



NCCN  
GUIDELINES  
FOR PATIENTS®

2025

# Invasive Breast Cancer



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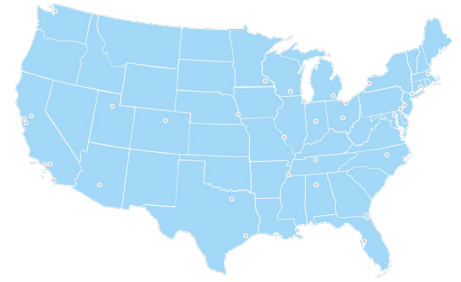


# About the NCCN Guidelines for Patients®



National Comprehensive  
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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 3.2025 – March 18, 2025.**

Learn how the NCCN Guidelines for Patients are developed

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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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# 1

## About invasive breast cancer

- 5 What is invasive breast cancer?
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**Invasive breast cancer is cancer that has spread from the milk ducts or milk glands (lobules) into the surrounding breast tissue or nearby lymph nodes. Invasive breast cancer is also called early-stage breast cancer.**

## What is invasive breast cancer?

Breast cancer starts in the cells of the breast. Over time, these cells form a mass called a tumor. In invasive breast cancer, cancer has grown outside the milk ducts or milk glands (lobules) into the surrounding breast tissue.

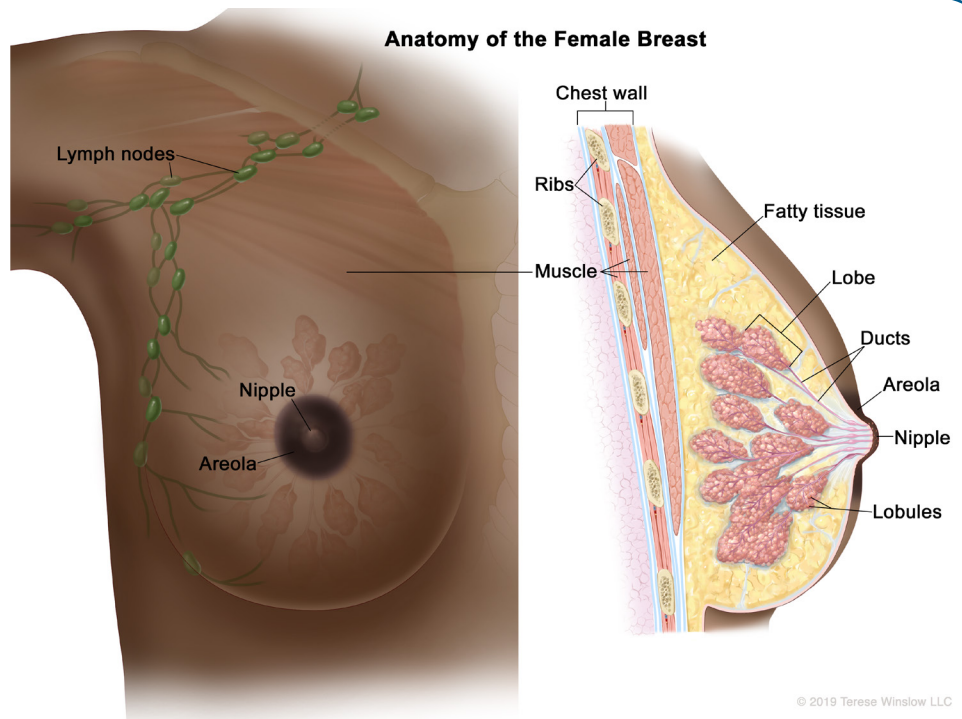
Once outside the ducts or lobules, breast cancer can spread through lymph or blood to lymph nodes or other parts of the body.

Almost all invasive breast cancers are carcinomas—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. A TDLU consists of a lobule connected to the end of a small milk duct. The most common types of invasive breast cancer are ductal carcinoma and lobular carcinoma.

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

### The breast

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



## What are the parts of the breast?

The breast is 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 are the pectoral (chest) muscle and ribs. Muscle and ligaments help hold the breast in place.

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 in the center of the breast 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.

Lymphatic fluid (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). Cancer cells can travel through blood and lymph to lymph nodes and other parts of the body.

## What's in this book?

This book is organized into the following chapters:

**Chapter 2: Testing for breast cancer** provides an overview of tests you might receive, and the role of HER2 status, hormone receptors, genetic cancer risk, and biomarker testing.

**Chapter 3: Breast cancer staging** provides information on how breast cancer is staged.

**Chapter 4: Types of treatment** gives a general overview of invasive breast cancer treatment and what to expect.

**Chapter 5: Supportive care** gives an overview of what supportive care is and possible side effects of treatment.

**Chapter 6: Your treatment options** provides specific surgery and systemic therapy options for your cancer based on hormone receptor (HR) and HER2 tumor status. It also discusses who might benefit from systemic therapy before surgery.

**Chapter 7: The breast after surgery** offers more information on volume displacement, flat closure, and breast reconstruction.

**Chapter 8: Recurrence** explains treatment options for cancer that has returned.

**Chapter 9: Other resources** provides information on patient advocacy groups and where to get help.



## What can you do to get the best care?

Advocate for yourself. You have an important role to play in your care. In fact, you're more likely to get the care you want by asking questions and making shared decisions with your care team. Consider seeking the opinion of a breast cancer specialist and team that specializes in diagnosis and management of breast cancer.

The NCCN Guidelines for Patients will help you understand cancer care. With better understanding, you'll be more prepared to discuss your care with your team and share your concerns. Many people feel more satisfied when they play an active role in their care.

You may not know what to ask your care team. That's common. Each chapter in this book ends with an important section called Questions to ask. These suggested questions will help you get more information on all aspects of your care.

Take the next step and keep reading to learn what is the best care for you!

## Why you should read this book

Making decisions about cancer care can be stressful. You may need to make tough decisions under pressure about complex choices.

The NCCN Guidelines for Patients are trusted by patients and providers. They clearly explain current care recommendations made by respected experts in the field. Recommendations are based on the latest research and practices at leading cancer centers.

Cancer care is not the same for everyone. By following expert recommendations for your situation, you are more likely to improve your care and have better outcomes as a result. Use this book as your guide to find the information you need to make important decisions.



**The NCCN Guidelines for Patients are seen as a trusted source by researchers, clinicians, and advocates. They set the standard for appropriate and effective breast cancer treatment, making them a good first step for newly diagnosed patients."**

# 2

## Testing for breast cancer

- 9 General health tests
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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.**

Tests are used to find cancer, plan treatment, and check how your cancer is responding to treatment. Results from a tumor biopsy and imaging studies will be used to determine what treatments are best for your type of breast cancer. Testing takes time. 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 with 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 doctor 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. It's important to know the specific type of cancer, or where the cancer started, if it was in multiple locations, how old they were when they had the cancer, 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

Tumor estrogen receptor (ER) and progesterone receptor (PR) status

Tumor HER2 status

Genetic counseling and testing if at risk for hereditary breast cancer or have triple-negative breast cancer (TNBC)

Address fertility and sexual health concerns

Pregnancy test in those of childbearing potential

Assess for distress

Lymphedema baseline screening

### 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

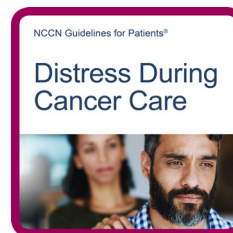
A clinical breast exam (CBE) is a physical exam of the bare breast performed by a health care provider to check for lumps or other changes. It is done while you are seated and/or lying down. Your provider should take time to palpate (feel) the entire breast, including the armpit. A nurse or assistant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

### Distress screening

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.

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, people, and medicine that can help you. Support and counseling are available. Your treatment team will ask about your level of distress. This is part of your cancer care.

More information on distress can be found in the *NCCN Guidelines for Patients: Distress During Cancer Care* at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



### Lymphedema baseline screening

Lymphedema is a condition in which lymph fluid builds up in tissues and causes swelling. A lymphedema baseline screening measures the fluid levels in your body. It is done to look for small changes in the body after surgery.

### Performance status

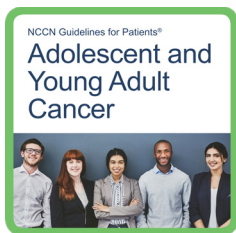
Performance status (PS) is a person's general level of fitness and ability to perform daily tasks. Your state of general health might be rated using a PS scale called the Eastern Cooperative Oncology Group (ECOG) score or the Karnofsky Performance Status (KPS). PS is one factor taken into consideration when choosing a treatment plan.

## Fertility (all genders)

Some types of treatment such as chemotherapy can affect fertility, or 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 can be found at *NCCN Guidelines for Patients: Adolescent and Young Adult Cancer* 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

Preventing pregnancy during treatment is important. Cancer treatment can affect the ovaries, damage sperm, and hurt a developing baby. Therefore, becoming pregnant or having one's partner become pregnant during treatment should be avoided. Non-hormonal birth control methods such as intrauterine devices (IUDs) and barrier methods are preferred in those with a breast cancer diagnosis. Types of barrier methods include condoms, diaphragms, cervical caps, and the contraceptive sponge. If you are pregnant at the time of your cancer diagnosis, treatment will need to be tailored to protect your unborn child. If you are breastfeeding at the time of cancer diagnosis, you may need to stop breastfeeding during treatment.

