



NCCN  
GUIDELINES  
FOR PATIENTS®

2023

# Invasive Breast Cancer



Presented with support from



NATIONAL COMPREHENSIVE CANCER NETWORK®  
**FOUNDATION**  
Guiding Treatment. Changing Lives.

Available online at

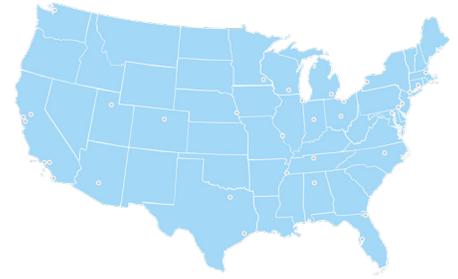
[NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines)



## About the NCCN Guidelines for Patients®



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



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

**These NCCN Guidelines for Patients are based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer, Version 4.2023 – March 23, 2023.**

View the NCCN Guidelines  
for Patients free online  
[NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines)

Find an NCCN Cancer  
Center near you  
[NCCN.org/cancercenters](https://www.nccn.org/cancercenters)

Connect with us     YouTube 

# Supporters



NCCN Guidelines for Patients are supported by funding from the  
NCCN Foundation®

**NCCN Foundation gratefully acknowledges the following corporate supporters for helping to make available these NCCN Guidelines for Patients: AstraZeneca, Daiichi Sankyo, Exact Sciences, Gilead Sciences Inc., and Novartis Pharmaceuticals Corporation.**

NCCN independently adapts, updates, and hosts the NCCN Guidelines for Patients. Our corporate supporters do not participate in the development of the NCCN Guidelines for Patients and are not responsible for the content and recommendations contained therein.

To make a gift or learn more visit online or email

[NCCNFoundation.org/donate](https://www.nccnfoundations.org/donate)

[PatientGuidelines@NCCN.org](mailto:PatientGuidelines@NCCN.org)

## Contents

- 4 Breast cancer basics
- 8 Testing for breast cancer
- 26 Breast cancer staging
- 32 Treating breast cancer
- 54 Surgery first
- 63 Preop treatment first
- 73 The breast after surgery
- 78 Recurrence
- 82 Making treatment decisions
- 93 Words to know
- 98 NCCN Contributors
- 99 NCCN Cancer Centers
- 101 Index

© 2023 National Comprehensive Cancer Network, Inc. All rights reserved. NCCN Guidelines for Patients and illustrations herein may not be reproduced in any form for any purpose without the express written permission of NCCN. No one, including doctors or patients, may use the NCCN Guidelines for Patients for any commercial purpose and may not claim, represent, or imply that the NCCN Guidelines for Patients that have been modified in any manner are derived from, based on, related to, or arise out of the NCCN Guidelines for Patients. The NCCN Guidelines are a work in progress that may be redefined as often as new significant data become available. NCCN makes no warranties of any kind whatsoever regarding its content, use, or application and disclaims any responsibility for its application or use in any way.

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).

National Comprehensive Cancer Network (NCCN) and NCCN Foundation  
3025 Chemical Road, Suite 100, Plymouth Meeting, PA 19462 USA

# 1

## Breast cancer basics

- 5 The breast
- 6 Breast cancer
- 6 How breast cancer spreads
- 7 Key points

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

## The breast

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

ribs. Muscle and ligaments help hold the breast in place.

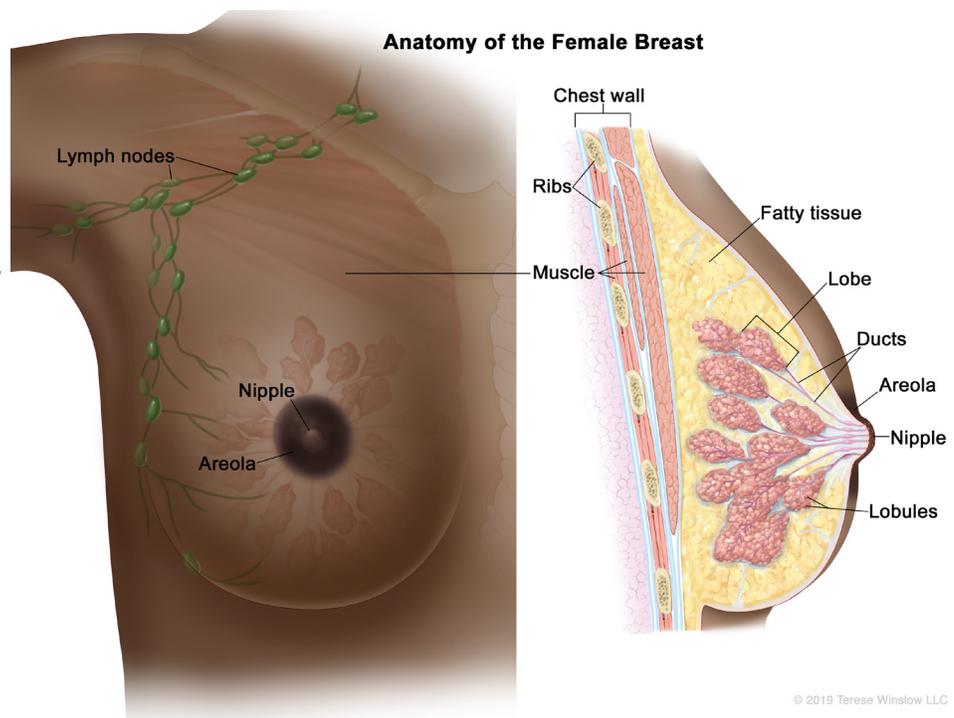
Breast tissue contains glands that can make milk. These milk glands are called lobules. Lobules look like tiny clusters of grapes. Small tubes called ducts connect the lobules to the nipple.

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

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

### The breast

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



## Breast cancer

Breast cancer starts in the cells of the breast. Almost all breast cancers are a subtype called carcinomas. Carcinomas are cancers that start in the cells that line the inner or outer surfaces of the body.

There are different types of breast carcinoma. The most common types are either ductal or lobular.

- **Ductal carcinoma** starts in the cells that line the milk ducts. Milk ducts are thin tubes that carry milk from the lobules of the breast to the nipple. It is the most common type of breast cancer.
- **Lobular carcinoma** starts in the lobules (milk glands) of the breast. It is the second most common type of breast cancer.

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

## How breast cancer spreads

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

### Primary tumor

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

### Invasive

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

### Metastasis

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

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

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

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



## Key points

- Anyone can develop breast cancer, but breast cancer occurs more frequently in persons assigned female at birth.
- Inside breasts are lobules, ducts, fat, blood and lymph vessels, ligaments, and connective tissue. Lobules are structures that make breast milk. Ducts carry breast milk from the lobules to the nipple.
- Breast cancer often starts in the ducts or lobules and then spreads into the surrounding tissue.
- Invasive breast cancer has grown outside the ducts or lobules into surrounding tissue. Once outside the ducts or lobules, breast cancer can spread through lymph or blood to lymph nodes or other parts of the body.
- Metastatic breast cancer has spread to distant sites in the body.

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



# 2

## Testing for breast cancer

9	Test results	20	Hormone receptor status
10	General health tests	21	HER2 status
12	Fertility (all genders)	21	Biomarker testing
12	Preventing pregnancy during treatment	23	Genetic risk testing
13	Blood tests	24	Distress screening
14	Imaging tests	24	Performance status
17	Biopsy	25	Key points

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

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

## Test results

Results from imaging studies and biopsy will be used to determine your treatment plan. It is important you understand what these tests mean. Ask questions and keep copies of your test results. Online patient portals are a great way to access your test results.

Keep these things in mind:

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

- Organize your papers. Create files for insurance forms, medical records, and test results. You can do the same on your computer.
- Keep a list of contact information for everyone on your care team. Add it to your phone. Hang the list on your refrigerator or keep it in a place where someone can access it in an emergency. Keep your primary care physician (PCP) informed of changes to this list. You are encouraged to keep your PCP in the loop. They are great partners in your care.
- In your contact list, include information on the exact type of cancer, as well as any treatments and the date they started.

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

## General health tests

### Medical history

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

### Family history

Some cancers and other diseases can run in families. Your 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, and at what age they were diagnosed. It's important to know the specific type of cancer or where the cancer started, if it is in multiple locations, and if they had genetic testing.

#### Guide 1 Possible tests

Medical history and physical exam (H&P)

Diagnostic mammogram, ultrasound, breast MRI, and other imaging studies as needed

Possible scans such as PET-CT, CT, and bone scan to rule out distant metastasis

Biopsy with pathology review

Determine tumor status including:

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

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

Address fertility, birth control, and sexual health concerns

Pregnancy test in those of childbearing potential

Assess for distress

## Physical exam

During a physical exam, your health care provider may:

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

## Clinical breast exam

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



## Create a medical binder

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

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

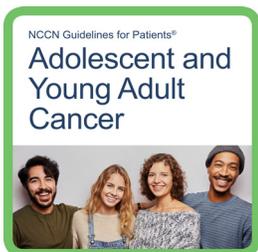
Bring your medical binder to appointments. You never know when you might need it!

## Fertility (all genders)

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

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

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



### Changes in fertility

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

## Preventing pregnancy during treatment

Preventing pregnancy during treatment is important. Cancer and cancer treatment can affect the ovaries and damage sperm. Hormonal birth control may or may not be recommended, so ask your doctor about options such as intrauterine devices (IUDs) and barrier methods. Types of barrier methods include condoms, diaphragms, cervical caps, and the contraceptive sponge.

### Those with ovaries

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

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

### Those with testicles

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

## Blood tests

Blood tests check for signs of disease and how well organs are working. They require a sample of your blood, which is removed through a needle placed into your vein. 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 14 different substances in your blood. It is usually done on the plasma part of your blood. A CMP provides important information about how well your kidneys and liver are working, among other things.

### Liver function tests

Liver function tests (LFTs) look at the health of your liver by measuring chemicals that are made or processed by the liver. Levels that are too high or low signal that the liver is not working well or that cancer has spread to the liver.

### Pregnancy test

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

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



## Imaging tests

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

A radiologist, an expert in interpreting imaging tests, will write a report and send this report to your doctor. While these reports are available to you through your portal, please wait to discuss these results with the doctor.

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

### Bone scan

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

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

### Bone x-ray

An x-ray uses low-dose radiation to take one picture at a time. A tumor changes the way radiation is absorbed and will show up on the x-ray. X-rays are also good at showing bone issues. Your care team may order x-rays if your bones hurt or were abnormal on a bone scan.

### Diagnostic mammogram

A mammogram is a picture of the insides 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.

### MRI scan

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

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

**Breast MRI**

If needed, a breast MRI will be used in addition to a mammogram. Contrast should be used. You will be positioned face down in the machine with your arms above your head.

