



NCCN
GUIDELINES
FOR PATIENTS®

2022

Breast Cancer Metastatic

Presented with support from:



Available online at [NCCN.org/patients](https://www.nccn.org/patients)



**It's easy to
get lost in the
cancer world**



**Let
NCCN Guidelines
for Patients[®]
be your guide**

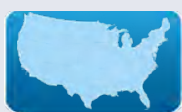
- ✓ Step-by-step guides to the cancer care options likely to have the best results
- ✓ Based on treatment guidelines used by health care providers worldwide
- ✓ Designed to help you discuss cancer treatment with your doctors

Metastatic Breast Cancer



National Comprehensive
Cancer Network®

NCCN Guidelines for Patients® are developed by the National Comprehensive Cancer Network® (NCCN®)



NCCN

- ✓ An alliance of leading cancer centers across the United States devoted to patient care, research, and education

**Cancer centers
that are part of NCCN:**
[NCCN.org/cancercenters](https://www.nccn.org/cancercenters)



NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

- ✓ Developed by experts from NCCN cancer centers using the latest research and years of experience
- ✓ For providers of cancer care all over the world
- ✓ Expert recommendations for cancer screening, diagnosis, and treatment

Free online at
[NCCN.org/guidelines](https://www.nccn.org/guidelines)



NCCN Guidelines for Patients

- ✓ Present information from the NCCN Guidelines in an easy-to-learn format
- ✓ For people with cancer and those who support them
- ✓ Explain the cancer care options likely to have the best results

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

These NCCN Guidelines for Patients are based on the NCCN Guidelines® for Breast Cancer, Version 2.2022 – December 20, 2021.

© 2022 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) / NCCN Foundation
3025 Chemical Road, Suite 100
Plymouth Meeting, PA 19462
215.690.0300

Metastatic Breast Cancer



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

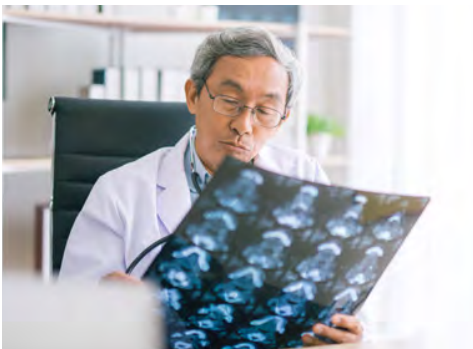
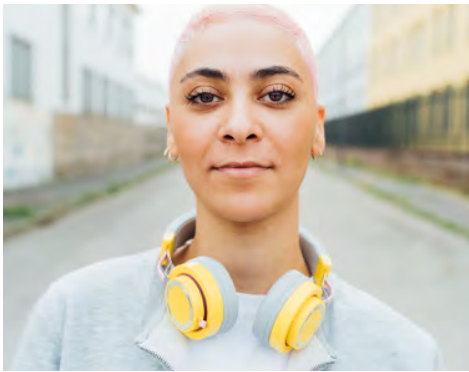
To make a gift or learn more, please visit NCCNFoundation.org/donate
or e-mail PatientGuidelines@NCCN.org.

Brem Foundation

The Brem Foundation teaches women about the need for personalized screening, opens access to breast care for women in need, and advocates for public policies that increase women's opportunities to screen for breast cancer. The Brem Foundation prides itself on reaching women from all socio-economic backgrounds and has made social determinants of health a large focus in all of its work. bremfoundation.org

With additional support from Dr. Wui-Jin Koh

In honor of Judy Anne Hanada Koh



Contents

6	Breast cancer basics
10	Testing for metastatic breast cancer
27	Breast cancer staging
33	Treatment overview
50	Hormone receptor-positive with HER2-
57	Hormone receptor-positive with HER2+
63	Hormone receptor-negative with HER2+
67	Triple-negative breast cancer
71	Making treatment decisions
84	Words to know
88	NCCN Contributors
89	NCCN Cancer Centers
90	Index

1

Breast cancer basics

- 7 The breast
- 8 Breast cancer
- 8 How breast cancer spreads
- 9 Key points



Anyone can develop breast cancer. Metastatic breast cancer is breast cancer that has spread to other parts of the body. Metastatic breast cancer is also called stage 4 or advanced breast cancer.

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.

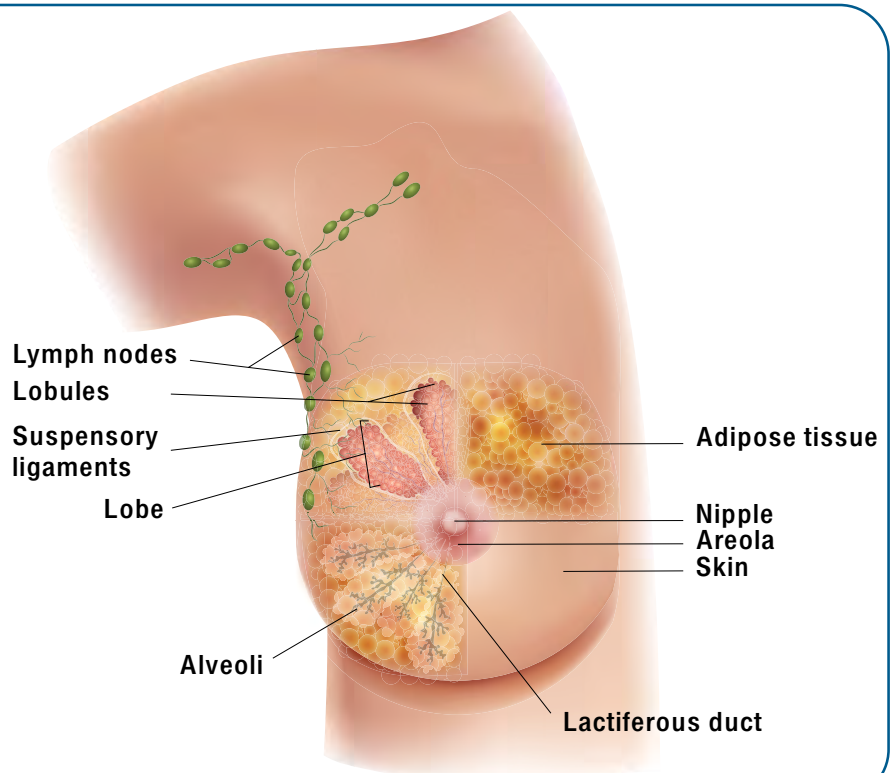
Breast tissue contains glands that can make milk. These milk glands are called lobules. Lobules look like tiny clusters of grapes. Small tubes called ducts connect the lobules to the nipple.

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 granular 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 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.

Anyone can have breast cancer, including males. Although there are some differences between males and females, treatment is very similar for all genders.

How breast cancer spreads

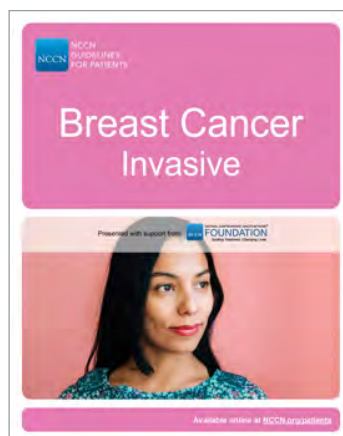
Cancer cells don't behave like normal cells. Cancer cells differ from normal cells in the following ways.

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 breast tissue or nearby lymph nodes.



For more information on invasive breast cancer, read the *NCCN Guidelines for Patients: Breast Cancer – Invasive*, available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines).

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 spread 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.

Key points

- Anyone can develop breast cancer.
- 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.
- Breast cancer that is limited and found only in the ducts or lobules is called noninvasive. Ductal carcinoma in situ (DCIS) is found only in the ducts.
- Invasive breast cancer is cancer that has grown outside the ducts or lobules into surrounding tissue. Once outside the ducts or lobules, breast cancer can spread through lymph or blood to lymph nodes or other parts of the body.
- Metastatic breast cancer has spread to distant sites in the body.



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)

2

Testing for metastatic breast cancer

11 Test results

12 General health tests

14 Fertility

14 Preventing pregnancy

15 Blood tests

15 Imaging tests

18 Biopsy

20 Hormone receptor status

22 HER2 status

22 Biomarker testing

24 Genetic testing

25 Distress screening

25 Performance status

26 Key points



Not all metastatic breast cancers are the same. Treatment planning starts with testing. This chapter presents an overview of the tests you might receive and what to expect.

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:

- Bring someone with you to doctor visits, if possible.
- Write down questions and take notes during appointments. Don't be afraid to ask your care team questions. Get to know your care team and help them get to know you.
- Get copies of blood tests, imaging results, and reports about the specific type of cancer you have.
- Organize your papers. Create files for insurance forms, medical records, and test types. Place items in order by date. 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



Create a medical binder

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

- Make copies of blood tests, imaging results, and reports about your specific type of cancer. It will be helpful when getting a second opinion.
- Choose a binder that meets your needs. Consider a zipper pocket to include a pen, small calendar, and insurance cards.
- Create folders for insurance forms, test types (blood, imaging, pathology, radiology, genetics), treatments, and procedures. Organize items in the folder by date.
- Add a section for questions and to take notes.
- Use online patient portals to view your test results and other records. Download or print the records to add to your binder.
- Bring your medical binder to appointments. You never know when you might need it!

encouraged to keep your PCP. They are great partners in care.

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 medicines, herbals, or supplements you take. Some supplements interact and affect prescriptions that your doctor may give you. Tell your doctor 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 is 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.

Bring a list of any medications, vitamins, over-the-counter drugs, herbals, or supplements you are taking.

Physical exam

During a physical exam, your health care provider may:

- Check your temperature, blood pressure, pulse, and breathing rate
- Check your weight and height
- 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. Tell your doctor if you feel pain.
- Examine your breasts to look for lumps, nipple discharge or bleeding, or skin changes. Tell your doctor if you have noticed changes in your breast(s).
- Feel for enlarged lymph nodes in your neck and underarm. Tell your doctor if you have felt any lumps or have any pain.

For possible tests, [see Guide 1](#).

Guide 1

Possible tests: Metastatic (M1) disease

Medical history and physical exam

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

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

Diagnostic 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, if needed

FDG 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

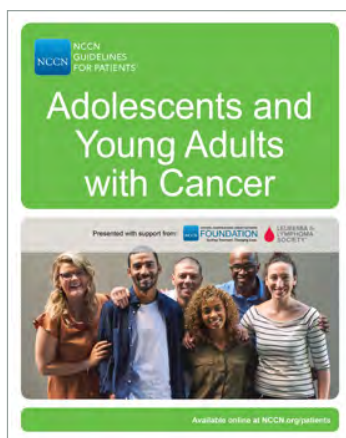
Genetic counseling if at risk for hereditary breast cancer

Assess for distress

Fertility

Treatment can affect your fertility, the ability to have children. If you think you want children in the future, ask your doctor how cancer and cancer treatment might change your fertility. In order 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 can be found in the *NCCN Guidelines for Patients: Adolescents and Young Adults with Cancer*, available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines).