## Blood tests

Blood tests check for signs of disease and how well organs are working. Some blood tests you might have are described next.

### 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 substances in your blood. It 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.

### **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, a medical expert, will interpret the test and send a report to your doctor. While these reports might be available to you through your patient portal or patient access system, please wait to discuss these results with your care team

The following imaging tests are not in order of importance. You may not need all of these tests.

### **Bone scan**

A bone scan uses a radiotracer to highlight areas of bone damage or loss. 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 material is a substance used to improve the quality of the pictures of the inside of the body. It is used to make the pictures clearer. Contrast might be taken by mouth (oral) or given through a vein (IV). Oral contrast does not get absorbed from your intestines and will be passed with your next bowel movements. IV contrast will leave the body in the urine immediately after the test.



The types of contrast vary and are different for CT and MRI. Not all imaging tests require contrast, but many do.

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. Contrast might not be used if you have a serious allergy or if your kidneys aren't working well.

### 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. Intravenous (IV) contrast is often used.

### Diagnostic mammogram

A mammogram is a picture of the inside of your breast. The pictures are made using x-rays. A computer combines the x-rays to make detailed pictures. A bilateral mammogram includes pictures of both breasts. 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. They are 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 tests may include a breast MRI or ultrasound.

### 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 mammogram

- Done on a regular basis when there are no signs or symptoms of breast cancer. Results take a few days.

#### Diagnostic mammogram

- Used for those who have symptoms such as a lump, pain, nipple thickening or discharge, or those whose breasts have changed shape or size. An ultrasound is often used with a diagnostic mammogram.
- 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.

### 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, which means there is no radiation delivered to your body during the test. Because of the very strong magnets used in the MRI machine, tell the technologist if you have any metal or a pacemaker 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 used.

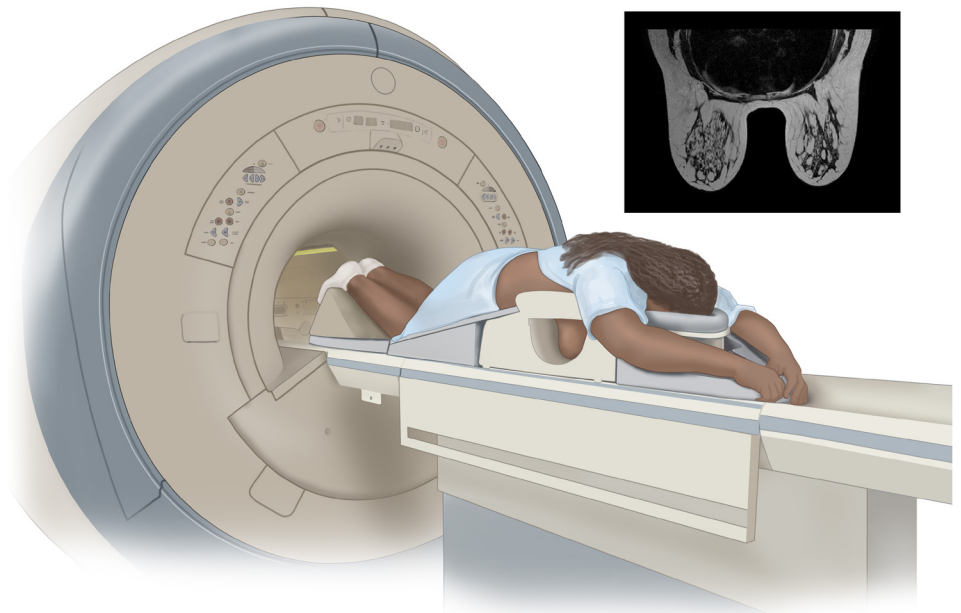
A closed MRI has a capsule-like design where the magnet surrounds you. The space is small and enclosed. An open MRI has a magnetic top and bottom, which allows for an opening on each end. Closed MRIs are more common than open MRIs, so if you have claustrophobia (a dread or fear of enclosed spaces), be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

to talk to your care team about it. MRI scans take longer to perform than CT scans.

- **A breast MRI** might be used in addition to a mammogram. 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 (metastasized) to the spine or brain.

### Breast MRI

If needed, a breast MRI will be done in addition to a mammogram. In a breast MRI, you are positioned face down with your arms overhead.



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### PET scan

A PET (positron emission tomography) 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 how much sugar is being taken up by the cancer cells. This gives an idea about how fast the cancer cells are growing. 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 found on the PET scan 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 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.
- **A sodium fluoride PET/CT** uses a radiotracer made of sodium fluoride.
- **An FES-PET/CT uses FES**, which is a radioactive form of the hormone estrogen. An FES-PET/CT might be used when cancer is estrogen receptor-positive (ER+).

**Testing takes time. It might take days or weeks before all test results come in.**

### 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 is painless and does not use x-rays, so it can be repeated as needed. Ultrasound is good at showing small areas of cancer in the breast and abnormal lymph nodes. Sometimes, a breast ultrasound or MRI is used to guide a biopsy.

## Biopsy

A biopsy is the removal of a sample of tissue from your body 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 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 from a special vacuum device is used to remove the sample through a needle.
- **Incisional biopsy** removes a small amount of tissue through a 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. An excisional biopsy is usually done under anesthesia by a surgeon in an operating room.

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 possible future treatment and imaging. The clips will 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.

### 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. The tissue may be benign (not cancer), atypical (not typical), or cancerous. If the tissue is benign, likely this area can be observed. If the tissue is atypical, you may be recommended to have a surgical (open) biopsy of the area for further evaluation. If

tissue shows cancer, your health care provider will discuss next steps. Your pathology report will contain information about histology and the grade (how abnormal the tumor looks) of the cancer.

### 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-negative (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 invasive 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 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+), progesterone receptor-positive (PR+), or both (ER+/PR+).

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

**Other systemic therapies** are used with those listed above to treat invasive breast cancer.

### Immunohistochemistry

Immunohistochemistry (IHC) is a special staining process that involves adding a chemical marker to cancer or immune cells. The 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.

### FISH or ISH

Fluorescence in situ hybridization (FISH) or other ISH methods like dual ISH are testing methods that involve special dyes called probes that attach to pieces of DNA, the genetic material in a person's cells.

## 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 substances such as hormones attach (bind) to these 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 (hormone-blocking) therapy.

There are 2 types of hormone receptors:

- **Estrogen** plays a role in ovary, uterus, and breast development
- **Progesterone** plays a role in menstrual cycle and pregnancy

### 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.

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

### Hormone receptor-positive

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

- **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. An ER-/PR+ tumor is relatively uncommon.

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

### Hormone receptor-negative

Hormone receptor-negative (HR-) breast cancer cells do not have 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-.

## Biomarker testing

Biomarker testing or tumor mutation testing is more commonly done in metastatic breast cancer. For more information, see *NCCN Guidelines for Patients: Metastatic Breast Cancer* at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.

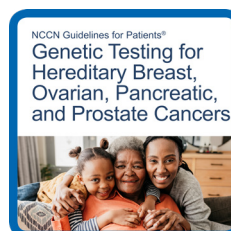


## Genetic cancer risk testing

About 1 out of 20 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 with you about the results. Tests results may be used to guide treatment planning.

Genetic testing is done using blood or saliva (spitting into a cup or using a cheek swab). The goal is to look for gene mutations inherited from your biological (birth) 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 family members might carry these mutations. Tell your care team if there is a family history of cancer.

More information on genetic cancer risk testing can be found in the *NCCN Guidelines for Patients: Genetic Testing for Hereditary Breast, Ovarian, Pancreatic, and Prostate Cancers* at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.

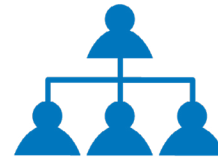


### **BRCA tests**

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, colorectal, pancreatic, and melanoma skin cancers. Mutated *BRCA* genes can also affect how some treatments work. These tests might be repeated if you tested negative for a gene mutation over 10 years ago, as genetic testing technology has improved.

### **Other genes**

Other genes such as *PALB2*, *p53*, *CHEK2*, and *ATM* might be tested. For example, *PALB2* normally helps prevent cancer. When *PALB2* mutates, it no longer works correctly. Those with a *PALB2* mutation have a higher risk of developing breast cancer.



### **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 (birth) 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?



## Key points

- Tests are used to find cancer, plan treatment, and check how your cancer is responding to treatment.
- You will have a physical exam, including a breast exam, to see if anything feels or looks abnormal.
- Treatment can affect your fertility or the ability to have children. You might be referred to a fertility specialist to discuss fertility preservation.
- A diagnostic 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 histology. This provides information about the behavior of your cancer, as well as treatments to which your cancer may respond. Other biomarker tests may be performed.
- About 1 out of 20 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 or to speak with a genetic counselor.

## Questions to ask

- What type(s) of imaging scans will I have?
- What type(s) of biopsy will I have?
- What tests will be done on the tumor?
- When will the test results be ready and who will discuss the results with me?
- What is the tumor HER2 and hormone receptor (HR) status?

# 3

## Breast cancer staging

- 23 How is breast cancer staged?
- 24 TNM scores
- 26 Numbered stages
- 27 Key points
- 27 Questions to ask



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 and standard-of-care treatment results.

## How is breast cancer staged?

A cancer stage is a way to describe the extent of the cancer at the time you are first diagnosed. 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.

