is a decrease in neutrophils, a type of white blood cell. This puts you at risk for infection.
- **Thrombocytopenia** is a condition where there are not enough platelets found in the blood. This puts you at risk for bleeding.

Lymphedema

Lymphedema is a condition in which lymph fluid builds up in tissues and causes swelling. It may be caused when part of the lymph system is damaged or blocked, such as during surgery to remove lymph nodes, or by radiation therapy. Cancers that block lymph vessels can also cause lymphedema. Swelling

usually develops slowly over time. It may develop during treatment, or it may start years after treatment. If you have lymphedema, you may be referred to an expert in lymphedema management. The swelling may be reduced by exercise, massage, compression devices, and other means.

Nausea and vomiting

Nausea and vomiting are common side effects of treatment. You will be given medicine to prevent nausea and vomiting.

Neurocognitive or neuropsychological effects

Some treatments can damage the nervous system (neurotoxicity) causing problems with concentration, memory, and thinking. Survivors are at risk for neurotoxicity and might be recommended for neuropsychological testing. Neuropsychology looks at how the health of your brain affects your thinking and behavior. Neuropsychological testing can identify your limits and a health care professional can create a plan to help with these limits.

Neuropathy

Neuropathy is a nerve problem that causes pain, numbness, tingling, swelling, or muscle weakness in different parts of the body. It usually begins in the hands or feet and gets worse over time. Neuropathy may be caused by cancer or cancer treatment. Most of the time, neuropathy goes away after treatment.

Organ issues

Treatment might cause your kidneys, liver, heart, and pancreas to not work as well as they should.

Pain

Tell your care team about any pain or discomfort. You might meet with a palliative care specialist or with a pain specialist to manage pain.

QOL

Cancer and its treatment can affect your overall well-being or quality of life (QOL). For more information on quality of life, see the *NCCN Guidelines for Patients: Palliative Care* at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



Survivorship

A person is a cancer survivor from the time of diagnosis until the end of life. After treatment, your health will be monitored for side effects of treatment and the return of cancer. This is part of your survivorship care plan. It is important to keep any follow-up doctor visits and imaging test appointments. Seek good routine medical care, including regular doctor visits for preventive care and cancer screening.

A personalized survivorship care plan will contain a summary of possible long-term effects of treatment called late effects and a list of follow-up tests. Find out how your primary care provider will coordinate with specialists for your follow-up care.

Tell your care team about any symptoms such as headaches, menstrual spotting between periods or new onset of spotting after menopause (if prior tamoxifen), shortness of breath that you notice with walking, or bone pain. Side effects can be managed. Continue to take all medicine such as endocrine therapy exactly as prescribed and do not miss or skip doses.



Warnings about supplements and drug interactions

You might be asked to stop taking or avoid certain herbal supplements when on a systemic therapy. Some supplements can affect the ability of a drug to do its job. This is called a drug interaction.

It is critical to speak with your care team about any supplements you may be taking. Some examples include:

- Turmeric
- Ginkgo biloba
- Green tea extract
- St. John's Wort
- Antioxidants

Certain medicines can also affect the ability of a drug to do its job. Antacids, heart or blood pressure medicine, and antidepressants are just some of the medicines that might interact with a systemic therapy or supportive care medicines given during systemic therapy. Therefore, it is very important to tell your care team about any medicines, vitamins, over-the-counter (OTC) drugs, herbals, or supplements you are taking.

Bring a list with you to every visit.

Key points

- Treatment takes a team approach. Get to know your care team and help them get to know you.
- Surgery is the main treatment for invasive breast cancer. This is only one part of a treatment plan.
- Radiation therapy (RT) uses high-energy radiation from x-rays (photons, electrons), protons, and other sources to kill cancer cells.
- Some breast cancers grow because of estrogen. These cancers are estrogen receptor-positive (ER+) and are often treated with endocrine therapy to reduce the risk of cancer recurrence.
- A clinical trial is a type of research that studies a treatment to see how safe it is and how well it works.
- Supportive care is health care that relieves symptoms caused by treatment and improves quality of life. Supportive care is always given.
- All cancer treatments can cause unwanted health issues called side effects. It is important for you to tell your care team about all your side effects so they can be managed.
- Eating a balanced diet, drinking enough fluids, and exercise can help manage side effects.



Let us know what you think!

Please take a moment to complete an online survey about the NCCN Guidelines for Patients.

[NCCN.org/patients/response](https://www.nccn.org/patients/response)

5

Surgery first

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Surgery is the main or primary treatment for invasive breast cancer. Radiation therapy (RT) and/or systemic therapy are possible after surgery. Together, you and your care team will choose a treatment plan that is best for you.

Not all cancers need treatment before surgery. This chapter is for those who will have surgery first.

Surgery with radiation therapy

Surgery is the main or primary treatment for invasive breast cancer. It involves removing the tumor from the breast and assessing the lymph nodes.

There are 2 breast surgery options:

- Lumpectomy
- Total mastectomy

Both options include axillary lymph node (ALN) staging with either sentinel lymph node biopsy (SLNB), axillary lymph node dissection (ALND), or both. After surgery, a pathologist will examine the removed tissue and any lymph nodes to determine the pathologic stage. This information will help plan next steps for treatment. Treatment after

surgery might include radiation therapy and/or systemic therapy.

An example of a tumor stage after surgery might be pT2. Lymph node micrometastases are written as pN1mi. Ipsilateral means on the same side of the body.

Lumpectomy followed by radiation therapy

A lumpectomy, also called breast-conserving surgery (BCS), is surgery to remove a tumor in the breast. Treatment after a lumpectomy is based on the type of cancer and if cancer is found in the axillary lymph nodes (ALNs). If there is a positive surgical margin, you might have more surgery to remove any remaining cancer. A lumpectomy is usually followed by radiation therapy (RT) to part of or the whole breast and sometimes the lymph nodes. A boost is extra radiation to the tumor area. Chemotherapy might be given before RT.

Total mastectomy followed by radiation therapy

A total mastectomy is a surgery that removes the whole breast. Treatment after a mastectomy is based on if cancer was found in the axillary lymph nodes (ALNs), the number of lymph nodes that tested positive, and the size of the removed tumor. Radiation therapy and/or systemic therapy are possible following a mastectomy.

Systemic therapy after surgery

Adjuvant systemic therapy is drug treatment after surgery or radiation therapy. It is given to kill any remaining cancer cells and to help reduce the risk of cancer returning. This treatment is based on cancer subtype called tumor histology and hormone receptor (HR) status. Histology is the study of the anatomy (structure) of cells, tissues, and organs under a microscope. Depending on the histology, HER2 status may also be a factor. If cancer is hormone receptor-positive (ER+ and/or PR+) and HER2-, then oncologists also take into account if there is cancer in lymph nodes called node positive (node+).

Systemic therapies might be used alone or in combination. Ask your medical oncologist why one treatment might be preferred over another for your type of cancer.

For those in menopause (natural or induced) with high-risk node-negative or node-positive tumors, bone-strengthening therapy might be given to reduce the risk of distant metastasis.

Favorable histologies

A favorable histology is one that has a favorable or good prognosis. A prognosis is the course your cancer will likely take. These tumor types are not high grade, are HER2-, and might respond better to treatment than other tumors. They also might have less risk of returning. Ask your care team what this might mean for your treatment. Those with estrogen receptor-positive (ER+) and/or progesterone receptor-positive (PR+) tumors will likely have endocrine therapy as listed in Guide 6. Other systemic therapies are possible.

Favorable histology types include:

- Pure tubular
- Pure mucinous
- Pure cribriform
- Encapsulated or solid papillary carcinoma (SPC)
- Adenoid cystic (conventional), secretory carcinoma, and other salivary carcinomas
- Rare low-grade forms of metaplastic carcinoma
- Other rare forms

Common histologies

Ductal and lobular carcinoma are the most common types of invasive breast cancer.