Impaired fertility

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

Preventing pregnancy

Preventing pregnancy during treatment is important. Cancer and cancer treatment can affect the ovaries and damage sperm. Hormonal birth control 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 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 40 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 after cancer treatment. If you think you want children in the future, talk to your doctor now. Sperm banking is an option.

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.

Pregnancy test

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

Complete blood count

A complete blood count (CBC) measures the levels of red blood cells, white blood cells, and platelets in your blood. Your doctor will want to know if you have enough red blood cells to carry oxygen throughout your body, white blood cells to fight infection, and platelets to control bleeding.

Comprehensive metabolic panel

A comprehensive metabolic panel (CMP) is a test that measures 14 different substances in your blood. A CMP provides important information about how well your kidneys and liver are working, and measure your electrolytes among other things. Creatinine is often part of a CMP. This test measures the health of your kidneys.

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.

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.

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. Your doctor will discuss the results with you.

The following imaging tests are listed in alphabetical order and not in order of importance.

Bilateral diagnostic mammogram

A mammogram is a picture of the inside of your breast. The picture is made using x-rays. A computer combines the x-rays to make detailed pictures. Diagnostic mammograms look at specific areas of your breasts, which may not be clearly seen on screening mammograms. A radiologist will evaluate the diagnostic mammogram while you wait so if additional testing is needed, it can be done right away. Mammogram results are used to plan treatment. Other tests may include a breast MRI or ultrasound.

Bone scan

Breast cancer can spread to bones. A bone scan is an imaging test that can show if cancer has spread to your bones. This test may be used if you have bone pain, are at high risk for bone metastases, or if there are changes in certain test results. Bone scans might be used to monitor treatment. Your entire skeleton will be checked.

A bone scan uses a radiotracer to make pictures of the inside areas of your bone that are abnormal. 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.

A special camera will take pictures of the tracer in your bones as it moves over your body. Areas of bone damage use 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 problems. These tests can help identify areas that might need further testing.

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 problems. Your doctor may order x-rays if your bones hurt or were abnormal on a bone scan.

Imaging and other tests are not always accurate. A multidisciplinary team should review the results.

CT scan

A computed tomography (CT or CAT) scan uses x-rays and computer technology to take pictures of the inside of the body. It takes many x-rays of the same body part from different angles. All the images are combined to make one detailed picture.

A CT scan of your chest, abdomen, and/or pelvis may be one of the tests to look for cancer. In most cases, contrast will be used.

Contrast

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 but are different for CT than MRI.

Tell your doctors if you have had allergic reactions to contrast in the past - especially to iodine or shellfish like shrimp. This is important. You might be given medicines, such as Benadryl and prednisone, 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.

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. Tell your doctor if you have any metal in your body.

Breast MRI

If needed, a breast MRI would 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.

PET/CT 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. 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

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. Scans are not sensitive enough to pick up microscopic deposits, but can detect larger metastases.

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 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 for showing small areas of cancer that are near the skin. Sometimes, a breast ultrasound or MRI is used to guide a biopsy.

Biopsy

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

There are different types of biopsies. Some biopsies are guided using imaging, such as an 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. If metastatic disease is identified on imaging, other sites like the lungs, liver, or bones may be biopsied.

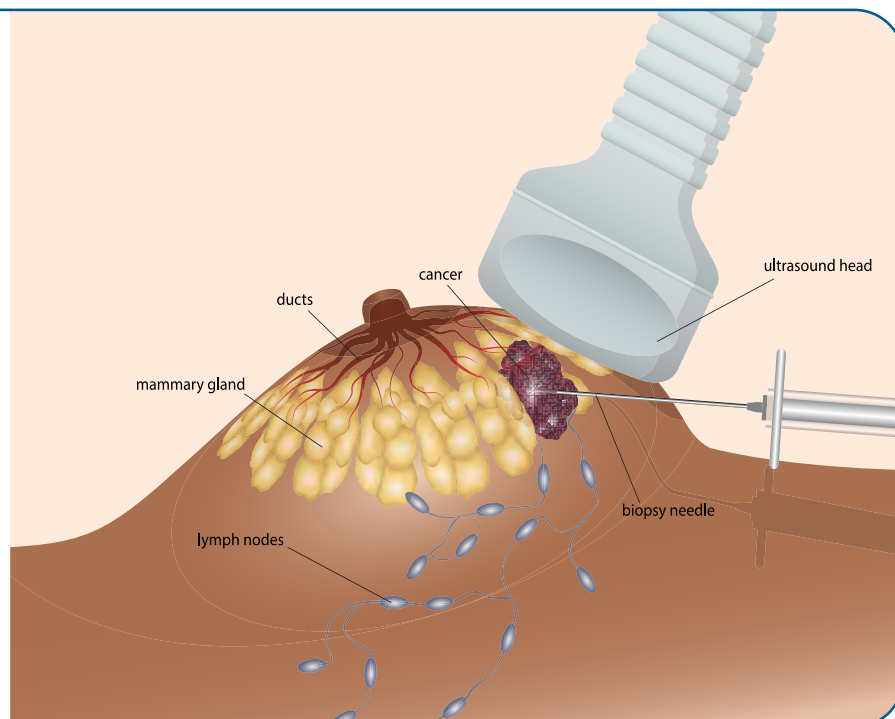
Types of possible biopsies include:

- **Fine-needle aspiration (FNA) or core biopsy (CB)** uses needles of different sizes to remove a sample of tissue or fluid.
- **Incisional biopsy** removes a small amount of tissue through a cut in the skin or body.
- **Liquid biopsy** uses a sample of blood for testing.

A core needle biopsy removes more than one tissue sample. The samples are small. A “vacuum” may be used to remove a larger sample. The needle is often guided into the tumor with imaging. When mammography is used during the biopsy, it is called a stereotactic needle biopsy.

Biopsy

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



2 Testing for metastatic breast cancer 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 and may be in your body for a period of time.

Biopsy of metastasis

A metastasis is the spread of cancer to an area of the body such as the bones, lungs, or liver. A biopsy of the metastasis may be needed to confirm the presence of cancer. If there is more than one metastasis, more than one site may be biopsied. The type of biopsy used depends on the location of the suspected metastases and other factors.

Liquid biopsy

Some abnormal changes (mutations) can be found by testing circulating tumor DNA (ctDNA) in the blood. In a liquid biopsy, a sample of

blood is taken to look for cancer cells or for pieces of DNA from tumor cells. Sometimes, testing can quickly use up a tumor sample and a liquid biopsy might be an option in this case.

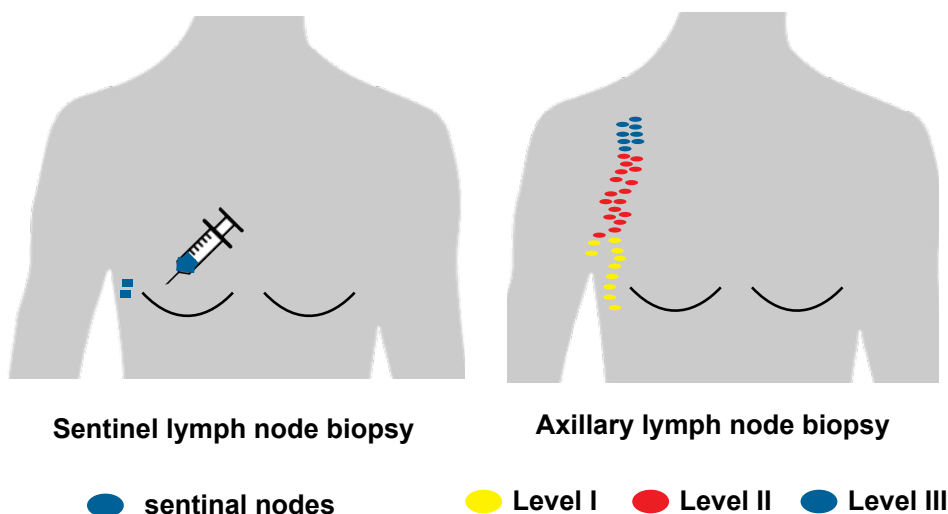
Sentinel lymph node biopsy

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. A sentinel lymph node biopsy (SLNB) 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. It is also called a sentinel node biopsy (SNB).

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.



To find the sentinel lymph nodes, a radioactive material and other dyes are injected into the body near the breast where they travel 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, one is removed and tested by a pathologist. If cancer is found, more than one lymph node may be removed.

Axillary lymph node biopsy

An axillary lymph node (ALN) drains lymph 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+).

Targeted axillary node biopsy

A new phrase that surgeons use is targeted axillary node biopsy. This typically includes all nodes in a sentinel lymph node biopsy (SLNB) and any nodes that were positive or considered suspicious, but stops short of a full axillary lymph node dissection (ALND) described next.

Axillary lymph node dissection

An axillary lymph node dissection (ALND) is surgery to remove axillary lymph nodes. This is performed after an ALN 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.

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.

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.

There are 2 types of hormone receptors:

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

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

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 in at least 1 out of every 100 cancer cells. These cancers are sometimes simply called hormone positive. 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 suggests that the tumor is estrogen dependent.

Hormone receptor-positive 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. Hormone receptor-negative cancers often grow faster than hormone receptor-positive cancers.

There are 2 types of HR- cells:

- **Estrogen receptor-negative (ER-)**
cancer cells do not have an estrogen receptor. These cancer cells do not need estrogen to grow and continue to grow despite treatment to block estrogen.
- **Progesterone receptor-negative (PR-)**
cancer cells do not need progesterone to grow.

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.

You might have more than one HER2 test. HER2 tests are done using a tumor biopsy sample.

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, tumor 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. Not all of the tests listed below are done for all patients. Your treatment team will recommend the best types of biomarker testing that are important for you.

Tumor markers

Your blood or biopsy may be tested for proteins. These proteins are called tumor markers.

Tumor mutation burden

When there are 10 or more mutations per million base pairs of tumor DNA, it is called tumor mutational burden-high (TMB-H). TMB-H can be used to help predict response to cancer treatment using immune checkpoint inhibitors that target the proteins called programmed death protein 1 (PD-1) and programmed death-ligand 1 (PD-L1).

Tumor mutation testing

A sample of your tumor or blood may be used to see if the cancer cells have any specific mutations. In tumor mutation testing, only the tumor is tested and not the rest of your body.

MSI-H/dMMR

Microsatellites are short, repeated strings of DNA. When errors or defects occur, they are fixed by mismatch repair (MMR) proteins. Some cancers 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 microsatellite instability-high (MSI-H). This is often due to dMMR genes. This is uncommon in breast cancer.

