NCCN GUIDELINES FOR PATIENTS®

2025

Metastatic Breast Cancer

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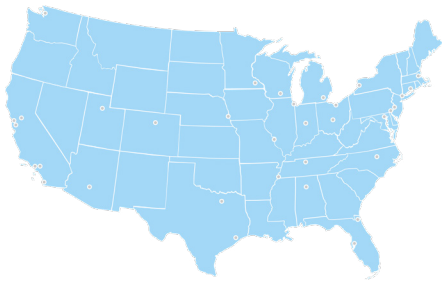
About the NCCN Guidelines for Patients®

National Comprehensive Cancer Network®



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

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

These NCCN Guidelines for Patients are based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer Version 4.2025 – April 17, 2025.

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NCCN.org/patient-guidelines-process

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Contents

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.

National Comprehensive Cancer Network (NCCN) and NCCN Foundation
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1

About metastatic breast cancer

Metastatic breast cancer (MBC) is breast cancer that has spread to other parts of the body. Metastatic breast cancer is also called advanced breast cancer.

What is metastatic breast cancer?

Breast cancer starts in the cells of the breast. Over time, these cells form a mass called a primary tumor. Breast cancer cells can spread through lymph or blood to other parts of the body. It can spread locally to nearby lymph nodes but also to more distant sites of the body (metastasis). Since cancer cells can spread through the blood, it is still possible to develop distant metastases even when the lymph nodes near the breast are negative for cancer.

- **Local metastasis** is cancer that has spread to a nearby body part such as the axillary lymph nodes.
- **Distant metastasis** is cancer that has spread to a body part far from the primary (main) tumor.

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

Why you should read this book

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

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

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

Almost all breast cancers are carcinomas—cancers that start in the cells that line the inner or outer surfaces of the body. There are different types of breast carcinoma, most of which arise in cells that make up the lining (epithelial cells) in the terminal duct lobular units (TDLUs) of the breast. A TDLU consists of a lobule connected to the end of a small milk duct. The most common types of breast cancer are ductal carcinoma and lobular carcinoma.

What's in this book?

This book is organized into the following chapters:

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

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

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

Chapter 5: Supportive care gives an overview of what supportive care is, possible side effects of treatment, and living with metastatic breast cancer.

Chapter 6: Your treatment options discusses systemic (drug) therapy options specific to your cancer. Treatment is based on the cancer's hormone receptor (HR) and HER2 status, and any biomarkers that might be found.

Chapter 7: Other resources provides information on patient advocacy groups and where to get help.

What can you do to get the best care?

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

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

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

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

2
Testing for MBC

Not all breast cancers are the same. Treatment planning starts with testing. It takes time for your care team to gather all the information needed to treat your cancer. This chapter presents an overview of the tests you might receive and what to expect.

Breast cancer treatment is becoming more individualized and it is important to get the right testing. This takes time, but will be very helpful in making sure you get the best treatment for your type of breast cancer. A tumor biopsy and imaging studies are an important part of testing. For possible tests, **see Guide 1.**

General health tests

Medical history

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

Family history

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

Physical exam

During a physical exam, your health care provider may:

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

Clinical breast exam

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

Distress screening

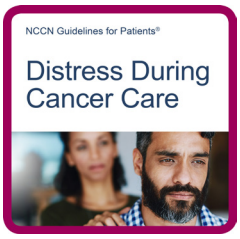
Distress is an unpleasant experience of a mental, physical, social, or spiritual nature. It can affect how you feel, think, and act. Distress might include feelings of sadness, fear, helplessness, worry, anger, and guilt. You may also experience depression, anxiety, and sleep issues.

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

Guide 1
Possible tests

Medical history and physical exam
Complete blood count (CBC), comprehensive metabolic panel (CMP) including liver function tests (LFTs), and alkaline phosphatase (ALP)
Imaging tests • Chest CT. Contrast might be used. • CT or MRI of abdomen with or without pelvis. Contrast will be used. • Other imaging tests as needed such as x-ray, bone scan, or PET/CT
Biopsy with tumor biomarker and testing including: • Estrogen receptor (ER) and progesterone receptor (PR) status • HER2 status • Other biomarker and mutation testing for targeted therapies
Genetic counseling and testing if at risk for hereditary breast cancer
Assess for distress

More information on distress can be found in the *NCCN Guidelines for Patients: Distress During Cancer Care* at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer



Performance status

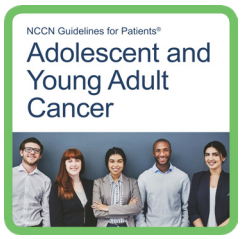
Performance status (PS) is a person's general level of fitness and ability to perform daily tasks. Your state of general health might be rated using a PS scale called the Eastern Cooperative Oncology Group (ECOG) score or the Karnofsky Performance Status (KPS). PS is one factor taken into consideration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

Fertility (all genders)

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

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

More information on fertility preservation can be found at *NCCN Guidelines for Patients: Adolescent and Young Adult Cancer* at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer



Changes in fertility

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

Preventing pregnancy during treatment

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

Blood tests

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

Alkaline phosphatase

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

Complete blood count

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

Comprehensive metabolic panel

A comprehensive metabolic panel (CMP) measures substances in your blood. It provides important information about how well your kidneys and liver are working, among other things

Liver function tests

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

Pregnancy test

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

Imaging tests

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

A radiologist, a medical expert, will interpret the test and send a report to your doctor. While these reports might be available to you through your patient portal or patient access system, please wait to discuss these results with your care team. They will be able to explain what the results mean for your care.