Common histology types include:

- Ductal/no special type (NST) (NST includes medullary pattern, cancers with neuroendocrine expression, and other rare patterns)
- Lobular
- Mixed
- Micropapillary
- Metaplastic (includes various subtypes)

Adjuvant treatment options for common histologies are described next.

HR+ with HER2+

In hormone receptor-positive (HR+) and HER2-positive (HER2+) breast cancer, estrogen (ER+) and/or progesterone receptors (PR+) and HER2 receptors are found. It might be written as HR+ with HER2+ or called triple-positive breast cancer.

- Chemotherapy with a HER2-targeted therapy is used to treat HER2+ cancer. Trastuzumab and pertuzumab are examples of HER2-targeted therapy.
- Endocrine therapy is used to treat HR+ breast cancer. It is given after chemotherapy.

HER2-targeted therapy options can be found in **Guide 4**.

Endocrine therapy options can be found in **Guide 5**.

HR- with HER2+

In hormone receptor-negative (HR-) cancer, there are no receptors for estrogen (ER-) and progesterone (PR-). When HER2 receptors are found, it is HER2-positive (HER2+). Since this cancer is HR- and HER2+, treatment will focus on targeting HER2. HER2-targeted therapy usually includes chemotherapy.

HER2-targeted therapy options can be found in **Guide 4**.

It is important to tell your care team about all side effects so they can be managed.

HR+ with HER2-

In hormone receptor-positive (HR+) cancer, estrogen (ER+) and/or progesterone receptors (PR+) are found. Endocrine therapy is used to treat HR+ breast cancer. Since the tumor is HER2-, therapy targeting HER2 is not used. Sometimes, chemotherapy is used instead. When cancer is found in the lymph nodes, it is node positive (node+).

- Those who are premenopausal might have ovarian suppression or ablation in addition to endocrine therapy.
- If chemotherapy is given, it is given before endocrine therapy.

Chemotherapy and other systemic therapies specific to HER2- breast cancer are found in **Guide 6**.

Endocrine therapy options can be found in **Guide 5**.

Guide 4**HER2-targeted therapy options: HER2+ cancer**

Preferred options	<ul style="list-style-type: none"> • Paclitaxel and trastuzumab • Docetaxel, carboplatin, and trastuzumab (TCH) • Docetaxel, carboplatin, trastuzumab, and pertuzumab (TCHP) <hr/> <p>If no residual disease after preoperative therapy or no preoperative therapy:</p> <ul style="list-style-type: none"> • Complete up to 1 year of HER2-targeted therapy with trastuzumab. Pertuzumab might be added. <hr/> <p>If residual disease after preoperative therapy:</p> <ul style="list-style-type: none"> • Ado-trastuzumab emtansine alone. If ado-trastuzumab emtansine discontinued for toxicity, then trastuzumab with or without pertuzumab to complete one year of therapy. • If node positive at initial staging, trastuzumab with pertuzumab
Other recommended	<ul style="list-style-type: none"> • Doxorubicin with cyclophosphamide (AC) followed by docetaxel with trastuzumab • Doxorubicin with cyclophosphamide (AC) followed by docetaxel with trastuzumab and pertuzumab • Paclitaxel or carboplatin with trastuzumab and pertuzumab
Used in some cases	<ul style="list-style-type: none"> • Docetaxel, cyclophosphamide, and trastuzumab • Doxorubicin and cyclophosphamide followed by paclitaxel with trastuzumab • Doxorubicin and cyclophosphamide followed by docetaxel with paclitaxel, trastuzumab, and pertuzumab • Neratinib • Paclitaxel with trastuzumab and pertuzumab • Ado-trastuzumab emtansine (TDM-1)
Notes	<ul style="list-style-type: none"> • Alternative taxanes (ie, docetaxel, paclitaxel, albumin-bound paclitaxel) might be substituted in some cases • An FDA-approved biosimilar or substitute might be used for trastuzumab.

Guide 5**Endocrine therapy options: HR+ cancer**

Premenopause at diagnosis	<p>Option 1</p> <ul style="list-style-type: none"> Tamoxifen alone for 5 years or with ovarian suppression or ablation 	<ul style="list-style-type: none"> After 5 years, if in postmenopause, then an aromatase inhibitor for 5 years or consider tamoxifen for another 5 years (for a total of 10 years on tamoxifen)
	<p>Option 2</p> <ul style="list-style-type: none"> Aromatase inhibitor for 5 years with ovarian suppression or ablation, then consider aromatase inhibitor for an additional 3 to 5 years 	<ul style="list-style-type: none"> After 5 years, if still in premenopause, then consider tamoxifen for another 5 years (for a total of 10 years on tamoxifen) or stop endocrine therapy
Menopause at diagnosis	<p>Option 1</p> <ul style="list-style-type: none"> Aromatase inhibitor for 5 years, then consider aromatase inhibitor for 3 to 5 more years Aromatase inhibitor for 2 to 3 years, then tamoxifen to complete 5 years total of endocrine therapy Tamoxifen for 2 to 3 years, then an aromatase inhibitor to complete 5 years of endocrine therapy Tamoxifen for 2 to 3 years, then up to 5 years of an aromatase inhibitor 	
	<p>Option 2</p> <ul style="list-style-type: none"> Tamoxifen for 4.5 to 6 years, then an aromatase inhibitor for 5 years or consider tamoxifen for another 5 years (for a total of 10 years on tamoxifen) 	
	<p>Option 3</p> <ul style="list-style-type: none"> For those who can't have aromatase inhibitors or who don't want aromatase inhibitors, take tamoxifen for 5 years or consider tamoxifen for up to 10 years 	

Guide 6**Systemic therapy options: HER2- cancer**

Preferred options	<ul style="list-style-type: none"> • Doxorubicin and cyclophosphamide (AC) with paclitaxel • Docetaxel and cyclophosphamide (TC) • Olaparib, if germline <i>BRCA1</i> or <i>BRCA2</i> mutations <hr/> <ul style="list-style-type: none"> • High-risk triple-negative breast cancer (TNBC): Preoperative pembrolizumab with carboplatin and paclitaxel, followed by preoperative pembrolizumab and cyclophosphamide with doxorubicin or epirubicin, followed by adjuvant pembrolizumab • If TNBC and residual disease after preoperative therapy with taxane-, alkylator-, and anthracycline-based chemotherapy, then capecitabine
Other recommended	<ul style="list-style-type: none"> • Doxorubicin and cyclophosphamide (AC) with docetaxel • Epirubicin and cyclophosphamide (EC) • Docetaxel, doxorubicin, and cyclophosphamide (TAC) <hr/> <p>For TNBC:</p> <ul style="list-style-type: none"> • Paclitaxel with carboplatin • Docetaxel with carboplatin
Used in some cases	<ul style="list-style-type: none"> • Doxorubicin and cyclophosphamide (AC) • Cyclophosphamide, methotrexate, and fluorouracil (CMF) • Doxorubicin and cyclophosphamide (AC) with paclitaxel • Capecitabine (maintenance therapy for TNBC after adjuvant chemotherapy)

Triple-negative breast cancer

In triple-negative breast cancer (TNBC), receptors for estrogen, progesterone, and HER2 are not found. This means that the breast cancer cells have tested negative for HER2 and both hormone receptors. It is written as ER- and/or PR- with HER2-.

TNBC is cancer that is:

- Estrogen receptor-negative (ER-),
- Progesterone receptor-negative (PR-), and
- HER2-negative (HER2-).