***NTRK* gene fusions**

In a tumor with an *NTRK* gene fusion, a piece of the *NTRK* gene and a piece of another gene fuse, or join. This activates the *NTRK* gene in a way that causes uncontrolled cell growth. Larotrectinib (Vitrakvi) and entrectinib (Rozlytrek) might be used to target advanced or metastatic cancer that is *NTRK* gene fusion-positive. *NTRK* gene fusions are rare.

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

PD-1 and PD-L1 testing

Programmed death protein 1 (PD-1) and programmed death-ligand 1 (PD-L1) are proteins that regulate the immune system. 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. When PD-1 is bound to called PD-L1, it prevents your immune system from attacking cancer cells. 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.

Genetic 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 a 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). 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, family members might carry these mutations. Tell your doctor if there is a family history of cancer.

BRCA tests

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

What is your family health history?

Some cancers and other diseases run in families – those who are related to you through genes passed down from parent to child. This information is called a family health history. You can ask family members about their health issues like heart disease, cancer, and diabetes, and at what age they were diagnosed. For relatives who have died, ask about the cause and age of death.

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

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

Some of the questions to ask include:

- Do you have any chronic diseases, such as heart disease or diabetes, or health conditions such as high blood pressure or high cholesterol?
- Have you had any other diseases, such as cancer or stroke?
- 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 day to day and week to week. Talk to your doctor and with 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 sleeping problems.



For more information, read the *NCCN Guidelines for Patients: Distress Management – Distress During Cancer Care*, available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines).

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) or the Karnofsky Performance Status (KPS).

ECOG PS

The ECOG PS scores range from 0 to 4.

- PS 0 means you are fully active.
- PS 1 means you are still able to perform light to moderate activity.
- PS 2 means you can still care for yourself but are not active.
- PS 3 means you are limited to the chair or bed more than half of the time.
- PS 4 means you need someone to care for you and are limited to a chair or bed.

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

Karnofsky PS

The KPS score ranges from 0 to 100.

- 10 to 40 means you cannot care for yourself without the help of others.
- 50 to 70 means you cannot work and need some help to take care of yourself.
- 80 to 100 means you are completely independent and can carry out daily tasks.

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 and grade (histology).
- Some breast cancers grow because of hormones such as estrogen and progesterone. Testing will be done to see if you have hormone receptor-positive (HR+) breast cancer.
- Some breast cancers have too many hormone receptors, HER2s, or both.
- A sample from a biopsy of your tumor will be tested to look for biomarkers or proteins, such as HER2.
- 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 or to speak with a genetic counselor.
- A sentinel lymph node (SLN) is the first lymph node 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.
- Online portals are a great way to access your test results.

3

Breast cancer staging

- 28 Overview
- 31 Stages
- 32 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. In metastatic breast cancer, the tumor can be any size, cancer may be found in the lymph nodes, and has spread to other parts of the body.

Overview

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 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 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.

- **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. 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: T2N0M1 or T2, N0, M1.

- **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

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 lower risk of recurrence. A high-grade tumor has a higher risk for recurrence (of cancer returning).

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

Numbered stages

Numbered stages are based on TNM scores. Stages range from stage 1 to stage 4, with 4 being the most advanced. Doctors write these stages as stage I, stage II, stage III, and stage IV. For example, ductal carcinoma in situ (DCIS) is stage 0 or Tis, N0, M0.

Stage 0 is noninvasive

Noninvasive breast cancer is rated stage 0. 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.

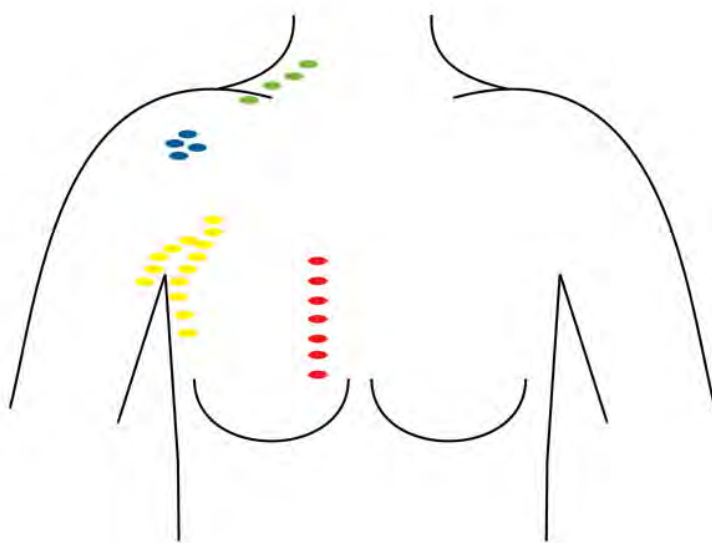
Stage 4 is metastatic

In stage 4 breast cancer, cancer has spread to distant sites (M1), but can also be found in the axillary lymph nodes. The tumor can be any size (any T). Your first diagnosis can be stage 4 metastatic breast cancer (called de novo) or it can develop from earlier stages.

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



Stages

Stage 4 breast cancer is metastatic breast cancer or MBC. In stage 4 breast cancer, cancer has spread to distant sites (M1), but can also be found in the axillary lymph nodes. The tumor can be any size (any T). Your first diagnosis can be stage 4 metastatic breast cancer (called de novo) or it can develop from earlier stages.

Anatomic staging of breast cancer is complex. 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. Keep copies of your pathology reports. The pathology report might include a lot of abbreviations such as pN0(mol+), ypT2, or cN3. Your doctor can help explain what they mean.

T = Tumor

The primary tumor size can be measured in centimeters (cm) or millimeters (mm). A large pea is 1 cm (10 mm). A golf ball is 4 cm (40 mm). A micrometastasis is a very small cancerous cell that is smaller than 2 mm. It might be written as T1mi.

- **T1** Tumor is 2 cm or less
- **T1mi** Tumor is microinvasive of 2 mm or less
- **T2** Tumor is 2.1 cm to 5 cm
- **T3** Tumor is more than 5 cm
- **T4** Tumor is of any size and has invaded nearby structures such as the chest wall and skin of the breast

N = Regional lymph node

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 breast bone. 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.
- **N1, N2, N3** means regional lymph node metastases are found. The higher the number, the more lymph nodes that have metastases.
- **N1mi** means micrometastases are found in lymph nodes.

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 distant metastasis.
- **M1** means distant metastasis is found. This is metastatic breast cancer.

Key points

- Staging helps to predict prognosis and to guide treatment decisions.
- Doctors classify breast cancer in the body using the tumor, node, metastasis (TNM) system.
- 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.
- The pathologic stage (p) is based on the results of 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.
- Doctors may explain your cancer stage in different ways to make it less confusing.



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)

4

Treatment overview

34 Treatment team

36 Overview

36 Surgery

37 Radiation therapy

38 HER2-targeted therapy

39 Chemotherapy

40 Endocrine therapy

42 Bone-strengthening therapy

43 Inhibitors

43 Immunotherapy

44 Clinical trials

46 Supportive care

48 Survivorship

49 Key points



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

Treatment team

Treating breast cancer takes a team approach. Treatment decisions should involve a multidisciplinary team (MDT). An MDT is a team of doctors, health care workers, and social care professionals from different professional backgrounds who have knowledge (expertise) and experience with 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, your team might include the following:

- **A pathologist** analyzes the cells, tissues, and organs removed during a biopsy or surgery and provides cancer diagnosis, staging, and information about biomarker testing.
- **A diagnostic radiologist** interprets the results of x-rays and other imaging tests.
- **An interventional radiologist** performs needle biopsies, endoscopies and ablation procedures, and places ports for treatment.
- **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.
- **A radiation oncologist** prescribes and plans 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 and physician assistants** are health care providers who work alongside doctors and other members of the medical team. 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. Sometimes, these experts are called nurse navigators.
- **Oncology pharmacists** provide medicines used to treat cancer and to manage symptoms and side effects.
- **Palliative care nurses, advanced practice providers, and physicians** help provide an extra layer of support with your cancer-related symptoms.

- **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 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 workers, can help navigate the complexities of financial and insurance stresses.
- **Research team** helps to collect research data and coordinate care if you are in a clinical trial.

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

Your physical, mental, and emotional well-being are important. You know yourself better than anyone. 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 who to contact with questions or concerns.

Overview

Metastatic breast cancer is treatable. Treatment can be local, systemic, or a combination of both. It is important to have regular talks with your doctor about your goals for treatment and your treatment plan.

There are 2 types of treatment:

- **Local therapy** focuses on a certain area. It includes surgery, ablation, and radiation therapy.
- **Systemic therapy** works throughout the body. It includes endocrine therapy, chemotherapy, targeted therapy, and immunotherapy.

There are many treatment options. However, not everyone will respond to treatment in the same way. Some people will do better than expected. Others will do worse. Many factors play a role in how you will respond to treatment.

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, use 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 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 the options before starting chemotherapy and/or endocrine therapy.

You should not become pregnant during treatment with radiation therapy or systemic therapy.

Surgery

Surgery is an operation or procedure to remove cancer from the body. Surgery is not the main or primary treatment for metastatic breast cancer. Surgery might be considered as a supportive care option. This means that if the primary tumor is causing pain, discomfort, or a health issue, then surgery might be an option. Radiation therapy might be an alternative to surgery.

For the treatment of metastases, surgery might be an option to remove a metastasis.

When preparing for surgery, seek the opinion of an experienced surgeon. The surgeon should be an expert in performing your type of surgery. Hospitals that perform many surgeries often have better results. You can ask for a referral to a hospital or cancer center that has experience in treating your type of cancer.

Radiation therapy

Radiation therapy (RT) uses high-energy radiation from x-rays, photons, protons, electrons, and other sources to kill cancer cells and shrink tumors. It is given over a certain period of time. Sometimes, radiation is given with certain systemic therapies. It may be used as supportive care to help ease pain or discomfort caused by cancer. RT is not the main treatment for metastatic disease.

Types of radiation therapy:

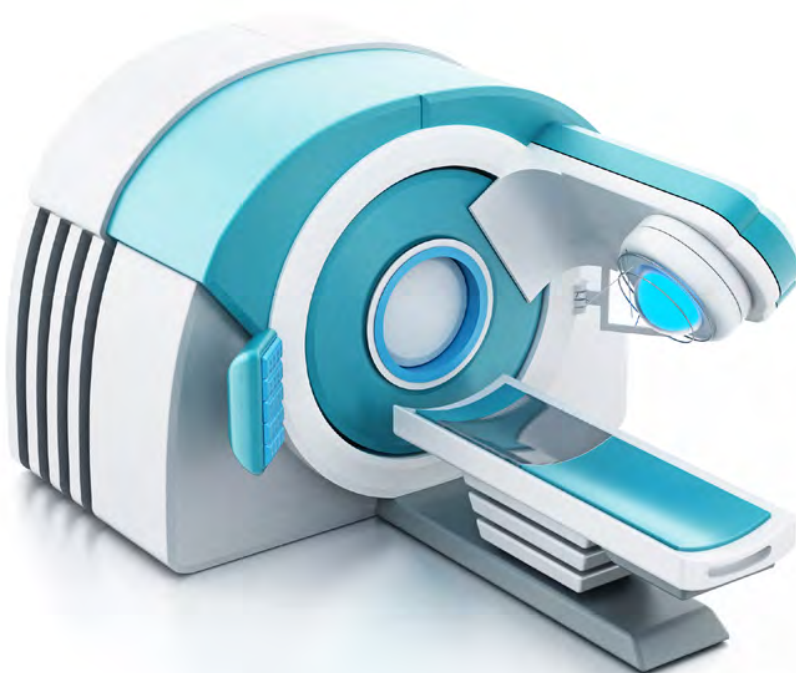
- **Whole breast radiation therapy (WBRT)** is used to treat the whole breast. Sometimes, additional treatments may be given to the tumor area. This is called a “boost.”