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) and progesterone receptor (PR) tumor status:** Does the cancer have the protein called an estrogen or progesterone receptor?
- **Human epidermal growth factor receptor 2 (HER2) tumor 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 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.

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. 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. The pathologic stage and clinical stage may be different, if imaging was not completely accurate. If you are given drug therapy before surgery, then the stage might look like ypT2.

## TNM scores

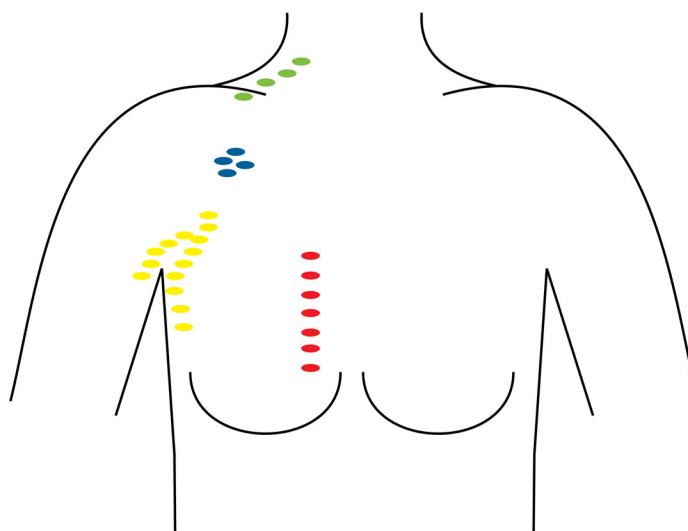
The tumor, node, metastasis (TNM) system is used to stage breast cancer. In this system, the letters T, N, and M describe different areas of cancer growth. Based on cancer test results, your doctor will assign a score or number to each letter. The higher the number, the larger the tumor or the more the 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

#### 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

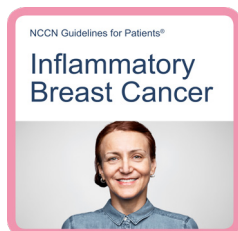


#### T = Tumor

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
- **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)

For more information on inflammatory breast cancer, see *NCCN Guidelines for Patients: Inflammatory Breast Cancer* 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. A low-grade tumor has a low risk of recurrence. A high-grade tumor has a higher risk of recurrence (of cancer returning).

- **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.

## Questions to ask

- What is the cancer stage and tumor grade?
- What does the cancer stage and grade mean in terms of treatment options and prognosis?
- Is there more than one known cancer site?
- Is cancer in the lymph nodes? If so, which lymph nodes?
- What is the tumor HER2 and hormone status?

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



# 4

## Types of treatment

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**There is more than one treatment for breast cancer. Treatment is usually a combination of surgery and other therapies. This chapter provides a general overview of the types of treatment 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 the planning and implementing of 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.

## 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
- Radiation therapy (RT)

**Systemic therapy** works throughout the body. It includes:

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

Treatment options are often described in the following ways:

- **Preferred therapies** have the most evidence they work better and may be safer than other therapies.
- **Other recommended therapies** may not work quite as well as preferred therapies, but they can still help treat cancer.
- **Therapies used in certain cases** work best for people with specific cancer features or health circumstances.

Many factors play a role in how cancer responds to treatment. It is important to have regular talks with your care team about your goals for treatment and your treatment plan.

# Surgery

Surgery is an operation or procedure to remove cancer from the body. It 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 who is 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.

## 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. A clear or negative margin (R0) is when 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.

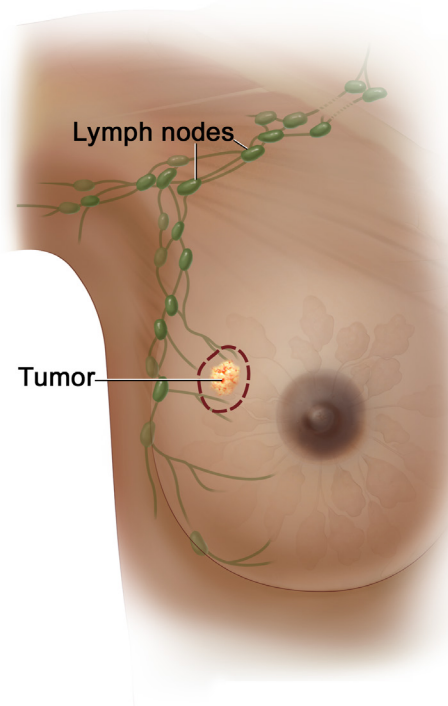
After surgery, you may receive treatment such as radiation to kill any remaining cancer cells. You might have a wound drain to prevent fluid from collecting in the body after surgery. These drains are usually removed a few days after surgery.

## Lumpectomy

Lumpectomy is the removal of abnormal cells or a tumor. It does not remove the whole

## 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).



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breast. A lumpectomy is also called a partial mastectomy, breast-conserving therapy, or breast-conserving surgery (BCS). In a lumpectomy, the surgeon aims to remove the tumor with a 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 is removed.

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 surgeon.

### Mastectomy

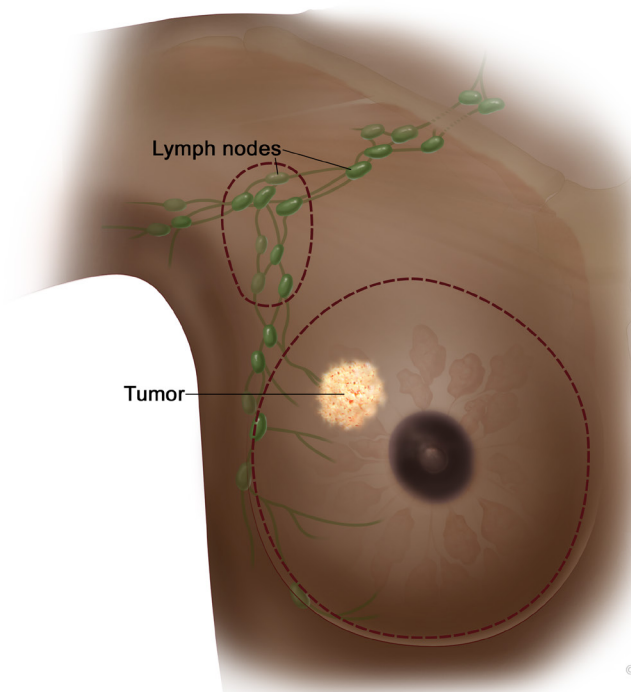
A mastectomy removes all or part of the breast tissue. Before removing the breast, the surgeon may do a sentinel lymph node biopsy (SLNB). Sentinel lymph nodes are the first lymph nodes cancer cells are likely to have spread from the primary tumor.

Types of mastectomies include:

- **A total mastectomy or simple mastectomy** removes the whole breast with a flat skin closure.
- **A modified radical mastectomy** removes the breast and axillary lymph nodes.
- **A skin-sparing mastectomy** removes the breast but not all of the skin, in order

#### Total (simple) mastectomy

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



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to have breast reconstruction that might include flaps and/or implants.

- **Nipple-sparing mastectomy** preserves the nipple-areola complex (NAC) as well as all of the skin. Not everyone is a candidate for nipple-sparing mastectomy. This is based upon location of cancer, breast size, and breast ptosis (degree of drooping).

Breast reconstruction is an option after a mastectomy. If you opt for reconstruction, it can be done during the initial surgery to remove your breast, or after finishing cancer treatment. If it is done after cancer treatment, this is called delayed reconstruction. Breast reconstruction is often done in multiple stages, requiring multiple procedures. You will need to consult with a plastic surgeon.