There are many variations within TNBC. It is a group of diseases that we are learning more about all the time. Since there are no HER2 receptors, HER2- targeted therapy is not used. And since there are no estrogen or progesterone hormone receptors, endocrine therapy is not used.

Treatment after surgery (adjuvant) will likely be chemotherapy as found in **Guide 6**.

Endocrine therapy

Endocrine therapy is used to treat hormone receptor-positive (HR+) breast cancer. This is cancer that tests positive for estrogen receptors (ER+) and/or progesterone receptors (PR+). Endocrine therapy blocks estrogen and progesterone, which can slow tumor growth or shrink the tumor for a period of time. It might also help prevent the risk of cancer returning in the breasts and elsewhere in the body.

- If chemotherapy is given, it is given before endocrine therapy.
- Those with high-risk breast cancer that is HR+ and HER2- might have 2 years of adjuvant abemaciclib with endocrine therapy.
- Those receiving an aromatase inhibitor who are at risk for osteoporosis will likely have bone density tests and bone-strengthening therapy.

Endocrine therapy options can be found in **Guide 5**.

Follow-up care

Follow-up care can be found in **Guide 7**.

After treatment, you will receive follow-up care. During this time, your health will be monitored for side effects of treatment called late effects and the possible return of cancer called recurrence. This is part of your survivorship care plan. It is important to keep any follow-up

doctor visits and imaging test appointments. Seek routine medical care, including regular doctor visits for preventive care and cancer screening.

Tell your care team about any symptoms such as headaches, menstrual spotting between periods or new onset of spotting after menopause (if prior tamoxifen use), shortness of breath that you notice with walking, or bone

Guide 7 Follow-up care

Medical history and physical exam (H&P) 1 to 4 times per year as needed for 5 years, then every year

Screen for changes in family history

Genetic testing and referral to genetic counseling, as needed

Monitor for lymphedema and refer for lymphedema management, as needed

Mammogram every 12 months, may start as soon as 6 months after breast-conserving therapy (mammogram not needed after mastectomy or on reconstructed breast)

Heart tests, as needed

Information on risk of future health issues (comorbidities)

If signs and symptoms of metastases, then blood and imaging tests

If taking endocrine therapy, continue to take endocrine therapy. Do not miss or skip doses

Annual gynecology exam for those on tamoxifen

Bone density tests for those on an aromatase inhibitor or who's ovaries stop working

A personalized survivorship plan that includes treatment summary of possible long-term side effects, clear follow-up recommendations, and coordination of care between the primary care provider and specialists.

Be active, eat a mostly plant-based diet, exercise, limit alcohol use, and achieve and maintain an ideal body weight (BMI of 20 to 25)

pain. Side effects can be managed. Continue to take all medicine such as endocrine therapy exactly as prescribed and do not miss or skip doses.

You should receive a personalized survivorship care plan. It will provide a summary of possible long-term effects of treatment and list follow-up tests. Find out how your primary care provider will coordinate with specialists for your follow-up care.

Key points

- Surgery is the main or primary treatment for invasive breast cancer. Radiation therapy (RT) and/or systemic therapy are possible following surgery.
- Adjuvant treatment is given after surgery to kill any remaining cancer cells in the body and to help prevent the return of cancer.
- In hormone receptor-positive (HR+) cancer, estrogen (ER+) and/or progesterone receptors (PR+) are found.
- Endocrine therapy is used to treat HR+ cancer.
- If chemotherapy is given, it is given before radiation therapy and endocrine therapy.
- In triple-negative breast cancer (TNBC), receptors for estrogen, progesterone, and HER2 are not found. It is almost always treated with chemotherapy.
- It is important to keep follow-up visits and imaging test appointments. Seek good routine medical care, including preventative care and cancer screenings. Continue to take all medicines as prescribed.

6

Preop treatment first

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This chapter is for those who would benefit from treatment before surgery. Treatment before surgery is called preoperative or neoadjuvant therapy. It can be systemic therapy or radiation therapy. Together, you and your care team will choose the best option for you.

In stage 3 breast cancer, the cancer can be large and in the lymph nodes, the lymph nodes can be fixed (or not moveable), or the cancer can involve the skin or chest wall. It is sometimes called advanced disease. It is not metastatic (stage 4).

Testing

Not everyone will benefit from preoperative therapy. If preoperative systemic therapy is an option for you, then you will have blood and imaging tests before starting treatment. Testing will include an axillary lymph node exam. An ultrasound and biopsy of lymph nodes suspected of cancer are possible.

You will have the following before starting preoperative systemic therapy:

- Core biopsy of breast
- Placement of clips or markers to help the surgeon know where to operate in case

the tumor goes away with preoperative therapy. Clips are also placed at the time of surgery for radiation planning.

- Axillary lymph node ultrasound or magnetic resonance imaging (MRI) (if not done before)
- Biopsy of suspicious lymph nodes with clip placement (if not done before)

Your preferences about treatment are always important. Talk to your care team and make your wishes known.



Treatment before surgery

Treatment before surgery is called preoperative or neoadjuvant therapy. It can be systemic (drug) therapy or radiation therapy. Preoperative systemic therapy is based on hormone receptor (HR) and HER2 status. Preoperative systemic therapy has benefits.

It can:

- Help preserve the breast
- Shrink the tumor
- Shrink the tumor so it can be removed with a smaller surgery (lumpectomy)
- Provide important information about how your tumor responds to therapy, which is very helpful in those with triple-negative (TNBC) and HER2-positive (HER2+) breast cancer
- Help choose adjuvant regimens in those with HER2+ and TNBC with residual disease
- Allow time for genetic testing
- Allow time to plan breast reconstruction in those choosing mastectomy
- Allow time for fewer lymph nodes to be removed at the time of surgery
- Allow time for you to decide about and prepare for surgery

There are risks with any treatment. While rare, cancer can still progress during preoperative systemic therapy.

During and after preoperative therapy, you will have tests to monitor treatment.

- If the tumor shrinks or the cancer burden is reduced, then surgery might be possible. Options are a lumpectomy or mastectomy. Both options include axillary lymph node (ALN) staging. After surgery, a pathologist will examine the removed tissue and any lymph nodes to determine the pathologic stage. Systemic therapy and radiation therapy will follow surgery.
- If the tumor did not shrink enough to be removed with surgery, then you will have more systemic therapy and/or radiation therapy (RT).

Surgery

Surgery options depend on how your cancer responded to preoperative therapy. A complete response means there is no evidence of cancer. In a partial response, the tumor in the breast or lymph nodes has shrunk in size. A lumpectomy or mastectomy are options depending on the size and location of the tumor, as well as the size of your breast before surgery. After surgery, most will have both systemic therapy and radiation therapy.

Treatment after surgery

Many people have treatment after surgery. Treatment after surgery is called adjuvant therapy. Adjuvant therapy is based on the size of the tumor, if cancer remains (residual disease), and if cancer in the lymph nodes is found. A complete response means there is no evidence of cancer.

Your tumor will be restaged after preoperative therapy. Staging will be done by looking at tissue removed during surgery. This is called the pathologic stage or surgical stage. It might look like this: ypT0N0. The y means you had preoperative therapy.

Hormone receptor-positive (HR+) cancer is often treated with adjuvant endocrine therapy. HER2-targeted therapy is often used to treat HER2+ cancer. Systemic therapies might be used alone or in combination. When chemotherapy is used, it is given before endocrine therapy. Ask your medical oncologist why one treatment might be preferred over another for your type of cancer.

For those in menopause (natural or induced) with high-risk node-negative (node-) or node-positive (node+) tumors, bone-strengthening therapy might be given to reduce the risk of distant metastasis.

Adjuvant treatment options based on HR and HER2 status are described on the following pages.

Order of treatments

Most people with cancer will receive more than one type of treatment. Below is an overview of the order of treatments.