- **Accelerated partial breast irradiation (APBI)** is used to treat the area where the tumor was removed.
- **Lymph node radiation therapy** is used to treat the lymph nodes. It is also called regional nodal radiation.

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

Radiation therapy

Radiation therapy uses high-energy radiation from x-rays, gamma rays, protons, and other sources to kill cancer cells and shrink tumors. It is also used to treat pain caused by cancer.



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 breast cancer (HER2+). HER2-targeted therapy or anti-HER2 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. These drugs include trastuzumab (Herceptin) or trastuzumab substitutes (biosimilars) such as Kanjinti, Ogivri, Herzuma, Ontruzant, and Trazimera. Margetuximab-cmkb (Margenza) and pertuzumab (Perjeta) are also included in this class. Phesgo might be used as a substitute for combination therapy of trastuzumab with pertuzumab.
- **HER2 inhibitors** stop growth signals from HER2 from within the cell. Lapatinib (Tykerb), neratinib (Nerlynx), and tucatinib (Tukysa) are examples of these drugs.
- **HER2 conjugates or antibody drug conjugates (ADCs)** deliver cell-specific chemotherapy. They attach to HER2s then enter the cell. Once inside, chemotherapy is released. Ado-trastuzumab emtansine (Kadcyla), fam-trastuzumab deruxtecan-nxki (Enhertu), and sacituzumab (Trodelvy) are included in this class.

Treatment options by cell receptor type

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

Hormone receptors include estrogen and progesterone. A tumor is considered hormone receptor-positive (HR+) if an increased number of estrogen receptors or progesterone receptors, or both, are found.

HER2 is a protein involved in normal cell growth. There might be higher amounts of HER2 in your breast cancer. If this is the case, it is called HER2-positive breast cancer (HER2+).

- **Endocrine therapy** stops cancer growth caused by hormones. It is a standard treatment for hormone receptor-positive (HR+) cancers. HR+ cancer can be estrogen receptor-positive (ER+) and/or progesterone receptor-positive (PR+).
- **HER2-targeted therapy** is a standard treatment for HER2+ cancers.
- **Chemotherapy** is often the first treatment for hormone receptor-negative (HR-) cancers.

Chemotherapy

Chemotherapy kills fast-growing cells throughout the body, including cancer cells and some normal cells. More than one chemotherapy may be used to treat 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.

There are different types of chemotherapy used to treat metastatic breast cancer:

- **Alkylating agents** damage DNA by adding a chemical to it. This group of drugs includes cyclophosphamide. Platinum-based alkylating agents contain a heavy metal that prevents cancer cells from dividing. These drugs include carboplatin and cisplatin (Platinol).
- **Anthracyclines** damage and disrupt the making of DNA causing cell death of both cancerous and non-cancerous cells. These drugs include doxorubicin (Adriamycin, Rubex), doxorubicin liposomal injection (Doxil), and epirubicin (Ellence).
- **Anti-metabolites** prevent the “building blocks” of DNA from being used. These drugs include capecitabine (Xeloda), fluorouracil (FU or 5FU), gemcitabine (Gemzar, Infugem), and methotrexate.
- **Microtubule inhibitors** stop a cell from dividing into two cells. These drugs include docetaxel (Taxotere), eribulin (Halaven), ixabepilone (Ixempra Kit), paclitaxel

(Taxol), and vinorelbine (Navelbine). Docetaxel, paclitaxel, and albumin-bound paclitaxel (called nab-paclitaxel or Abraxane) are also called taxanes.

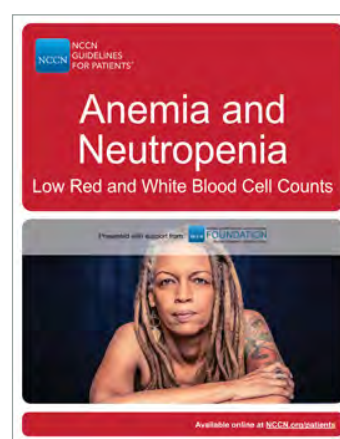
More than one drug may be used to treat metastatic breast cancer. When only one drug is used, it's called a single agent. A combination regimen is the use of two or more chemotherapy drugs.

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 varies.

Myeloid growth factors

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

For more information on myeloid growth factors, see *NCCN Guidelines for Patients: Anemia and Neutropenia*, available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines).



Endocrine therapy

Endocrine therapy blocks estrogen and 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.
- **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 can 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.

More than one endocrine therapy might be used. Other treatments might be added to endocrine therapy.

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** permanently stops the ovaries from making hormones. Ablation uses extreme hot or cold to stop the ovaries from working.
- **Ovarian suppression** temporarily stops 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.
- **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) is a SERD.
- **Hormones** may be used to treat breast cancer when taken in high doses. It is not known how hormones stop breast cancer from growing. They include ethinyl estradiol, fluoxymesterone, and megestrol acetate.

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

Menopausal status

Options for endocrine therapy are partly based on if you started or were in menopause before beginning treatment. In menopause, the ovaries permanently stop producing hormones and menstrual periods stop. After menopause, estrogen and progesterone levels continue to stay low.

Premenopause

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

Perimenopause is the transitional period before menopause. During perimenopause, levels of estrogen start to decrease.

Tamoxifen is the endocrine treatment for those in premenopause and perimenopause.

Menopause

Cancer treatment can cause a temporary menopause. When menstrual periods stop for 12 months or more, it is called menopause. If you don't have periods, a test using a blood sample may be needed to confirm your status. Menstrual periods may stop during treatment and for up to 2 years after treatment, but often returns in those 40 years of age and under. In menopause, your adrenal glands, liver, and body fat make small amounts of estrogen.

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

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.

Bone-strengthening therapy

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 or weakness called osteoporosis, fractures, bone pain, and squeezing (compression) of the spinal cord. Some treatments for breast cancer, like endocrine therapy, can cause bone loss, which put you at an increased risk for fractures.

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.

Drugs used to prevent bone loss and fractures:

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

Drugs used to treat bone metastases:

- Zoledronic acid (Zometa)
- Pamidronate (Aredia)
- Denosumab (Xgeva)

Zoledronic acid, pamidronate, and denosumab

Zoledronic acid, pamidronate, and denosumab are used to prevent bone loss (osteoporosis) and fractures caused by endocrine therapy. Zoledronic acid and denosumab are also used in those with metastatic breast cancer who have bone metastases to help prevent fractures or spinal cord compression. 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 doctor 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 doctor about any planned trips to the dentist and any procedures or surgeries that might affect the jaw bone. It will be important to take care of your teeth and to see a dentist before starting treatment with any of these drugs.

Inhibitors

CDK4/6 inhibitors

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

EGFR inhibitors

An EGRF inhibitor blocks the activity of a protein called epidermal growth factor receptor (EGFR).

mTOR inhibitors

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

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

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.

PIK3CA inhibitor

The *PIK3CA* gene is one of the most frequently mutated genes in breast cancers. A mutation in this gene can lead to increased growth of cancer cells and resistance to various treatments. Alpelisib (Piqray) is an example of a *PIK3CA* inhibitor. It is given in combination with the anti-estrogen drug fulvestrant to help delay tumor growth for a longer period of time compared to fulvestrant alone.

Immunotherapy

Immunotherapy is a type of systemic treatment that increases 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) and dostarlimab-gxly (Jemperli) target MSI-H or dMMR tumors, or those that express PD-1 or PD-L1. Pembrolizumab also targets tumor mutational burden-high (TMB-H).

Clinical trials

A clinical trial is a type of medical research study. After being developed and tested in a laboratory, potential new ways of fighting 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.

Who can enroll?

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

Informed consent

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

Start the conversation

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

Frequently asked questions

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

Will I get a placebo?

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

Are clinical trials free?

There is no fee to enroll in a clinical trial. The study sponsor pays for research-related costs, including the study drug. You may, however, have costs indirectly related to the trial, such as the cost of transportation or child care due to extra appointments. During the trial, you will continue to receive standard cancer care. This care is billed to—and often covered by—insurance. You are responsible for copays and any costs for this care that are not covered by your insurance.



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://cancer.gov/about-cancer/treatment/clinical-trials/search)

Worldwide

**The U.S. National Library of Medicine
(NLM)**
clinicaltrials.gov/

Need help finding a clinical trial?
NCI's Cancer Information Service (CIS)
1.800.4.CANCER (1.800.422.6237)
cancer.gov/contact

Supportive care

Supportive care is health care given during all cancer stages. It aims to prevent, reduce, and relieve suffering, and to improve quality of life. Supportive care might include pain relief (palliative care), emotional or spiritual support, financial aid, or family counseling. Tell your care team how you are feeling and about any side effects so they can be managed. 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.

Anemia, neutropenia, and thrombocytopenia

Some cancer treatments can cause low blood cell counts.

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

For more information on anemia, neutropenia and thrombocytopenia, see *NCCN Guidelines for Patients: Anemia and Neutropenia*, available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines).

Distress

Depression, anxiety, and sleeping problems are common in cancer. Talk to your doctor 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.

For more information, see *NCCN Guidelines for Patients: Distress During Cancer Care*, available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines).

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, 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

Scalp cooling (or scalp hypothermia) might help lessen hair loss in those receiving certain types of chemotherapy. Some people find scalp cooling uncomfortable and have headaches as a side effect from the cold. You may experience hair loss even with scalp cooling treatment.

Lymphedema

Lymphedema is a condition in which extra lymph fluid builds up in tissues and causes swelling. It may be caused when part of the lymph system is damaged or blocked, such as during surgery to remove lymph nodes, or radiation therapy. Cancers that block lymph vessels can also cause lymphedema. Swelling usually develops slowly over time. It may develop during treatment or it may start years after treatment. If you have lymphedema, you may be referred to an expert in lymphedema management. The swelling may be reduced by exercise, massage, compression sleeves, and other means. Ask your care team about the ways to treat lymphedema.

Nausea and vomiting

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

For more information, see *NCCN Guidelines for Patients: Nausea and Vomiting*, available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines).

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. They may prescribe medicine to help with the pain, or encourage applying heat or ice, or suggest exercise.

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
- Describe 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?
- Rate 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?