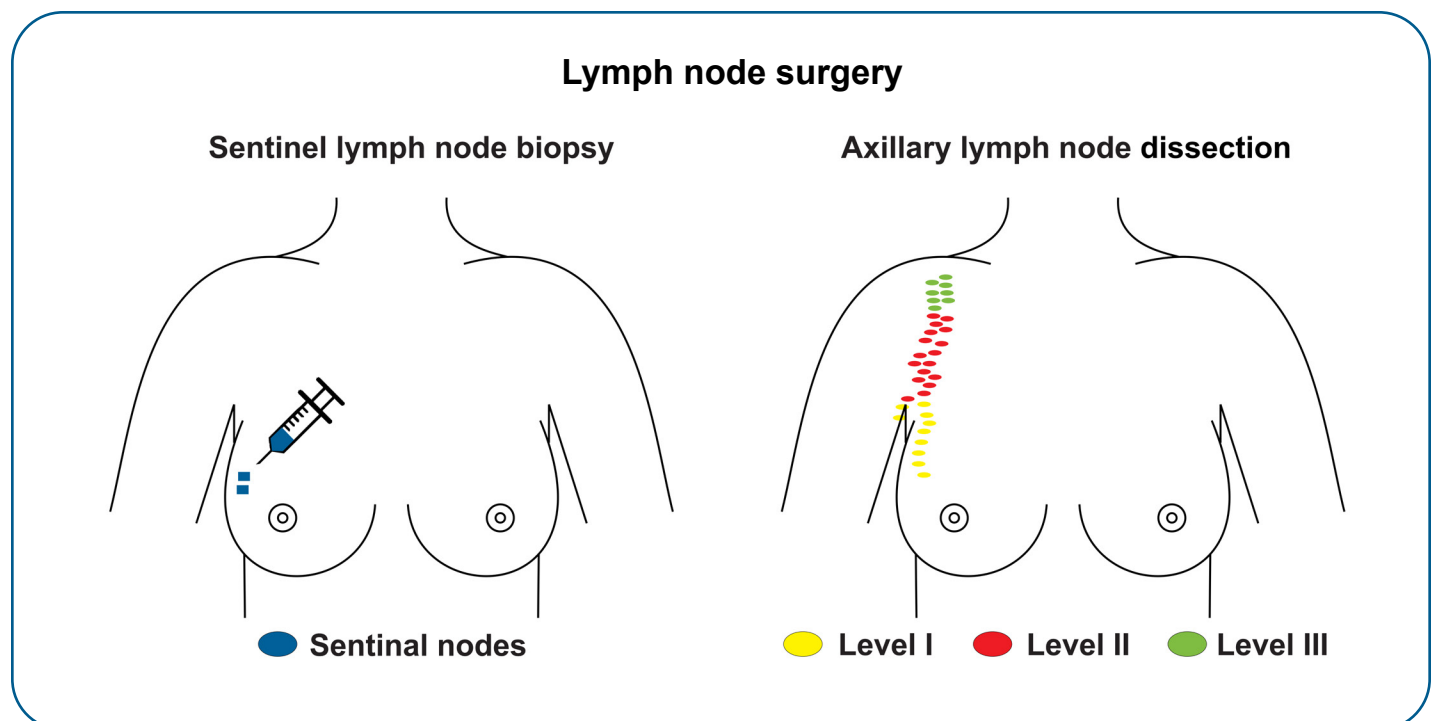
## Lymph node surgery

### Sentinel lymph node biopsy

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

A sentinel lymph node (SLN) is the first lymph node(s) 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 tracer 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 may contain cancer. Removing lymph nodes can cause lymphedema (fluid buildup) and other health issues.

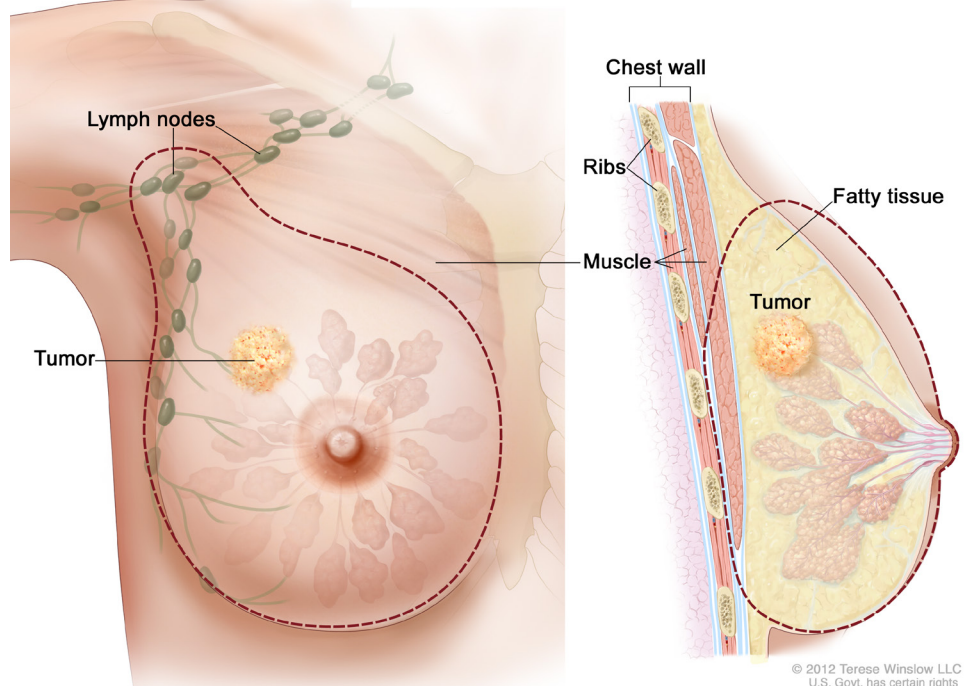
There are 3 levels of axillary lymph nodes:

- **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. Level III nodes are not typically removed unless there is a lot of disease. For more information about the timing of biopsies, talk with your care team.

### Modified radical mastectomy

The dotted line shows where the entire breast and some lymph nodes are 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 after surgery to treat or slow cancer growth. Treatment is given in small daily doses on weekdays, with weekends off.

At least weekly, you will meet with your radiation oncologist to review treatment results and to help with side effects, such as sunburn-like rash. Ask your care team which radiation option(s) are best for your situation, if RT will be combined with chemotherapy, 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.
- **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.
- **Postmastectomy radiation therapy (PMRT)** is given after a mastectomy. It targets the chest wall and possible mastectomy scar.
- **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), or lymph nodes found inside the

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

### External beam radiation therapy

External beam radiation therapy (EBRT) uses a machine outside of the body called a linear accelerator (linac) to aim radiation at the whole breast (called whole breast radiation therapy or WBRT) and lymph nodes (called regional nodal irradiation or 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

Systemic therapy is drug therapy that works throughout the body. Types include chemotherapy, targeted therapy, immunotherapy, and endocrine therapy. For a general list of systemic therapies, **see Guide 2.**

Systemic therapy might be used alone or with other therapies. Goals of systemic therapy should be discussed before starting treatment.

The choice of therapy takes into consideration many factors, including HER2 and hormone receptor tumor status, if the tumor can be removed with surgery (resectable), your preferences about treatment, and if you have any other serious health conditions.

**Guide 2****Systemic therapy examples**

<b>Chemotherapy examples</b>	<ul style="list-style-type: none"> <li>• Capecitabine (Xeloda)</li> <li>• Carboplatin</li> <li>• Cisplatin</li> <li>• Cyclophosphamide (Frindovyx)</li> <li>• Docetaxel (Taxotere, Docivyx)</li> <li>• Doxorubicin (Adriamycin)</li> <li>• Epirubicin (Ellence)</li> <li>• Eribulin (Halaven)</li> <li>• Fluorouracil</li> <li>• Gemcitabine</li> <li>• Methotrexate</li> <li>• Paclitaxel</li> <li>• Vinorelbine</li> </ul>
<b>Targeted therapy examples</b>	<p>Antibody drug conjugates</p> <ul style="list-style-type: none"> <li>• Ado-trastuzumab emtansine (T-DM1, Kadcyla), fam-trastuzumab deruxtecan-nxki (T-DXd, Enhertu), and sacituzumab govitecan-hziy (Trodelvy)</li> </ul> <p>CDK4/6 inhibitors</p> <ul style="list-style-type: none"> <li>• Abemaciclib (Verzenio), palbociclib (Ibrance), and ribociclib (Kisqali)</li> </ul> <p>PARP inhibitors</p> <ul style="list-style-type: none"> <li>• Olaparib (Lynparza) and talazoparib (Talzenna)</li> </ul> <p>PIK3CA, AKT1, PTEN, and mTOR inhibitors</p> <ul style="list-style-type: none"> <li>• Alpelisib (Piqray), capivasertib (Truqap), and everolimus (Afinitor)</li> </ul>
<b>HER2-targeting therapy (antibody, inhibitor, and conjugate) examples</b>	<ul style="list-style-type: none"> <li>• Pertuzumab (Perjeta)</li> <li>• Trastuzumab (Herceptin) or trastuzumab substitutes (biosimilars) such as Kanjinti, Ogivri, Herzuma, Ontruzant, and Trazimera</li> <li>• Ado-trastuzumab emtansine</li> <li>• Fam-trastuzumab deruxtecan-nxki</li> <li>• Lapatinib (Tykerb)</li> <li>• Margetuximab-cmkb (Margenza)</li> <li>• Neratinib (Nerlynx)</li> <li>• Tucatinib (Tukysa)</li> <li>• Phesgo as a substitute for combination therapy of trastuzumab with pertuzumab</li> </ul>
<b>Immunotherapy</b>	<ul style="list-style-type: none"> <li>• Pembrolizumab (Keytruda)</li> </ul>
<b>Endocrine therapy</b>	<ul style="list-style-type: none"> <li>• Endocrine therapy can be found in <a href="#">Guide 3</a>.</li> </ul>

Systemic therapy might be given before or after surgery. Systemic therapies are described in more detail below and in the following pages.

## 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 (IV) 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 (Adriamycin), doxorubicin liposomal injection (Doxil), and epirubicin (Ellence)
- **Taxanes** include docetaxel, paclitaxel, and albumin-bound paclitaxel.
- **Antimetabolites** include capecitabine (Xeloda), 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. ADCs are given in cycles. Examples include ado-trastuzumab emtansine (Kadcyla), fam-trastuzumab deruxtecan-nxki (Enhertu, T-DXd), and sacituzumab govitecan-hziy (Trodelvy).

## 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.

HER2 therapies may affect your heart's pumping function. 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

This section is for inhibitors that are different from inhibitors used in HER2-targeted therapy.

### CDK4/6 inhibitors

Cyclin-dependent kinase (CDK) is a cell protein that helps cells grow and divide. For hormone receptor-positive (HR+), HER2-negative (HER2-) 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).