**Spine and brain MRI**

An MRI can be used to detect breast cancer that has spread (metastasize) to your spine or brain. For a brain MRI, a device is placed around your head. For a spine MRI, no device is worn. Contrast should be used in an MRI.

**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.

**Contrast material**

Contrast material is used to improve the pictures of the inside of the body. Contrast materials are not dyes, but substances that help enhance and improve the images of several organs and structures in the body. It is used to make the pictures clearer. The contrast is not permanent and will leave the body in your urine immediately after the test. The types of contrast vary and are different for CT and MRI.

Tell your doctors if you have had allergic reactions to contrast in the past, especially to iodine or to shellfish such as shrimp. 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.

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

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

- Screening mammograms are done on a regular basis when there are no signs or symptoms of breast cancer. Results take a few days.
- Diagnostic mammograms are used for those who have symptoms such as a lump, pain, nipple thickening or discharge, or whose breasts have changed shape or size.
- Diagnostic mammograms are also used to take a closer look at an abnormal area found in a screening mammogram.
- A radiologist will evaluate the diagnostic mammogram while you wait so if additional testing is needed, it can be done right away.
- Both types of mammograms use low-dose x-rays to examine the breast. They may use either the standard 2-dimensional (2D) digital mammography or 3-dimensional (3D) mammograms known as tomosynthesis.

## PET scan

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

### Sodium fluoride PET-CT

A sodium fluoride PET-CT might be used instead of a bone scan. In this test, the radiotracer is made of sodium fluoride.

### FDG PET-CT

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

### FES PET-CT

FES is a radioactive form of the hormone estrogen. It might be used instead of FDG PET-CT when cancer is estrogen receptor-positive (ER+).

## 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 that are near the skin. Sometimes, a breast ultrasound or MRI is used to guide a biopsy.



### 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)

## Biopsy

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

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

Types of possible biopsies include:

- **Fine-needle aspiration (FNA) or core biopsy (CB)** uses needles of different sizes to remove a sample of

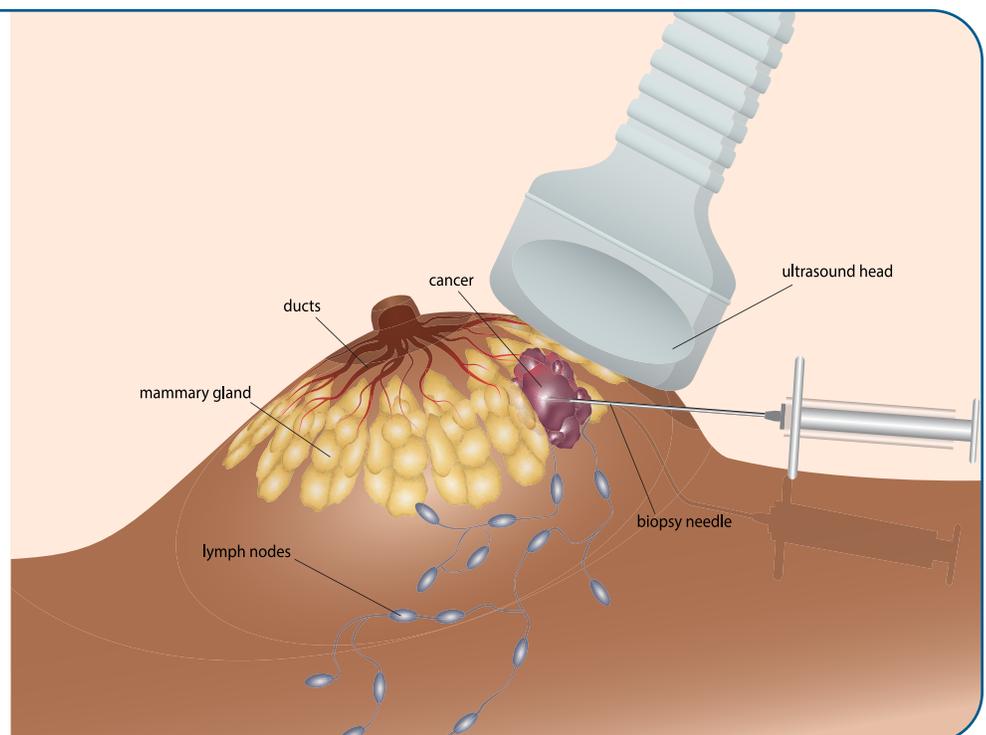
tissue or fluid. In a vacuum-assisted core biopsy (VACB), suction is used to remove the sample with a special vacuum device.

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

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

### Biopsy

In a biopsy, a sample of tumor is removed. There are different types of biopsy. This image shows an ultrasound-guided needle biopsy.



a biopsy, it is called a stereotactic needle biopsy.

One or more clips may be placed near the breast tumor during a biopsy. The clips are small, painless, and made of metal. They will mark the site for future treatment and imaging. The clips stay in place until surgery. If the area biopsied is benign, the clip will remain in place to mark the biopsy site on future imaging. The clip causes 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.

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

to take the day off to recover emotionally and physically from the experience.

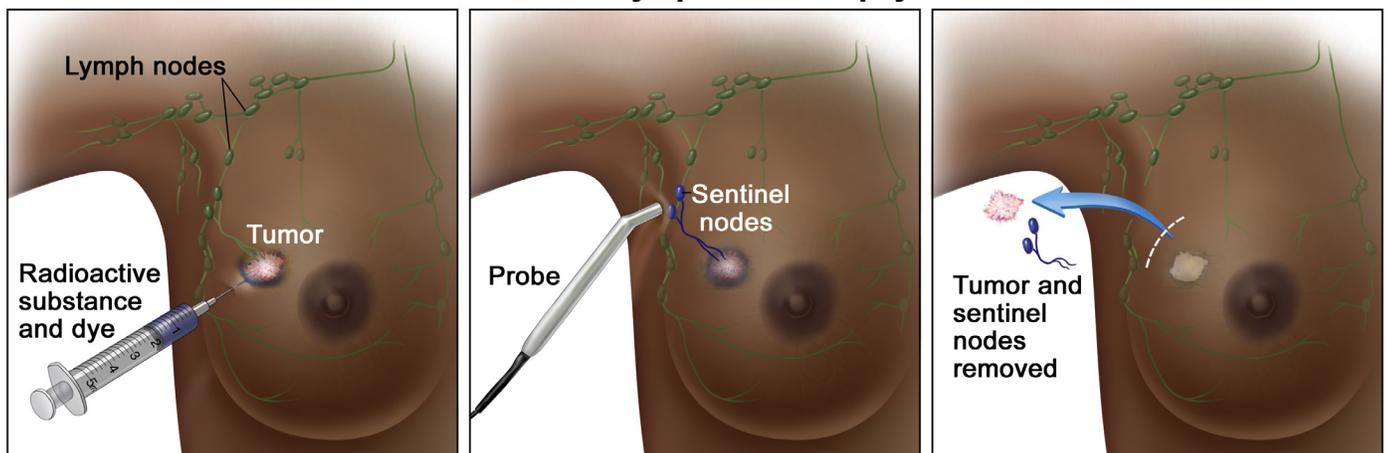
### Axillary lymph node needle biopsy

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.

### Sentinel lymph node biopsy

**A sentinel lymph node (SLN) is the first lymph node that cancer cells are most likely to spread to from a primary tumor. Often, there can be more than one sentinel lymph node. Removal of the sentinel lymph nodes during surgery is called a sentinel lymph node biopsy (SLNB or SNB).**

#### Sentinel Lymph Node Biopsy



© 2019 Terese Winslow

## Sentinel lymph node biopsy

A sentinel lymph node (SLN) is the first lymph node that cancer cells are most likely to spread to from a primary tumor. Sometimes, there can be more than one sentinel lymph node. Removal of the sentinel lymph nodes during surgery is called a sentinel lymph node biopsy (SLNB or SNB). This procedure is done during surgery such as a mastectomy (surgery to remove the breast) or lumpectomy (surgery to remove the tumor) to determine if any cancer cells have traveled to the lymph nodes. The lymph nodes removed are called the sentinel nodes. They may or may not contain any cancer cells. Just because these nodes are removed, it does not mean that they are positive for cancer.

To find the sentinel lymph nodes, a radioactive material and other dyes are injected into the area where breast tumor is located. From here, the dye travels through the lymphatics in the breast to the lymph nodes. This helps the surgeon find which of the nodes are the sentinel lymph nodes. Once the nodes are found, those containing the radioactive material or dye are removed and tested by a pathologist. If cancer is found, then more than the sentinel lymph nodes may be removed.

## Biopsy results

Histology is the study of the anatomy (structure) of cells, tissues, and organs under a microscope. It is used to make treatment decisions. Your pathology report will contain information about histology. You may be recommended to have an open biopsy (surgery) to remove (excise) the tumor to confirm histology. Talk to your health care provider for more information on next steps.

## Estrogen receptor-positive (ER+) breast cancer cells

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

## Hormone receptor status

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

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

There are 2 types of hormone receptors:

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

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

### Immunohistochemistry

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

## Hormone receptor-positive

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

There are 2 types of HR+ cells:

- **Estrogen receptor-positive (ER+)** cancer cells may need estrogen to grow. These cells may stop growing or die with treatment to block estrogen production or estrogen receptor signaling.
- **Progesterone receptor-positive (PR+)** cancer cells need progesterone to grow. It is thought that PR expression also suggests the tumor is estrogen dependent.

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

## Hormone receptor-negative

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

## HER2 status

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

There are 2 tests for HER2:

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

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

## Biomarker testing

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

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

### Tumor markers

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

## Tumor mutation testing

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

### MSI-H/dMMR mutation

Microsatellites are short, repeated strings of DNA. When errors or defects occur, they are fixed by mismatch repair (MMR) proteins. Some cancers have DNA mutations for changes that prevent these errors from being fixed. This is called microsatellite instability (MSI) or deficient mismatch repair (dMMR). When cancer cells have more than a normal number of microsatellites, it is called MSI-H (microsatellite instability-high). This is often due to dMMR genes.

### PD-1 and PD-L1 testing

Programmed death protein 1 (PD-1) and programmed death-ligand 1 (PD-L1) are immune proteins. If either protein is expressed on the surface of cancer cells, it can cause your immune cells to ignore the cancer and suppress the anti-tumor immune response. If your cancer expresses either protein, you might have treatment that combines chemotherapy and a checkpoint inhibitor therapy. This is designed to activate your immune system to better fight off the cancer cells.

## FISH

Fluorescence in situ hybridization (FISH) is a testing method that involves special dyes called probes that attach to pieces of DNA, the genetic material in a person's cells.

## 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.

## Next-generation sequencing

Next-generation sequencing (NGS) is a high-throughput method used to determine the DNA sequence or gene changes of cancer cells in your tumor. This method would only be used if enough tumor tissue remains after other biomarker testing has been completed.

## PCR

A polymerase chain reaction (PCR) is a lab process that can make millions or billions of copies of your DNA (genetic information). PCR is very sensitive. It can find 1 abnormal cell among more than 100,000 normal cells. These copies called PCR product might be used for NGS.

