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NCCN
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FOR PATIENTS®

2020

Breast Cancer Metastatic



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

About



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

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These NCCN Guidelines for Patients® are based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer (Version 3.2020, March 6, 2020).

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Endorsed by

Breast Cancer Alliance

Receiving a cancer diagnosis can be overwhelming, both for the patient and their family. We support the NCCN Guidelines for Patients: Metastatic Breast Cancer with the knowledge that these tools will help to equip patients with many of the educational resources, and answers to questions, they may seek. breastcanceralliance.org

Breastcancer.org

Breastcancer.org is a leading resource for people to make sense of the complex medical and personal information about breast health and breast cancer. Our mission is to engage, educate, and empower people with expert information and our dynamic peer support community to help everyone make the best decisions for their lives. breastcancer.org

DiepCFoundation

DiepCFoundation applauds the National Comprehensive Cancer Network (NCCN) for their ongoing work in the development of Patient Guidelines. We endorse the NCCN Guidelines for Patients: Metastatic Breast Cancer for patients seeking information about all options for breast reconstruction after cancer. The Principles of Breast Reconstruction Following Surgery in the NCCN Guidelines directly aligns with the mission of the Foundation to educate and empower more patients with the information needed to make an informed decision about breast reconstruction after surgical treatment for breast cancer. diepcfoundation.org

FORCE: Facing Our Risk of Cancer Empowered

As the nation's leading organization serving the hereditary cancer community, FORCE is pleased to endorse the NCCN Guidelines for Patients: Metastatic Breast Cancer. This guide provides valuable, evidence-based, expert reviewed information on the standard of care, empowering patients to make informed decisions about their treatment. facingourrisk.org

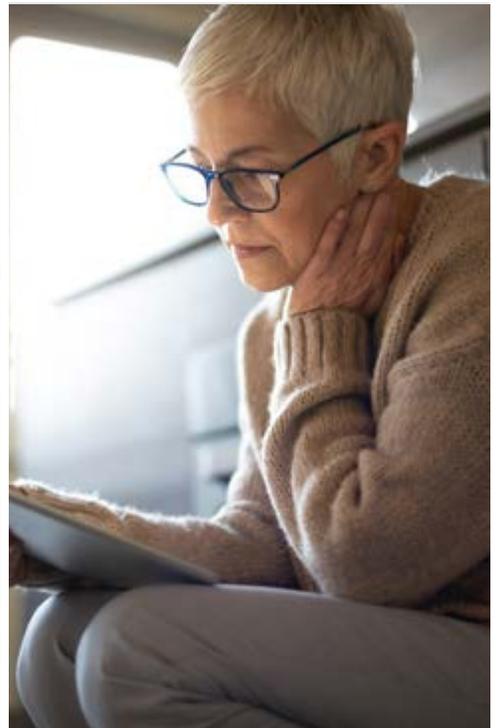
Sharsheret

Sharsheret is proud to endorse this important resource, the NCCN Guidelines for Patients: Metastatic Breast Cancer. With this critical tool in hand, women nationwide have the knowledge they need to partner with their healthcare team to navigate the often complicated world of breast cancer care and make informed treatment decisions. sharsheret.org

With generous support from

- Benjamin Anderson, MD, in honor of Joan McClure
- Kristina Griffin
- Patricia Andrews
- Kate Townsend

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Breast cancer basics

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

The breast

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

Breast tissue contains glands that can make milk. These milk glands are called lobules.