### 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 examples of a PARP inhibitor (PARPi).

### PIK3CA, PTEN, and AKT1 inhibitors

The *PIK3CA* gene is one of the most frequently mutated genes in breast cancers. PTEN and AKT are also part of this important pathway in cancer cells and can be altered less commonly



### 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.**

in breast cancers. A mutation or alteration in these genes can lead to increased growth of cancer cells and resistance to various treatments. Alpelisib (Piqray) and inavolisib (Itovebi) are examples of a PIK3CA inhibitors and capivasertib (Truqap) is an AKT1 inhibitor.

### mTOR inhibitors

mTOR is a cell protein that helps cells grow and divide. Endocrine therapy may stop working if mTOR becomes overactive. mTOR inhibitors are used to get endocrine therapy working again.

Everolimus (Afinitor) is an mTOR inhibitor. Most often, it is taken with exemestane. For some, it may be taken with fulvestrant or tamoxifen.

## Immunotherapy

Immunotherapy is a type of systemic treatment that tries to reactivate the immune system against tumor cells. The immune system has many on and off switches. Tumors take advantage of off switches. Immunotherapy can block off switches, which helps the immune system turn on. Immunotherapy can be given alone or with other types of treatment. Pembrolizumab (Keytruda) is an example of immunotherapy.

## Endocrine therapy

Endocrine therapy blocks estrogen or progesterone to treat hormone receptor-positive (HR+) breast cancer. 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 is 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).
- **Androgen** is made by the adrenal glands, testicles, and ovaries.

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 slow tumor growth or shrink the tumor for a period of time.

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

Those who want to have children in the future should discuss fertility plans with their doctor



and may need to be referred to a fertility specialist before starting endocrine therapy.

Types of endocrine therapy can be found in **Guide 3**.

## Testosterone

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

### Guide 3 Endocrine therapy types

<b>Bilateral oophorectomy</b>	Surgery to remove both ovaries.
<b>Ovarian ablation</b>	Radiation to permanently stop the ovaries from making hormones.
<b>Ovarian or testosterone suppression</b>	<p>Drugs to temporarily stop the ovaries or testicles from making hormones such as LHRH and GnRH.</p> <ul style="list-style-type: none"> <li>• LHRH agonists include goserelin (Zoladex) and leuprolide (Lupron Depot). These are injected every 4 or 12 weeks. They do not affect estrogen made by the ovaries.</li> <li>• GnRH agonists might be used to suppress ovarian hormone or testosterone production.</li> </ul>
<b>Aromatase inhibitors (AIs)</b>	<p>Drugs to 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 AIs include anastrozole (Arimidex) and letrozole (Femara). Exemestane (Aromasin) is a steroidal AI.</p>
<b>Estrogen receptor (ER) modulators or anti-estrogens</b>	<ul style="list-style-type: none"> <li>• <b>Selective estrogen receptor modulators (SERMs)</b> block estrogen from attaching to hormone receptors. Tamoxifen and toremifene (Fareston) are SERMs.</li> <li>• <b>Selective estrogen receptor degraders (SERDs)</b> block and destroy estrogen receptors. Fulvestrant (Faslodex) and elacestrant (Orserdu) are SERDs.</li> </ul>
<b>Hormones</b>	Hormone examples include ethinyl estradiol, fluoxymesterone, and megestrol acetate (Megace).

### Premenopause

If you have menstrual periods, you are in premenopause. In premenopause, the ovaries are the main source of estrogen and progesterone.

GnRH agonists may be used to temporarily induce menopause for those in premenopause. A combination of GnRH agonists and tamoxifen or aromatase inhibitors (AIs) may be considered as endocrine therapy 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.

## Bone-strengthening therapy

Medicines that target the bones may be given to help relieve bone pain or reduce the risk of bone-related 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 fractures, bone pain, high calcium levels in the blood, and squeezing (compression) of the spinal cord. Some treatments for breast cancer, like aromatase inhibitors or GnRH agonists, can cause bone loss (osteoporosis), 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 may 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.

### **Zoledronic acid, pamidronate, and denosumab**

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



### **We want your feedback!**

**Our goal is to provide helpful and easy-to-understand information on cancer.**

**Take our survey to let us know what we got right and what we could do better.**

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

**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.**



# Clinical trials

A clinical trial is a type of medical research study. After being developed and tested in a lab, 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 and are done in phases.

- **Phase 1** trials study the safety and side effects of an investigational drug or treatment approach.
- **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 safety and benefit of an FDA-approved treatment.

## Who can enroll?

It depends on the clinical trial's rules, called eligibility criteria. The rules may be about age, cancer type and stage, treatment history, or general health. They 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 research team. This group of experts 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 it with people you trust. Keep in mind that you can leave and seek treatment outside of the clinical trial at any time.

## 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.

## Are clinical trials free?

There is no fee to enroll in a clinical trial. The study sponsor pays for research-related costs, including the study drug. But you may need to pay for other services, like transportation or childcare, due to extra appointments. During the trial, you will continue to receive standard cancer care. This care is often covered by insurance.

## Key points

- Surgery is the main or primary treatment for invasive breast cancer.
- Systemic treatment is based on estrogen receptor (ER), progesterone receptor (PR), and HER2 expression.
- 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.

## Questions to ask

- What is your experience treating breast cancer?
- How many breast cancer surgeries have you done?
- What treatment will I have before and after surgery?
- Is there a social worker or someone who can help me decide about treatment?
- How much time do I have to decide about treatment? Are there any decisions that must be made today?



### 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/](https://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)

# 5

## Supportive care

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50 Questions to ask

**Supportive care helps manage the symptoms of invasive breast cancer and the side effects of treatment. This chapter discusses possible side effects.**

## What is supportive care?

Supportive care helps improve your quality of life during and after cancer treatment. The goal is to prevent or manage side effects and symptoms, like pain and cancer-related fatigue. It also addresses the mental, social, and spiritual concerns faced by those with cancer.

Supportive care is available to everyone with cancer and their families, not just those at the end of life. Palliative care is another name for supportive care.

Supportive care can also help with:

- Making treatment decisions
- Coordinating your care
- Paying for care
- Planning for advanced care and end of life

## 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 just be unpleasant. Others may be harmful to one's health. Treatment can cause several side effects. Some are very serious. Tell your care team about any new or worsening symptoms.

### 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 breathing problems, 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 or constipation

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. Constipation is also common, especially if taking certain pain medicines. Drinking fluids, staying active, and taking medicines for constipation are often recommended.

### 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.

### 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 at first. Scalp cooling (or scalp hypothermia) might help lessen

**It is important to tell your care team about all of your side effects, including new or worsening symptoms.**

hair loss in those receiving certain types of chemotherapy.

### Infections

Infections occur more frequently and are more severe in those with a weakened immune system. Drug treatment for breast cancer can weaken the body's natural defense against infections. If not treated early, infections can be fatal.

Neutropenia, a low number of white blood cells, can lead to frequent or severe infections. When someone with neutropenia also develops a fever, it is called febrile neutropenia (FN). With FN, your risk of infection may be higher than normal. This is because a low number of white blood cells leads to a reduced ability to fight infections. FN is a side effect of some types of systemic therapy.

### Loss of appetite

Sometimes side effects from surgery, cancer, or its treatment might cause you to feel not hungry or sick to your stomach (nauseated). You might have a sore mouth. 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 weight.

### 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 red blood cells, resulting in less oxygen being carried to your body tissues. You might tire easily or feel short of breath if you are anemic.
- **Neutropenia** is a decrease in neutrophils, the most common 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.

**“Recovery is the goal. Life will be forever altered because of your cancer experience. There will come a day that your cancer isn’t the first thing that you think of in the morning and the day you realize that happened will be powerful.”**



## Neurocognitive or neuropsychological effects

Some treatments can damage the nervous system (neurotoxicity) causing problems with concentration and memory. 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 doctors can create a plan to help with these limits.

## Neuropathy and neurotoxicity

Some treatments can damage the nervous system (neurotoxicity) causing neuropathy and problems with concentration, memory, and thinking. 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 with additional cycles of treatment. Most of the time, neuropathy improves gradually and may eventually go away after treatment.

## Organ issues

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

## Pain

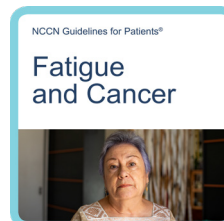
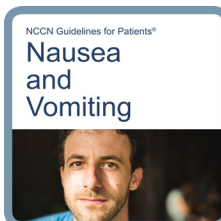
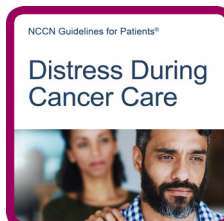
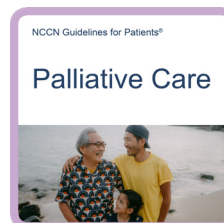
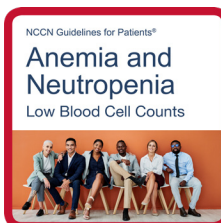
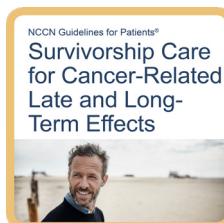
Tell your care team about any pain or discomfort. You might meet with a palliative care specialist or with a pain specialist to manage pain.

## Palliative care

Palliative care is appropriate for anyone, regardless of age, cancer stage, or the need for other therapies. It focuses on physical, emotional, social, and spiritual needs that affect quality of life.