- ✓ **Preoperative or neoadjuvant (before) therapy** is given to shrink the tumor before a primary treatment such as surgery.
- ✓ **Perioperative therapy** is systemic therapy, such as chemotherapy, given before and after surgery.
- ✓ **Primary treatment** is the main treatment given to rid the body of cancer.
- ✓ **Postoperative or adjuvant (after) therapy** is given after primary treatment to rid the body of any cancer cells left behind from surgery. It is also used when the risk of cancer returning (recurrence) is felt to be high.
- ✓ **First-line therapy** is the first set of systemic (drug) treatment given.
- ✓ **Second-line therapy** is the next set of treatment given if cancer progresses during or after systemic therapy.

Talk to your care team about your treatment plan and what it means for your stage and type of cancer.

HR+ with HER2+

Hormone receptor-positive (HR+) with HER2+ is also called triple-positive breast cancer. Receptors for HER2, estrogen, and/or progesterone are found. It is treated with HER2-targeted therapy and endocrine therapy.

HER2-targeted therapy options can be found in **Guide 8**.

- If no disease remains after preoperative therapy, then you will have endocrine therapy and up to 1 year of HER2-targeted therapy with trastuzumab alone or with pertuzumab.
- If disease remains after preoperative therapy, then you will have ado-trastuzumab emtansine. If ado-trastuzumab emtansine was discontinued for toxicity, then HER2-targeted therapy with trastuzumab alone or with pertuzumab will be given to complete 1 year of therapy. Endocrine therapy will be added. Adjuvant neratinib (HER2 inhibitor) may also be considered for high-risk disease.

Adjuvant endocrine therapy options can be found in **Guide 9**.

HR- with HER2+

Hormone receptor-negative (HR-) breast cancer can be ER- and/or PR-. Since this cancer is HER2+, it is treated with targeted therapy.

HER2-targeted therapy options can be found in **Guide 8**.

- If no disease remains after preoperative therapy, then you will complete up to 1 year of HER2-targeted therapy with trastuzumab alone or with pertuzumab.
- If disease remains after preoperative therapy, then you will have ado-trastuzumab emtansine. If ado-trastuzumab emtansine is discontinued for toxicity, then you will receive HER2-targeted therapy with trastuzumab alone or with pertuzumab to complete 1 year of therapy.

HR+ with HER2-

Hormone receptor-positive (HR+) breast cancer can be ER+ and/or PR+. It is treated with adjuvant endocrine therapy. Olaparib (Lynparza) or abemaciclib (Verzenio) might be added in some cases.

Adjuvant endocrine therapy options can be found in **Guide 9**.

Guide 8**HER2-targeted therapy options: HER2+ cancer**

Preferred options	<ul style="list-style-type: none"> • Paclitaxel and trastuzumab • Docetaxel, carboplatin, and trastuzumab (TCH) • Docetaxel, carboplatin, trastuzumab, and pertuzumab (TCHP) <hr/> <p>If no residual disease after preoperative therapy or no preoperative therapy:</p> <ul style="list-style-type: none"> • Complete up to 1 year of HER2-targeted therapy with trastuzumab. Pertuzumab might be added. <hr/> <p>If residual disease after preoperative therapy:</p> <ul style="list-style-type: none"> • Ado-trastuzumab emtansine alone. If ado-trastuzumab emtansine discontinued for toxicity, then trastuzumab with or without pertuzumab to complete one year of therapy. • If node positive at initial staging, trastuzumab with pertuzumab
Other recommended	<ul style="list-style-type: none"> • Doxorubicin with cyclophosphamide (AC) followed by docetaxel with trastuzumab • Doxorubicin with cyclophosphamide (AC) followed by docetaxel with trastuzumab and pertuzumab • Paclitaxel or carboplatin with trastuzumab and pertuzumab
Used in some cases	<ul style="list-style-type: none"> • Docetaxel, cyclophosphamide, and trastuzumab • Doxorubicin and cyclophosphamide followed by paclitaxel with trastuzumab • Doxorubicin and cyclophosphamide followed by docetaxel with paclitaxel, trastuzumab, and pertuzumab • Neratinib • Paclitaxel with trastuzumab and pertuzumab • Ado-trastuzumab emtansine (TDM-1)
Notes	<ul style="list-style-type: none"> • Alternative taxanes (ie, docetaxel, paclitaxel, albumin-bound paclitaxel) might be substituted in some cases • An FDA-approved biosimilar or substitute might be used for trastuzumab.

Guide 9

Endocrine therapy options

Premenopause
at diagnosis

Option 1

- Tamoxifen alone for 5 years or with ovarian suppression or ablation



- After 5 years, if in postmenopause, then an aromatase inhibitor for 5 years or consider tamoxifen for another 5 years (for a total of 10 years on tamoxifen)

- After 5 years, if still in premenopause, then consider tamoxifen for another 5 years (for a total of 10 years on tamoxifen) or stop endocrine therapy

Option 2

- Aromatase inhibitor for 5 years with ovarian suppression or ablation, then consider aromatase inhibitor for an additional 3 to 5 years

Menopause at
diagnosis

Option 1

- Aromatase inhibitor for 5 years, then consider aromatase inhibitor for 3 to 5 more years
- Aromatase inhibitor for 2 to 3 years, then tamoxifen to complete 5 years total of endocrine therapy
- Tamoxifen for 2 to 3 years, then an aromatase inhibitor to complete 5 years of endocrine therapy
- Tamoxifen for 2 to 3 years, then up to 5 years of an aromatase inhibitor

Option 2

- Tamoxifen for 4.5 to 6 years, then an aromatase inhibitor for 5 years or consider tamoxifen for another 5 years (for a total of 10 years on tamoxifen)

Option 3

- For those who can't have aromatase inhibitors or who don't want aromatase inhibitors, take tamoxifen for 5 years or consider tamoxifen for up to 10 years

Guide 10**Systemic therapy options: HER2- cancer**

Preferred options	<ul style="list-style-type: none"> • Doxorubicin and cyclophosphamide (AC) with paclitaxel • Docetaxel and cyclophosphamide (TC) • Olaparib, if germline <i>BRCA1</i> or <i>BRCA2</i> mutations <hr/> <ul style="list-style-type: none"> • High-risk triple-negative breast cancer (TNBC): Preoperative pembrolizumab with carboplatin and paclitaxel, followed by preoperative pembrolizumab and cyclophosphamide with doxorubicin or epirubicin, followed by adjuvant pembrolizumab • If TNBC and residual disease after preoperative therapy with taxane-, alkylator-, and anthracycline-based chemotherapy, then capecitabine
Other recommended	<ul style="list-style-type: none"> • Doxorubicin and cyclophosphamide (AC) with docetaxel • Epirubicin and cyclophosphamide (EC) • Docetaxel, doxorubicin, and cyclophosphamide (TAC) <hr/> <p>For TNBC:</p> <ul style="list-style-type: none"> • Paclitaxel with carboplatin • Docetaxel with carboplatin
Used in some cases	<ul style="list-style-type: none"> • Doxorubicin and cyclophosphamide (AC) • Cyclophosphamide, methotrexate, and fluorouracil (CMF) • Doxorubicin and cyclophosphamide (AC) with paclitaxel • Capecitabine (maintenance therapy for TNBC after adjuvant chemotherapy)

Triple-negative breast cancer

In triple-negative breast cancer (TNBC), the tumor has tested negative for HER2, estrogen receptors, and progesterone receptors. It is written as ER- and/or PR- with HER2-. This cancer does not respond to endocrine therapy or HER2-targeted therapy. It is treated with chemotherapy and other systemic therapies found in **Guide 10**.