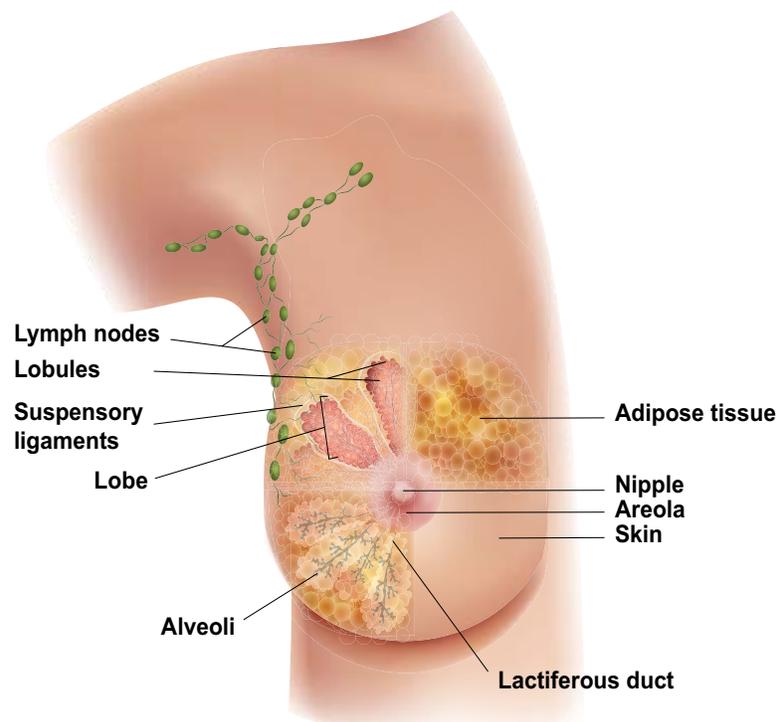
Lobules look like tiny clusters of grapes. Small tubes called ducts connect the lobules to the nipple.

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

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

The breast

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



Breast cancer

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

There is more than one type of breast carcinoma.

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

Anyone can have breast cancer, including men. Although there are some differences between men and women, treatment is very similar.

How breast cancer spreads

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

Primary tumor

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

Invasive

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

Metastasis

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

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

Breast cancer can metastasize to the bones, lungs, liver, spine, or brain. Breast cancer that has metastasized to other parts of the body is still called breast cancer.

Cancer stages

The American Joint Committee on Cancer (AJCC) created a way to determine how much cancer is in your body, where it is located, and what subtype you have. This is called staging. Based on testing, your cancer will be assigned a stage. Staging is needed to make treatment decisions.

Cancer staging is often done twice.

- **Clinical stage (c)** is the rating given before any treatment. It is based on a physical exam, biopsy, and imaging tests.
- **Pathologic stage (p)** or surgical stage is determined by examining tissue removed during an operation.

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?
- **The spread (metastasis) to distant sites (M):** Has the cancer spread to distant organs such as the lungs or liver?
- **Estrogen receptor (ER) status:** Does the cancer have the protein called an estrogen receptor?
- **Progesterone receptor (PR) status:** Does the cancer have the protein called a progesterone receptor?
- **Human epidermal growth factor receptor 2 (HER2) status:** Does the cancer make too much of a protein called HER2?

- **Grade of the cancer (G):** How much do the cancer cells look like normal cells?

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: T2, N1, M1.

- **T (tumor)** - Size of the main (primary) tumor
- **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

Numbered stages

Number stages range from stage 1 to stage 4, with 4 being the most advanced. Doctors write these stages as stage I, stage II, stage III, and stage IV.

Stage 0 is noninvasive

Noninvasive breast cancer is rated stage 0. This cancer is found only inside the ducts or lobules. It has not spread to the surrounding breast tissue.

Stages 1, 2, and 3 are invasive

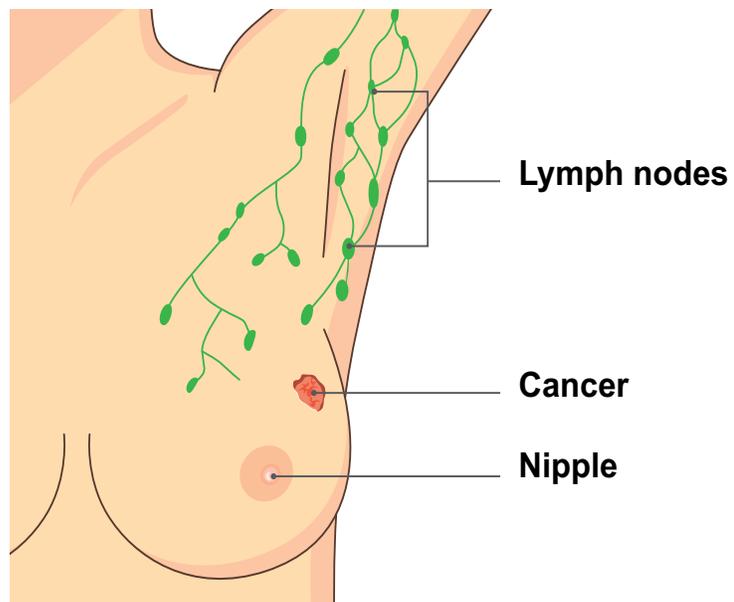
Invasive breast cancer is rated stage 1, 2, or 3. It has grown outside the ducts, lobules, or breast skin. Cancer might be in the axillary lymph nodes.