Treatment side effects

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

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

Trouble eating

Sometimes side effects from surgery, cancer, or other treatments 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 your weight.

Survivorship

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

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

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.

For more information on survivorship, see [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines).



Key points

- Treatment takes a team approach. Get to know your care team and let them get to know you.
- Metastatic breast cancer is treatable. The goal of treatment is to prevent or slow the spread of cancer.
- Treatment for metastatic breast cancer is a combination of therapies, but often given in a specific order (sequential).
- Local therapy focuses on a certain area. It includes surgery, ablation, and radiation therapy.
- Systemic therapy works throughout the body. It includes endocrine therapy, chemotherapy, targeted therapy, and immunotherapy.
- Radiation therapy (RT) uses high-energy radiation from x-rays, photons, protons, electrons, and other sources to kill cancer cells and shrink tumors.
- Chemotherapy kills fast-growing cells throughout the body, including cancer cells and some normal cells.
- Targeted therapies can block the ways cancer cells grow, divide, and move in the body.
- HER2 is a protein involved in normal cell growth. HER2-targeted therapy is drug therapy that treats HER2-positive (HER2+) breast cancer.
- Endocrine therapy blocks estrogen or progesterone to treat hormone receptor-positive (HR+) breast cancer.
- Those who want to have children in the future should be referred to a fertility specialist before starting chemotherapy and/or endocrine therapy to discuss the options.
- Bone-strengthening therapy is used to prevent bone loss and fractures and to treat bone metastases.
- 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 cancer or its 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

Hormone receptor-positive with HER2-

51	Treatment
54	Monitoring
54	Disease progression
56	Key points



In hormone receptor-positive (HR+) cancer, hormone receptors for estrogen (ER+) and/or progesterone (PR+) are found. When HER2 receptors are not found, it is HER2-negative (HER2-). Treatment for ER+ and/or PR+ with HER2- is endocrine therapy that might be used with another systemic therapy. Together, you and your doctor will choose a treatment plan that is best for you.

Treatment

Treatment for ER+ and/or PR+ with HER2- is endocrine therapy alone or with another systemic therapy.

Treatment is based on if:

- You are in visceral crisis (organs aren't working as well as they should)
- You had endocrine therapy and if yes, then how long ago and what type

For treatment options, [see Guide 2](#).

Most people will be able to have many lines of systemic therapy. You will continue therapy until disease progression or there is an unacceptable toxicity. An unacceptable toxicity is one that puts your overall health at risk.

Guide 2

Treatment options: ER+ and/or PR+ with HER2-

Visceral crisis	Consider initial systemic therapy (See Guide 3)
No visceral crisis and had endocrine therapy within the past 12 months	If premenopause, then ovarian ablation or suppression with systemic therapy (See Guide 4)
	If menopause, then systemic therapy (See Guide 4)
No visceral crisis and no endocrine therapy within the past 12 months	If premenopause, then one from below: <ul style="list-style-type: none"> • Ovarian ablation or suppression with systemic therapy (See Guide 4) • Select ER modulators (See Guide 4)
	If menopause, then systemic therapy (See Guide 4)

Visceral crisis

Cancer can stop organs from working as they should. This is called a visceral crisis. If you are in visceral crisis, the goal is to get you stable. This is done using systemic therapy in [Guide 3](#).

Guide 3 Systemic therapy options: Visceral crisis

Preferred options

- Anthracyclines such as doxorubicin or liposomal doxorubicin
- Taxanes such as paclitaxel
- Anti-metabolites such as capecitabine or gemcitabine
- Microtubule inhibitors such as vinorelbine or eribulin
- For germline *BRCA1* or *BRCA2* mutations: olaparib or talazoparib
- For *PIK3CA* activating mutation: alpelisib with fulvestrant

Other recommended

- Cyclophosphamide
- Docetaxel
- Albumin-bound paclitaxel
- Epirubicin
- Ixabepilone

Used in some cases

- Doxorubicin and cyclophosphamide (AC)
- Epirubicin and cyclophosphamide (EC)
- Cyclophosphamide, methotrexate, and fluorouracil (CMF)
- Docetaxel and capecitabine
- Gemcitabine and paclitaxel (GT)
- Gemcitabine and carboplatin
- Carboplatin with paclitaxel or albumin-bound paclitaxel
- For *NTRK* fusion: larotrectinib or entrectinib
- For MSI-H/dMMR: pembrolizumab or dostarlimab-gxly
- For TMB-H: pembrolizumab

No visceral crisis

First-line therapy is the first treatment tried. If cancer progresses while on first-line endocrine therapy, then you will likely switch to a different endocrine therapy for second-line therapy. Endocrine therapy may be combined with another systemic therapy. If you are not in visceral crisis, then systemic therapy options can be found in [Guide 4](#).

If you are in premenopause, then systemic therapy will be given with ovarian ablation or suppression.

Guide 4**Systemic therapy options: No visceral crisis**

Preferred first-line therapy options	<ul style="list-style-type: none"> • Aromatase inhibitor with CDK4/6 inhibitor (abemaciclib, palbociclib, or ribociclib) • ER down-regulator (fulvestrant) with non-steroidal aromatase inhibitor (anastrozole, letrozole) • Fulvestrant with CDK4/6 inhibitor (abemaciclib, palbociclib, or ribociclib) • For <i>BRCA1</i> or <i>BRCA2</i> mutations: olaparib or talazoparib
Preferred second-line and next-line options	<ul style="list-style-type: none"> • Fulvestrant with CDK4/6 inhibitor (abemaciclib, palbociclib, or ribociclib) if CDK4/6 inhibitor not used before • For <i>PIK3CA</i> tumor mutation, alpelisib and fulvestrant • Everolimus with endocrine therapy (exemestane, fulvestrant, tamoxifen)
Other recommended	<ul style="list-style-type: none"> • Selective ER down-regulator (fulvestrant) • Non-steroidal aromatase inhibitor (anastrozole, letrozole) • Selective estrogen receptors modulator (tamoxifen) • Steroidal aromatase inactivator (exemestane)
Used in some cases	<ul style="list-style-type: none"> • Megestrol acetate • Ethinyl estradiol • Abemaciclib • For <i>NTRK</i> fusion: larotrectinib or entrectinib • For MSI-H/dMMR: pembrolizumab or dostarlimab-gxly • For TMB-H: pembrolizumab

Monitoring

You will be monitored throughout treatment. Monitoring includes physical exams, blood tests, imaging scans, and tumor testing (if needed). Monitoring is used to see if your cancer is responding to treatment, is stable, or is progressing.

Monitoring is important. You will be monitored for symptoms caused by cancer such as pain from bone metastases. The goal of monitoring is to determine if treatment provides benefit. Benefit includes keeping your cancer stable.

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.

Disease progression

Disease progression is defined by the growth or spread of cancer as shown on imaging tests or physical exam of the tumor.

Treatment is based on if cancer progressed while:

- On endocrine therapy or
- In visceral crisis

For treatment options, [see Guide 5](#).

Guide 5

Progression: ER+ and/or PR+ with HER2-

Progression or unacceptable toxicity on first-line endocrine therapy

If not endocrine-resistant, consider a different line of endocrine therapy alone or with targeted therapy (See Guide 4)



If no benefit after 3 lines of endocrine therapy or visceral disease with symptoms, then systemic therapy (See Guide 3)



Consider no more systemic therapy and continue supportive care

For visceral crisis: progression or unacceptable toxicity on first-line systemic therapy

Try a different line of systemic therapy (See Guide 3)



Continue systemic therapy until progression



Consider no more systemic therapy and continue supportive care

Progression or toxicity on endocrine therapy

If cancer progressed while you were on endocrine therapy, then you will likely switch to a different endocrine therapy. Targeted therapy might be added. Sometimes, your body becomes resistant to endocrine therapy. If this happens, endocrine therapy will be stopped and a systemic therapy will be used.

After 3 rounds of endocrine therapy

If cancer progresses after 3 rounds of endocrine therapy or you are having severe cancer symptoms in internal organs, then it might be time to consider switching to systemic therapy alone. As cancer progresses, you will switch to different systemic therapies. This may continue until there is no longer a benefit or there is an unacceptable toxicity. At this point, the focus will be supportive care.

Before another round of systemic therapy is given, you and your doctor will discuss:

- Your wishes to continue treatment
- The risks and benefits of treatment
- Your performance status
- Your preferences on types of treatment

Visceral crisis and progression or toxicity

Chemotherapy may be started when the cancer within internal organs causes severe symptoms. This is called a visceral crisis. Most people will be able to have many lines (rounds) of systemic therapy. You will be monitored throughout treatment.

Before starting another line of therapy, you and your doctor will discuss:

- Your wishes to continue treatment
- The risks and benefits of treatment
- Your performance status
- Your preferences on types of treatment

Systemic therapy has side effects that might affect your quality of life. Even if you decide to stop systemic therapy, supportive care will continue.

Did you know?

The terms “chemotherapy” and “systemic therapy” are often used interchangeably, but they are not the same.

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

Key points

- In hormone receptor-positive (HR+) cancer, hormone receptors for estrogen (ER+) and/or progesterone (PR+) are found. When HER2 receptors are not found, it is HER2-negative (HER2-). It is written as ER+ and/or PR+ with HER2-.
- HR+ with HER2- metastatic breast cancer is initially treated with endocrine therapy alone or with another systemic therapy. Later therapy may include chemotherapy or other agents.
- If you are in premenopause, then systemic therapy will be given with ovarian ablation or suppression.
- In a visceral crisis, cancer in the internal organs causes severe symptoms.
- You will continue therapy until disease progression or there is an unacceptable toxicity. An unacceptable toxicity is one that puts your overall health at risk.
- Supportive care is always given.
- Your preferences about treatment are always important.

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

6

Hormone receptor-positive with HER2+

58	Treatment
60	Monitoring
60	Disease progression
62	Key points



In hormone receptor-positive cancer, estrogen (ER+) and/or progesterone receptors (PR+) are found. When HER2 receptors are found, it is also HER2+. This cancer is sometimes called triple-positive breast cancer. Together, you and your doctor will choose a treatment plan that is best for you.

Treatment

Treatment for ER+ and/or PR+ with HER2+ is usually a combination of endocrine and systemic therapies that target hormone receptors and HER2.

Guide 6

Systemic therapy with HER2-targeted therapy options

First-line options

- Pertuzumab, trastuzumab, and docetaxel (preferred)
- Pertuzumab, trastuzumab, and paclitaxel (preferred)
- Fam-trastuzumab deruxtecan-nxki (in some cases)

Second-line and beyond

- Fam-trastuzumab deruxtecan-nxki (preferred)
- Ado-trastuzumab emtansine (T-DM1)
- Tucatinib, trastuzumab, and capecitabine
- Trastuzumab and docetaxel or vinorelbine
- Trastuzumab and paclitaxel with or without carboplatin
- Trastuzumab and capecitabine
- Capecitabine with trastuzumab or lapatinib
- Trastuzumab and lapatinib (without cytotoxic therapy)
- Trastuzumab with other agents
- Neratinib and capecitabine
- Margetuximab-cmkb with chemotherapy (capecitabine, eribulin, gemcitabine, or vinorelbine)
- Ado-trastuzumab emtansine (T-DM1)

Other options

- For *BRCA1* or *BRCA2* mutations, olaparib or talazoparib
- For *NTRK* fusion, larotrectinib or entrectinib
- For MSI-H/dMMR, pembrolizumab
- For TMB-H: pembrolizumab

Note: An FDA-approved biosimilar might be used for trastuzumab.