- ▶ **If no disease remains** after preoperative therapy and you are at high risk for the return of cancer, then you will have pembrolizumab (if a pembrolizumab-containing regimen was given before surgery).
- ▶ **If disease remains or there is cancer in the lymph nodes (node positive)**, then you will have capecitabine. Olaparib might be given if a *BRCA1* or *BRCA2* mutation was found. Pembrolizumab is an option if a pembrolizumab-containing regimen was given before surgery.

Endocrine therapy

Endocrine therapy is used to treat hormone receptor-positive (HR+) breast cancer. This is cancer that tests positive for estrogen receptors (ER+) and/or progesterone receptors (PR+). Endocrine therapy blocks estrogen and progesterone to treat HR+ breast cancer. This can slow tumor growth or shrink the tumor for a period of time. It might also help prevent the risk of cancer returning. Endocrine therapy is often used with other systemic therapies.

Endocrine therapy options can be found in **Guide 9**.

Follow-up care

After treatment, you will enter follow-up care. During this time, your health will be monitored for side effects of treatment and the possible return of cancer called recurrence. This is part of your survivorship care plan. It is important to keep any follow-up doctor visits and imaging test appointments and seek good routine medical care, including regular doctor visits for preventive care and cancer screening.

Tell your care team about any symptoms such as headaches or bone pain. Side effects can be managed. Continue to take all medicine such as endocrine therapy exactly as prescribed and do not miss or skip doses.

You should receive a personalized survivorship care plan. It will provide a summary of possible long-term effects of treatment and a list of follow-up tests. Find out how your primary care provider will coordinate with specialists for your follow-up care.

Follow-up care can be found in **Guide 11**.

Guide 11 Follow-up care

Medical history and physical exam (H&P) 1 to 4 times per year as needed for 5 years, then every year

Screen for changes in family history

Genetic testing and referral to genetic counseling, as needed

Monitor for lymphedema and refer for lymphedema management, as needed

Mammogram every 12 months, may start as soon as 6 months after breast-conserving therapy (mammogram not needed after mastectomy or on reconstructed breast)

Heart tests, as needed

Information on risk of future health issues (comorbidities)

If signs and symptoms of metastases, then blood and imaging tests

If taking endocrine therapy, continue to take endocrine therapy. Do not miss or skip doses

Annual gynecology exam for those on tamoxifen

Bone density tests for those on an aromatase inhibitor or who's ovaries stop working

A personalized survivorship plan that includes treatment summary of possible long-term side effects, clear follow-up recommendations, and coordination of care between the primary care provider and specialists.

Be active, eat a mostly plant-based diet, exercise, limit alcohol use, and achieve and maintain an ideal body weight (BMI of 20 to 25)

Key points

- In stage 3 breast cancer, the cancer can be large and in the lymph nodes, the lymph nodes can be fixed (or not moveable), or the cancer can involve the skin or chest wall. It is not metastatic.
- Treatment before surgery is called preoperative (neoadjuvant) therapy. It can be systemic therapy or radiation therapy. The goal of treatment is to shrink the tumor before surgery.
- Systemic therapy after surgery is called adjuvant therapy. Adjuvant therapy is based on how the tumor responded to preoperative treatment.
- All treatment is based on HER2 and hormone receptor (HR) status.
- In hormone receptor-positive (HR+) breast cancer, tests find hormone receptors for estrogen and/or progesterone on the tumor.
- HR+ breast cancer is treated with endocrine therapy.
- HER2-positive (HER2+) breast cancer is treated with HER2-targeted therapy.
- It is important to keep follow-up visits and imaging test appointments. Seek good routine medical care, including preventative care and cancer screenings. Continue to take all medicines as prescribed.



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7

The breast after surgery

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The look of your breast after surgery will depend on the type of surgery, the amount of tissue removed, and other factors such as your body type, age, and size and shape of the area before surgery. You might consider speaking with a plastic surgeon before surgery. This chapter offers more information on volume displacement, flat closure, and breast reconstruction.

The recovery time for each procedure differs. This can affect your ability to return to work or participate in activities. You might consider speaking with a plastic surgeon before surgery to discuss your options and what to expect.

Volume displacement

With a lumpectomy, most people have a scar with some volume loss. However, if you need a large lumpectomy and your surgeon thinks your breast will look more abnormal afterwards, your breast may be able to be reshaped at the time of surgery. This procedure is called volume displacement or oncoplasty. Only a limited number of cancer centers perform this procedure. It is often done by the cancer surgeon or plastic surgeon right after the lumpectomy. The surgeon will shift the

remaining breast tissue to fill the space left by the removed tumor.

If volume displacement is planned, a larger piece of your breast will need to be removed. Despite a larger piece being removed, the natural look of your breast will be kept. However, with large amounts of tissue removed, your breast may be smaller than before.

You may not like the results of the volume displacement. In this case, breast revision surgery may help. This surgery is done by a plastic surgeon. A second volume displacement may be an option, too. Another option is to get breast implants or mastectomy with reconstruction.

Flat closure

In a total mastectomy with a flat closure, the entire breast, including nipple, extra skin, fat, and other tissue in the breast area, is removed. The remaining skin is tightened and sewn together. No breast mound is created, and no implant is added. The scar will be slightly raised and differ in color than the surrounding skin. A flat closure is not completely flat or smooth. The result varies from person to person. Ask to look at pictures from flat closures so you know what to expect.

You might decide to have a flat closure procedure later or after having breast implants removed. Talk to your care team to learn more.

Breast reconstruction

Breast reconstruction is surgery to rebuild the shape and look of the breast after a mastectomy. In many cases, breast reconstruction involves a staged approach. It might require more than one procedure.

You may have a choice as to when breast reconstruction is done. Immediate reconstruction is finished within hours after removing the breast. Delayed reconstruction can occur months or years after the cancer surgery. Reconstruction can also be done in a staged fashion, with part of the reconstruction done at the time of the original cancer surgery and finished with another surgery later. A plastic surgeon performs breast reconstruction.

Breasts can be reconstructed with implants and flaps. All methods are generally safe, but as with any surgery, there are risks. Ask your treatment team for a complete list of side effects.

Implants

Breast implants are small bags filled with salt water, silicone gel, or both. They are placed under the breast skin or muscle to look like a new breast following a mastectomy. A balloon-like device, called an expander, may be used first to stretch out tissue. It will be placed under your skin or muscle and enlarged every few weeks for 2 to 3 months. When your skin is stretched to the proper size, you will have surgery to place the final implant.

Implants have a small risk of leaking or causing other issues. You may feel pain from the implant or expander. Scar tissue or tissue death can occur.

Take care of yourself. This is a stressful time. Seek out support groups at your local hospital, through social media, or from those listed in the back of this book. Look to friends, relatives, neighbors, and coworkers for social support.



Flaps

Sometimes breast fullness can be recreated after a skin-sparing mastectomy. In a skin-sparing mastectomy, breast tissue is removed from underneath the skin. The nipple remains intact, if possible. The remaining skin flaps are used to create a breast mound. This technique does not use implants or skin transferred from other parts of the body and may be completed in a single surgery. This technique, called a Goldilocks mastectomy, is best suited for those with larger breasts who are willing to have much smaller breasts as a result.

Breasts can be remade using tissue from other parts of your body, known as flaps. These flaps are taken from the abdomen, buttocks, thigh, or from under the shoulder blade. Some flaps are completely removed and then sewn in place. Other flaps stay attached to your body but are slid over and sewn into place.

There are several risks associated with flaps, including death of fat in the flap, which can cause lumps. A hernia may result from muscle weakness. Problems are more likely to occur among those who have diabetes or who smoke.

Implants and flaps

Some breasts are reconstructed with both implants and flaps. This method may give the reconstructed breast more volume to match the other breast. For any reconstruction, you may need surgery on your remaining breast to match the two breasts in size and shape.