## Genetic risk testing

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

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

### **BRCA tests**

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

While it can be confusing, just know that testing done to look for an inherited gene mutation or an inherited risk of cancer is different than genetic testing done on cancer cells or testing to look for proteins produced by cancer cells.



## What is your family cancer health history?

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

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

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

Some of the questions to ask include:

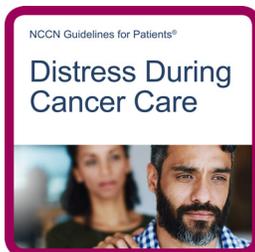
- ✓ How old were you when each of these diseases and health conditions was diagnosed?
- ✓ What is our family's ancestry – from what countries did our ancestors originate?

## Distress screening

It is normal to have strong feelings about being diagnosed with cancer and your feelings can also change from day to day and week to week. Talk to your care team and those whom you feel most comfortable about how you are feeling. There are services and people who can help you. Support and counseling are available. Dealing with a cancer diagnosis may sometimes be stressful and may cause distress. Your treatment team will screen your level of distress. This is part of your cancer care.

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.

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



## Performance status

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

### ECOG PS

The ECOG PS scores range from 0 to 5.

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

In breast cancer, PS might be referred to as good or poor. Good PS is usually PS 0 or PS 1.

## Key points

- Tests are used to find cancer, plan treatment, and check how well treatment is working.
- You will have a physical exam, including a breast exam, to see if anything feels or looks abnormal.
- Treatment can affect your fertility, the ability to have children.
- Blood tests check for signs of disease and how well organs are working.
- Imaging tests take pictures of the inside of your body.
- A diagnostic bilateral mammogram includes detailed pictures of both breasts. It is different than a screening mammogram.
- During a biopsy, tissue or fluid samples are removed for testing. Samples are needed to confirm the presence of cancer and to perform cancer cell tests.
- A sample from a biopsy of your tumor will be tested for estrogen receptor (ER) status, progesterone receptor (PR) status, HER2 status, and grade (histology). This provides information about the behavior of your cancer, as well as treatments to which your cancer may respond.
- About 1 out of 10 breast cancers are hereditary. Depending on your family history or other features of your cancer, you might be referred for genetic testing, to speak with a genetic counselor, and possibly to have genetic testing.
- A sentinel lymph node (SLN) is the first lymph node(s) that cancer cells are most likely to spread to from a primary tumor. A sentinel lymph node biopsy (SNLB) might be done to look for cancer in your lymph node(s).
- Online portals are a great way to access your test results.



### **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)

# 3

## Breast cancer staging

27 How breast cancer is staged

28 TNM scores

31 Key points

**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 and HER2 status.**

## How breast cancer is staged

A cancer stage is a way to describe the extent of the cancer at the time you are first diagnosed. The American Joint Committee on Cancer (AJCC) created a staging system to determine how much cancer is in your body, where it is located, and what subtype you have. This is called staging. Based on testing, your cancer will be assigned a stage. Staging helps to predict prognosis and is needed to make treatment decisions. A prognosis is the course your cancer will likely take. AJCC is just one type of staging system.

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.

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

- **Clinical stage (c)** is the rating given before any treatment. It is based on a physical exam, biopsy, and imaging tests. An example might look like cN2 or cM1.
- **Pathologic stage (p)** or surgical stage is determined by examining tissue removed during surgery. An example might be pN2. If you are given drug therapy before surgery, then the stage might look like ypT3.

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. Doctors may explain your cancer stage in different ways than described next.

Information gathered during staging:

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

## 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

## T = Tumor

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

- **T1** Tumor is 2 cm (20 mm) or less
  - **T1mi** Tumor is micrometastasis of 1 mm or less
  - **T1a** Tumor is 1.1 mm to 5 mm
  - **T1b** Tumor is 5.1 mm to 10 mm
  - **T1c** Tumor is 10.1 mm to 20 mm
- **T2** Tumor is 2.1 cm to 5 cm
- **T3** Tumor is more than 5 cm

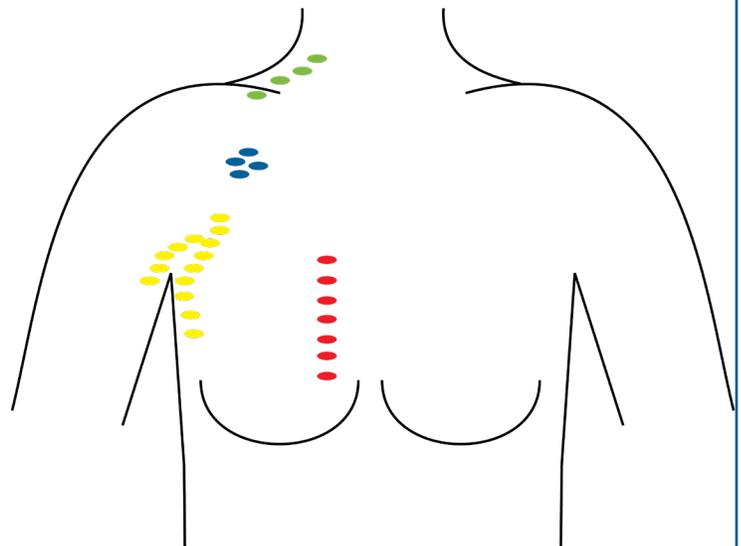
- **T4** Tumor is of any size and has invaded nearby structures such as the chest wall and skin of the breast
- **T4d** Tumor is inflammatory carcinoma (inflammatory breast cancer)
  - More information on inflammatory breast cancer is available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



## 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



## 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. There are hundreds of lymph nodes throughout your body. They work as filters to help fight infection and remove harmful things from your body. Regional lymph nodes are those located near the tumor in the breast. 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. 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.

Keep copies of your pathology reports. The pathology report might include a lot of abbreviations such as pN0(mol+), ypT2, or cN3. Ask your care team to explain what they mean.

# 4

## Treating breast cancer

33	Care team	43	Immunotherapy
35	Treatment overview	44	Endocrine therapy
36	Surgery	45	Bone-strengthening therapy
41	Radiation therapy	47	Clinical trials
42	Chemotherapy	49	Supportive care
42	Myeloid growth factors	50	Side effects
43	HER2-targeted therapy	53	Key points
43	PARP inhibitors		

**There is more than one treatment for invasive breast cancer.**

**This chapter describes general treatment options and what to expect. Together, you and your care team will choose a treatment plan that is best for you.**

## Care team

Treating breast cancer takes a team approach. Treatment decisions should involve a multidisciplinary team (MDT). An MDT is a team of health care and psychosocial care professionals from different professional backgrounds who have knowledge (expertise) and experience in your type of cancer. This team is united in 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.

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

- **A diagnostic radiologist** interprets the results of mammograms, ultrasounds, and other imaging tests.
- **An interventional radiologist** performs needle biopsies and places intravenous (IV) ports for treatment.
- **A pathologist** analyzes the cells and tissues removed during a biopsy and provides cancer diagnosis, staging, and information about biomarker testing.
- **A surgical oncologist** performs operations to remove cancer.
- **A reconstructive (plastic) surgeon** performs breast reconstruction, if desired, for those who undergo mastectomy.
- **A medical oncologist** treats cancer in adults using systemic therapy such as endocrine, chemotherapy, immunotherapy, or targeted therapy.
- **A radiation oncologist** prescribes and delivers radiation therapy to treat cancer.
- **An anesthesiologist** gives anesthesia, a medicine so you do not feel pain during surgery or procedures.
- **Residents and fellows** are doctors who are continuing their training, some to become specialists in a certain field of medicine.
- **Nurse practitioners (NPs) and physician assistants (PAs)** are health care providers. Some of your clinic visits may be done by a nurse practitioner or physician assistant.
- **Oncology nurses** provide your hands-on care, like giving systemic therapy, managing your care, answering questions, and helping you cope with side effects.
- **Oncology pharmacists** are experts in knowing how to use medicines to treat cancer and to manage symptoms and side effects.

- **Palliative care nurses, advanced practice providers (APPs), and physicians** help provide an extra layer of support with cancer-related care.
- **Nutritionists and dietitians** can provide guidance on what foods are most suitable for your condition.
- **An occupational therapist** helps people with the tasks of daily living.
- **A physical therapist** helps people move with greater comfort and ease.
- **A certified lymphedema therapist** gives a type of massage called manual lymph drainage.
- **Psychologists and psychiatrists** are mental health experts who can help manage issues such as depression, anxiety, or other mental health conditions that can affect how you think and feel.
- **Social workers** help people solve and cope with problems in their everyday lives. Clinical social workers also diagnose and treat mental, behavioral, and emotional issues. The anxiety a person feels when diagnosed with cancer might be managed by a social worker in some cancer centers. They, or other designated professionals, can help navigate the complexities of financial and insurance stresses.
- **A research team** helps to collect research data and coordinate care if you are in a clinical trial. Clinical trials help bring new therapies to patients and advance the treatment for everyone. Consider asking your care team about access to clinical trials.

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

Your physical, mental, and emotional well-being are important. Help other team members understand:

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

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

## 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:

- Mastectomy (surgery)
- Radiation therapy

Systemic therapy works throughout the body. It includes:

- HER2-targeted therapy
- Endocrine therapy
- Chemotherapy
- Immunotherapy
- Myeloid growth factors

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

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

### Guide 2 Systemic therapy examples

#### Chemotherapy examples

- |                         |   |                                |
|-------------------------|---|--------------------------------|
| • Capecitabine (Xeloda) | • Doxorubicin (Adriamycin, Rubex Doxorubicin) | • Eribulin (Halaven)           |
| • Carboplatin           | • Doxorubicin liposomal injection (Doxil)     | • Fluorouracil                 |
| • Cisplatin (Platinol)  | • Epirubicin (Ellence)                        | • Methotrexate                 |
| • Cyclophosphamide      |   | • Paclitaxel (Taxol, Abraxane) |
| • Docetaxel (Taxotere)  |   | • Vinorelbine (Navelbine)      |

#### HER2-targeted therapy (antibody, inhibitor, and conjugate) examples

- |  |   |   |
|--|---|---|
| • Pertuzumab (Perjeta)   | • Ado-trastuzumab emtansine (T-DM1) (Kadcyla) | • Neratinib (Nerlynx)   |
| • Trastuzumab (Herceptin) or trastuzumab substitutes (biosimilars) such as Kanjinti, Ogivri, Herzuma, Ontruzant, and Trazimera | • Fam-trastuzumab deruxtecan-nxki (Enhertu)   | • Tucatinib (Tukysa)  |
|  | • Lapatinib (Tykerb)                          | • Phesgo as a substitute for combination therapy of trastuzumab with pertuzumab |
|  | • Margetuximab-cmkb (Margenza)                |   |

## Birth control during treatment

If you become pregnant during chemotherapy, radiation therapy, endocrine therapy, or other types of systemic therapy, serious birth defects can occur. If you had menstrual periods before starting chemotherapy, choose birth control without hormones. Condoms are an option. “The pill” or other types of hormonal birth control are usually not recommended, especially in hormone receptor-positive (HR+) cancers. Speak to your doctor about preventing pregnancy while being treated for breast cancer.