Treatment options are as follows:

- Usually treatment consists of anti-HER2 therapy plus chemotherapy followed by anti-estrogen therapy, [see Guide 6](#).
- Endocrine therapy
- Endocrine therapy with HER2-targeted therapy, [see Guide 7](#).

If you are in premenopause, then ovarian ablation or suppression are recommended with endocrine and HER2-targeted therapy.

You will continue therapy until disease progression or there is an unacceptable toxicity. An unacceptable toxicity is one that puts your overall health at risk.

It is important to keep follow-up visits and imaging test appointments. Seek good routine medical care, including preventative care and cancer screenings.

Guide 7 Endocrine therapy with HER2-targeted therapy options

Aromatase inhibitor alone or with

- Trastuzumab
- Lapatinib
- Lapatinib and trastuzumab

Fulvestrant alone or with trastuzumab

Tamoxifen alone or with trastuzumab

Monitoring

Monitoring includes physical exams, blood tests, imaging scans, and tumor testing (if needed). Monitoring is used to see if your cancer is responding to treatment, is stable, or is progressing.

Monitoring is important. You will be monitored for symptoms caused by cancer such as pain from bone metastases. The goal of monitoring is to determine if treatment provides benefit. Benefit includes stopping cancer from spreading.

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.

Disease progression

Disease progression is defined by the growth or spread of cancer as shown on imaging tests or physical exam of the tumor.

Treatment is based on if cancer progressed while you were taking:

- First-line endocrine therapy or
- First-line systemic therapy with HER2-targeted therapy

Most people will be able to have many lines of systemic therapy. You will be monitored throughout treatment. For treatment options, [see Guide 8](#).

Guide 8

Progression: ER+ and/or PR+ with HER2+

Progression on first-line endocrine therapy	If not endocrine-resistant, consider a different line of endocrine therapy alone (See Guide 7) or with HER2-targeted therapy (See Guide 6)	➔	If no benefit after 3 lines of endocrine therapy alone or with HER2-targeted therapy or visceral disease with symptoms, then systemic therapy with HER2-targeted therapy (See Guide 6)	➔	Consider no more HER2-targeted therapy and continue supportive care
Progression on first-line systemic therapy with HER2-targeted therapy	Try a different line of systemic therapy with HER2-targeted therapy (See Guide 6)	➔	Continue systemic therapy until progression	➔	Consider no more HER2-targeted therapy and continue supportive care

Cancer progresses on first-line endocrine therapy

First-line therapy is the first treatment tried. If cancer progresses while on first-line endocrine therapy, then you will likely switch to a different endocrine therapy for second-line.

Endocrine therapy might be given with HER2-targeted therapy. At some point, this cancer becomes resistant to endocrine therapy and only systemic therapy with HER2-targeted therapy will be used. [See Guide 6.](#)

After 3 rounds of endocrine therapy

If cancer progresses after 3 rounds of endocrine therapy or you are having severe cancer symptoms in internal organs (visceral crisis), then it might be time to consider stopping endocrine therapy and focus on systemic therapy and supportive care.

Cancer progresses on systemic therapy with HER2-targeted therapy

If cancer progresses while you are on systemic and HER2-targeted therapy, then another line of therapy is an option. In this case, a different systemic and HER2-targeted therapy will be tried. Sometimes, only HER2-targeted therapy will be given.

Continue HER2-targeted therapy until disease progression. [See Guide 6.](#)

When cancer progresses, consider ending HER2-targeted therapy and continuing supportive care.

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

After multiple lines of systemic therapy

After multiple lines of systemic therapy, it might be time to consider ending HER2-targeted therapy and focus on supportive care. The possible side effects of continuing with more lines of HER2-targeted therapy may outweigh the benefits.

Before a new line of systemic therapy is tried, you and your doctor will discuss:

- Your wishes to continue treatment
- The risks and benefits of treatment
- Your performance status
- Your preferences on types of treatment

Systemic therapy has side effects that may impact your quality of life. If you and your doctor decide to stop HER2-targeted therapy, supportive care will still continue.

Key points

- In hormone receptor-positive (HR+) cancer, estrogen (ER+) and/or progesterone receptors (PR+) are found. When HER2 receptors are found, it is also HER2-positive (HER2+).
- ER+ and/or PR+ with HER2+ breast cancer is sometimes called triple-positive breast cancer.
- Treatment is usually a combination of endocrine and systemic therapies that target hormone receptors and HER2.
- You will continue systemic therapy until disease progression or there is an unacceptable toxicity. An unacceptable toxicity is one that puts your overall health at risk.
- Supportive care is always given.
- Your preferences about treatment are always important.

Since your type of breast cancer may change over time, a repeat biopsy may be needed to guide treatment.

7

Hormone receptor-negative with HER2+

-
- | | |
|----|-----------|
| 64 | Treatment |
|----|-----------|
-
- | | |
|----|------------|
| 65 | Monitoring |
|----|------------|
-
- | | |
|----|---------------------|
| 65 | Disease progression |
|----|---------------------|
-
- | | |
|----|------------|
| 66 | Key points |
|----|------------|



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+). This cancer is sometimes written as ER- and/or PR- with HER2+. Together, you and your doctor will choose a treatment plan that is best for you.

Treatment

Treatment for cancer that is HR- with HER2+ is systemic therapy with HER2-targeted therapy. Endocrine therapy is not used in ER-.

- For systemic therapy with HER2-targeted therapy options, [see Guide 9](#).

Guide 9

Systemic therapy with HER2-targeted therapy options

First-line options	<ul style="list-style-type: none"> • Pertuzumab, trastuzumab, and docetaxel (preferred) • Pertuzumab, trastuzumab, and paclitaxel (preferred) • Fam-trastuzumab deruxtecan-nxki (in some cases)
Second-line and beyond	<ul style="list-style-type: none"> • Fam-trastuzumab deruxtecan-nxki (preferred) • Ado-trastuzumab emtansine (T-DM1) • Tucatinib, trastuzumab, and capecitabine • Trastuzumab and docetaxel or vinorelbine • Trastuzumab and paclitaxel with or without carboplatin • Trastuzumab and capecitabine • Capecitabine with trastuzumab or lapatinib • Trastuzumab and lapatinib (without cytotoxic therapy) • Trastuzumab with other agents • Neratinib and capecitabine • Margetuximab-cmkb with chemotherapy (capecitabine, eribulin, gemcitabine, or vinorelbine) • Ado-trastuzumab emtansine (T-DM1)
Other options	<ul style="list-style-type: none"> • For <i>BRCA1</i> or <i>BRCA2</i> mutations, olaparib or talazoparib • For <i>NTRK</i> fusion, larotrectinib or entrectinib • For MSI-H/dMMR, pembrolizumab • For TMB-H: pembrolizumab

Note: An FDA-approved biosimilar might be used for trastuzumab.

You will continue therapy until disease progression or there is an unacceptable toxicity. An unacceptable toxicity is one that puts your overall health at risk.

Monitoring

Most people will be able to have many lines of systemic therapy. You will be monitored throughout treatment. Monitoring includes physical exams, blood tests, imaging scans, and tumor testing (if needed). Monitoring is used to see if your cancer is responding to treatment, is stable, or is progressing.

Monitoring is important. You will be monitored for symptoms caused by cancer such as pain from bone metastases. The goal of monitoring is to determine if treatment provides benefit. Benefit includes keeping your cancer stable.

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.

Disease progression

Disease progression is defined by the growth or spread of cancer as shown on imaging tests or physical exam of the tumor.

When this cancer progresses, treatment is another line of systemic therapy with HER2-targeted therapy. You will have a different therapy than before. There are many options. Most people will be able to have many lines of systemic therapy. Systemic therapy is used to prevent the growth and spread, and to relieve pain and discomfort in metastatic breast cancer.

Before a new line of systemic therapy is given, you and your doctor will discuss:

- Your wishes to continue treatment
- The risks and benefits of treatment
- Your performance status
- Your preferences on types of treatment

Systemic therapy has side effects. When performance status is poor, the side effects of HER2-targeted therapy might affect your quality of life. Even if you stop HER2-targeted therapy, supportive care will continue.

After multiple lines of systemic therapy

After multiple lines of systemic therapy, it might be time to consider ending HER2-targeted therapy and focus on supportive care. The possible side effects of continuing with more lines of HER2-targeted therapy may outweigh the benefits. Your wishes are always important.

Key points

- In hormone receptor-negative (HR-) with HER2-positive (HER2+) breast cancer, there are no receptors for estrogen (ER-) and progesterone (PR-), but HER2 tests are positive (HER2+).
- Endocrine therapy is not used when cancer is estrogen receptor-negative (ER-).
- Since this cancer is HER2+, systemic therapy that targets HER2 is used. This is called HER2-targeted therapy.
- Most people will be able to have many lines of systemic therapy. Before each new line of therapy, you and your doctor will discuss goals of treatment, risks and benefits of treatment, your overall health, and your goals for treatment.
- Your preferences about treatment are always important.
- Supportive care is always given.

Need help paying
for medicine or
treatment?

Ask your care team
what options are
available.