Nipple replacement

Like your breast, a nipple can be remade. To rebuild a nipple, a plastic surgeon can use surrounding tissues. Also, nipples can be remade with tissue from the thigh or other nipple. Tissue can be darkened with a tattoo to look more like a nipple. It is important to note that while you can remake something to look like a nipple, it will not have the sensation of your real nipple. Also, a tattoo can be done to look like a nipple without having to take tissue from another part of the body.

What to consider

Some things to consider when deciding to have flat closure or reconstruction after mastectomy:

- **Your desire** – You may have a strong feeling towards flat closure or one form of reconstruction after being given the options. Breast reconstruction should be a shared decision between you and your care team. Make your wishes known.
- **Health issues** – You may have health issues such as diabetes or a blood disorder that might affect or delay healing, or make longer procedures unsafe.
- **Tobacco use** – Smoking delays wound healing and can cause mastectomy flap death (necrosis), nipple-areola complex (NAC) necrosis in a nipple-sparing mastectomy, infection, and failure of implant-based reconstruction. In free flap reconstruction, smoking increases the risk of complications. You are encouraged to stop smoking prior to reconstruction.
- **Breast size and shape** – There are limits to the available sizes of breast implants. Very large breasts or breasts that lack tone or droop (called ptosis) might be difficult to match. Breast reduction surgery might be an option.
- **Body mass index (BMI)** – Those with an elevated BMI have an increased risk of infections and complications with breast reconstruction.

Key points

- Volume displacement is a shifting of the breast tissue to fill the space left by a lumpectomy.
- Flat closure is done after a mastectomy in which the skin is tightened and sewn together without the addition of a breast implant.
- Breast reconstruction is surgery to rebuild the shape and look of the breast.
- Breasts that are fully removed in a mastectomy can be remade with breast implants, flaps, or both.
- Removed nipples can be remade with body tissue and/or tattooing.

8

Recurrence

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When cancer returns, it is called a recurrence. Treatment is based on the types of treatment you had before. Together, you and your care team will choose a treatment plan that is best for you.

Overview

Breast cancer can return in the following areas:

- It can return to the breast or chest wall of the breast that had cancer before.
- It can return to axillary lymph nodes or lymph nodes in or near the breast.
- It can return to other distant parts of the body. This is called metastatic breast cancer.
- You can also have a new breast cancer that is not a recurrence of an earlier cancer.

This chapter presents treatment options for local and regional recurrence.

Tests

You will have tests to learn more about your cancer. Many tests you had when you were first diagnosed will be repeated. This is called restaging. Tests such as a brain or spine MRI might be done based on your symptoms. Tests for recurrence can be found in **Guide 12**.

Guide 12

Possible tests: Recurrence

Medical history and physical exam (H&P)

Blood tests such as CBC and comprehensive metabolic panel (including liver function tests and alkaline phosphatase)

Chest CT with or without contrast

CT with contrast of abdomen with or without pelvis (MRI with contrast might be done instead)

Other imaging as needed

Biopsy tumor or metastasis and test for biomarkers

Determine tumor status including:

- Estrogen receptor (ER) and progesterone receptor (PR) status
- HER2 status

Genetic counseling if at risk for hereditary breast cancer

Assess for distress

Treatment

Treatment is based on where the cancer has returned and what type of treatment you had before. Surgery followed by radiation therapy (RT) and systemic therapy are possible. Systemic and endocrine therapy options will be based on tumor hormone receptor (HR) status, HER2 status, and previous treatments given during your initial cancer treatment. Supportive care will be given. Supportive care aims to relieve side effects such as pain and to improve quality of life.

Local recurrence

Treatment for cancer that has returned to the same breast as before is based on if your first treatment was breast-conserving surgery (lumpectomy) with radiation therapy or a mastectomy with or without radiation therapy (RT). More surgery might be an option. However, if you had RT before, then it may not be possible to have it again in the same area. Systemic and endocrine therapy options will be based on what you had before.

Regional recurrence

If the recurrence is in or near the armpit (axilla), then surgery to remove the tumor might be an option before RT. Systemic therapy might be given before surgery to help reduce the disease burden.

Both local and regional

Cancer that is both local and regional might be referred to as a locoregional recurrence. Treatment for a locoregional recurrence is surgery and RT when possible. Some people

receive systemic therapy or RT if surgery is not possible.

Unresectable

An unresectable tumor cannot be removed with surgery. It is treated with systemic therapy. For treatment of unresectable recurrent disease, see *NCCN Guidelines for Patients: Metastatic Breast Cancer*, available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



Key points

- When cancer returns, it is called a recurrence.
- Cancer that returns to the breast that had cancer before is called a local recurrence.
- Cancer that returns to axillary lymph nodes or lymph nodes in or near the breast is called a regional recurrence.
- Cancer that returns to distant parts of the body is called metastatic breast cancer.
- Treatment is based on where the cancer has returned and what type of treatment you had before.
- Surgery followed by radiation therapy and systemic therapy are possible. Systemic and endocrine therapy options will be based on hormone receptor and HER2 status, and any mutations found.
- Supportive care will be given. Supportive care aims to relieve side effects such as pain and to improve quality of life.
- An unresectable tumor cannot be removed with surgery. Unresectable recurrent disease is treated as metastatic disease with systemic therapy.

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Making treatment decisions

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It's important to be comfortable with the cancer treatment you choose. This choice starts with having an open and honest conversation with your care team.

It's your choice

In shared decision-making, you and your team share information, discuss the options, and agree on a treatment plan. It starts with an open and honest conversation between you and your care team.

Treatment decisions are very personal. What is important to you may not be important to someone else. Some things that may play a role in your decision-making:

- What you want and how that might differ from what others want
- Your religious and spiritual beliefs
- Your feelings about certain treatments
- Your feelings about pain or side effects
- Cost of treatment, travel to treatment centers, and time away from school or work
- Quality of life and length of life
- How active you are and the activities that are important to you

Think about what you want from treatment. Discuss openly the risks and benefits of specific treatments and procedures. Weigh options and share concerns with your

care team. If you take the time to build a relationship with your care team, it will help you feel supported when considering options and making treatment decisions.

Second opinion

It is normal to want to start treatment as soon as possible. While cancer can't be ignored, there is time to have another doctor review your test results and suggest a treatment plan. This is called getting a second opinion, and it's a normal part of cancer care. Even doctors get second opinions!

Things you can do to prepare:

- Check with your insurance company about its rules on second opinions. There may be out-of-pocket costs to see doctors who are not part of your insurance plan.
- Make plans to have copies of all your records sent to the doctor you will see for your second opinion.

Support groups

Many people diagnosed with cancer find support groups to be helpful. Support groups often include people at different stages of treatment. Some people may be newly diagnosed, while others may be finished with treatment. If your hospital or community doesn't have support groups for people with cancer, check out the websites listed in this book.

Questions to ask

Possible questions to ask your care team are listed on the following pages. Feel free to use these questions or come up with your own.

Questions about your care team’s experience

1. What is your experience treating breast cancer? What else do you treat?
2. What is the experience of those on your team?
3. How many people like me have you treated?
4. Will you be consulting with experts to discuss my care? Whom will you consult?
5. How many procedures like the one you’re suggesting have you done?
6. Is this treatment a major part of your practice?
7. How often is a complication expected? What are the complications?
8. How many breast cancer surgeries have you done?
9. Who will manage my day-to-day care?

Questions about options

1. What will happen if I do nothing?
2. Which option is proven to work best for my cancer, age, overall health, and other risk factors?
3. What are the possible complications and side effects? Are any life-threatening?
4. What can be done to prevent or relieve the side effects of treatment?
5. Am I a candidate for a clinical trial?
6. Can I join a clinical trial at any time?
7. What decisions must be made today?
8. Is there a social worker or someone who can help me decide about treatment?
9. Is there a hospital or treatment center you can recommend for breast cancer treatment?
10. Can I go to one hospital for surgery and a different center for radiation therapy?