Stage 4 is metastatic

In stage 4 breast cancer, cancer has spread to distant sites. Your first diagnosis can be stage 4 metastatic breast cancer or it can develop from earlier stages.

Axillary lymph nodes

Lymph is a clear fluid. It drains from breast tissue into lymph vessels where it travels to lymph nodes. Most of the breast lymph nodes are located near the armpit. These are called axillary lymph nodes.



Review

- Inside breasts are lobules, ducts, fat, blood and lymph vessels, ligaments, and connective tissue. Lobules are structures that make breast milk. Ducts carry breast milk from the lobules to the nipple.
- Breast cancer often starts in the ducts or lobules and then spreads into the surrounding tissue.
- Breast cancer that is found only in the ducts or lobules is called noninvasive.
- Invasive breast cancer is cancer that has grown outside the ducts or lobules into surrounding tissue. Once outside the ducts or lobules, breast cancer can spread through lymph or blood to lymph nodes or other parts of the body.
- Metastatic breast cancer has spread to distant sites in the body.
- Anyone can have breast cancer, including men. Although there are some differences between men and women, treatment is very similar.

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Tests for metastatic breast cancer

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

General health tests

Medical history

A medical history is a record of all health issues and treatments you have had in your life. Be prepared to list any illness or injury and when it happened. Bring a list of old and new medicines and any over-the-counter medicines, herbs, or supplements you take. Tell your doctor about any symptoms you have. A medical 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. You can ask family members about their health issues like heart disease, cancer, and diabetes, and at what age they were diagnosed.

Physical exam

A physical exam is a study of your body. A doctor will check your body for signs of disease.

A health care provider may:

- Check your temperature, blood pressure, pulse, and breathing rate
- Weigh you
- Listen to your lungs and heart
- Look in your eyes, ears, nose, and throat
- Feel and apply pressure to parts of your body to see if organs are of normal size, are soft or hard, or cause pain when touched. Tell your doctor if you feel pain.
- Feel for enlarged lymph nodes in your neck and underarm. Tell the doctor if you have felt any lumps or have any pain.
- Complete a breast exam

Doctors should perform a thorough physical exam along with a complete health history. For recommended tests, [see Guide 1](#).

Performance status

Your state of general health will be rated using a performance status (PS) scale. PS is based on your overall health, cancer symptoms, and the ability to do daily activities.

PS scale scores range from 0 to 4.

- PS 0 means you are fully active.
- PS 1 means you are still able to perform light to moderate activity.
- PS 2 means you can still care for yourself but are not active.

- PS 3 means you are limited to the chair or bed more than half of the time.
- PS 4 means you need someone to care for you and are limited to a chair or bed.

If you have a PS of 3 or more, then consider supportive care. Supportive care is health care that relieves symptoms caused by cancer and improves quality of life.

Guide 1 Testing for metastatic breast cancer

Medical history and physical exam

Discuss goals of therapy and engage in shared decision-making

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

Chest CT with contrast (for diagnosis)