Those who want to become pregnant in the future should be referred to a fertility specialist to discuss options before starting chemotherapy and/or endocrine therapy.

## Surgery

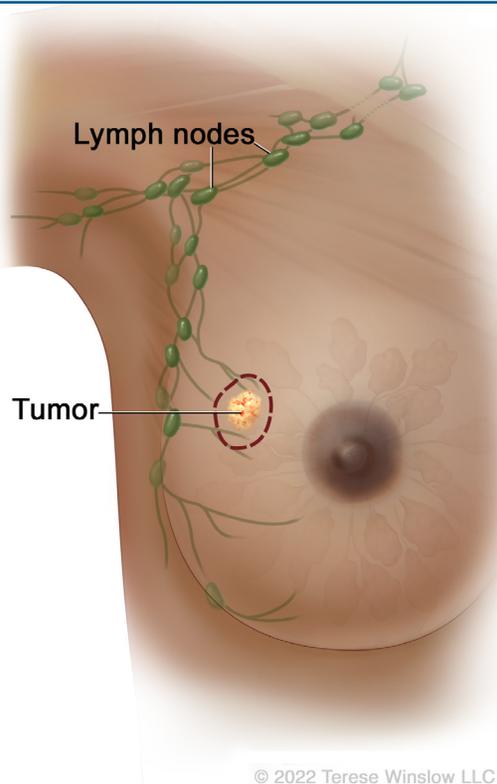
Surgery is an operation or procedure to remove cancer from the body. Surgery is the main or primary treatment for invasive breast cancer. This is only one part of a treatment plan. Systemic therapy or radiation therapy might be used before surgery to shrink the tumor or reduce the amount of cancer (called cancer burden).

- **Preoperative** is systemic (drug) treatment before surgery. It is also called neoadjuvant therapy.
- **Postoperative** is systemic (drug) treatment after surgery. It is also called adjuvant therapy.

When preparing for surgery, seek the opinion of an experienced surgeon. The surgeon

## Breast-conserving surgery

The dotted line shows where the tumor is removed. Lumpectomy is the removal of abnormal cells or tumor. It is also called a partial mastectomy, breast-conserving therapy, or breast-conserving surgery (BCS).



© 2022 Terese Winslow LLC  
U.S. Govt. has certain rights

should be an expert in performing your type of surgery. Hospitals that perform many surgeries often have better results. You can ask for a referral to a hospital or cancer center that has experience in treating your type of cancer.

The removal of the cancer through surgery can be accomplished in different ways depending on the specific circumstances, such as the size and location of the tumor, and if there is cancer in any surrounding organs and tissues.

Surgery might be a lumpectomy or mastectomy. It is based on the safest and best way to remove the cancer and your choice. Your preferences about treatment are always important. Make your wishes known.

If you are considering breast reconstruction, surgery requires collaboration between a breast surgeon and the reconstructive (plastic) surgeon.

### Goal of surgery

The goal of surgery or tumor resection is to remove all of 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. If there is a positive margin, you may require another surgery to try to remove the remaining tumor cells. Surgery usually includes removal of some lymph nodes.

### Surgical margins

The goal of surgery is a cancer-free surgical margin. After surgery, you may receive treatment such as radiation to kill any remaining cancer cells.

- **In a clear or negative margin (R0),** no cancerous cells are found in the tissue around the edge of the tumor.
- **In an R1 resection,** the surgeon removes all the visible tumor, but the microscopic margins are still positive for tumor cells. Despite best efforts this can happen.
- **In an R2 resection,** the surgeon is unable to remove all the visible tumor or there is metastatic disease.

Your surgeon will look carefully for cancer not only along the surgical margin, but in other nearby areas. Despite best efforts, it is not always possible to find all of the cancer. Sometimes, surgeons can't safely remove the tumor with a cancer-free margin.

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

## Lumpectomy

Lumpectomy is the removal of abnormal cells or tumor. It is also called breast-conserving therapy or breast-conserving surgery (BCS). In a lumpectomy, only the tumor with an area of normal-looking tissue is removed. The rest of your breast is left alone. Extra tissue is removed around the tumor to create a cancer-free area. This cancer-free area is called a surgical margin. Having a surgical margin will decrease the chance that cancer may return in that area of the breast. You may have more than one surgery to ensure all of the cancer was removed.

A lumpectomy is usually followed by radiation therapy to part of or the whole breast and sometimes the lymph nodes. A boost is extra radiation to the tumor area.

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. Certain reconstruction options, such as volume displacement, might be available.

## Breastfeeding or Chestfeeding

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



## 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
- Gingko biloba
- Green tea extract
- St. John's Wort
- Antioxidants

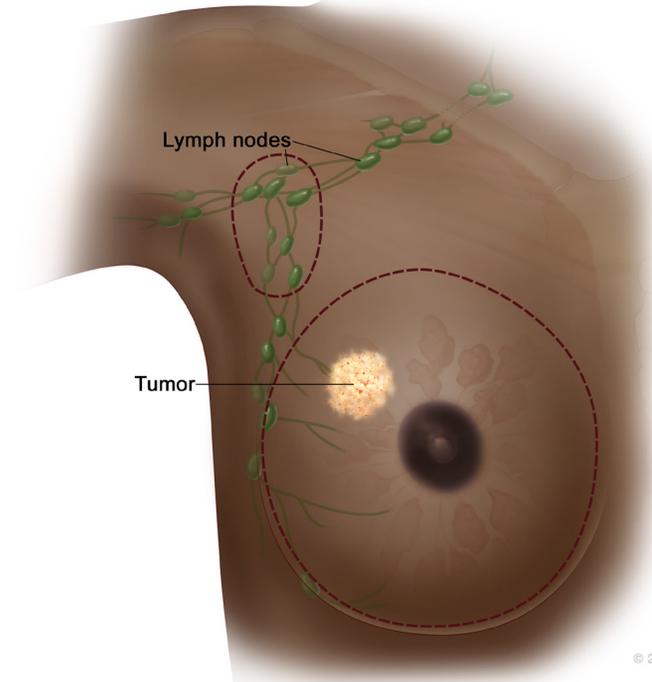
Certain medicines can also affect the ability of a drug to do its job. Antacids, heart or blood pressure medicine, and antidepressants are just some of the medicines that might interact with a systemic therapy. Therefore, it is very important to tell your care team about any medicines, vitamins, over-the-counter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

**Bring a list with you to every visit.**

### Total (Simple) Mastectomy

#### Total (simple) mastectomy

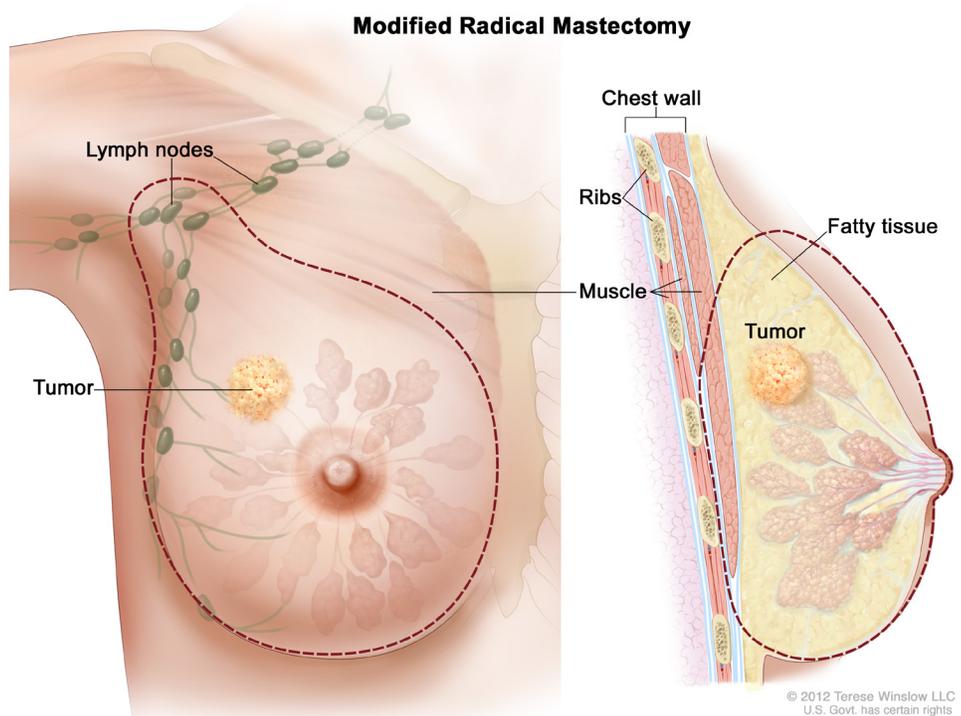
The dotted line shows where the entire breast is removed. Some lymph nodes under the arm may also be removed.



### Modified Radical Mastectomy

#### Modified radical mastectomy

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



## Mastectomy

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

Types of mastectomy include:

- **A total mastectomy or simple mastectomy** is a surgery that removes the whole breast with an aesthetic flat skin closure.
- **A skin-sparing mastectomy** removes the breast but not all of the skin,

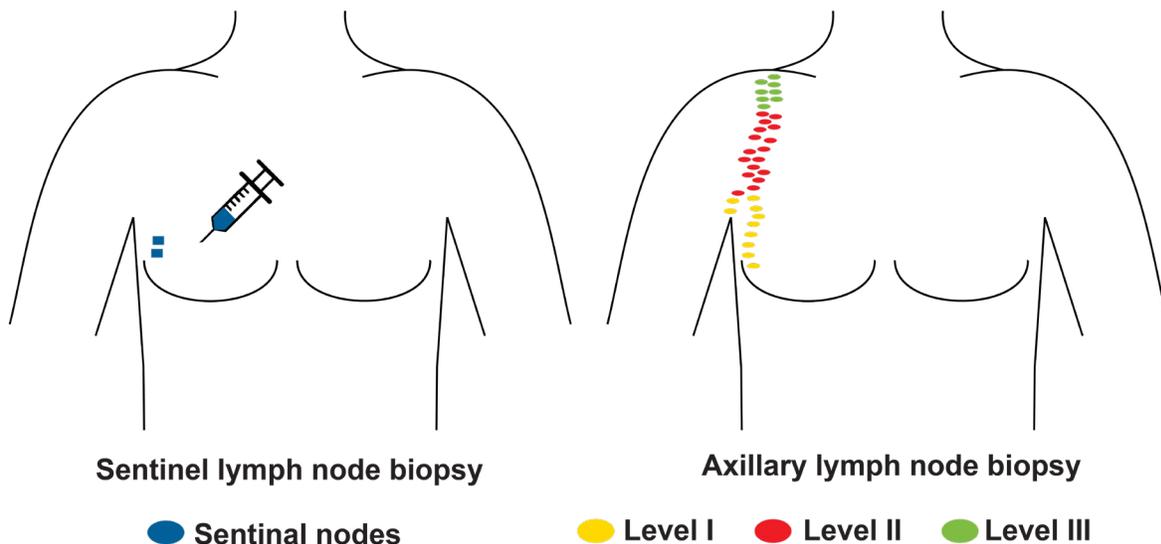
in order to have breast reconstruction that might include flaps and/or implants.