Questions about treatment

1. Which treatment(s) do you recommend and why?
2. Does the order of treatment matter?
3. When will I start treatment?
4. How long will treatment take?
5. What should I expect from treatment?
6. What will you do to make me comfortable during treatment?
7. How much will my insurance pay for treatment?
8. Are there programs to help me pay for treatment?
9. What are the chances my cancer will return after treatment?
10. I would like a second opinion. Is there someone you can recommend?

Questions about surgery

1. How much of my breast will be removed?
2. What will my breast look like after surgery?
3. What lymph nodes might be removed during surgery?
4. What are the chances you can remove the whole tumor with a negative margin?
5. How can I prepare for surgery?
6. How long will recovery take and what should I expect?
7. When will I be able to return to work or normal activities after surgery?
8. How much pain will I be in and what will be done to manage my pain?
9. What complications can occur from this surgery?
10. What options are available if I do not like the look of my breast after surgery?

Questions about radiation therapy

1. What type of radiation therapy (RT) will I have?
2. What will you target?
3. What is the goal of this RT?
4. How many treatment sessions will I require?
5. Can you do a shorter course of RT?
6. Do you offer this type of RT here? If not, should I be referred to someone who does?
7. What side effects can I expect from RT?
8. Will I be given medicine to help me relax during RT?
9. What should I wear?

Questions about clinical trials

1. What clinical trials are available for my type and stage of breast cancer?
2. What are the treatments used in the clinical trial?
3. What does the treatment do?
4. Has the treatment been used before? Has it been used for other types of cancer?
5. What are the risks and benefits of this treatment?
6. What side effects should I expect? How will the side effects be controlled?
7. How long will I be in the clinical trial?
8. Will I be able to get other treatments if this doesn't work?
9. How will you know the treatment is working?
10. Will the clinical trial cost me anything? If so, how much?

Questions about resources and support

- 1. Who can I talk to about help with housing, food, and other basic needs?
- 2. What help is available for transportation, childcare, and home care?
- 3. How much will I have to pay for treatment?
- 4. What help is available to pay for medicines and other treatment?
- 5. What other services are available to me and my caregivers?
- 6. How can I connect with others and build a support system?
- 7. How can I find in-person or online support?
- 8. Who can help me with my concerns about missing work or school?
- 9. Who can I talk to if I don't feel safe at home, at work, or in my neighborhood?
- 10. How can I get help to stop smoking or vaping?

Resources

Breast Cancer Alliance

[Breastcanceralliance.org](https://breastcanceralliance.org)

Breastcancer.org

[Breastcancer.org](https://breastcancer.org)

CanCare

[Cancare.org](https://cancare.org)

CancerCare

[Cancercares.org](https://cancercares.org)

Cancer Hope Network

cancerhopenetwork.org

DiepC Foundation

diepcfoundation.org

FORCE: Facing Our Risk of Cancer

Empowered

facingourrisk.org

GPAC Global Patient Advocacy Coalition

[GPACunited.org](https://gpacunited.org)

Inflammatory Breast Cancer Research

Foundation

ibcresearch.org

Lobular Breast Cancer Alliance

lobularbreastcancer.org

National Coalition for Cancer Survivorship

canceradvocacy.org

Sharsheret

sharsheret.org

Triage Cancer

[Triagecancer.org](https://triagecancer.org)

Unite for HER

uniteforher.org

Young Survival Coalition

youngsurvival.org



Words to know

accelerated partial breast irradiation (APBI)

Treatment with radiation to the part of the breast with cancer. It is given over a shorter period of time compared to whole breast radiation therapy.

anti-estrogen

A drug that stops estrogen from attaching to cells.

areola

A darker, round area of skin on the breast around the nipple.

aromatase inhibitor (AI)

A drug that lowers the level of estrogen in the body.

axillary lymph node (ALN)

A small disease-fighting structure that is near the armpit (axilla).

axillary lymph node dissection (ALND)

An operation that removes the disease-fighting structures (lymph nodes) near the armpit.

bilateral diagnostic mammogram

Pictures of the insides of both breasts that are made from a set of x-rays.

bilateral oophorectomy

An operation that removes both ovaries.

biopsy

A procedure that removes fluid or tissue samples to be tested for a disease.

biosimilar

A drug that is almost an identical drug made by another company. It has been approved by the U.S. Food and Drug Administration (FDA) and

must be used in the exact same way and at the same dose as the other drug.

bone mineral density

A test that measures the strength of bones.

bone scan

A test that makes pictures of bones to assess for health problems.

boost

An extra dose of radiation to a specific area of the body.

breast-conserving surgery (BCS)

A cancer treatment that includes removing a breast lump.

breast implant

A small bag filled with salt water, gel, or both that is used to remake breasts.

breast reconstruction

An operation that creates new breasts.

cancer stage

A rating of the outlook of a cancer based on its growth and spread.

carcinoma

A cancer of cells that line the inner or outer surfaces of the body.

chest wall

The layer of muscle, bone, and fat that protects the vital organs.

clinical breast exam (CBE)

Touching of a breast by a health expert to feel for diseases.

clinical stage (c)

The rating of the extent of cancer before treatment is started.

clinical trial

A type of research that assesses health tests or treatments.

connective tissue

Supporting and binding tissue that surrounds other tissues and organs.

contrast

A substance put into your body to make clearer pictures during imaging tests.

core needle biopsy (CNB)

A procedure that removes tissue samples with a hollow needle. Also called core biopsy.

diagnostic bilateral mammogram

Pictures of the insides of both breasts that are made from a set of x-rays.

duct

A tube-shaped structure through which milk travels to the nipple.

ductal carcinoma

A breast cancer that starts in the cells that line the ducts.

endocrine therapy

A cancer treatment that stops the making or action of estrogen. Also called hormone therapy.

estrogen

A hormone that plays a role in breast development.

estrogen receptor (ER)

A protein inside cells that binds to estrogen.

estrogen receptor-negative (ER-)

A type of breast cancer that doesn't use estrogen to grow.

estrogen receptor-positive (ER+)

A type of breast cancer that uses estrogen to grow.

fine-needle aspiration (FNA)

A procedure that removes tissue samples with a very thin needle.

flat closure

Procedure done after a mastectomy in which the skin is tightened and sewn together without the addition of a breast implant.

gene

Coded instructions in cells for making new cells and controlling how cells behave.

genetic counseling

Expert guidance on the chance for a disease that is passed down in families.

hereditary breast cancer

Breast cancer likely caused by abnormal genes passed down from biological parent to child.

histology

The structure of cells, tissue, and organs as viewed under a microscope.

hormone

A chemical in the body that triggers a response from cells or organs.

hormone receptor-negative cancer (HR-)

Cancer cells that don't use hormones to grow.

hormone receptor-positive cancer (HR+)

Cancer cells that use hormones to grow.

human epidermal growth factor receptor 2 (HER2)

A protein on the surface of a cell that sends signals for the cell to grow.

immunohistochemistry (IHC)

A lab test of cancer cells to find specific cell traits involved in abnormal cell growth.

invasive breast cancer

The growth of breast cancer into the breast's supporting tissue (stroma).

lobule

A gland in the breast that makes breast milk.

lobular carcinoma

A breast cancer that starts in the lobules (milk glands) of the breast.

lumpectomy

An operation that removes a small breast cancer tumor. Also called breast-conserving surgery.

lymph

A clear fluid containing white blood cells.

lymph node

A small, bean-shaped disease-fighting structure.

lymphadenopathy

Lymph nodes that are abnormal in size or consistency.