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

Bone scan

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

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

Bone x-ray

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

Contrast material

Contrast material is a substance used to improve the quality of the pictures of the inside of the body. It is used to make the pictures clearer. Contrast might be taken by mouth (oral) or given through a vein (IV). Oral contrast does not get absorbed from your intestines and will be passed with your next bowel movements. IV contrast will leave the body in the urine immediately after the test. The types of contrast vary and are different for CT and MRI. Not all imaging tests require contrast, but many do.

Tell your care team if you have had allergic reactions to contrast in the past. This is important. You might be given medicines to avoid the effects of those allergies. Contrast might not be used if you have a serious allergy or if your kidneys aren't working well.

CT scan

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

MRI scan

A magnetic resonance imaging (MRI) scan uses radio waves and powerful magnets to take pictures of the inside of the body. It does not use x-rays, which means there is no radiation delivered to your body during the test. Because of the very strong magnets used in the MRI machine, tell the technologist if you have any metal or a pacemaker in your body. During the test, you will likely be asked to hold your breath for 10 to 20 seconds as the technician collects the images. Contrast is often used.

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

- **A spine or brain MRI** can be used to detect breast cancer that has spread (metastasized) to the spine or brain.

PET scan

A PET (positron emission tomography) scan uses a radioactive drug called a tracer. A tracer is a substance injected into a vein to see where cancer cells are in the body and how much sugar is being taken up by the cancer cells. This gives an idea about how fast the cancer cells are growing. Cancer cells show up as bright spots on PET scans. However, not all tumors will appear on a PET scan. Also, not all bright spots found on the PET scan are cancer. It is normal for the brain, heart, kidneys, liver, and bladder to be bright on PET. Inflammation or infection can also show up as a bright spot. When a PET scan is combined with CT, it is called a PET/CT scan.

- **An FDG-PET/CT** uses a radiotracer called fluorodeoxyglucose (FDG). It is made of fluoride and a simple form of sugar called glucose. You cannot eat or drink for at least 4 hours before the scan. This scan is most helpful when other imaging results are unclear.
- **A sodium fluoride PET/CT** uses a radiotracer made of sodium fluoride.
- **An FES-PET/CT** uses FES, which is a radioactive form of the hormone estrogen. An FES-PET/CT might be used when cancer is estrogen receptor-positive (ER+).

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

Ultrasound

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

Biopsy

A biopsy is the removal of a sample of tissue from your body for testing. A pathologist will examine the biopsy for cancer and write a report called a pathology report. While these reports might be available to you through your patient portal or patient access system, please wait to discuss these results with your care team. They will be able to explain what the results mean for your care.

There are different types of biopsies. Some biopsies are guided using imaging, such as ultrasound or MRI. Tumors found in different areas may be biopsied. You may have tissue removed from the breast, lymph nodes, or both.

Types of possible biopsies include:

- **Fine-needle aspiration (FNA) or core biopsy (CB)** uses needles of different sizes to remove a sample of tissue or fluid.
- **Vacuum-assisted core biopsy (VACB)** uses suction from a special vacuum device to remove the sample through a needle.

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

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.

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

The clips will stay in place until surgery. If the area biopsied is benign, the clip will remain in place to mark the biopsy site on future imaging. The clips cause no problems, even if they are left in place for a long time. You will be able to go through airport security and have an MRI.

Biopsy of metastasis

Metastasis is the spread of cancer to an area of the body such as the bones, lungs, or liver. A biopsy of the metastasis is typically 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. These biopsies are usually guided by imaging tests like ultrasound (US) or CT.

Biopsy results

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

HER2 status

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

There are 2 tests for HER2:

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

HER2 testing should be done on all new tumors. A tumor biopsy sample will be used. You might have more than one HER2 test. Newer drugs that target HER2 have recently been shown to be effective in some people with metastatic breast cancer with lower levels of HER2 expression (0, 1+, and 2+ by IHC) called HER2-low or HER2-ultralow.

Immunohistochemistry

Immunohistochemistry (IHC) is a special staining process that involves adding a chemical marker to cancer or immune cells. The cells are then studied using a microscope. IHC can find estrogen, progesterone, and HER2 receptors in breast cancer cells. A

Treatment options by cell receptor type

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

- ✓ Hormone receptors include estrogen and progesterone. A tumor is considered hormone receptor-positive (HR+) if an increased number of estrogen receptors, progesterone receptors, or both are found.
- ✓ HER2 is a protein involved in normal cell growth. There might be higher amounts of HER2 in your breast cancer. HER2 is categorized as negative, 0+, low, or positive.

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

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

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

pathologist will measure how many cells have estrogen and/or progesterone receptors and the number of receptors inside each cell.

FISH or ISH

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

Hormone receptor status

Your blood carries hormones throughout your body. A hormone is a substance made by a gland in your body. A receptor is a protein found inside or on the surface of a cell. When substances such as hormones attach (bind) to these receptors, it causes changes within the cell. When hormones attach to receptors inside breast cancer cells, they can cause cancer to grow. If found, these receptors may be targeted using endocrine (hormone-blocking) therapy.

There are 2 types of hormone receptors:

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

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

Hormone receptor-positive

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

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

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

Hormone receptor-negative

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

Biomarker testing

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

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

Tumor mutation testing

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

Testing is done using a variety of methods such as FISH, ISH, IHC, next-generation sequencing (NGS), and/or polymerase chain reaction (PCR). These methods are used to identify the presence of gene mutations, alterations, rearrangements, or fusions.