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

Breast reconstruction is an option after a mastectomy. It might be done at the same time as mastectomy (“immediate”) or at some time following the completion of cancer treatment (“delayed”). Breast reconstruction is often done in stages.

## Lymph node surgery

There are two types of surgeries to remove lymph nodes. A sentinel lymph node biopsy finds and removes the lymph nodes where breast cancer first spreads. An axillary lymph node dissection removes lymph nodes from levels I and II.



## Sentinel lymph node biopsy

A sentinel lymph node biopsy (SLNB or SNB) is done during surgery such as a mastectomy or lumpectomy to determine if any cancer cells have traveled to the lymph nodes. The lymph nodes removed are called the sentinel nodes. They may or may not contain any cancer cells. Just because these nodes are removed, it does not mean that they are positive for cancer.

## Axillary lymph node dissection

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

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

There are 3 levels of axillary lymph nodes:

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

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

## Radiation therapy

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

Types of radiation therapy include:

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

Radiation may be given to the breast and chest wall, infraclavicular region (below the collarbone), supraclavicular area (above the collarbone), lymph nodes found inside the breast (intramammary), behind the ribcage (internal mammary), or axillary bed (armpit).

## External beam radiation therapy

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

## Internal radiation

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

## Chemotherapy

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

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

Some examples of chemotherapy drugs include the following:

- Doxorubicin (Adriamycin), doxorubicin liposomal injection (Doxil), and epirubicin (Ellence) are **anthracyclines**.
- Docetaxel, paclitaxel, and albumin-bound paclitaxel are **taxanes**.

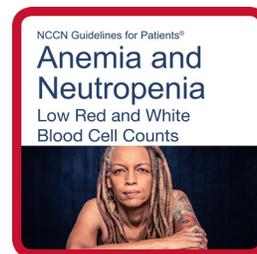
- Capecitabine (Xeloda), fluorouracil, gemcitabine (Gemzar, Infugem), and methotrexate are **anti-metabolites**.

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.

## Myeloid growth factors

Certain chemotherapies can reduce the cells that fight infection. Treatments with myeloid growth factors (MGFs) can help increase the number of white blood cells and prevent infections.

More information on myeloid growth factors can be found in the *NCCN Guidelines for Patients: Anemia and Neutropenia*, at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



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

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

### Did you know?

The terms “chemotherapy” and “systemic therapy” are often used interchangeably, but they are not the same. Systemic therapy works throughout the body and includes chemotherapy, targeted therapy, immunotherapy, endocrine therapy, and others.

## PARP inhibitors

Cancer cells often become damaged. PARP is a cell protein that repairs cancer cells and allows them to survive. Blocking PARP can cause cancer cells to die. Olaparib (Lynparza) and talazoparib (Talzenna) are PARP inhibitors. You must have the *BRCA1* or *BRCA2* mutation and your breast cancer must be HER2- for PARP inhibitors to be considered.

## Immunotherapy

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

## Endocrine therapy

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, and also by other tissues in the body such as the 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. It is not the same as hormone replacement therapy used for menopause.

There is one type of surgical endocrine therapy:

- **Bilateral oophorectomy** is surgery to remove both ovaries.

Other main types of endocrine therapy include:

- **Ovarian ablation** uses radiation to permanently stop the ovaries from making hormones.
- **Ovarian suppression** uses drugs to temporarily stop the ovaries from making hormones. It is achieved with drugs called LHRH agonists. These drugs stop LHRH from being made, which stops the ovaries from making hormones. LHRH agonists include goserelin (Zoladex) and leuprolide (Lupron Depot). Gonadotropin-releasing hormone (GnRH) agonists might be used to suppress ovarian hormone or testosterone production.
- **Aromatase inhibitors (AIs)** stop a type of hormone called androgen from changing into estrogen by interfering with an enzyme called aromatase. They do not affect estrogen made by the ovaries. Non-steroidal aromatase inhibitors include anastrozole (Arimidex) and letrozole (Femara). Exemestane (Aromasin) is a steroidal aromatase inhibitor.
- **Estrogen receptor (ER) modulators** or anti-estrogens prevent hormones from binding to receptors. SERMs and SERDs are types of ER modulators.
  - **Selective estrogen receptor modulators (SERMs)** block estrogen from attaching to hormone receptors. They include tamoxifen and toremifene (Fareston).
  - **Selective estrogen receptor degraders (SERDs)** block and destroy estrogen receptors. Fulvestrant (Faslodex) and elacestrant (Orserdu) are SERDs.

- **Gonadotropin-releasing hormone (GnRH) agonists** might be used to suppress ovarian hormone or testosterone production.

Those who want to have children in the future should be referred to a fertility specialist before starting endocrine therapy to discuss the options.

## Testosterone

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

## Premenopause

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

Tamoxifen is the endocrine treatment for those in premenopause. GnRH agonists may be used to temporarily induce menopause for those in premenopause. Combination of GnRH agonists and tamoxifen/aromatase inhibitors 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 a temporary menopause.

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

## Bone-strengthening therapy

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

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

Drugs used to prevent bone loss and fractures:

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

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

density tests look for osteoporosis and help predict your risk for bone fractures.

A baseline DEXA scan is recommended before starting endocrine therapy.

### Zoledronic acid, pamidronate, and denosumab

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

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

### Endocrine therapy

<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>	Drugs to temporarily stop the ovaries or testicles from making hormones such as LHRH and GnRH agonists.
<b>Aromatase inhibitors (AIs)</b>	Drugs to stop a type of hormone called androgen from changing into estrogen by interfering with an enzyme called aromatase.
<b>Estrogen receptor (ER) modulators</b>	<ul style="list-style-type: none"> <li>• Selective estrogen receptor modulators (SERMs) block estrogen from attaching to hormone receptors. Tamoxifen and toremifene (Fareston) are SERMs.</li> <li>• Selective estrogen receptor degraders (SERDs) block and destroy estrogen receptors. Fulvestrant (Faslodex) and elacestrant (Orserdu) are SERDs.</li> </ul>
<b>Hormones</b>	It is not known how hormones stop breast cancer from growing. They include ethinyl estradiol, fluoxymesterone, and megestrol acetate (Megace ES).

## Clinical trials

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

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

## Phases

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

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

**Standard of care is the best known way to treat 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.**



## Who can enroll?

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

## Informed consent

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

## Start the conversation

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



## 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)

## Frequently asked questions

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

### Will I get a placebo?

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

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

Rarely. It depends on the study, your health insurance, and the state in which you live. In general, procedures, drugs, or tests that are considered standard of care will be billed to you or your insurance, whereas those considered research are covered by the trial sponsor. Your treatment team and the research team can help determine if you are responsible for any costs.

## Supportive care

Supportive care will be specific to your needs. Supportive care is health care that relieves symptoms caused by cancer or its treatment and improves quality of life. It might include pain relief, palliative care, emotional or spiritual support, financial aid, or family counseling. Tell your care team how you are feeling and about any side effects so they can be managed. Best supportive care, supportive care, and palliative care are often used interchangeably.

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

## Side effects

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

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

## Late effects

Late effects are side effects that occur months or years after a disease is diagnosed or after treatment has ended. Late effects may be caused by cancer or cancer treatment. They may include physical, mental, and social problems, and second cancers. The sooner late effects are treated the better. Ask your care team about what late effects could occur. This will help you know what to look for.

## Survivorship

A person is a cancer survivor from the time of diagnosis until the end of life. When treatment leads to remission (or no evidence of disease), you will need follow-up or survivorship care for late effects. During survivorship care you will still have a care team, but it will look different. Seek out peer support groups, whether online or in-person.

## Side effects

### Blood clots

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

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

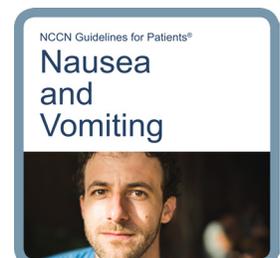
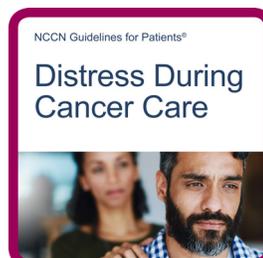
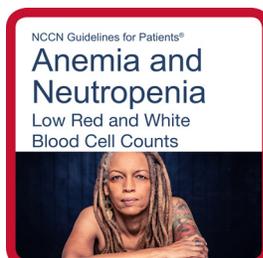
thromboembolism (VTE) refers to blood clots in the veins.

### 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

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.



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 doctor first.

## Diarrhea

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

## Difficulty eating

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.

## Distress

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

## Fatigue

Fatigue is extreme tiredness and inability to function due to lack of energy. Fatigue may be caused by cancer or it may be a side effect of treatment. Let your care team know how you are feeling and if fatigue is getting in the way of doing the things you enjoy. Eating a

balanced diet, exercise, yoga, acupuncture, and massage therapy can help. You might be referred to a nutritionist or dietitian to help with fatigue.

## Hair loss

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

## Low blood cell counts

Some cancer treatments can cause low blood cell counts.

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

## Lymphedema

Lymphedema is a condition in which extra lymph fluid builds up in tissues and causes swelling (edema). It may occur when part of the lymph system is damaged or blocked, such as during surgery to remove lymph nodes or due to radiation therapy. 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 sleeves, and other means. Ask your care team about the ways to treat lymphedema.

## Nausea and vomiting

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

## Neurocognitive or neuropsychological effects

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

## Neuropathy

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

## Organ issues

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

## Pain

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

## Keep a pain diary

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

Include in your pain diary:

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

## Key points

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

# 5

## Surgery first

- 55 Surgery and radiation therapy
- 56 Adjuvant systemic therapy
- 57 HR+ with HER2+
- 60 HR+ with HER2-
- 60 HR- with HER2+
- 60 Triple-negative breast cancer
- 60 Adjuvant endocrine therapy
- 61 Follow-up care
- 62 Key points

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

Not all cancers need treatment before surgery. If your oncologist is considering treatment before surgery (preoperative), then *Chapter 6* is where you can find that information. This chapter is for those who will not have preoperative therapy.

## Surgery and radiation therapy

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

There are 2 breast surgery options:

- Lumpectomy
- Total mastectomy

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

include radiation therapy and/or systemic therapy.