CT with contrast of abdomen with or without pelvis or MRI with contrast

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

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

Bone scan or sodium fluoride PET/CT, if needed

FDG PET/CT, if needed

X-rays if bone pain and if bones look abnormal on bone scan

First recurrence of disease should be biopsied

Determine tumor ER/PR and HER2 status on area of metastasis

Biomarker testing to identify those that would benefit from targeted therapy

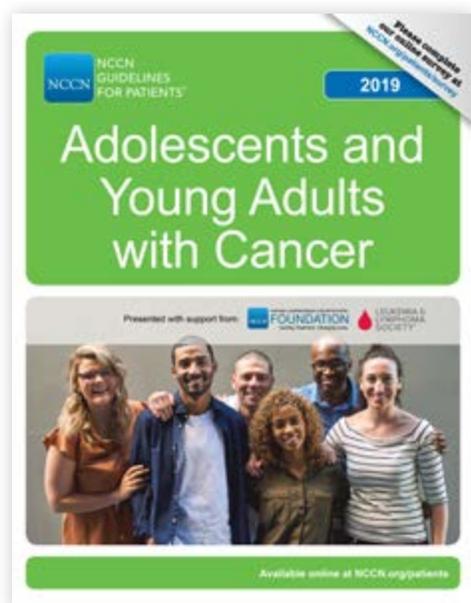
Genetic counseling if at risk for hereditary breast cancer

Fertility and birth control

Treatment can affect your fertility or your ability to have children. If you think you want children in the future, ask your doctor how cancer and cancer treatment will change your fertility and sexual health.

In order to preserve your fertility, you may need to take action before starting cancer treatment. Those who want to have children in the future should be referred to a fertility specialist before starting treatment to discuss the options.

More information can be found in *NCCN Guidelines for Patients® Adolescents and Young Adults with Cancer*, available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines).



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

Those with ovaries

Those who can have children will have a pregnancy test before starting treatment. Cancer treatment can hurt the baby if you are or become pregnant during treatment. Therefore, birth control to prevent pregnancy during and after treatment is recommended. Hormonal birth control may not be recommended, so ask your doctor about options.

Those with testicles

Cancer and cancer treatment can damage sperm. Therefore, use birth control to prevent pregnancy during and after treatment. If you think you want children in the future, talk to your doctor now. Sperm banking is an option.

Infertility

Infertility is the complete loss of the ability to have children. The actual risk of infertility is related to your age at time of diagnosis, treatment type(s), treatment dose, and treatment length. Chemotherapy with alkylating agents has a higher risk of infertility. Sometimes, there isn't time for fertility preservation before you start treatment. Talk to your doctor about your concerns.

Blood tests

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

Complete blood count

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

Comprehensive metabolic panel

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

Liver function tests

Liver function tests 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.

Imaging tests

Imaging tests take pictures of the inside of your body. These tests are used to find and treat breast cancer and metastases. Imaging tests show the primary tumor, or where the cancer started, and look for cancer in other parts of the body.

A radiologist, an expert who looks at test images, will write a report. The radiologist will send this report to your doctor who will discuss the results with you. Feel free to ask as many questions as you like.

CT scan

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

A CT scan of your chest, abdomen, and/or pelvis may be one of the tests to look for cancer. In most cases, contrast will be used. Contrast material is used to improve the pictures inside the body. Contrast materials are not dyes, but substances that help certain areas in the body stand out. Contrast is used to make the pictures clearer.

Tell your doctors if you have had bad reactions to contrast in the past. This is important. You might be given medicines, such as Benadryl® and prednisone, for an allergy to contrast. Contrast might not be used if you have a serious allergy or if your kidneys aren't working well.

MRI scan

A magnetic resonance imaging (MRI) scan uses radio waves and powerful magnets to take pictures of the inside of the body. It does not use x-rays. Contrast might be used.

Spine and brain MRI

Breast cancer can spread (metastasize) to your spine or brain. Contrast should be used in these MRIs. For a brain MRI, a device will be placed around your head that sends and receives radio waves. For a spine MRI, no device is worn.

Bone scan

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

A bone scan uses a radiotracer to make pictures of the inside areas of your bone which are abnormal. A radiotracer is a substance that releases small amounts of radiation. Before the pictures are taken, the tracer will be injected into your vein. It can take a few hours for the tracer to enter your bones.

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

Bone x-ray

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

PET/CT scan

A positron emission tomography (PET) scan uses a radioactive drug called a tracer. A tracer is a substance put into your body to see how cancer is growing and where it is in the body. Cancer cells show up as bright spots on PET scans. Not all bright spots are cancer.