lymphatic system

Germ-fighting network of tissues and organs that includes the bone marrow, spleen, thymus, lymph nodes, and lymphatic vessels. Part of the immune system.

lymphedema

Swelling in the body caused by a buildup of fluid called lymph.

magnetic resonance imaging (MRI)

A test that uses radio waves and powerful magnets to make pictures of the insides of the body.

mammogram

A picture of the insides of the breast that is made using x-rays.

mastectomy

An operation that removes the whole breast.

menopause

The point in time 12 months after a last menstrual period.

mutation

An abnormal change.

nipple-areola complex (NAC)

The ring of darker breast skin is called the areola. The raised tip within the areola is called the nipple.

noninvasive breast cancer

Breast cancer that has not grown into tissue from which it can spread.

palpable adenopathy

Lymph nodes that feel abnormal in size or consistency.

partial breast irradiation

Treatment with radiation that is received at the site of the removed breast tumor.

pathologic stage (p)

A rating of the extent of cancer given after examining tissue removed during surgery.

pathologist

A doctor who's an expert in testing cells and tissue to find disease.

postmenopause

The state of having no more menstrual periods.

premenopause

The state of having menstrual periods.

primary tumor

The first mass of cancer cells.

prognosis

The likely course and outcome of a disease based on tests.

radiation therapy (RT)

A treatment that uses high-energy rays. Also called radiotherapy.

recurrence

The return of cancer after a cancer-free period.

sentinel lymph node (SLN)

The first lymph node to which cancer cells spread after leaving a tumor.

sentinel lymph node biopsy (SLNB)

An operation to remove the disease-fighting structures (lymph nodes) to which cancer first spreads. Also called sentinel lymph node dissection.

side effect

An unhealthy or unpleasant physical or emotional response to treatment.

skin-sparing mastectomy

An operation that removes all breast tissue but saves as much breast skin as possible.

supportive care

Health care that includes symptom relief but not cancer treatment. Also called palliative care or best supportive care.

surgical margin

The normal-looking tissue around a tumor removed during an operation.

systemic therapy

Drug treatment that works throughout the body.

total mastectomy

An operation that removes the entire breast with a flat closure. Also called simple mastectomy.

ultrasound

A test that uses sound waves to take pictures of the inside of the body.

vacuum-assisted core biopsy (VACB)

A procedure in which a small sample of tissue is removed from the breast with the aid of a vacuum device.

volume displacement

A method to shift breast tissue during an operation to fill a space left from a lumpectomy.

whole breast radiation therapy (WBRT)

Treatment with radiation of the entire breast.

NCCN Contributors

This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer Version 1.2024. It was adapted, reviewed, and published with help from the following people:

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NCCN Cancer Centers

Abramson Cancer Center
at the University of Pennsylvania
Philadelphia, Pennsylvania
800.789.7366 • penncancer.org

**Case Comprehensive Cancer Center/
University Hospitals Seidman Cancer Center and
Cleveland Clinic Taussig Cancer Institute**
Cleveland, Ohio
UH Seidman Cancer Center
800.641.2422 • uhhospitals.org/services/cancer-services
CC Taussig Cancer Institute
866.223.8100 • my.clevelandclinic.org/departments/cancer
Case CCC
216.844.8797 • case.edu/cancer

City of Hope National Medical Center
Duarte, California
800.826.4673 • cityofhope.org

**Dana-Farber/Brigham and Women's Cancer Center |
Mass General Cancer Center**
Boston, Massachusetts
877.442.3324 • youhaveus.org
617.726.5130 • massgeneral.org/cancer-center

Duke Cancer Institute
Durham, North Carolina
888.275.3853 • dukecancerinstitute.org

Fox Chase Cancer Center
Philadelphia, Pennsylvania
888.369.2427 • foxchase.org

Fred & Pamela Buffett Cancer Center
Omaha, Nebraska
402.559.5600 • unmc.edu/cancercenter

Fred Hutchinson Cancer Center
Seattle, Washington
206.667.5000 • fredhutch.org

Huntsman Cancer Institute at the University of Utah
Salt Lake City, Utah
800.824.2073 • healthcare.utah.edu/huntsmancancerinstitute

**Indiana University Melvin and Bren Simon
Comprehensive Cancer Center**
Indianapolis, Indiana
888.600.4822 • www.cancer.iu.edu

Mayo Clinic Comprehensive Cancer Center
Phoenix/Scottsdale, Arizona
Jacksonville, Florida
Rochester, Minnesota
480.301.8000 • Arizona
904.953.0853 • Florida
507.538.3270 • Minnesota
mayoclinic.org/cancercenter

Memorial Sloan Kettering Cancer Center
New York, New York
800.525.2225 • mskcc.org

Moffitt Cancer Center
Tampa, Florida
888.663.3488 • moffitt.org

O'Neal Comprehensive Cancer Center at UAB
Birmingham, Alabama
800.822.0933 • uab.edu/onealcancercenter

**Robert H. Lurie Comprehensive Cancer Center
of Northwestern University**
Chicago, Illinois
866.587.4322 • cancer.northwestern.edu

Roswell Park Comprehensive Cancer Center
Buffalo, New York
877.275.7724 • roswellpark.org

**Siteman Cancer Center at Barnes-Jewish Hospital
and Washington University School of Medicine**
St. Louis, Missouri
800.600.3606 • siteman.wustl.edu

**St. Jude Children's Research Hospital/
The University of Tennessee Health Science Center**
Memphis, Tennessee
866.278.5833 • stjude.org
901.448.5500 • uthsc.edu

Stanford Cancer Institute
Stanford, California
877.668.7535 • cancer.stanford.edu

**The Ohio State University Comprehensive Cancer Center -
James Cancer Hospital and Solove Research Institute**
Columbus, Ohio
800.293.5066 • cancer.osu.edu

**The Sidney Kimmel Comprehensive
Cancer Center at Johns Hopkins**
Baltimore, Maryland
410.955.8964
www.hopkinskimmelmcc.org

The UChicago Medicine Comprehensive Cancer Center
Chicago, Illinois
773.702.1000 • uchicagomedicine.org/cancer

The University of Texas MD Anderson Cancer Center
Houston, Texas
844.269.5922 • mdanderson.org

UC Davis Comprehensive Cancer Center
Sacramento, California
916.734.5959 • 800.770.9261
health.ucdavis.edu/cancer

UC San Diego Moores Cancer Center

La Jolla, California

858.822.6100 • cancer.ucsd.edu

UCLA Jonsson Comprehensive Cancer Center

Los Angeles, California

310.825.5268 • uclahealth.org/cancer

UCSF Helen Diller Family Comprehensive Cancer Center

San Francisco, California

800.689.8273 • cancer.ucsf.edu

University of Colorado Cancer Center

Aurora, Colorado

720.848.0300 • coloradocancercenter.org

University of Michigan Rogel Cancer Center

Ann Arbor, Michigan

800.865.1125 • rogelcancercenter.org

University of Wisconsin Carbone Cancer Center

Madison, Wisconsin

608.265.1700 • uwhealth.org/cancer

UT Southwestern Simmons Comprehensive Cancer Center

Dallas, Texas

214.648.3111 • utsouthwestern.edu/simmons

Vanderbilt-Ingram Cancer Center

Nashville, Tennessee

877.936.8422 • vicc.org

Yale Cancer Center/Smilow Cancer Hospital

New Haven, Connecticut

855.4.SMILOW • yalecancercenter.org

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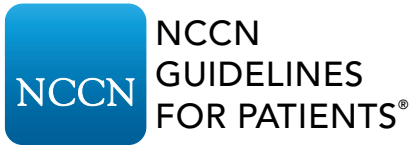
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Invasive Breast Cancer

2024

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