8

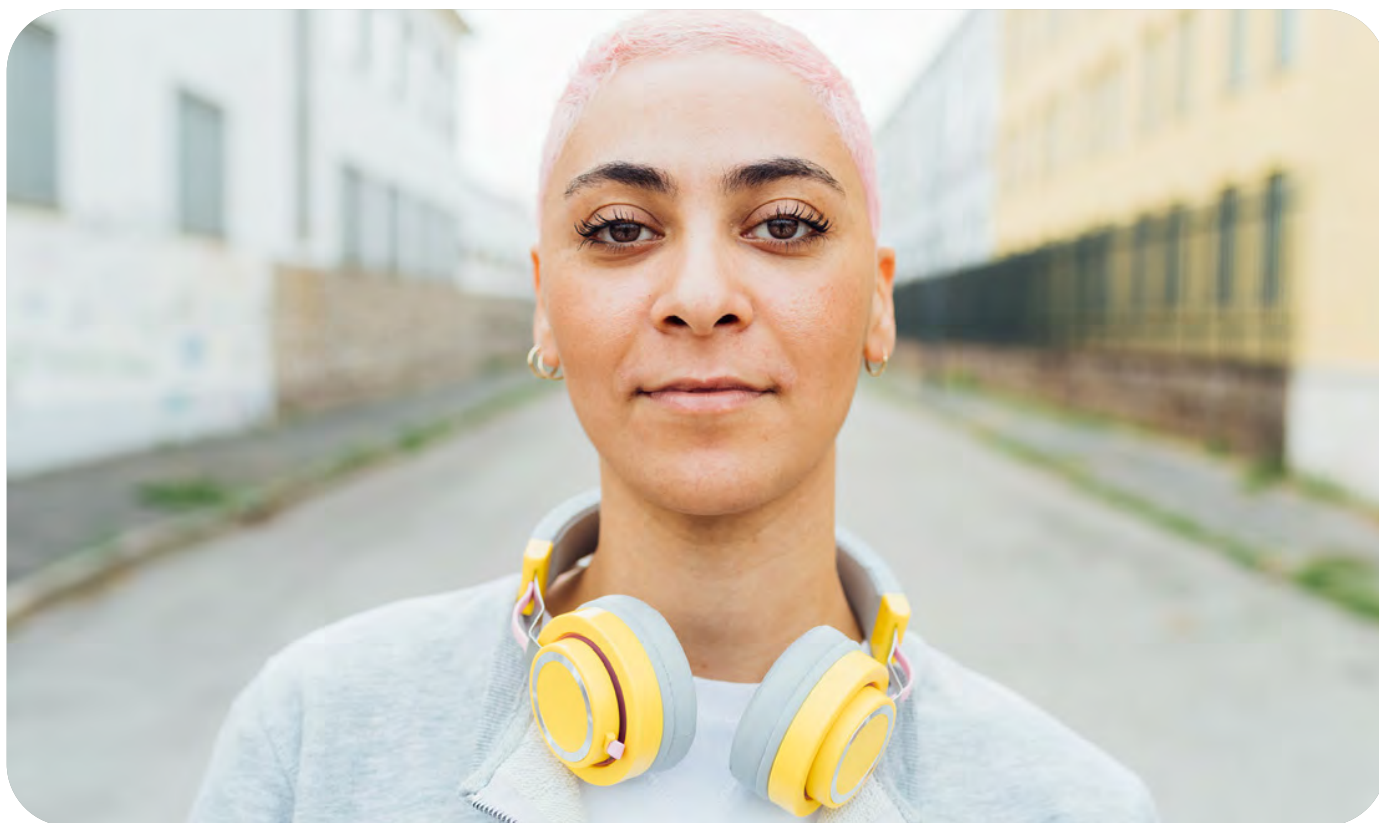
Triple-negative breast cancer

68 Treatment

68 Monitoring

70 Disease progression

70 Key points



In triple-negative breast cancer (TNBC), cancer cells have tested negative for HER2, estrogen hormone receptors, and progesterone hormone receptors. TNBC is sometimes written as ER- and PR- with HER2-. Together, you and your doctor will choose a treatment plan that is best for you.

Triple-negative breast cancer (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.

Treatment

Since there are no HER2 receptors, HER2-targeted therapy is not an option. And since there are no estrogen or progesterone hormone receptors, endocrine therapy is not an option. Without any of these receptors it is more challenging to treat. Treatment is usually chemotherapy or immunotherapy. Multiple lines of systemic therapy will be given until disease progression or there is an unacceptable toxicity. An unacceptable toxicity is one that puts your overall health at risk.

Systemic therapy options are found in [Guide 10](#).

Monitoring

Monitoring includes physical exams, blood tests, imaging scans, and tumor testing (if needed). Monitoring is used to see if your cancer is responding to treatment, is stable, or is progressing.

Monitoring is important. You will be monitored for symptoms caused by cancer, such as pain from bone metastases. The goal of monitoring is to determine if treatment provides benefit. Benefit includes keeping cancer stable.

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.

Guide 10

Systemic therapy options: ER- and PR- with HER2-

Preferred options

- Anthracyclines such as doxorubicin or liposomal doxorubicin
- Taxanes such as paclitaxel
- Anti-metabolites such as capecitabine or gemcitabine
- Microtubule inhibitors such as vinorelbine or eribulin
- Sacituzumab govitecan-hziy
- For germline *BRCA1* or *BRCA2* mutations: olaparib, talazoparib, carboplatin, or cisplatin
- For PD-L1–positive: pembrolizumab with chemotherapy (albumin-bound paclitaxel, paclitaxel, or gemcitabine with carboplatin)

Other recommended

- Cyclophosphamide
- Docetaxel
- Albumin-bound paclitaxel
- Epirubicin
- Ixabepilone

Useful in some cases

- Doxorubicin and cyclophosphamide (AC)
- Epirubicin and cyclophosphamide (EC)
- Cyclophosphamide, methotrexate, and fluorouracil (CMF)
- Docetaxel and capecitabine
- Gemcitabine and paclitaxel (GT)
- Gemcitabine and carboplatin
- Carboplatin with paclitaxel or albumin-bound paclitaxel
- For *NTRK* fusion: larotrectinib or entrectinib
- For MSI-H/dMMR: pembrolizumab or dostarlimab-gxly
- For TMB-H: pembrolizumab

Disease progression

Disease progression is defined by the growth or spread of cancer as shown on imaging tests or physical exam of the tumor.

Before a new line of systemic therapy is given, you and your doctor will discuss:

- Your wishes to continue treatment
- The risks and benefits of treatment
- Your performance status
- Your preferences on types of treatment

After multiple lines of systemic therapy, it might be time to consider ending systemic therapy and focus on supportive care. The possible side effects of continuing with more lines of systemic therapy may outweigh the benefits. Your preferences and goals of treatment are always important.

Key points

- In triple-negative breast cancer (TNBC), receptors for estrogen, progesterone, and HER2 are not found.
- TNBC is usually treated with chemotherapy.
- Multiple lines of systemic therapy will be given until disease progression or there is an unacceptable toxicity. An unacceptable toxicity is one that puts your overall health at risk.
- Before each new line of therapy, you and your doctor will discuss goals of treatment, risks and benefits of treatment, your overall health, and your goals for treatment.
- Your preferences about treatment are always important.
- Supportive care is always given.

9

Making treatment decisions

72 It's your choice

72 Questions to ask your doctors

81 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 doctor.

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 doctor.

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 like surgery or chemotherapy
- Your feelings about pain or side effects such as nausea and vomiting
- 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 doctor. If you take the time to build a relationship with your doctor, 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, including imaging scans and pathology slides, 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 your doctors

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

Questions to ask about testing and diagnosis

1. What tests will I have? How often will they be repeated? Will my insurance pay for these tests?
2. What will you do to make me comfortable during testing?
3. What if I am pregnant or want to become pregnant?
4. When will I have a biopsy? Will I have more than one? What are the risks?
5. How will my biopsy be performed? What else might be done at this time?
6. How soon will I know the results and who will explain them to me?
7. How can I get a copy of the pathology report and other test results?
8. Who will talk with me about the next steps? When?
9. What can I do before my next appointment?

Questions to ask your care team about their experience

1. What is your experience treating metastatic breast cancer?
2. What is the experience of those on your team?
3. Do you only treat metastatic breast cancer? What else do you treat?
4. How many patients like me (of the same age, gender, race) have you treated?
5. Will you be consulting with experts to discuss my care? Whom will you consult?
6. How many procedures like the one you're suggesting have you done?
7. Is this treatment a major part of your practice?
8. How often is a complication expected? What are the complications?
9. How many breast cancer surgeries have you done? What type of surgeries have you done? How many per year?
10. Who will manage my day-to-day care?

Questions to ask about options

1. What will happen if I do nothing?
2. How do my age, overall health, and other factors affect my options?
3. What if I am pregnant? What if I'm planning to get pregnant in the near future?
4. Which option is proven to work best for my cancer, age, and other risk factors?
5. What are the possible complications and side effects?
6. How do you know if the treatment worked? How will I know?
7. What can be done to prevent or relieve the side effects of treatment?
8. Are there any life-threatening side effects of this treatment? How will I be monitored?
9. Am I a candidate for a clinical trial? Can I join a clinical trial at any time?
10. Does any option offer a long-term cancer control? Are the chances any better for one option than another? Less time-consuming? Less expensive?
11. Is there a social worker or someone who can help me decide?
12. Is there a hospital or treatment center you can recommend for breast cancer treatment?
Can I go to one hospital for surgery and a different center for radiation therapy?

Questions to ask about treatment

1. What are my treatment choices? What are the benefits and risks? Which treatment do you recommend and why?
2. How will my age, performance status, cancer stage, and other health conditions limit my treatment choices?
3. Does the order of treatment matter?
4. How long do I have to decide about treatment?
5. Will I have to go to the hospital or elsewhere for treatment? How often? How long is each visit? Will I have to stay overnight in the hospital or make travel plans?
6. Do I have a choice of when to begin treatment? Can I choose the days and times of treatment? Should I bring someone with me?
7. How much will the treatment hurt? What will you do to make me comfortable?
8. Can I stop treatment at any time? What will happen if I stop treatment?
9. How much will this treatment cost me? How much will my insurance pay for this treatment? Are there any programs to help me pay for treatment?
10. Will I miss work or school? Will I be able to drive? When will I be able to return to my normal activities?
11. What are the chances my cancer will return after this treatment? How will it be treated if it returns?
12. I would like a second opinion. Is there someone you can recommend? Who can help me gather all of my records for a second opinion?

Questions to ask about surgery

1. What will be removed during surgery? What will this mean in terms of my recovery?
2. What kind of surgery will I have? Will I have more than one surgery?
3. Does my cancer involve any veins or arteries? How might this affect surgery?
4. How long will it take me to recover from surgery? When will I be able to return to work?
5. How much pain will I be in? What will be done to manage my pain?
6. What is the chance that this surgery will shorten my life?
7. What other side effects can I expect from surgery? What complications can occur from this surgery?
8. What treatment will I have before, during, or after surgery? What does this treatment do?

Questions to ask about radiation therapy

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

Questions to ask about side effects

1. What are the side effects of treatment?
2. What are the side effects of this cancer?
3. How long will these side effects last? Do any side effects lessen or worsen in severity over time?
4. What side effects should I watch for? What side effects are expected and which are life threatening?
5. When should I call the doctor? Can I text? What should I do on weekends and during non-office hours?
6. What emergency department or ER should I go to? Will my treatment team be able to communicate with the ER team?
7. What medicines can I take to prevent or relieve side effects?
8. What can I do to help with pain and other side effects?
9. Will you stop treatment or change treatment if there are side effects? What do you look for?
10. What can I do to lessen or prevent side effects? What will you do?
11. What medicines may worsen side effects of treatment?
12. What are some of the likely permanent side effects that I might have from the treatment?