Sometimes, CT is combined with PET. This combined test is called a PET/CT scan. It may be done with one or two machines depending on the cancer center.

Sodium fluoride PET/CT

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

FDG PET/CT

An FDG PET/CT uses a radiotracer called F-18 fluorodeoxyglucose (FDG). It is made of fluoride and a simple form of sugar called glucose. You cannot eat or drink for at least 4 hours before the scan.

This scan is most helpful when other imaging is unclear. It may help find cancer in lymph nodes and distant sites. If it clearly shows cancer in the bone, a bone scan and sodium fluoride PET/CT may not be needed. FDG PET/CT can be done at the same time as a CT used for diagnosis.

Ultrasound

An ultrasound uses high-energy sound waves to form pictures of the inside of the body. Ultrasound is good at showing small areas of cancer that are on or near the surface of the body.

Tissue tests

To confirm cancer is present, a tissue sample needs to be removed and tested. If cancer is confirmed, more lab tests will be done to learn about the cancer. Not all breast cancers are alike. Your doctor will use the lab results to decide which treatment options are right for you.

Biopsy

A biopsy is a procedure that removes a sample of tissue or fluid. The samples are sent to a lab for testing. A sample from the area of the suspected metastasis will also be taken. A pathologist will test the biopsy and write a report called a pathology report. Ask questions about your biopsy results and what it means for your treatment.

A biopsy is needed even if you were treated for earlier stages of breast cancer. The tumor can change or mutate. Such changes can greatly impact treatment options. However, sometimes it is unsafe to biopsy a tumor or metastasis. In this case, treatment might start without a biopsy.

Hormone receptor tests

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

Hormone receptors

Hormones recognize and bind to specific hormone receptors.

There are 2 types of hormone receptors:

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

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

Immunohistochemistry

Immunohistochemistry (said immunohistochemistry or IHC) is a special staining process that involves adding a chemical marker to cells. These cells are then studied using a microscope. IHC can find hormone receptors in breast cancer cells. A pathologist will measure how many cells have hormone receptors and the amount of hormone receptors inside each cell. Test results will either be hormone receptor-positive or hormone receptor-negative.

Hormone receptor–positive

In hormone receptor–positive breast cancer, IHC finds estrogen and/or progesterone hormone receptors in at least 1 out of every 100 cancer cells. These cancers are sometimes simply called hormone positive (HR+). Most breast cancers are hormone positive.

There are 2 types of hormone-positive cells:

- Estrogen-positive (ER+) cancer cells may need estrogen to grow. These cells may stop growing or die with treatment to block estrogen.
- Progesterone-positive (PR+) cancer cells need progesterone to grow. These cells stop growing with treatment to block progesterone.

Hormone receptor–negative

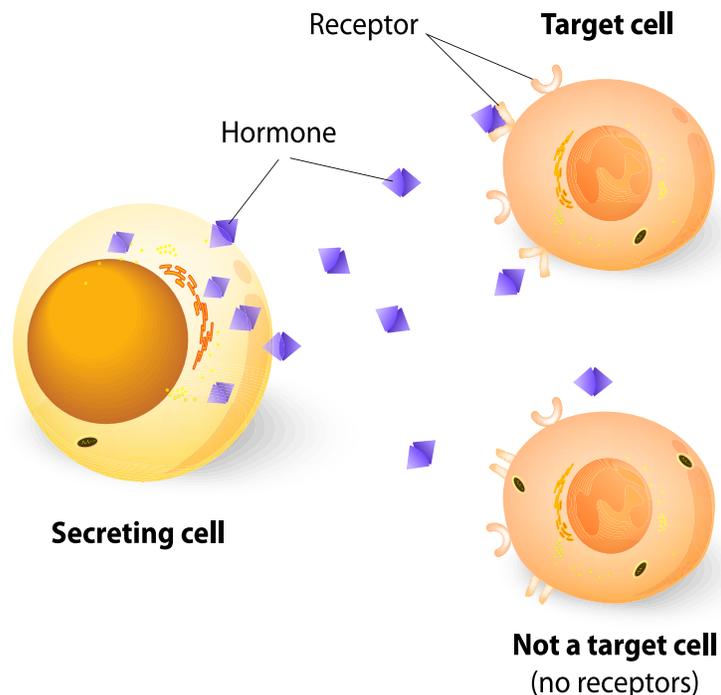
Hormone receptor–negative breast cancer cells do not have estrogen or progesterone hormone receptors. These cancers are sometimes simply called hormone negative (HR-). Hormone-negative cancers often grow faster than hormone-positive cancers.