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

### Lumpectomy

A lumpectomy, also called breast-conserving surgery (BCS), is surgery to remove a tumor in the breast. Treatment after a lumpectomy is based on the type of cancer and if cancer is found in the axillary lymph nodes (ALNs). If there is a positive surgical margin, you might have more surgery to remove any remaining cancer. Whole breast radiation therapy (WBRT) is usually recommended after a lumpectomy. Regional node irradiation (RNI) might be added. Chemotherapy might be given before RT.

### Total mastectomy

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

## Adjuvant systemic therapy

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

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

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

### Favorable histologies

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

Favorable histology types include:

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

### Common histologies

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

Common histology types include:

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

Adjuvant treatment options for common histologies are described next.

## HR+ with HER2+

In hormone receptor-positive (HR+) cancer, estrogen (ER+) and/or progesterone receptors (PR+) are found. If HER2 receptors are

overexpressed, the cancer is also HER2+. It might be written as HR+ with HER2+ or called triple-positive breast cancer.

### Guide 4

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

<b>Preferred options</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>
	<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>
	<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 followed by docetaxel with trastuzumab</li> <li>• Doxorubicin with cyclophosphamide followed by docetaxel with 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 followed by paclitaxel with trastuzumab</li> <li>• Doxorubicin and cyclophosphamide followed by docetaxel with paclitaxel, trastuzumab, and pertuzumab</li> <li>• Neratinib</li> <li>• Paclitaxel with trastuzumab and pertuzumab</li> <li>• Ado-trastuzumab emtansine (TDM-1)</li> </ul>
<b>Notes</b>	<ul style="list-style-type: none"> <li>• Alternative taxanes (ie, docetaxel, paclitaxel, albumin-bound paclitaxel) might be substituted in some cases</li> <li>• An FDA-approved biosimilar or substitute might be used for trastuzumab.</li> </ul>

Endocrine therapy is used to treat HR+ breast cancer. Chemotherapy with a HER2-targeted therapy is used to treat HER2+ cancer. Examples of HER2-targeted therapy used after surgery include trastuzumab and pertuzumab.

Systemic therapies might be used alone or in combination. If chemotherapy is given, it is given before endocrine therapy. Ask your medical oncologist why one treatment might be preferred over another for your type of cancer.

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

Endocrine therapy options can be found in **Guide 6**.

## Guide 5

### Adjuvant therapy options: HER2-

<b>Preferred options</b>	<ul style="list-style-type: none"> <li>• Doxorubicin and cyclophosphamide (AC) with paclitaxel</li> <li>• Docetaxel and cyclophosphamide (TC)</li> <li>• Olaparib, if germline <i>BRCA1</i> or <i>BRCA2</i> mutations</li> </ul>
	<ul style="list-style-type: none"> <li>• High-risk triple-negative breast cancer (TNBC): Preoperative pembrolizumab with carboplatin and paclitaxel, followed by preoperative pembrolizumab and cyclophosphamide with doxorubicin or epirubicin, followed by adjuvant pembrolizumab</li> <li>• If TNBC and 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>
	<p>Only in certain TNBC cases:</p> <ul style="list-style-type: none"> <li>• Paclitaxel with carboplatin</li> <li>• Docetaxel with carboplatin (preoperative only)</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> <li>• Capecitabine (maintenance therapy for TNBC after adjuvant chemotherapy)</li> </ul>

**Guide 6****Endocrine therapy options****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

## HR+ with HER2-

In hormone receptor-positive (HR+) cancer, estrogen (ER+) and/or progesterone receptors (PR+) are found. Endocrine therapy is used to treat HR+ breast cancer. Since there are no HER2 receptors, therapy targeting the HER2 receptors is not used. Sometimes, chemotherapy is used instead. When cancer is found in the lymph nodes, it is node positive (node+).

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

Chemotherapy and other systemic therapies specific to HER2- are found in **Guide 5**.

Endocrine therapy options can be found in **Guide 6**.

## HR- with HER2+

In hormone receptor-negative (HR-) cancer, there are no receptors for estrogen (ER-) and progesterone (PR-). When HER2 receptors are found, it is HER2-positive (HER2+). Since this cancer is HR- and HER2+, treatment will focus on targeting HER2. HER2-targeted therapy usually includes chemotherapy. HER2-targeted therapy options can be found in Guide 4.

## Triple-negative breast cancer

In triple-negative breast cancer (TNBC), receptors for estrogen, progesterone, and HER2 are not found. This means that the breast cancer cells have tested negative for

HER2 and both hormone receptors. It is written as ER- and/or PR- with HER2-.

TNBC is cancer that is:

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

There are many variations within TNBC. It is a group of diseases that we are learning more about all the time. Since there are no HER2 receptors, HER2- targeted therapy is not used. And since there are no estrogen or progesterone hormone receptors, endocrine therapy is not used. Adjuvant treatment will likely be chemotherapy as found in **Guide 5**.

## Adjuvant endocrine therapy

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

Those with high-risk breast cancer that is HR+ and HER2- might have 2 years of adjuvant abemaciclib with endocrine therapy.

Those receiving an aromatase inhibitor who are at risk for osteoporosis will likely have bone density tests and bone-strengthening therapy.

Adjuvant endocrine therapy options 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 called late effects and the possible return of cancer called recurrence. This is part of your survivorship care plan. It is important to keep any follow-up doctor visits and imaging test appointments. Seek routine medical care, including regular doctor visits for preventive care and cancer screening.

Tell your care team about any symptoms such as headaches, menstrual spotting between periods or new onset of spotting after

menopause (if prior tamoxifen use), shortness of breath that you notice with walking, or bone pain. Side effects can be managed. Continue to take all medicine such as endocrine therapy exactly as prescribed and do not miss or skip doses.

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

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

### Guide 7 Follow-up care

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

Screen for changes in family history

Genetic testing and referral to genetic counseling, as needed

Monitor for lymphedema and refer for lymphedema management, as needed

Mammogram every 12 months (not needed after mastectomy or on reconstructed breast)

Heart tests, as needed

Information on risk of future health issues (comorbidities)

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

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

Annual gynecology exam for those on tamoxifen

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

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. Radiation therapy (RT) and/or systemic therapy are possible following surgery.
- Treatment after surgery is called adjuvant treatment. It is based on the pathologic stage and other factors. Your tumor will be tested to determine the pathologic stage.
- Adjuvant systemic therapy is given after surgery to kill any remaining cancer cells in the body and to help prevent the return of cancer.
- Adjuvant treatment is based on the stage, histology, and hormone receptor status. Histology is the study of the anatomy (structure) of cells, tissues, and organs under a microscope.
- A favorable histology is one that has a favorable or good prognosis.
- In hormone receptor-positive (HR+) cancer, estrogen (ER+) and/or progesterone receptors (PR+) are found.
- Endocrine therapy is used to treat HR+ cancer.
- If chemotherapy is given, it is given before radiation therapy and endocrine therapy.
- In triple-negative breast cancer (TNBC), receptors for estrogen, progesterone, and HER2 are not found. It is almost always treated with chemotherapy.
- It is important to keep follow-up visits and imaging test appointments. Seek good routine medical care, including preventative care and cancer screenings. Continue to take all medicines as prescribed.



**share with us.**

**Take our survey,  
and help make the  
NCCN Guidelines for Patients  
better for everyone!**

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

# 6

## Preop treatment first

- 64 Testing
- 65 Preoperative therapy
- 65 Surgery
- 66 Adjuvant treatment
- 67 HR+ with HER2+
- 68 HR+ with HER2-
- 68 HR- with HER2+
- 69 Triple-negative breast cancer
- 70 Adjuvant endocrine therapy
- 71 Follow-up care
- 72 Key points

**This chapter is for those who have stage 3 breast cancer or for those who would benefit from treatment before surgery. Treatment before surgery is called preoperative or neoadjuvant therapy. It can be systemic therapy or radiation therapy. Preoperative therapy is not for everyone. Together, you and your care team will choose the best option for you.**

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

## Testing

Not everyone will benefit from preoperative therapy. If preoperative systemic therapy is an option for you, then you will have blood and imaging tests before starting treatment. These tests will determine if your cancer can be removed with surgery (operable) or cannot be removed with surgery at this time (inoperable). Testing will include an axillary lymph node exam with ultrasound and biopsy of lymph nodes suspected of cancer.

Talk with your care team about what types of preoperative therapy are right for you.

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 MRI (if not done before)
- Biopsy of suspicious lymph nodes with clip placement (if not done before)

## Preoperative therapy

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

It can:

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

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

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

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

## Surgery

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

## Adjuvant treatment

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

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

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

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

Adjuvant treatment options are described next.

### Order of treatments

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

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

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

## HR+ with HER2+

Hormone receptor-positive (HR+) with HER2+ is also called triple-positive breast cancer. Receptors for HER2, estrogen, and/

or progesterone are found. It is treated with HER2-targeted therapy and endocrine therapy.

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

### Guide 8

#### Preop and adjuvant HER2-targeted therapy options: HER2+

<b>Preferred options</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>
	<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> <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 followed by docetaxel with trastuzumab</li> <li>• Doxorubicin with cyclophosphamide followed by docetaxel with 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 followed by paclitaxel with trastuzumab</li> <li>• Doxorubicin and cyclophosphamide followed by docetaxel with paclitaxel, trastuzumab, and pertuzumab</li> <li>• Neratinib</li> <li>• Paclitaxel with trastuzumab and pertuzumab</li> <li>• Ado-trastuzumab emtansine (TDM-1)</li> </ul>
<b>Notes</b>	<ul style="list-style-type: none"> <li>• Alternative taxanes (ie, docetaxel, paclitaxel, albumin-bound paclitaxel) might be substituted in some cases</li> <li>• An FDA-approved biosimilar or substitute might be used for trastuzumab</li> </ul>

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

## HR+ with HER2-

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

## HR- with HER2+

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

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

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

## Triple-negative breast cancer

In triple-negative breast cancer (TNBC), the tumor has tested negative for HER2, estrogen receptors, and progesterone receptors. It is written as ER- and/or PR- with HER2-. This cancer does not respond to endocrine therapy or HER2-targeted therapy. It is treated with chemotherapy and other systemic therapies found in **Guide 9**.

- ▶ If no disease remains after preoperative therapy and you are at high risk for

the return of cancer, then you will have pembrolizumab (if a pembrolizumab-containing regimen was given before surgery).

- ▶ If disease remains or there is cancer in the lymph nodes (node positive), then you will have capecitabine. Olaparib might be given if a *BRCA1* or *BRCA2* mutation was found. Pembrolizumab is an option if a pembrolizumab-containing regimen was given before surgery.