Estrogen receptor-positive (ER+) breast cancer cells

- ✓ In ER+ breast cancer, testing finds estrogen hormone receptors in at least 1 out of every 100 cancer cells.
- ✓ In ER-low–positive invasive breast cancer, testing finds estrogen hormone receptors in 1 to 10 out of every 100 cancer cells.

- Certain mutations such as *BRCA1/2, PIK3CA, AKT1, PTEN, NTRK,* and *RET* can be targeted with specific therapies.
- Germline *BRCA1/2* and *PALB2* testing is recommended for all patients with metastatic breast cancer, unless it has already been done (more recently than 2014).

PD-1 and PD-L1 testing

Programmed cell death protein 1 (PD-1) and programmed death-ligand 1 (PD-L1) are immune proteins. If either protein is expressed on the surface of cancer cells, it can cause your immune cells to ignore the cancer and suppress the anti-tumor immune response. If your cancer expresses either protein, you might have treatment that combines chemotherapy and immune checkpoint inhibitors. This is designed to activate your immune system to better fight off the cancer cells. Usually this test is done when hormone receptors and HER2 testing are negative (like in triple-negative tumors).

MSI-H/dMMR mutation

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

Tumor mutational 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 PD-1 and PD-L1.

Next-generation sequencing

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

PCR

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

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

Tumor markers

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

Liquid biopsy

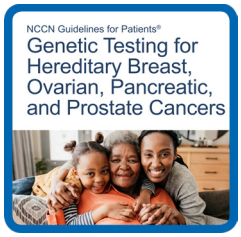
Some abnormal changes (mutations) can be found by testing circulating tumor DNA (ctDNA) in the blood. In a liquid biopsy, a sample of blood is taken to look for cancer cells or for pieces of DNA from tumor cells. A liquid biopsy can provide information about the tumor cells without the need for a tumor biopsy.

Genetic cancer risk testing

About 1 out of 20 breast cancers are hereditary. Depending on your family history or other features of your cancer, your health care provider might refer you for hereditary genetic testing to learn more about your cancer. A genetic counselor or trained provider will speak with you about the results. Test results may be used to guide treatment planning.

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

More information on genetic cancer risk testing can be found in the *NCCN Guidelines for Patients: Genetic Testing for Hereditary Breast, Ovarian, Pancreatic, and Prostate Cancer*s at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.



BRCA tests

Everyone has *BRCA* genes. Normal *BRCA* genes help to prevent tumor growth. They help fix damaged cells and help cells grow normally. *BRCA* mutations put you at risk for more than one type of cancer. Mutations in *BRCA1* or *BRCA2* increase the risk of breast, ovarian, prostate, colorectal, pancreatic, and melanoma skin cancers. These tests might be repeated if you tested negative for a gene mutation over 10 years ago, as genetic testing technology has improved.

Other genes

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

Key points

- Tests are used to find cancer, plan treatment, and check how your cancer is responding to treatment.
- You will have a physical exam, including a breast exam, to see if anything feels or looks abnormal.
- During a biopsy, tissue or fluid samples are removed for testing. Samples are needed to confirm the presence of cancer and to perform cancer cell tests.
- A sample from a biopsy of your tumor will be tested for estrogen receptor (ER) status, progesterone receptor (PR) status, HER2 status, and histology. This provides information about the behavior of your cancer, as well as treatments to which your cancer may respond. Other biomarker tests may be performed.
- About 1 out of 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.

Questions to ask

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

3
Breast cancer staging

Cancer staging is used to reflect prognosis and to guide treatment decisions. It describes the size and location of the tumor and if cancer has spread to lymph nodes, organs, or other parts of the body. It also takes into account hormone receptor (HR) and HER2 status, and standard-of-care treatment results.

How is breast cancer staged?

A cancer stage is a way to describe the extent of the cancer at the time you are first diagnosed. Based on testing, your cancer will be assigned a stage. Staging helps to predict prognosis and is needed to make treatment decisions. A prognosis is the course your cancer will likely take.

Information gathered during staging:

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

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

Staging includes:

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

TNM scores

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

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

T = Tumor

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

- **T1** – Tumor is 2 cm (20 mm) or less
- **T2** – Tumor is 2.1 cm to 5 cm
- **T3** – Tumor is more than 5 cm
- **T4** – Tumor is of any size and has invaded nearby structures such as the chest wall and skin of the breast
- **T4d** – Tumor is inflammatory carcinoma (inflammatory breast cancer)

For more information on inflammatory breast cancer, see *NCCN Guidelines for Patients: Inflammatory Breast Cancer* at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.

N = Regional lymph node

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

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

- **N0** means no cancer is in the regional lymph nodes. Isolated tumor cells (ITCs) may be present. These are malignant cell clusters no larger than 0.2 mm.

- **N1mi** means micrometastases (approximately 200 cells, larger than 0.2 mm, but not larger than 2.0 mm) are found in lymph nodes.
- **N1, N2, N3** means regional lymph node metastases are found. The higher the number, the more lymph nodes that have metastases.

M = Metastasis

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

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

Grade

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

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

Numbered stages

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

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

Key points

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

Questions to ask

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

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

4
Types of treatment

This chapter provides a general overview of the types of systemic therapy used to treat metastatic breast cancer (MBC). Systemic therapy is drug therapy that works throughout the body.

Care team

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

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

Systemic therapy

Systemic therapy is the main or primary treatment for metastatic breast cancer. The goal of treatment is to prevent or slow the spread of cancer.