There are 2 types of hormone-negative cells:

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

Hormone receptors

Cells in the ovaries, testes, and adrenal glands secrete hormones. Hormones recognize and bind to specific hormone receptors.



Genetic tests

Anything that increases your chances of cancer is called a risk factor. Risk factors can be activities that people do, things you have contact with in the environment, or traits passed down from parents to children through genes (inherited or hereditary). Genes are coded instructions that tell your cells what to do and what to become. An abnormal change in these instructions—called a gene mutation—can cause cells to grow and divide out of control.

Genetics can increase the risk of breast cancer. Your disease or family history may suggest you have hereditary breast cancer. About 1 out of 10 breast cancers are hereditary.

Your health care provider might refer you for genetic testing to learn more about your cancer. A genetic counselor will speak to you about the results. A genetic counselor is an expert who has special training in genetic diseases and will explain your chances of having hereditary breast cancer.

Genetic counseling

Your genetic counselor or oncologist might recommend genetic testing. *BRCA1* and *BRCA2* gene mutations are related to breast cancer. Other genes may be tested as well. Tests results may be used to guide treatment planning.

BRCA tests

Everyone has genes called *BRCA1* and *BRCA2*. Normal *BRCA* genes help to prevent tumor growth. They help fix damaged cells and help cells grow normally. *BRCA1* and *BRCA2* mutations put you at risk for more than one type of cancer. Mutations in *BRCA1* or *BRCA2*

Genetic testing
is recommended
for all men with
breast cancer.

increase the risk of breast, ovarian, prostate, colorectal, or melanoma skin cancer. Mutated *BRCA* genes can also affect how well some treatments work. Your doctor might choose a platinum-based systemic therapy or other treatment that is known to work better for your mutation.

If you have metastatic breast cancer, then you might be referred for *BRCA* tests. These tests do not need to be repeated if done before. They are done using blood or saliva (spitting into a cup).

Tumor tests

A sample from a biopsy of your tumor will be tested to look for biomarkers or proteins. This information is used to choose the best treatment for you. It is sometimes called molecular testing.

HER2 testing

Human epidermal growth factor receptor 2 (HER2) is a protein found on the surface of breast cells. When amounts are high, it causes cells to grow and divide. Normal breast cells have two copies of the gene that makes HER2. They also have a normal number of HER2 on the cell surface.

Some breast cancers have too many HER2 genes or receptors. Too many HER2s is called HER2-positive (HER2+).

There are 2 tests for HER2:

- Immunohistochemistry (IHC) measures receptors. If the IHC score is 3+, the cancer is HER2+.
- In situ hybridization (ISH) counts the number of copies of the HER2 gene.

Anyone with new metastatic breast cancer should have HER2 testing. You might have more than one HER2 test. HER2 tests are done using a biopsy sample.

Tumor mutation testing

A sample of your tumor or blood may be used to see if the cancer cells have any specific mutations. Some mutations can be targeted with specific therapies. This is separate from the genetic testing for mutations that you may have inherited from your parents. An example of this is a mutation in a gene known as *PIK3CA*. *PIK3CA* is targeted by a drug called alpelisib. With other gene mutations, you may qualify to enter a clinical trial.

PD-L1 testing

Programmed death-ligand 1 (PD-L1) is an immune system protein. This protein can cause your immune cells to ignore the cancer cells and suppress the anti-tumor immune response. If any of the cells in your tumor sample have (express) the PD-L1 protein, you might have treatment that combines chemotherapy and immunotherapy. This is designed to activate your immune system to better fight off the cancer cells.