### Guide 9

#### Preop and adjuvant therapy options: HER2-

<b>Preferred options</b>	<ul style="list-style-type: none"> <li>• Doxorubicin and cyclophosphamide (AC) with paclitaxel</li> <li>• Docetaxel and cyclophosphamide (TC)</li> <li>• Olaparib, if germline <i>BRCA1</i> or <i>BRCA2</i> mutations</li> </ul>
	<ul style="list-style-type: none"> <li>• High-risk triple-negative breast cancer (TNBC): Preoperative pembrolizumab with carboplatin and paclitaxel, followed by preoperative pembrolizumab and cyclophosphamide with doxorubicin or epirubicin, followed by adjuvant pembrolizumab</li> <li>• If TNBC and 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>
	<p>Only in certain TNBC cases:</p> <ul style="list-style-type: none"> <li>• Paclitaxel with carboplatin</li> <li>• Docetaxel with carboplatin (preoperative only)</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> <li>• Capecitabine (maintenance therapy for TNBC after adjuvant chemotherapy)</li> </ul>

## Adjuvant endocrine therapy

Adjuvant endocrine therapy is used to treat hormone receptor-positive (HR+) breast cancer. This is cancer that tests positive for estrogen receptors (ER+) and/or progesterone receptors (PR+). Endocrine therapy blocks estrogen and progesterone to treat HR+

breast cancer. This can slow tumor growth or shrink the tumor for a period of time. It might also help prevent the risk of cancer returning. Endocrine therapy is often used with other systemic therapies.

Adjuvant endocrine therapy options can be found in **Guide 10**.

### Guide 10 Endocrine therapy options

Premenopause at diagnosis	Option 1	<ul style="list-style-type: none"> <li>• 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)</li> </ul>
	<ul style="list-style-type: none"> <li>• Tamoxifen alone or with ovarian suppression or ablation for 5 years</li> </ul>	
Menopause at diagnosis	Option 2	<ul style="list-style-type: none"> <li>• 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</li> </ul>
	Option 1	<ul style="list-style-type: none"> <li>• Aromatase inhibitor for 5 years with ovarian suppression or ablation, then consider aromatase inhibitor for an additional 3 to 5 years</li> </ul>
	Option 1	<ul style="list-style-type: none"> <li>• Aromatase inhibitor for 5 years, then consider aromatase inhibitor for 3 to 5 more years</li> <li>• Aromatase inhibitor for 2 to 3 years, then tamoxifen to complete 5 years total of endocrine therapy</li> <li>• Tamoxifen for 2 to 3 years, then an aromatase inhibitor to complete 5 years of endocrine therapy</li> <li>• Tamoxifen for 2 to 3 years, then up to 5 years of an aromatase inhibitor</li> </ul>
	Option 2	<ul style="list-style-type: none"> <li>• 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)</li> </ul>
	Option 3	<ul style="list-style-type: none"> <li>• 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</li> </ul>

## Follow-up care

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

Tell your care team about any symptoms such as headaches or bone pain. Side effects can be managed. Continue to take all

medicine such as endocrine therapy exactly as prescribed and do not miss or skip doses.

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

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

### Guide 11 Follow-up care

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

Screen for changes in family history

Genetic testing and referral to genetic counseling, as needed

Monitor for lymphedema and refer for lymphedema management, as needed

Mammogram every 12 months (not needed after mastectomy or on reconstructed breast)

Heart tests, as needed

Information on risk of future health issues (comorbidities)

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

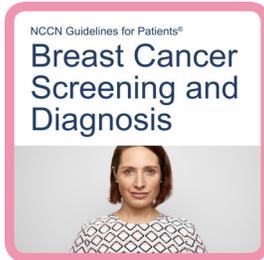
If taking endocrine therapy, continue to take endocrine therapy. Do not miss or skip doses

Annual gynecology exam for those on tamoxifen

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

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

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



- HER2-positive (HER2+) breast cancer is treated with HER2-targeted therapy.
- It is important to keep follow-up visits and imaging test appointments. Seek good routine medical care, including preventative care and cancer screenings. Continue to take all medicines as prescribed.

## Key points

- In stage 3 breast cancer, the cancer can be large and in the lymph nodes, the lymph nodes can be fixed (or not moveable), or the cancer can involve the skin or chest wall. It is not metastatic.
- Treatment before surgery is called preoperative (neoadjuvant) therapy. It can be systemic therapy or radiation therapy. The goal of treatment is to shrink the tumor before surgery.
- Systemic therapy after surgery is called adjuvant therapy. Adjuvant therapy is based on how the tumor responded to preoperative treatment.
- All treatment is based on HER2 and hormone receptor (HR) status.
- In hormone receptor-positive (HR+) breast cancer, tests find hormone receptors for estrogen and/or progesterone on the tumor.
- HR+ breast cancer is treated with endocrine therapy.

# 7

## The breast after surgery

- 74 Volume displacement
- 75 Flat closure
- 75 Breast reconstruction
- 76 Nipple replacement
- 76 What to consider
- 77 Key points

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

The recovery time for each procedure differs. This can affect your ability to return to work or participate in activities. You might consider

speaking with a plastic surgeon before surgery to discuss your options and what to expect.

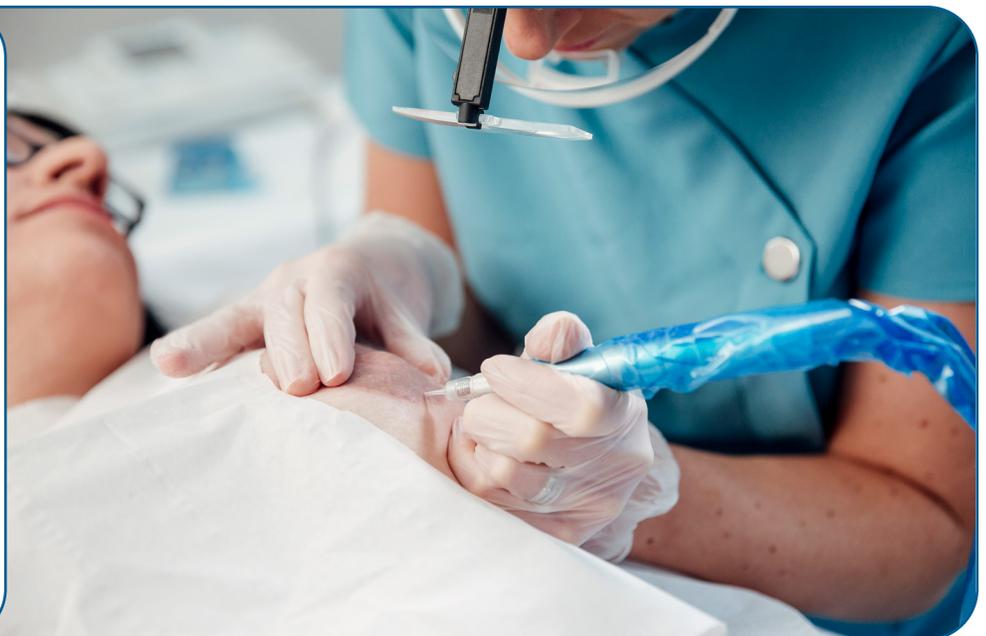
## Volume displacement

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

If volume displacement is planned, a larger piece of your breast will need to be removed. Despite a larger piece being removed, the natural look of your breast will be kept.

### Tattoo

**Removed nipples can be remade with body tissue and/or tattooing.**



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 are 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 end result varies from person to person. Ask to look at “after” pictures from flat closures so you know what to expect.

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

## Breast reconstruction

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

You may have a choice as to when breast reconstruction is done. Immediate reconstruction is finished within hours after removing the breast. Delayed reconstruction can occur months or years after the cancer surgery. Reconstruction can also be done in a

staged fashion, with part of the reconstruction done at the time of the original cancer surgery, and finished with another surgery at a later time. 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 two to three 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. Textured implants can cause breast implant-associated anaplastic large cell lymphoma (BIA-ALCL), a type of cancer.

### Flaps

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

with larger breasts who are willing to have much smaller breasts as a result.

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

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

## Implants and flaps

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

## Nipple replacement

Like your breast, a nipple can be remade. To rebuild a nipple, a plastic surgeon can use surrounding tissues. Also, nipples can be remade with tissue from the thigh or 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.

## Key points

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

### **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. Marijuana 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.

For online support, try these websites:

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

# 8

## Recurrence

- 79 Overview
- 79 Tests
- 79 Treatment
- 81 Key points

**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 3 places:

- It can return to the breast that had cancer before. This is called a **local recurrence**.
- It can return to axillary lymph nodes or lymph nodes in or near the breast. This is called a **regional recurrence**.
- It can return to other distant parts of the body. This is called **metastatic breast cancer**.

This chapter presents treatment options for local and regional recurrence.

## Tests

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

## Treatment

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

### Local only

Treatment for a local recurrence is based on if your first treatment was breast-conserving surgery (lumpectomy) with radiation therapy or a mastectomy with or without radiation therapy (RT). More surgery might be an option. However, if you had RT before, then it may not be possible to have it again in the same area.

### Regional only

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

### Both local and regional

Cancer that is both local and regional might be referred to as a locoregional recurrence. Treatment for a locoregional recurrence is surgery and RT when possible. Some people receive systemic therapy or RT if surgery is not possible.

## Unresectable

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



### Guide 12

#### Possible tests: Recurrence

Medical history and physical exam (H&P)

Discuss goals of therapy, engage in shared decision-making, and document course of care

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)

Brain MRI with contrast if suspicious central nervous system (CNS) symptoms

Spine MRI with contrast if back pain or symptoms of cord compression

Bone scan or sodium fluoride PET-CT, as needed

FDG PET-CT or FES PET-CT, as needed

X-rays of symptomatic bones and long and weight-bearing bones abnormal on bone scan

Biopsy tumor or metastasis and test for biomarkers

Determine tumor status including:

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

Genetic counseling if at risk for hereditary breast cancer

Assess for distress

## Key points

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

Supportive care aims to prevent, reduce, and relieve side effects and to improve quality of life.

# 9

## Making treatment decisions

- 83 It's your choice
- 83 Questions to ask
- 91 Resources

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

## It's your choice

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

Treatment decisions are very personal. What is important to you may not be important to someone else.

Some things that may play a role in your decision-making:

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

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

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

## Second opinion

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

Things you can do to prepare:

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

## Support groups

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

## Questions to ask

Possible questions to ask your doctors are listed on the following pages. Feel free to use these questions or come up with your own. Be clear about your goals for treatment and find out what to expect from treatment.















## Resources

Many of these resources are also available en español and other languages.