System therapy is drug therapy that works throughout the body. It includes:

- Chemotherapy
- Antibody drug conjugates
- HER2-targeted therapy
- Other targeted therapies
- Immunotherapy
- Endocrine therapy

Treatment for metastatic breast cancer is a combination of systemic therapies that are often given in a specific order (sequential). The choice of therapy takes into consideration many factors, including HER2 and hormone receptor tumor status, your preferences about treatment, and if you have any other serious health conditions. Goals of systemic therapy should be discussed before starting treatment.

Treatment options

Treatment options are often described in the following ways:

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

For a general list of systemic therapies, **see Guide 2.**

Guide 2
Systemic therapy examples

Chemotherapy examples	• Capecitabine (Xeloda) • Carboplatin • Cisplatin • Cyclophosphamide • Docetaxel (Taxotere) • Doxorubicin (Adriamycin) • Epirubicin (Ellence)	• Eribulin (Halaven) • Fluorouracil • Gemcitabine • Methotrexate • Paclitaxel • Vinorelbine
Targeted therapy examples	Antibody drug conjugates • Sacituzumab govitecan-hziy (Trodelvy), fam-trastuzumab deruxtecan-nxki (Enhertu, T-DXd), and datopotamab deruxtecan-dlnk (Datroway)	
	CDK4/6 inhibitors • Abemaciclib (Verzenio), palbociclib (Ibrance), and ribociclib (Kisqali)	
	PARP inhibitors • Olaparib (Lynparza) and talazoparib (Talzenna)	
	PIK3CA, AKT1, PTEN, and mTOR inhibitors • Alpelisib (Piqray), capivasertib (Truqap), everolimus (Afinitor), and inavolisib (Itovebi)	
HER2-targeting therapy (antibody, inhibitor, and conjugate) examples	• Pertuzumab (Perjeta) • Trastuzumab (Herceptin) or trastuzumab substitutes (biosimilars) such as Kanjinti, Ogivri, Herzuma, Ontruzant, and Trazimera • Ado-trastuzumab emtansine (T-DM1) (Kadcyla) • Fam-trastuzumab deruxtecan-nxki (Enhertu, T-DXd)	• Lapatinib (Tykerb) • Margetuximab-cmkb (Margenza) • Neratinib (Nerlynx) • Tucatinib (Tukysa) • Phesgo as a substitute for combination therapy of trastuzumab with pertuzumab
Immunotherapy	• Pembrolizumab (Keytruda) and dostarlimab-gxly (Jemperli)	
Endocrine therapy	• Endocrine therapy can be found in **Guide 3.**	

Endocrine therapy

Endocrine therapy blocks estrogen or progesterone to treat hormone receptor-positive (HR+) breast cancer. The endocrine system is made up of organs and tissues that produce hormones. Hormones are natural chemicals released into the bloodstream.

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

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

Hormones may cause breast cancer to grow. Endocrine therapy will stop your body from making hormones or it will block what hormones do in the body. This can slow tumor growth or shrink the tumor for a period of time.

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

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

Systemic therapy is based on the cancer's hormone receptor (HR) and HER2 status, and any biomarkers that might be found.

Those who want to have children in the future should discuss fertility plans with their doctor and may need to be referred to a fertility specialist before starting endocrine therapy.

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

Testosterone

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

Premenopause

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

GnRH agonists may be used to temporarily induce menopause for those in premenopause. A combination of GnRH

agonists and tamoxifen or aromatase inhibitors (AIs) may be considered as endocrine therapy for those in premenopause.

Menopause

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

Guide 3
Endocrine therapy types

Bilateral oophorectomy	Surgery to remove both ovaries.
Ovarian ablation	Radiation to permanently stop the ovaries from making hormones.
Ovarian or testosterone suppression	Drugs to temporarily stop the ovaries or testicles from making hormones such as LHRH and GnRH. • LHRH agonists include goserelin (Zoladex) and leuprolide (Lupron Depot). These are injected every 4 or 12 weeks. They do not affect estrogen made by the ovaries. • GnRH agonists might be used to suppress ovarian hormone or testosterone production.
Aromatase inhibitors (AIs)	Drugs to stop a type of hormone called androgen from changing into estrogen by interfering with an enzyme called aromatase. They do not affect estrogen made by the ovaries. Nonsteroidal AIs include anastrozole (Arimidex) and letrozole (Femara). Exemestane (Aromasin) is a steroidal AI.
Estrogen receptor (ER) modulators or anti-estrogens	• **Selective estrogen receptor modulators (SERMs)** block estrogen from attaching to hormone receptors. Tamoxifen and toremifene (Fareston) are SERMs. • **Selective estrogen receptor degraders (SERDs)** block and destroy estrogen receptors. Fulvestrant (Faslodex) and elacestrant (Orserdu) are SERDs.
Hormones	Hormone examples include ethinyl estradiol, fluoxymesterone, and megestrol acetate (Megace).

Chemotherapy

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

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

Some examples of chemotherapy drugs include the following:

- **Anthracyclines** include doxorubicin (Adriamycin), doxorubicin liposomal injection (Doxil), and epirubicin (Ellence)
- **Taxanes** include docetaxel, paclitaxel, and albumin-bound paclitaxel.
- **Antimetabolites** include capecitabine (Xeloda), fluorouracil, gemcitabine, and methotrexate.

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

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

Antibody drug conjugates

An antibody drug conjugate (ADC) delivers cell-specific chemotherapy. It attaches to a protein found on the outside of the cancer cell, then enters the cell. Once inside the cell, chemotherapy is released. ADCs are given in cycles. ADC examples include ado-trastuzumab emtansine (Kadcyla), fam-trastuzumab deruxtecan-nxki (Enhertu, T-DXd), sacituzumab govitecan-hziy (Trodelvy), and datopotamab deruxtecan-dlnk (Datroway).