## 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.



## Quality of life

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

## 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 health concerns, and second cancers. The sooner late effects are treated the better. Ask the care team about what late effects could occur. This will help you know what to look for.

## 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 care 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.



**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)

## Key points

- 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. Side effects depend on many factors. These factors include the drug type and dose, length of treatment, and the person.
- Some side effects are very rare. Ask your care team what to expect.
- Tell your care team about any new or worsening symptoms.

## Questions to ask

- Who will coordinate my care?
- Who should I call when I have questions or notice changes in my condition?
- How long should I wait if I notice changes in my condition?
- What should I do on weekends and other non-office hours?
- Will my care team be able to communicate with the emergency department or urgent care team?

# 6

## Your treatment options

- 52 Surgery first
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**Surgery is the main or primary treatment for invasive breast cancer. Some people benefit from systemic therapy before surgery. Radiation therapy (RT), systemic therapy, or both are possible after surgery. Together, you and your care team will choose a treatment plan that is best for your situation.**

This chapter provides specific treatment options based on hormone receptor (HR) and HER2 tumor status. It also discusses who might benefit from treatment before surgery.

### Surgery first

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
- Mastectomy

Surgery might 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 systemic therapy, radiation therapy, or both.

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 first

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 (histology), the size of the tumor, if cancer is found in the axillary lymph nodes, your age, and if you are in menopause. Many factors play a role in treatment decisions. Most people have radiation therapy (RT) to the breast and sometimes lymph nodes after a lumpectomy. A boost is extra radiation to the tumor area. Systemic (drug) therapy might be given before RT.

### Mastectomy first

A total mastectomy is a surgery that removes the whole breast. A nipple-sparing or skin-sparing mastectomy may be possible. Treatment after a mastectomy is based on if cancer was found in the axillary lymph nodes, the number of lymph nodes that tested positive, and the size of the removed tumor. Radiation therapy to the chest wall and lymph nodes, systemic therapy, or both are possible following a mastectomy.



## Systemic therapy before surgery

Some cancers benefit from treatment before surgery. These cancers include those with large tumors, aggressive tumors, cancer in the lymph nodes called nodal or node-positive (N+) disease, or the cancer that involves the breast skin or chest wall. Treatment before surgery is called preoperative or neoadjuvant therapy.

### 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)



### Order of treatments

Most people with cancer will receive more than one type of treatment. Below is an overview words you might hear to describe treatment.

- **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.

## Treatment before surgery

Treatment before surgery is systemic (drug) therapy. It is based on hormone receptor (HR) and HER2 status. Preoperative systemic

therapy has benefits. The goal is to shrink the tumor or the amount of cancer before surgery. How the tumor responds to drug therapy may also affect treatments after surgery.

### Guide 4

#### HER2-targeted therapy options: HER2+ cancer

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

For preoperative systemic therapy options,  
see **Guide 4** and **Guide 5**.

### Guide 5 Systemic therapy options: HER2- cancer

<b>Preferred</b>	<ul style="list-style-type: none"> <li>• Doxorubicin and cyclophosphamide (AC) with paclitaxel</li> <li>• Docetaxel and cyclophosphamide (TC)</li> <li>• Adjuvant only: Olaparib, if germline <i>BRCA1</i> or <i>BRCA2</i> mutations</li> </ul> <hr/> <p>Triple-negative breast cancer (TNBC):</p> <ul style="list-style-type: none"> <li>• Options listed above</li> <li>• Preoperative pembrolizumab with carboplatin and paclitaxel, followed by preoperative pembrolizumab and cyclophosphamide with doxorubicin or epirubicin, followed by adjuvant pembrolizumab</li> <li>• If residual disease after preoperative therapy with taxane-, alkylator-, and anthracycline-based chemotherapy, then capecitabine</li> </ul>
<b>Other recommended</b>	<ul style="list-style-type: none"> <li>• Doxorubicin and cyclophosphamide (AC) with docetaxel</li> <li>• Epirubicin and cyclophosphamide (EC)</li> <li>• Docetaxel, doxorubicin, and cyclophosphamide (TAC)</li> </ul> <hr/> <p>TNBC:</p> <ul style="list-style-type: none"> <li>• Options listed above</li> <li>• Paclitaxel with carboplatin</li> <li>• Docetaxel with carboplatin</li> </ul>
<b>Used in some cases</b>	<ul style="list-style-type: none"> <li>• Doxorubicin and cyclophosphamide (AC)</li> <li>• Cyclophosphamide, methotrexate, and fluorouracil (CMF)</li> <li>• Doxorubicin and cyclophosphamide (AC) with paclitaxel</li> </ul> <hr/> <p>TNBC:</p> <ul style="list-style-type: none"> <li>• Options listed above</li> <li>• Docetaxel, carboplatin, and pembrolizumab (preoperative only)</li> <li>• Doxorubicin and cyclophosphamide (AC) with carboplatin and docetaxel</li> <li>• Capecitabine (maintenance therapy after adjuvant chemotherapy)</li> </ul>
<b>Notes</b>	<p>Other taxanes (such as docetaxel, paclitaxel, albumin-bound paclitaxel) might be substituted in some cases.</p>

### 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. The choice between a lumpectomy or mastectomy is based on the size and location of the tumor, the size of your breast before surgery, and your preference.

If you had preoperative therapy, your tumor will be restaged using tissue removed during surgery. This is called the pathologic (p) stage or surgical stage. It might look like this: ypT2N1. The y means you had preoperative therapy. Treatment after surgery might be systemic therapy or radiation or both. It will likely include endocrine therapy if your tumor is HR+.

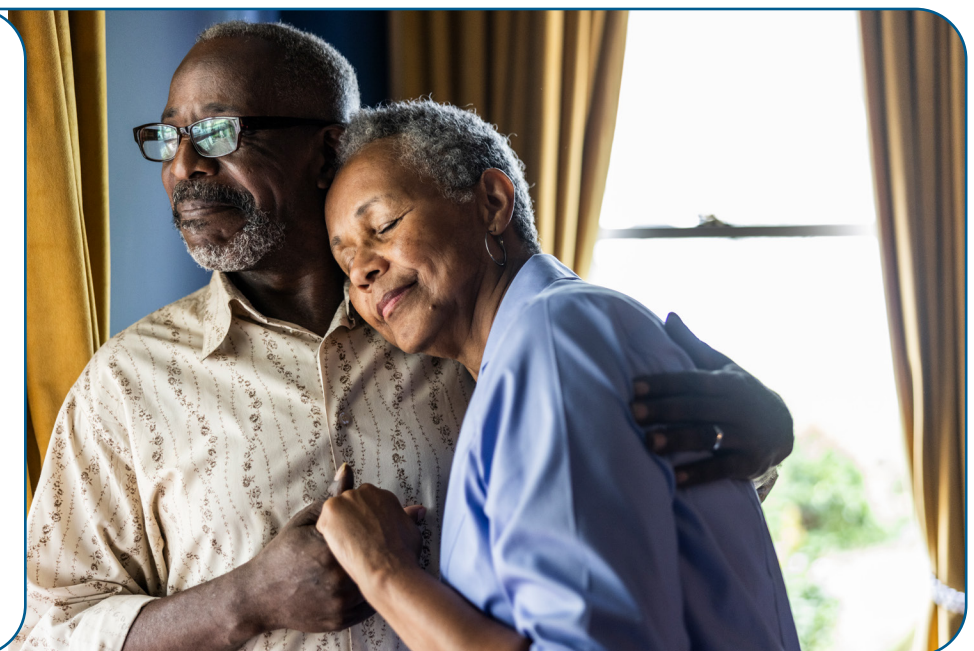
### Surgery is not an option

Surgery is not always possible. Even though surgery might not be an option, systemic therapy will continue. If the cancer is not responding to systemic therapy, then radiation may be considered to try to make the cancer resectable (able to be removed with surgery). The goal of treatment is to reduce the amount of cancer. Talk with your care team about your goals of treatment and your treatment preferences. Your wishes are always important.

### Systemic therapy after surgery

Adjuvant systemic therapy is drug treatment after surgery. It is given to kill any remaining cancer cells and to help reduce the risk of cancer returning. This treatment is based on

**“Take things one day or even one step at a time, it might get harder before it gets better, but it will get better.”**



cancer stage, including lymph node (nodal) hormone receptor (HR), and HER2 status.

Systemic therapy options are based on the tumor type (histology), tumor HR and HER2 status, and if you are in menopause. Systemic therapies might be used alone or in combination. Ask your care team why one treatment might be preferred over another for your type of cancer.

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

### Favorable histologies

A tumor with a favorable histology is one that has a 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 hormone receptor-positive (HR+) tumors will likely have endocrine therapy. Other systemic therapies or radiation therapy are possible.

Favorable histology includes the following:

- Pure tubular
- Pure mucinous
- Pure cribriform
- 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 includes the following:

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

### 21-gene assay

A 21-gene assay (such as Oncotype Dx) is a tumor test used to predict if your cancer might benefit from adjuvant chemotherapy in addition to endocrine therapy. There are other tests that might be helpful, but a 21-gene assay is the only test proven to predict who would benefit from chemotherapy.

### What's next?

The next pages describe systemic therapy treatment based on tumor HR and HER2 status for common histologies. Typically, the systemic therapy options are the same before and after surgery. Ask your care team for more information.