Questions to ask about clinical trials

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

Resources

American Association for Cancer Research (AACR)

aacr.org

American Breast Cancer Foundation

youandbreastcancer.com/en-bc/home

American Cancer Society (ACS)

cancer.org/cancer/breast-cancer.html

Breast Cancer Alliance (BCA)

breastcanceralliance.org

Breast Cancer Support Project

breastcancerportraitproject.org

Breastcancer.org

breastcancer.org

Brem Foundation

bremfoundation.org

CancerCare

cancercare.org

Cancer Support Community

cancersupportcommunity.org/living-cancer

Chemocare

chemocare.com

DiepCFoundation

diepcfoundation.org

Dr. Susan Love Foundation for Breast Cancer Research

drsusanloveresearch.org/love-research-army

FORCE - Facing Our Risk of Cancer Empowered

facingourrisk.org

GPAC - Global Patient Advocacy Coalition

GPACunited.org

Living Beyond Breast Cancer (LBBC)

lbbs.org

MedlinePlus

medlineplus.gov/breastcancer.html

My Survival Story

mysurvivalstory.org

National Cancer Institute (NCI)

cancer.gov/types/breast

National Center for Health Research

breastimplantinfo.org

National Coalition for Cancer Survivorship

canceradvocacy.org/toolbox

National Financial Resource Directory - Patient Advocate Foundation

patientadvocate.org/explore-our-resources/national-financial-resource-directory/

OncoLinkoncolink.org**Patient Access Network Foundation**panfoundation.org**Radiological Society of North America**radiologyinfo.org**SHARE Cancer Support**sharecancersupport.org**Sharsheret**sharsheret.org**Smart Patients**smartpatients.com/communities/breast-cancer**Susan G. Komen**komen.org**Testing.com**testing.com**The Male Breast Cancer Coalition**malebreastcancercoalition.org/men-have-breasts-too**Unite for HER**uniteforher.org**Young Survival Coalition (YSC)**youngsurvival.org

share with us.

Take our [survey](#)

And help make the
NCCN Guidelines for Patients
better for everyone!

NCCN.org/patients/comments



Words to know

accelerated partial breast irradiation (APBI)

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

anti-estrogen

A cancer 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.

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.

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.

chemotherapy

Cancer drugs that stop the cell life cycle so cells don't increase in number.

chest wall

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

clinical breast exam

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.

complete blood count (CBC)

A lab test that includes the number of blood cells.

computed tomography (CT)

A test that uses x-rays from many angles to make a picture of the insides of the body.

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.

Words to know

core needle biopsy

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 causes female body traits.

estrogen receptor (ER)

A protein inside of 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 to have babies.

fine-needle aspiration (FNA)

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

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 that was likely caused by abnormal genes passed down from 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 edge 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.

in situ hybridization (ISH)

A lab test of the number of a gene.

infraclavicular

The area right below the collarbone.

internal mammary

The area along the breastbone.

lobule

A gland in the breast that makes breast milk.

lobular carcinoma

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

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.

lymph node

A small, bean-shaped disease-fighting structure.

lymphadenopathy

Lymph nodes that are abnormal in size or consistency.

lymphatic system

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

lymphedema

Swelling in the body due to a buildup of fluid called lymph.

magnetic resonance imaging (MRI)

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

mammogram

A picture of the insides of the breast that is made by an x-ray test.

medical history

A report of all your health events and medications.

medical oncologist

A doctor who is an expert in cancer drugs.

menopause

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

mutation

An abnormal change.

nipple-areola complex (NAC)

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

ovarian ablation

Methods used to stop the ovaries from making hormones.

ovarian suppression

A drug treatment that lowers the amount of hormones made by the ovaries.

palpable adenopathy

Lymph nodes that feel abnormal in size or consistency.

partial breast irradiation

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

pathologic stage (p)

A rating of the extent of cancer based on tests given after treatment.

pathologist

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

pelvis

The body area between the hip bones.

physical exam

A study of the body by a health expert for signs of 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

A hormone in women that is involved in sexual development, periods, and pregnancy.

prognosis

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

radiation therapy (RT)

A treatment that uses high-energy rays.

recurrence

The return of cancer after a cancer-free period.

selective estrogen receptor degrader (SERD)

A drug that blocks and destroys estrogen receptors.

selective estrogen receptor modulator (SERM)

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

sentinel lymph node (SLN)

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

sentinel lymph node biopsy (SLNB)

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

side effect

An unhealthy or unpleasant physical or emotional response to treatment.

supportive care

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

supraclavicular

The area right above the collarbone.

systemic therapy

Drug treatment that works throughout the body.

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.

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 2.2022. It was adapted, reviewed, and published with help from the following people:

Dorothy A. Shead, MS
Senior Director
Patient Information Operations

Tanya Fischer, MEd, MSLIS
Medical Writer

Susan Kidney
Senior Graphic Design Specialist

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer Version 2.2022 were developed by the following NCCN Panel Members:

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

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

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

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

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

Kimberly H. Allison, MD
Stanford Cancer Institute

Bethany Anderson, MD
University of Wisconsin
Carbone Cancer Center

Sarah L. Blair, MD
UC San Diego Moores Cancer Center

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

Helen Chew, MD
UC Davis Comprehensive Cancer Center

Chau Dang, MD
Memorial Sloan Kettering Cancer Center

*Anthony D. Elias, MD
University of Colorado Cancer Center

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

Matthew P. Goetz, MD
Mayo Clinic Cancer Center

Lori J. Goldstein, MD
Fox Chase Cancer Center

Sara A. Hurvitz, MD
UCLA Jonsson Comprehensive Cancer
Center

Steven J. Isakoff, MD, PhD
Massachusetts General Hospital
Cancer Center

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

Sara H. Javid, MD
Fred Hutchinson Cancer Research
Center/Seattle Cancer Care Alliance

Jairam Krishnamurthy, MD
Fred & Pamela Buffett Cancer Center

Marilyn Leitch, MD
UT Southwestern Simmons
Comprehensive Cancer Center

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

Ingrid A. Mayer, MD
Vanderbilt-Ingram Cancer Center

Joanne Mortimer, MD
City of Hope National Medical Center

Sameer A. Patel, MD
Fox Chase Cancer Center

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

Laura H. Rosenberger, MD, MS
Duke Cancer Institute

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

Amy Sitapati, MD
UC San Diego Moores Cancer Center

Karen Lisa Smith, MD, MPH
The Sidney Kimmel Comprehensive
Cancer Center at Johns Hopkins

*Mary Lou Smith, JD, MBA
Patient Advocate
Research Advocacy Network

Hatem Soliman, MD
Moffitt Cancer Center

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

Melinda L. Telli, MD
Stanford Cancer Institute

John H. Ward, MD
Huntsman Cancer Institute
at the University of Utah

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

Jessica S. Young, MD
Roswell Park Comprehensive Cancer Center

NCCN Staff

Rashmi Kumar, PhD
Director, Clinical Information Operations

Jennifer Burns, BS
Manager, Guidelines Support

* 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 • pennmedicine.org/cancer

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

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

Dana-Farber/Brigham and Women's
Cancer Center | Massachusetts General
Hospital Cancer Center
Boston, Massachusetts
617.732.5500 • youhaveus.org
617.726.5130
massgeneral.org/cancer-center

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

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

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

Fred Hutchinson Cancer
Research Center/Seattle
Cancer Care Alliance
Seattle, Washington
206.606.7222 • seattlecca.org
206.667.5000 • fredhutch.org

Huntsman Cancer Institute
at the University of Utah
Salt Lake City, Utah
800.824.2073 • huntsmanccancer.org

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

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

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

Moffitt Cancer Center
Tampa, Florida
888.663.3488 • moffitt.org

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

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

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

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

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

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

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

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

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

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

UC San Diego Moores Cancer Center
La Jolla, California
858.822.6100 • cancer.ucsd.edu

UCLA Jonsson
Comprehensive Cancer Center
Los Angeles, California
310.825.5268 • cancer.ucla.edu

UCSF Helen Diller Family
Comprehensive Cancer Center
San Francisco, California
800.689.8273 • cancer.ucsf.edu

University of Colorado Cancer Center
Aurora, Colorado
720.848.0300 • coloradocancercenter.org

University of Michigan
Rogel Cancer Center
Ann Arbor, Michigan
800.865.1125 • rogelcancercenter.org

University of Wisconsin
Carbone Cancer Center
Madison, Wisconsin
608.265.1700 • uwhealth.org/cancer

UT Southwestern Simmons
Comprehensive Cancer Center
Dallas, Texas
214.648.3111 • utsouthwestern.edu/simmons

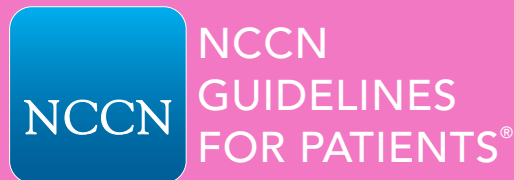
Vanderbilt-Ingram Cancer Center
Nashville, Tennessee
877.936.8422 • vicc.org

Yale Cancer Center/
Smilow Cancer Hospital
New Haven, Connecticut
855.4.SMILOW • yalecancercenter.org

Index

- axillary lymph node (ALN)** 7, 20
- axillary lymph node dissection (ALND)** 20
- bilateral diagnostic mammogram** 15
- biopsy** 18–20
- birth control** 14, 36
- blood tests** 15
- bone scan** 16
- bone-strengthening therapy** 42
- BRCA** 24
- cancer stages** 30–31
- chemotherapy** 39
- clinical stage (c)** 28
- clinical trial** 44–45
- computed tomography (CT)** 16
- contrast** 16–17
- distress** 25, 46
- endocrine therapy** 40–41
- estrogen receptor (ER)** 20–21
- family history** 12, 24
- fertility** 14
- genetic testing** 24
- hair loss** 46
- hormone receptor (HR)** 20–21
- hormone therapy (see endocrine therapy)**
- human epidermal growth factor receptor 2 (HER2)** 22, 38
- imaging tests** 15–17
- immunotherapy** 43
- impaired fertility** 14
- inhibitors** 43
- lymphedema** 47
- magnetic resonance imaging (MRI)** 17
- mammogram** 15
- medical history** 12
- menopause** 41
- mutations** 22–23
- pathologic stage (p)** 28
- positron emission tomography (PET)** 17
- pregnancy** 14
- premenopause** 41
- progesterone receptor (PR)** 20–21
- radiation therapy (RT)** 37
- sentinel lymph node biopsy (SLNB)** 19
- supportive care** 46–48
- surgery** 36
- TNM scores** 29
- triple-negative breast cancer (TNBC)** 68–70
- tumor tests** 22–23
- ultrasound** 17
- visceral crisis** 52





Breast Cancer Metastatic 2022

NCCN Foundation gratefully acknowledges the following corporate supporters for helping to make available these NCCN Guidelines for Patients: AstraZeneca, Exact Sciences, Gilead Oncology, Lilly, Pfizer Inc., Seagen Inc., and West Pharmaceutical Services, Inc. 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 support the NCCN Guidelines for Patients

DONATE NOW

Visit NCCNFoundation.org/Donate



National Comprehensive
Cancer Network®

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

NCCN.org/patients – For Patients | NCCN.org – For Clinicians