HER2-targeted therapy

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

HER2-targeted therapies include:

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

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

Other targeted therapies

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

CDK4/6 inhibitors

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

PARP inhibitors

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

PIK3CA, PTEN, and AKT1 inhibitors

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

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

mTOR inhibitors

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

Everolimus (Afinitor) is an mTOR inhibitor. It can be taken with exemestane, fulvestrant, or tamoxifen.

Immunotherapy

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

Warnings about supplements and drug interactions

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

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

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

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

Bring a list with you to every visit.

Bone-strengthening therapy

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

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

Drugs used to prevent bone loss and fractures:

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

Drugs used to treat bone metastases:

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

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

Zoledronic acid, pamidronate, and denosumab

Zoledronic acid, pamidronate, and denosumab are used to prevent bone loss (osteoporosis) and fractures caused by endocrine therapy. Zoledronic acid and denosumab are also used in those with metastatic breast cancer who have bone metastases to help reduce the likelihood of fractures, pain, or other complications arising from cancer in bone. You might have blood tests to monitor kidney function, calcium levels, and magnesium levels. A calcium and vitamin D supplement will likely be recommended by your doctor.

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

Clinical trials

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

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

Phases

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

- **Phase 1** trials study the safety and side effects of an investigational drug or treatment approach.
- **Phase 2** trials study how well the drug or approach works against a specific type of cancer.
- **Phase 3** trials test the drug or approach against a standard treatment. If the results are good, it may be approved by the FDA.
- **Phase 4** trials study the safety and benefit of an FDA-approved treatment.

Who can enroll?

It depends on the clinical trial's rules, called eligibility criteria. The rules may be about age, cancer type and stage, treatment history, or general health. They ensure that participants are alike in specific ways and that the trial is as safe as possible for the participants.

Informed consent

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

Will I get a placebo?

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

Are clinical trials free?

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

Key points

- Systemic therapy works throughout the body and is the main treatment for metastatic breast cancer.
- Systemic treatment is based on estrogen receptor (ER), progesterone receptor (PR), and HER2 expression.
- Treatment is a combination of systemic therapies that are often given in a specific order (sequential).
- HER2-targeted therapy is drug therapy that treats HER2+ breast cancer.
- Endocrine therapy blocks estrogen or progesterone to treat hormone receptor-positive (HR+) breast cancer.
- Medicines that target the bones may be given to help relieve bone pain or reduce the risk of bone-related problems.
- A clinical trial is a type of research that studies a treatment to see how safe it is and how well it works.

Questions to ask

- What is your experience treating breast cancer?
- Is there a social worker or someone who can help me decide about treatment?
- Who will coordinate my care?
- Am I a candidate for a clinical trial?

Finding a clinical trial

In the United States

NCCN Cancer Centers
NCCN.org/cancercenters

The National Cancer Institute (NCI)
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

5
Supportive care

Supportive care helps manage the symptoms of metastatic breast cancer (MBC) and the side effects of treatment. This chapter discusses possible side effects.

People are living longer with metastatic breast cancer (MBC). Since treatment can last many years, supportive care for side effects is important. Living with MBC also brings new meaning to survivorship.

What is supportive care?

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

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

Supportive care can also help with:

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

Side effects

All cancer treatments can cause unwanted health issues called side effects. Side effects depend on many factors. These factors include the drug type and dose, length of treatment, and the person. Some side effects may just be unpleasant. Others may be harmful to one's health. Treatment can cause several side effects. Some are very serious. Tell your care team about any new or worsening symptoms.

Blood clots

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

Bone health

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

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

Diarrhea or constipation

Diarrhea is frequent and watery bowel movements. Your care team will tell you how to manage diarrhea. It is important to drink lots of fluids. Constipation is also common, especially if taking certain pain medicines. Drinking fluids, staying active, and taking medicines for constipation are often recommended.

Distress

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

Fatigue

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

Hair loss

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

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

Infections

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

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

Loss of appetite

Sometimes side effects from surgery, cancer, or its treatment might cause you to feel not hungry or sick to your stomach (nauseated). You might have a sore mouth. Healthy eating is important during treatment. It includes eating a balanced diet, eating the right amount of food, and drinking enough fluids. A registered dietitian who is an expert in nutrition and food

can help. Speak to your care team if you have trouble eating or maintaining weight.

Low blood cell counts

Some cancer treatments can cause low blood cell counts.

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

Lymphedema

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

Nausea and vomiting

Nausea and vomiting are common side effects of treatment. You will be given medicine to prevent nausea and vomiting. Your care team can also provide information on non-medical ways to help with nausea and vomiting.

Neurocognitive or neuropsychological effects

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

Neuropathy and neurotoxicity

Some treatments can damage the nervous system (neurotoxicity) causing neuropathy and problems with concentration, memory, and thinking. Neuropathy is a nerve problem that causes pain, numbness, tingling, swelling, or muscle weakness in different parts of the body. It usually begins in the hands or feet and gets worse with additional cycles of treatment. Most of the time, neuropathy improves gradually and may eventually go away after treatment.

Organ issues

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

Pain

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

Palliative care

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

Quality of life

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

Late effects

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

Supportive care resources

More information on supportive care is available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.

Survivorship

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

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

Keep these things in mind:

- Tell your care team about any symptoms such as headaches, menstrual spotting between periods or new onset of spotting after menopause (if prior tamoxifen), shortness of breath when 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. If you are experiencing side effects, talk to your care team.