## HR+ with HER2+

HR+ with HER2+ breast cancer is sometimes called triple-positive breast cancer. It is treated with HER2-targeted therapy and endocrine therapy. A CDK4/6 inhibitor may be added.

- Chemotherapy with a HER2-targeted therapy is used to treat HER2+ cancer. Trastuzumab and pertuzumab are examples of HER2-targeted therapy. HER2-targeted therapy options can be found in **Guide 4**.
- Endocrine therapy is used to treat HR+ breast cancer. It is given after chemotherapy. Endocrine therapy options for HR+ cancer can be found in **Guide 6**.

## HR- with HER2+

In HER2-positive (HER2+) breast cancer, tumor cells have a larger than normal number of HER2 receptors. Since this cancer is HR- and HER2+, treatment focuses on targeting HER2. HER2-targeted therapy usually includes chemotherapy. HER2-targeted therapy options can be found in **Guide 4**.

## HR+ with HER2-

HER2-targeting therapy is not used when the tumor is HER2-negative (HER2-). Sometimes, chemotherapy is used. When cancer is found in the lymph nodes, it is node positive (node+).

- If chemotherapy is given, it is given before endocrine therapy. Chemotherapy and other systemic therapies specific to HER2- breast cancer can be found in **Guide 5**.
- Those who are premenopausal might have ovarian suppression or ablation in addition to endocrine therapy. Endocrine therapy options for HR+ cancer can be found in **Guide 6**.

## Triple-negative breast cancer

In triple-negative breast cancer (TNBC), the tumor tested negative for HER2, estrogen receptors, and progesterone receptors. It is written as ER- and/or PR- with HER2-. There are many variations within TNBC. It is a group of diseases that we are learning more about all the time. This cancer is treated with chemotherapy and other systemic therapies found in **Guide 5**.



# Endocrine therapy

Endocrine therapy is used to treat hormone receptor-positive (HR+) breast cancer. This is cancer that tests positive for estrogen receptors (ER+), progesterone receptors

(PR+), or both (ER+/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.

## Guide 6 Endocrine therapy options: HR+ cancer

### Premenopause at diagnosis

Option 1

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



- 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



- If chemotherapy is given, it is given before endocrine therapy.
- Those with high-risk breast cancer that is HR+ and HER2- might have endocrine therapy with 2 years of adjuvant abemaciclib or 3 years of ribociclib.
- Those receiving an aromatase inhibitor (AI) who are at risk for osteoporosis will likely have bone density tests and bone-strengthening therapy.

Endocrine therapy options for HR+ cancer can be found in **Guide 6**.

## Follow-up care

After treatment, you will receive follow-up care. During this time, your health will be monitored for side effects of treatment (late effects) and the possible return of cancer (recurrence).

It is important to keep any follow-up care and imaging test appointments. Seek routine medical care, including regular doctor visits for preventive care and cancer screening. Find out who 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 use), 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.

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

### Guide 7 Follow-up care

Medical history and physical exam 1 to 4 times a year as needed for 5 years, then every year

Screen for distress, anxiety, depression, and 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 (not needed for the side that underwent a mastectomy or on reconstructed breast)

Discuss any issues or questions related to fertility, birth control, or sexual health

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 (depending on age)

Bone density tests for those on an aromatase inhibitor or who later have ovarian issues

Maintain an ideal body weight (BMI of 20 to 25), be active, eat a mostly plant-based diet, exercise, limit alcohol, and quit smoking/vaping nicotine

## Key points

- Surgery is the main or primary treatment for invasive breast cancer. Some people benefit from systemic therapy before surgery. Treatment after surgery might include systemic therapy, radiation therapy, or both.
- In hormone receptor-positive (HR+) cancer, estrogen receptors (ER+), progesterone receptors (PR+), or both (ER+/PR+) are found. Endocrine therapy is given for HR+ cancers to reduce the risk of recurrence.
- HER2-positive (HER2) cancers are treated with a combination of chemotherapy and HER2-targeted therapy.
- 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 preventive care and cancer screenings. Continue to take all medicines as prescribed.

## Questions to ask

- What treatments do you recommend and why?
- Does the order of treatments matter?
- Which option is proven to work best for my type of cancer, age, overall health, and other factors?
- Are there resources to help me pay for treatment or other care I may need?
- How long will I be on this systemic (drug) therapy or endocrine therapy?

# 7

## The breast after surgery

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63 Flat closure

64 Breast reconstruction

65 What to consider

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66 Questions to ask

**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 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. A plastic surgeon performs oncoplastic (breast cancer surgery) reductions, balancing procedures, and breast reconstruction.

## 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 stages, 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.

## Flaps

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 size and shape of both breasts.

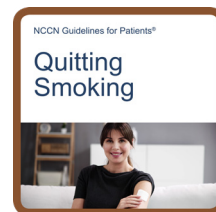
## Nipple replacement

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 the 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.



### If you smoke or vape, seek help to quit

Smoking or vaping nicotine greatly increases your chances of having side effects during and after surgery. Smoking and vaping can limit how well cancer treatment works and prevent wound healing. They also increase your chances of developing other cancers. Cannabis use might also affect the amount of anesthesia used during surgery.

Nicotine is the chemical in tobacco that makes you want to keep smoking and vaping. Nicotine withdrawal is challenging for most people who smoke or vape. The stress of having cancer may make it even harder to quit. If you smoke or vape, ask your care team about counseling and medicines to help you quit.

More information can be found in the *NCCN Guidelines for Patients: Quitting Smoking* at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](https://www.nccn.org/patientguidelines) app.

For online support, try these websites:

- [SmokeFree.gov](https://www.smokefree.gov)
- [CDC.gov/tobacco](https://www.cdc.gov/tobacco)

## 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. 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.

## Questions to ask

- What will my breast look like after surgery?
- How many breast surgeries or breast reconstructive surgeries have you done?
- How long will it take for me to recover from surgery and what should I expect?
- How much pain will I be in and what will be done to manage my pain?
- What options are available if I do not like the look of my breast after surgery?



# 8

## Recurrence

68 Overview

68 Tests

69 Treatment

70 Key points

70 Questions to ask

**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. This is called **local recurrence**.
- It can return to axillary lymph nodes or lymph nodes in or near the breast. This is called **regional recurrence**.
- 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 for recurrence can be found in **Guide 8**.

### Guide 8

#### Possible tests: Recurrence

Medical history and physical exam

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, including estrogen receptor (ER), progesterone receptor (PR), and 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 (drug) therapy are possible. Systemic and endocrine therapy options will be based on tumor hormone receptor (HR) status, HER2 status, and treatments given during your initial cancer treatment. Supportive care is always 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) or a mastectomy. More surgery might be an option. If you had radiation therapy before, then it may or may not be possible to have radiation again in the same area, which may limit your surgical options.

### Regional recurrence

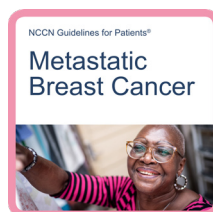
If the recurrence is in or near the armpit (axilla), then surgery to remove the tumor might be an option before radiation therapy. Systemic therapy might be given before surgery to help reduce the amount of cancer or the size of the tumor. Treatment after surgery might include radiation therapy to the lymph nodes. If you had radiation therapy before, then it may not be possible to have it again to the same area.

### 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 radiation therapy followed by systemic therapy.

### 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 systemic therapy and radiation therapy is possible for a locoregional recurrence. Systemic and endocrine therapy options are based on hormone receptor (HR) and HER2 status, and any mutations found.
- An unresectable tumor cannot be removed with surgery. Unresectable recurrent disease is treated as metastatic disease with systemic therapy.

## Questions to ask

- Where is the cancer located and what does this mean for my treatment options?
- Which course of treatment do you recommend and why?
- Is surgery an option? What treatment might I have before and after surgery?
- What role do previous treatments, my age, menopause status, and overall health play in treatment options?
- Am I a candidate for a clinical trial?

# 9

## Other resources

- 72 What else to know
- 72 What else to do
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- 73 Questions to ask about resources and support

**Want to learn more? Here's how you can get additional help.**

## What else to know

This book can help improve your cancer care. It plainly explains expert recommendations and suggests questions to ask your care team. But, it's not the only resource that you have.

You're welcome to receive as much information and help as you need. Many people are interested in learning more about:

- The details of treatment
- Being a part of a care team
- Getting financial help
- Finding an oncologist who is an expert in breast cancer
- Coping with side effects

## What else to do

Your health care center can help you with next steps. They often have on-site resources to help meet your needs and find answers to your questions. Health care centers can also inform you of resources in your community.