**Breast Cancer Alliance (BCA)**

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

**Unite for HER**

[uniteforher.org](https://uniteforher.org)

**Breastcancer.org**

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

**Cancer Hope Network**

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

**DiepC Foundation**

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

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

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

**GPAC Global Patient Advocacy Coalition**

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

**Inflammatory Breast Cancer Research  
Foundation**

[ibcresearch.org](https://ibcresearch.org)

**MedlinePlus**

[medlineplus.gov/breastcancer.html](https://medlineplus.gov/breastcancer.html)

**National Cancer Institute (NCI)**

[cancer.gov/types/breast](https://cancer.gov/types/breast)

**Sharsheret**

[sharsheret.org](https://sharsheret.org)

**Triage Cancer**

[tragecancer.org](https://tragecancer.org)



## Words to know

### **accelerated partial breast irradiation (APBI)**

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

### **adjuvant therapy**

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

### **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.

### **boost**

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

### **breast-conserving surgery (BCS)**

A cancer treatment that includes removing a breast lump.

### **breast implant**

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

### **breast reconstruction**

An operation that creates new breasts.

### **cancer stage**

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

### **carcinoma**

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

### **chest wall**

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

### **clinical breast exam (CBE)**

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

### **clinical stage (c)**

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

**clinical trial**

A type of research that assesses health tests or treatments.

**connective tissue**

Supporting and binding tissue that surrounds other tissues and organs.

**contrast**

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

**core needle biopsy (CNB)**

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

**deoxyribonucleic acid (DNA)**

A chain of chemicals in cells that contains coded instructions for making and controlling cells.

**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.

**imaging test**

A test that makes pictures (images) of the insides of the body.

**immune system**

The body's natural defense against infection and disease.

**immunohistochemistry (IHC)**

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

**inflammatory breast cancer**

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.

**intramammary lymph nodes**

Lymph nodes inside the breast and surrounded by breast tissue.

**invasive breast cancer**

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

**linear accelerator (linac)**

A machine that delivers radiotherapy treatments.

**lobular carcinoma**

A breast cancer that started in cells that line the breast glands (lobules).

**lobule**

A gland in the breast that makes breast milk.

**lumpectomy**

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

**luteinizing 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.

**lymphadenopathy**

Lymph nodes that are abnormal in size or consistency.

**lymphatic system**

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

**lymphedema**

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

**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 by using x-rays.

**mastectomy**

An operation that removes the whole breast.

**medical history**

A report of all your health events and medicines.

**medical oncologist**

A doctor who is an expert in cancer drugs.

**menopause**

12 months after the last menstrual period.

**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.

**nipple-sparing mastectomy**

An operation that preserves the nipple-areola complex (NAC) as well as all of the skin.

**noninvasive breast cancer**

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

**palpable adenopathy**

Lymph nodes that feel abnormal in size or consistency.

**partial breast irradiation (PBI)**

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

**pathologic stage (p)**

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

**pathologist**

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

**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.

**primary tumor**

The first mass of cancer cells.

**progesterone (PR)**

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

**prognosis**

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

**radiation therapy (RT)**

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

**recurrence**

The return of cancer after a cancer-free period.

**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.

**skin-sparing mastectomy**

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

**supportive care**

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

**supraclavicular**

The area right above the collarbone.

**surgical margin**

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

**systemic therapy**

Drug treatment that works throughout the body.

**total mastectomy**

An operation that removes the entire breast with an aesthetic 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.

**vacuum-assisted core biopsy (VACB)**

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

**volume displacement**

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

**whole breast radiation therapy (WBRT)**

Treatment with radiation of the entire breast.

# NCCN Contributors

This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer, Version 4.2023. It was adapted, reviewed, and published with help from the following people:

Dorothy A. Shead, MS  
Senior Director

Tanya Fischer, MEd, MSLIS  
Senior Medical Writer

Laura Phillips  
Graphic Design Specialist

The NCCN Guidelines® for Breast Cancer Version 4.2023 were developed by the following NCCN Panel Members:

William J. Gradishar, MD/Chair  
Robert H. Lurie Comprehensive Cancer  
Center of Northwestern University

Sharon H. Giordano, MD, MPH  
The University of Texas  
MD Anderson Cancer Center

Hope S. Rugo, MD  
UCSF Helen Diller Family  
Comprehensive Cancer Center

Meena S. Moran, MD/Vice-Chair  
Yale Cancer Center/Smilow Cancer Hospital

Matthew P. Goetz, MD  
Mayo Clinic Comprehensive Cancer Center

Bryan Schneider, MD  
Indiana University Melvin and Bren Simon  
Comprehensive Cancer Center

Jame Abraham, MD  
Case Comprehensive Cancer Center/  
University Hospitals Seidman Cancer Center  
and Cleveland Clinic Taussig Cancer Institute

Lori J. Goldstein, MD  
Fox Chase Cancer Center

Mary Lou Smith, JD, MBA  
Research Advocacy Network

Vandana Abramson, MD  
Vanderbilt-Ingram Cancer Center

Sara A. Hurvitz, MD  
UCLA Jonsson Comprehensive  
Cancer Center

Hatem Soliman, MD  
Moffitt Cancer Center

Rebecca Aft, MD, PhD  
Siteman Cancer Center at Barnes-  
Jewish Hospital and Washington  
University School of Medicine

Rachel C. Jankowitz, MD  
Abramson Cancer Center at the  
University of Pennsylvania

Erica M. Stringer-Reasor, MD  
O'Neal Comprehensive  
Cancer Center at UAB

Doreen Agnese, MD  
The Ohio State University Comprehensive  
Cancer Center - James Cancer Hospital  
and Solove Research Institute

Sara H. Javid, MD  
Fred Hutchinson Cancer Center

Melinda L. Telli, MD  
Stanford Cancer Institute

Kimberly H. Allison, MD  
Stanford Cancer Institute

Jairam Krishnamurthy, MD  
Fred & Pamela Buffet Cancer Center

Mei Wei, MD  
Huntsman Cancer Institute  
at the University of Utah

Bethany Anderson, MD  
University of Wisconsin  
Carbone Cancer Center

A. Marilyn Leitch, MD  
UT Southwestern Simmons  
Comprehensive Cancer Center

Kari B. Wisinski, MD  
University of Wisconsin  
Carbone Cancer Center

Harold J. Burstein, MD, PhD  
Dana-Farber/Brigham and Women's  
Cancer Center

\*Janice Lyons, MD  
Case Comprehensive Cancer Center/  
University Hospitals Seidman Cancer Center  
and Cleveland Clinic Taussig Cancer Institute

\*Jessica S. Young, MD  
\*Roswell Park Comprehensive Cancer Center

Helen Chew, MD  
UC Davis Comprehensive Cancer Center

Joanne Mortimer, MD  
City of Hope National Medical Center

\*Kay Yeung, MD  
UC San Diego Moores Cancer Center

Chau Dang, MD  
Memorial Sloan Kettering Cancer Center

Sameer A. Patel, MD  
Fox Chase Cancer Center

## NCCN

Rashmi Kumar, PhD  
Senior Director, Clinical Content

Anthony D. Elias, MD  
University of Colorado Cancer Center

Lori J. Pierce, MD  
University of Michigan  
Rogel Cancer Center

Mary Dwyer, MS  
Senior Director, Guidelines Operations

Laura H. Rosenberger, MD, MS  
Duke Cancer Institute

\* Reviewed this patient guide. For disclosures, visit [NCCN.org/disclosures](https://www.nccn.org/disclosures).

# NCCN Cancer Centers

**Abramson Cancer Center**  
at the University of Pennsylvania  
Philadelphia, Pennsylvania  
800.789.7366 • [penmedicine.org/cancer](http://penmedicine.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 |  
Massachusetts General Hospital Cancer Center**  
Boston, Massachusetts  
617.732.5500 • [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 • [huntsmancancer.org](http://huntsmancancer.org)

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

**Mayo Clinic Comprehensive Cancer Center**  
Phoenix/Scottsdale, Arizona  
Jacksonville, Florida  
Rochester, Minnesota  
480.301.8000 • Arizona  
904.953.0853 • Florida  
507.538.3270 • Minnesota  
[mayoclinic.org/cancercenter](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 Sidney Kimmel Comprehensive  
Cancer Center at Johns Hopkins**  
Baltimore, Maryland  
410.955.8964  
[www.hopkinskimmelcancercenter.org](http://www.hopkinskimmelcancercenter.org)

**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 • [cancer.ucla.edu](http://cancer.ucla.edu)

### 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)

# Index

- accelerated partial breast irradiation (APBI)** 41–42
- axillary lymph node (ALN)** 18
- axillary lymph node dissection (ALND)** 40–41
- biopsy** 17–19
- birth control** 12, 36
- bone scan** 14, 45–46
- bone-strengthening therapy** 45–46
- BRCA** 23
- breast-conserving surgery (BCS)** 36, 38
- breastfeeding** 38
- breast reconstruction** 75–76
- cancer stages** 27–30
- chemotherapy** 42
- chestfeeding** 38
- clinical stage (c)** 27
- clinical trials** 47–49
- clips or markers** 18
- computed tomography (CT)** 15
- contrast** 15
- DEXA scan** 45–46
- diagnostic mammogram** 14–15
- distress** 24, 51
- endocrine therapy** 44–46
- estrogen receptor (ER)** 20
- family history** 10, 23
- fertility** 12
- flat closure** 75
- genetic testing** 23
- germline mutations** 23
- hereditary breast cancer** 23
- histology** 56
- hormone receptor (HR)** 20
- hormone therapy (see endocrine therapy)**
- human epidermal growth factor receptor 2 (HER2)** 21, 43
- immunotherapy** 43
- inhibitors** 43
- isolated tumor cells (ITCs)** 30
- lumpectomy** 36, 38
- lymphedema** 52
- lymph node** 30, 41
- magnetic resonance imaging (MRI)** 14–15
- mammogram** 14–15
- mastectomy** 39–40
- menopause** 45
- menstruation** 12, 45
- micrometastases** 29–30
- mutations** 21–23
- myeloid growth factors** 42
- ovaries** 12, 44

**partial breast irradiation (PBI)** 41–42

**pathologic stage (p)** 27

**positron emission tomography (PET)** 16

**pregnancy** 12, 36

**premenopause** 45

**progesterone receptor (PR)** 20

**radiation therapy (RT)** 41–42

**recurrence** 79–80

**regional nodal irradiation (RNI)** 41–42

**sentinel lymph node biopsy (SLNB)** 19, 40–41

**side effects** 49–53

**supportive care** 49–50

**surgery** 36–41

**targeted therapy** 43

**testicles** 12, 44

**testosterone** 45

**those assigned male at birth** 6–7, 12, 45

**TNM scores** 27–30

**triple-negative breast cancer (TNBC)** 60, 69

**tumor tests** 21–22

**ultrasound** 16

**volume displacement** 74

**whole breast radiation therapy (WBRT)** 41–42





# Invasive Breast Cancer 2023

To support the NCCN Guidelines for Patients, visit

[NCCNFoundation.org/Donate](https://www.nccn.org/Donate)



National Comprehensive  
Cancer Network®

3025 Chemical Road, Suite 100  
Plymouth Meeting, PA 19462  
215.690.0300

[NCCN.org/patients](https://www.nccn.org/patients) – For Patients | [NCCN.org](https://www.nccn.org) – For Clinicians