Monitoring metastatic disease

You will be monitored during treatment for metastatic breast cancer. 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. It is important to keep follow-up visits and test appointments. Contact your doctor if you have any new or worsening symptoms.

Monitoring is important. You will be monitored for symptoms caused by cancer, such as pain

“My doctor reminded me that stress cannot help me, but it can hurt me! It helped me remember to control those things I could control and relax in front of those that I could not control.”

from bone metastases. The goal of monitoring is to determine if treatment provides benefit. Benefit includes keeping cancer stable.

Lifestyle changes

Changes in your lifestyle can help manage side effects and improve treatment results. Lifestyle changes include eating a balanced and nutritious diet, exercising regularly, limiting alcohol, and quitting smoking. Your care team can offer information and support on lifestyle changes.

Living with metastatic breast cancer

Those living with MBC often have unique challenges not experienced by other breast cancer survivors. Living with MBC can be stressful—financially, emotionally, physically, and spiritually. Take care of yourself. Seek out support groups at your local hospital, through social media, or from those listed in the back of this book. Look to friends, relatives, neighbors, and coworkers for social support. Your cancer care team or one of your primary health care providers can be a great source of information and support if you are experiencing any changes in your mental, physical, emotional, sexual, or financial health.

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

Key points

- Supportive care is health care that relieves symptoms caused by treatment and improves quality of life. Supportive care is always given.
- All cancer treatments can cause unwanted health issues called side effects. Side effects depend on many factors. These factors include the drug type and dose, length of treatment, and the person.
- Some side effects are very rare. Ask your care team what to expect.
- Tell your care team about any new or worsening symptoms.
- Late effects are side effects that occur months or years after a disease is diagnosed. Late effects may include physical, mental, and social health concerns, and second cancers.
- Those living with MBC often have unique challenges not experienced by other breast cancer survivors. Your cancer care team or one of your primary health care providers can be a great source of information and support if you are experiencing any changes in your mental, physical, emotional, sexual, or financial health.

Questions to ask

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

6
Your treatment options

Systemic therapy is the main or primary treatment for metastatic breast cancer (MBC). The goal of treatment is to prevent or slow the spread of cancer. Systemic therapy is based on the cancer's hormone receptor (HR) and HER2 status, and any biomarkers that might be found. Together, you and your care team will choose a treatment plan that is best for you.

This chapter provides specific treatment options based on hormone receptor (HR) and HER2 tumor status.

HR+ with HER2-

In hormone receptor-positive (HR+) breast cancer, estrogen (ER+), progesterone receptors (PR+), or both (ER+/PR+) are found. When no HER2 receptors are found, then it is HER2-negative (HER2-). Initial treatment for HR+ HER2- metastatic breast cancer is most often endocrine therapy plus a CDK4/6 inhibitor (abemaciclib, ribociclib, or palbociclib). The next treatment will depend on your tumor's response to the initial treatment, the types of mutations that are specific to your cancer, and if your situation or health has changed.

Treatment is based on:

- How aggressive the cancer is and if it is negatively affecting your organs (visceral crisis)
- If you had endocrine therapy and if yes, then how long ago and what type

Visceral crisis

When cancer within internal organs (metastasis) causes severe symptoms or causes organs to stop working as they should, it is called a visceral crisis. If you are in visceral crisis, the goal is to decrease the cancer quickly. This may be accomplished by using chemotherapy or other systemic therapies.

No visceral crisis

If you are not in visceral crisis, then endocrine therapy often combined with CDK4/6 inhibitors is usually given. CDK4/6 inhibitors include abemaciclib, palbociclib, and ribociclib. Later, systemic therapy specific to HER2- breast cancer will be given. Those who are premenopausal might have ovarian suppression or ablation in addition to endocrine therapy. Systemic therapy options (including endocrine therapy) can be found in **Guide 4.**

Sometimes, HR+ cancer does not respond or stops responding to endocrine therapy. If this happens, chemotherapy or antibody drug conjugates (ADCs) will be given. If an ER+ tumor is resistant to endocrine therapy (endocrine refractory), then triple-negative breast cancer (TNBC) systemic therapy options found on page 49 will be considered.

Guide 4
Systemic therapy options: HR+ and HER2- without visceral crisis

Preferred first-line options	• Aromatase inhibitor with CDK4/6 inhibitor • Fulvestrant with CDK4/6 inhibitor • For germline *BRCA1* or *BRCA2* mutations, olaparib, or talazoparib
Preferred second-line and next-line options	• Fulvestrant with CDK4/6 inhibitor if CKD4/6 inhibitor not used before • For *PIK3CA, AKT1,* or *PTEN* mutation, alpelisib with fulvestrant or capivasertib with fulvestrant • Everolimus with endocrine therapy (exemestane, fulvestrant, or tamoxifen) • For germline *BRCA1* or *BRCA2* mutations, olaparib, or talazoparib if not used before
Other recommended	• Selective ER down-regulator (fulvestrant). For an *ESR1* mutation, elacestrant. • Selective ER down-regulator with a non-steroidal aromatase inhibitor • Non-steroidal aromatase inhibitor (anastrozole or letrozole) • Selective ER modulator (tamoxifen) • Steroidal aromatase inactivator (exemestane) • For *PALB2,* olaparib
Used in some cases	• Megestrol acetate • Ethinyl estradiol • Abemaciclib • For *NTRK* fusion, larotrectinib, entrectinib, or repotrectinib • For MSI-H/dMMR, pembrolizumab or dostarlimab-gxly • For TMB-H, pembrolizumab • For *RET* fusion, selpercatinib • For *PIK3CA,* inavolisib, palbociclib, and fulvestrant • For somatic *BRCA1* or *BRCA2* mutations, olaparib • For *FGFR1-3* fusions or mutations, erdafitinib • For HER2 activating mutations, neratinib with trastuzumab and fulvestrant or neratinib alone or with fulvestrant
Notes	• Those who are in premenopause or perimenopause might have ovarian suppression or ablation in addition to endocrine therapy.