In addition to help from your providers, the resources listed in the next section provide support for many people like yourself. Look through the list and visit the provided websites to learn more about these organizations

## Where to get help

**Bone Marrow & Cancer Foundation**

[bonemarrow.org](http://bonemarrow.org)

**Breast Cancer Alliance**

[Breastcanceralliance.org](http://Breastcanceralliance.org)

**Breastcancer.org**

[Breastcancer.org](http://Breastcancer.org)

**CanCare**

[Cancare.org](http://Cancare.org)

**CancerCare**

[Cancercare.org](http://Cancercare.org)

**Cancer Hope Network**

[cancerhopenetwork.org](http://cancerhopenetwork.org)

**Cancer Survivor Care**

[Cancersurvivorcare.org](http://Cancersurvivorcare.org)

**DiepC Foundation**

[diepcfoundation.org](http://diepcfoundation.org)

**FORCE: Facing Our Risk of Cancer Empowered**

[facingourrisk.org](http://facingourrisk.org)

**GPAC Global Patient Advocacy Coalition**

[GPACunited.org](http://GPACunited.org)

**HIS Breast Cancer Awareness**

[Hisbreastcancer.org](http://Hisbreastcancer.org)

**Imerman Angels**  
[Imermanangels.org](http://Imermanangels.org)

**Inflammatory Breast Cancer Research Foundation**  
[ibcresearch.org](http://ibcresearch.org)

**Lobular Breast Cancer Alliance**  
[lobularbreastcancer.org](http://lobularbreastcancer.org)

**My Faulty Gene**  
[Myfaultygene.org](http://Myfaultygene.org)

**MedlinePlus**  
[medlineplus.gov](http://medlineplus.gov)

**National Cancer Institute (NCI)**  
[cancer.gov/types/breast](http://cancer.gov/types/breast)

**National Coalition for Cancer Survivorship**  
[canceradvocacy.org](http://canceradvocacy.org)

**Sharsheret**  
[sharsheret.org](http://sharsheret.org)

**Triage Cancer**  
[Triagecancer.org](http://Triagecancer.org)

**Unite for HER**  
[uniteforher.org](http://uniteforher.org)

**Young Survival Coalition (YSC)**  
[Youngsurvival.org](http://Youngsurvival.org)

## Questions to ask about resources and support

- Who can I talk to about help with housing, food, and other basic needs?
- What help is available for transportation, childcare, and home care?
- What other services are available to me and my caregivers?
- How can I connect with others and build a support system?
- Who can I talk to if I don't feel safe at home, at work, or in my neighborhood?





## Words to know

**adjuvant therapy**

Treatment that is given to lower the chances of the cancer returning.

**antibody drug conjugate (ADC)**

A substance made up of a protein linked to a drug that attaches and enters certain types of cancer cells.

**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.

**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.

**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.

**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 (CB).

**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 cancer derived from cells that line small tube-shaped vessels.

**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.

**fertility specialist**

An expert who helps people have babies.

**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.

**inflammatory breast cancer (IBC)**

A type of breast cancer in which the breast looks red and swollen and feels warm to the touch.

**infraclavicular**

The area right below the collarbone.

**in situ hybridization (ISH)**

A lab test of the number of a gene.

**internal mammary**

The area along the breastbone.

**lobule**

A gland in the breast that makes breast milk.

**lutinizing hormone-releasing hormone (LHRH)**

A hormone in the brain that helps control the making of estrogen by the ovaries.

**lymph**

A clear fluid containing white blood cells.

**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.

**lymph node**

A small, bean-shaped disease-fighting structure.

**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.

**medical oncologist**

A doctor who is an expert in cancer drugs.

**menopause**

12 months after the last menstrual period.

**modified radical mastectomy**

An operation that removes the whole breast and lymph nodes under the arm (axilla).

**mutation**

An abnormal change.

**neoadjuvant treatment**

A treatment that is given before the main treatment to reduce the cancer. Also called preoperative treatment if given before an operation.

**nipple-areola complex (NAC)**

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

**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.

**positron emission tomography (PET)**

A test that uses radioactive material to see the shape and function of body parts.

**postmenopause**

The state of having no more menstrual periods.

**premenopause**

The state of having menstrual periods.

**progesterone**

A hormone involved in sexual development, periods, and pregnancy.

**progesterone receptor (PR)**

A protein inside cells that binds to progesterone.

**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.

**radical mastectomy**

An operation that removes the whole breast, lymph nodes under the arm (axilla), and chest wall muscles under the breast.

**recurrence**

The return of cancer after a cancer-free period.

**selective estrogen receptor degrader (SERD)**

A drug that blocks and destroys estrogen receptors.

**selective estrogen receptor modulator (SERM)**

A drug that blocks the effect of estrogen inside of cells.

**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.

**supportive care**

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

**supraclavicular**

The area right above the collarbone.

**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.

**triple-negative breast cancer (TNBC)**

A breast cancer that does not use hormones or the HER2 protein to grow.

**ultrasound**

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

# NCCN Contributors

This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer, Version 3.2025. 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 • [pennmedicine.org/cancer](http://pennmedicine.org/cancer)

**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](http://uhhospitals.org/services/cancer-services)  
CC Taussig Cancer Institute  
866.223.8100 • [my.clevelandclinic.org/departments/cancer](http://my.clevelandclinic.org/departments/cancer)  
Case CCC  
216.844.8797 • [case.edu/cancer](http://case.edu/cancer)

**City of Hope National Medical Center**  
Duarte, California  
800.826.4673 • [cityofhope.org](http://cityofhope.org)

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

**Duke Cancer Institute**  
Durham, North Carolina  
888.275.3853 • [dukecancerinstitute.org](http://dukecancerinstitute.org)

**Fox Chase Cancer Center**  
Philadelphia, Pennsylvania  
888.369.2427 • [foxchase.org](http://foxchase.org)

**Fred & Pamela Buffett Cancer Center**  
Omaha, Nebraska  
402.559.5600 • [unmc.edu/cancercenter](http://unmc.edu/cancercenter)

**Fred Hutchinson Cancer Center**  
Seattle, Washington  
206.667.5000 • [fredhutch.org](http://fredhutch.org)

**Huntsman Cancer Institute at the University of Utah**  
Salt Lake City, Utah  
800.824.2073 • [healthcare.utah.edu/huntsmancancerinstitute](http://healthcare.utah.edu/huntsmancancerinstitute)

**Indiana University Melvin and Bren Simon**  
**Comprehensive Cancer Center**  
Indianapolis, Indiana  
888.600.4822 • [www.cancer.iu.edu](http://www.cancer.iu.edu)

**Johns Hopkins Kimmel Cancer Center**  
Baltimore, Maryland  
410.955.8964  
[www.hopkinskimmelcancercenter.org](http://www.hopkinskimmelcancercenter.org)

**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](http://mayoclinic.org/cancercenter)

**Memorial Sloan Kettering Cancer Center**  
New York, New York  
800.525.2225 • [mskcc.org](http://mskcc.org)

**Moffitt Cancer Center**  
Tampa, Florida  
888.663.3488 • [moffitt.org](http://moffitt.org)

**O'Neal Comprehensive Cancer Center at UAB**  
Birmingham, Alabama  
800.822.0933 • [uab.edu/onealcancercenter](http://uab.edu/onealcancercenter)

**Robert H. Lurie Comprehensive Cancer Center**  
**of Northwestern University**  
Chicago, Illinois  
866.587.4322 • [cancer.northwestern.edu](http://cancer.northwestern.edu)

**Roswell Park Comprehensive Cancer Center**  
Buffalo, New York  
877.275.7724 • [roswellpark.org](http://roswellpark.org)

**Siteman Cancer Center at Barnes-Jewish Hospital**  
**and Washington University School of Medicine**  
St. Louis, Missouri  
800.600.3606 • [siteman.wustl.edu](http://siteman.wustl.edu)

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

**Stanford Cancer Institute**  
Stanford, California  
877.668.7535 • [cancer.stanford.edu](http://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](http://cancer.osu.edu)

**The UChicago Medicine Comprehensive Cancer Center**  
Chicago, Illinois  
773.702.1000 • [uchicagomedicine.org/cancer](http://uchicagomedicine.org/cancer)

**The University of Texas MD Anderson Cancer Center**  
Houston, Texas  
844.269.5922 • [mdanderson.org](http://mdanderson.org)



UC Davis Comprehensive Cancer Center  
Sacramento, California  
916.734.5959 • 800.770.9261  
[health.ucdavis.edu/cancer](http://health.ucdavis.edu/cancer)

UC San Diego Moores Cancer Center  
La Jolla, California  
858.822.6100 • [cancer.ucsd.edu](http://cancer.ucsd.edu)

UCLA Jonsson Comprehensive Cancer Center  
Los Angeles, California  
310.825.5268 • [uclahealth.org/cancer](http://uclahealth.org/cancer)

UCSF Helen Diller Family  
Comprehensive Cancer Center  
San Francisco, California  
800.689.8273 • [cancer.ucsf.edu](http://cancer.ucsf.edu)

University of Colorado Cancer Center  
Aurora, Colorado  
720.848.0300 • [coloradocancercenter.org](http://coloradocancercenter.org)

University of Michigan Rogel Cancer Center  
Ann Arbor, Michigan  
800.865.1125 • [rogelcancercenter.org](http://rogelcancercenter.org)

University of Wisconsin Carbone Cancer Center  
Madison, Wisconsin  
608.265.1700 • [uwhealth.org/cancer](http://uwhealth.org/cancer)

UT Southwestern Simmons  
Comprehensive Cancer Center  
Dallas, Texas  
214.648.3111 • [utsouthwestern.edu/simmons](http://utsouthwestern.edu/simmons)

Vanderbilt-Ingram Cancer Center  
Nashville, Tennessee  
877.936.8422 • [vicc.org](http://vicc.org)

Yale Cancer Center/Smilow Cancer Hospital  
New Haven, Connecticut  
855.4.SMILOW • [yalecancercenter.org](http://yalecancercenter.org)



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