HER2+

When HER2 receptors are found (amplified or overexpressed), the cancer is HER2-positive (HER2+). It is treated with HER2-targeted therapy and other systemic therapies as found in **Guide 5.**

Those with HER2+ and HR+ disease may also benefit from treatment with endocrine therapy. These can include aromatase inhibitors (AIs), tamoxifen, fulvestrant, or CDK 4/6 inhibitors. Those who are premenopausal might have ovarian suppression or ablation in addition to endocrine therapy.

Triple-negative breast cancer

Triple-negative breast cancer (TNBC) 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 is usually chemotherapy, and sometimes immunotherapy or targeted therapy.

TNBC systemic therapy options are found in **Guide 6.**

Guide 5
HER2-targeted therapy options: HER2+

First-line options	• Pertuzumab, trastuzumab, and docetaxel (preferred) • Pertuzumab, trastuzumab, and paclitaxel (preferred)
Second-line options	• Fam-trastuzumab deruxtecan-nxki (T-DXd) (preferred)
Third-line options	• Tucatinib, trastuzumab, and capecitabine (preferred) • Ado-trastuzumab emtansine (T-DM1)
Next-line options	• Trastuzumab and docetaxel or vinorelbine • Trastuzumab and paclitaxel with or without carboplatin • Capecitabine with trastuzumab or lapatinib • Trastuzumab and lapatinib • Trastuzumab with chemotherapy • Neratinib and capecitabine • Margetuximab-cmkb with chemotherapy (capecitabine, eribulin, gemcitabine, or vinorelbine) • Abemaciclib with fulvestrant and trastuzumab (for HR+ only) • Targeted therapy might be used if specific mutations are found

Guide 6
Systemic therapy options: TNBC

Preferred first-line	• Anthracyclines such as doxorubicin or liposomal doxorubicin • Taxanes such as paclitaxel • Antimetabolites such as capecitabine or gemcitabine • Microtubule inhibitors such as vinorelbine or eribulin • For PD-L1–positive with a combined positive score (CPS) of 10 or more, pembrolizumab with chemotherapy (albumin-bound paclitaxel, paclitaxel, or gemcitabine with carboplatin) • For PD-L1–positive with a CPS of less than 10, systemic chemotherapy • For PD-L1–positive with a combined positive score (CPS) of 10 or more with germline *BRCA1* or *BRCA2* mutation, PARP inhibitors (olaparib or talazoparib) or platinum chemotherapy (cisplatin or carboplatin)
Preferred second-line	• For germline *BRCA1* or *BRCA2* mutation, PARP inhibitors (PARPi) • Sacituzumab govitecan-hziy
Third-line and beyond	• Systemic chemotherapy • For biomarker-positive tumors, targeted therapies
Other recommended	• Cyclophosphamide • Docetaxel • Albumin-bound paclitaxel • Epirubicin • Ixabepilone • For *PALB2,* olaparib • Systemic chemotherapy • Fam-trastuzumab deruxtecan-nxki (T-DXd)
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 and paclitaxel or albumin-bound paclitaxel • For *NTRK* fusion, larotrectinib, entrectinib, or repotrectinib • For MSI-H/dMMR, pembrolizumab or dostarlimab-gxly • For TMB-H, pembrolizumab • For *RET* fusion, selpercatinib • For *PIK3CA,* inavolisib, palbociclib, and fulvestrant
Notes	• Alternative taxanes (such as docetaxel, paclitaxel, albumin-bound paclitaxel) might be substituted in some cases • Targeted therapy might be used if specific mutations are found

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 cancer stable.

It is important to keep follow-up visits and imaging test appointments. Seek good routine medical care. 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.

Most people will be able to have many rounds (lines) of systemic therapy. After multiple lines of systemic therapy, it might be time to consider ending systemic therapy and focus on supportive care. Supportive care is sometimes called palliative care. Systemic therapy has side effects that may impact your quality of life. If you and your care team decide to stop systemic therapy, supportive care will continue.

Your preferences and goals of treatment are always important. The goals of treatment can be thought of as curative or palliative. This means that treatment aims to cure or in the case of palliative care, treatment aims to preserve function and/or maintain comfort. Goals of treatment may change over time. Talk with your care team and make your wishes known.

Progression or toxicity on endocrine therapy

First-line therapy is the first treatment given. If HR+ cancer progresses while on first-line endocrine therapy, then you will likely switch to a different endocrine therapy. Targeted therapy might be added. Sometimes, your cancer becomes resistant to endocrine therapy. If this happens, endocrine therapy will be stopped and another systemic therapy such as chemotherapy or an antibody drug conjugate will be used.

Cancer progresses on systemic therapy with HER2-targeted therapy

If HER2+ cancer progresses while on HER2-targeted therapy, then different HER2-targeted therapy will be given.

Key points

- In hormone receptor-positive (HR+) cancer, estrogen receptors (ER+), progesterone receptors (PR+), or both (ER+/PR+) are found.
- In HER2-positive (HER2+) cancer, HER2 is either overexpressed or amplified. HER2+ cancer is treated with HER2-targeted therapy and other systemic therapies.
- Initial treatment for HR+ with HER2- is most often endocrine therapy plus a CDK4/6 inhibitor.
- Those with HR+ and HER2+ disease may also benefit from treatment with both endocrine therapy and HER2-targeted therapies.
- In triple-negative breast cancer (TNBC), receptors for estrogen, progesterone, and HER2 are not found. TNBC is usually treated with chemotherapy and sometimes immunotherapy or targeted therapy.
- Before each new line of therapy, you and your care team will discuss the risks and benefits of treatment, your overall health, and your goals for treatment.
- It is important to keep follow-up visits and imaging test appointments. Seek good routine medical care, including preventive care and cancer screenings. Continue to take all medicines as prescribed.

Questions to ask

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

7
Other resources

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

What else to know

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

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

- The details of their health and treatment
- Being a part of a care team
- Getting financial help
- Finding a care provider who is an expert in their field
- Coping with health problems

What else to do

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

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

Where to get help

Bag It
Bagitcancer.org

Bone Marrow & Cancer Foundation
bonemarrow.org

Breast Cancer Alliance
Breastcanceralliance.org

Breastcancer.org
Breastcancer.org

CanCare, Inc.
Cancare.org

Cancer*Care*
Cancercare.org

Cancer Hope Network
cancerhopenetwork.org

Cancer Survivor Care
Cancersurvivorcare.org

DiepC Foundation
diepcfoundation.org

FORCE: Facing Our Risk of Cancer Empowered
facingourrisk.org

GPAC Global Patient Advocacy Coalition
GPACunited.org

HIS Breast Cancer Awareness
Hisbreastcancer.org

Imerman Angels
Imermanangels.org

Inflammatory Breast Cancer Research Foundation
ibcresearch.org

Lobular Breast Cancer Alliance
lobularbreastcancer.org

My Faulty Gene
Myfaultygene.org

National Coalition for Cancer Survivorship
canceradvocacy.org

Sharsheret
sharsheret.org

Triage Cancer
Triagecancer.org

Unite for HER
uniteforher.org

Young Survival Coalition (YSC)
Youngsurvival.org

Questions to ask

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

Words to know

antibody drug conjugate (ADC)
A substance made up of a protein linked to a drug that attaches and enters certain types of cancer cells.

anti-estrogen
A drug that stops estrogen from attaching to cells.

aromatase inhibitor (AI)
A drug that lowers the level of estrogen in the body.

axillary lymph node (ALN)
A small disease-fighting structure that is near the armpit (axilla).

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.

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

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

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

clinical breast exam (CBE)
Touching of a breast by a health expert to feel for diseases.

clinical trial
A type of research that assesses health tests or treatments.

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

core needle biopsy (CNB)
A procedure that removes tissue samples with a hollow needle. Also called core biopsy (CB).

deoxyribonucleic acid (DNA)
A chain of chemicals in cells that contains coded instructions for making and controlling cells.

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

ductal carcinoma
A cancer derived from cells that line small tube-shaped vessels.

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

estrogen
A hormone that plays a role in breast development.

estrogen receptor (ER)
A protein inside cells that binds to estrogen.

estrogen receptor-negative (ER-)
A type of breast cancer that doesn't use estrogen to grow.

estrogen receptor-positive (ER+)
A type of breast cancer that uses estrogen to grow.

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

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

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

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

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

hormone receptor-negative cancer (HR-)
Cancer cells that don't use hormones to grow.

hormone receptor-positive cancer (HR+)
Cancer cells that use hormones to grow.

human epidermal growth factor receptor 2 (HER2)
A protein on the surface of a cell that sends signals for the cell to grow.

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

infraclavicular
The area right below the collarbone.

in situ hybridization (ISH)
A lab test of the number of a gene.

internal mammary
The area along the breastbone.

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

lobule
A gland in the breast that makes breast milk.

luteinizing hormone-releasing hormone (LHRH)
A hormone in the brain that helps control the making of estrogen by the ovaries.

lymph
A clear fluid containing white blood cells.

lymphadenopathy
Lymph nodes that are abnormal in size or consistency.

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

lymph node
A small, bean-shaped disease-fighting structure.

magnetic resonance imaging (MRI)
A test that uses radio waves and powerful magnets to make pictures of the insides of the body.

medical oncologist
A doctor who is an expert in cancer drugs.

menopause
12 months after the 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.

palpable adenopathy
Lymph nodes that feel abnormal in size or consistency.

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

perimenopause
Refers to the time during which your body makes the natural transition to menopause.

positron emission tomography (PET)
A test that uses radioactive material to see the shape and function of body parts.

postmenopause
The state of having no more menstrual periods.

premenopause
The state of having menstrual periods.

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

progesterone receptor (PR)
A protein inside cells that binds to progesterone.

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

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.

side effect
An unhealthy or unpleasant physical or emotional response to treatment.

standard of care
The best-known way to treat a particular disease based on past clinical trials. There may be more than one treatment regimen that is considered standard of care.

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.

visceral crisis
When organs aren't working as well as they should.

NCCN Contributors

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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
UH Seidman Cancer Center
800.641.2422 • uhhospitals.org/services/cancer-services
CC Taussig Cancer Institute
866.223.8100 • my.clevelandclinic.org/departments/cancer
Case CCC
216.844.8797 • case.edu/cancer

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

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

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

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

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

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

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

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

Johns Hopkins Kimmel Cancer Center
Baltimore, Maryland
410.955.8964
www.hopkinskimmelcancercenter.org

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

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

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

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

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

UCLA Jonsson Comprehensive Cancer Center
Los Angeles, California
310.825.5268 • uclahealth.org/cancer

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

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

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

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

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

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

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

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