MSI/MMR testing

MSI

Microsatellites are short, repeated strings of DNA (the information inside genes). When errors or defects occur, they are fixed. Some cancers prevent these errors from being fixed. This is called microsatellite instability (MSI). Knowing this can help plan treatment.

MMR

Mismatch repair (MMR) helps fix mutations in certain genes. When MMR is lacking (dMMR), these mutations may lead to cancer. Knowing this can help plan treatment or predict how well treatment will work with your type of tumor. When cancer cells have more than a normal number of microsatellites, it is called MSI-H (microsatellite instability-high).

Other tumor testing

Your blood or biopsy may be tested for proteins. These proteins are called tumor markers. Knowing this information can help plan treatment. Examples of some tumor markers in breast cancer include carcinoembryonic antigen (CEA), CA 15-3, and CA 27.29. An increase in the level of certain tumor markers could mean that the cancer has grown or spread (progressed).

Test results

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

Whether you are going for a second opinion, test, or office visit, keep these things in mind:

- Bring someone with you to doctor visits. Encourage this person to ask questions and take notes. Perhaps, they can record the conversation with your doctor.
- Write down questions and take notes during appointments. Don't be afraid to ask your care team questions. Get to know your care team and let them get to know you.
- Get copies of blood tests, imaging results, and reports about the specific type of cancer you have. It will be helpful when getting a second opinion.
- Organize your papers. Create files for insurance forms, medical records, and test results. You can do the same on your computer.
- Keep a list of contact information for everyone on your care team. Add it to your binder or notebook. Hang the list on your fridge or keep it by the phone.

Review

- Tests are used to find cancer, plan treatment, and check how well treatment is working.
- You will have a physical exam, including a breast exam, to see if anything feels or looks abnormal.
- Treatment can affect your fertility or your ability to have children.
- Performance status (PS) is based on your overall health, cancer symptoms, and the ability to do daily activities.
- Blood tests check for signs of disease and how well organs are working.
- Imaging tests take pictures of the inside of your body.
- 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.
- Some breast cancers have too many hormone receptors, HER2s, or both.
- A sample from a biopsy of your tumor will be tested to look for biomarkers or proteins, such as HER2.
- Genetic mutations can increase the risk of breast cancer. Your doctor might refer you for genetic testing or to speak with a genetic counselor.



Create a medical binder

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

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

3

Treatment options

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There is more than one treatment for metastatic breast cancer. This chapter describes treatment options and what to expect. Not everyone will receive the same treatment. Discuss with your doctor which treatment might be best for you.

Metastatic breast cancer is treatable. The goal of treatment is to prevent or slow the spread of cancer and to relieve any pain or discomfort. It is important to have regular talks with your doctor about your goals for treatment and your treatment plan.

There are 2 types of treatment:

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

Treatment can be local, systemic, or a combination of both. Medical oncologists are cancer doctors trained in the use of systemic therapy. There are many systemic therapy options that work well for long-term cancer control. If one does not work or doesn't stop the spread of cancer, then another will be tried.

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

Surgery

Surgery is not the main or primary treatment for metastatic breast cancer. After systemic drug therapy, surgery might be considered as a supportive care option. This means that if the primary tumor is causing pain, discomfort, or a health issue, then surgery might be an option. Also, you might prefer to have the breast removed. This requires collaboration between a breast surgeon and the reconstructive (plastic) surgeon. Radiation therapy might be an alternative to surgery.

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

Radiation therapy

Radiation therapy (RT) uses high-energy radiation from x-rays, gamma rays, protons, and other sources to kill cancer cells and shrink tumors. It is given over a certain period of time. Radiation therapy can be given alone or before or after surgery to treat or slow the growth of cancer. Sometimes, radiation therapy is given with certain systemic therapies. It may be used as supportive care to help ease discomfort or pain from a primary tumor or a metastasis.

Endocrine therapy

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

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

- Estrogen is made mainly by the ovaries
- Progesterone is made mainly by the ovaries
- Luteinizing hormone-releasing hormone (LHRH) is made by a part of the brain called the hypothalamus. It tells the ovaries to make estrogen and progesterone.
- Androgen is made by the adrenal glands, testicles, and ovaries.

Hormones can cause breast cancer to grow. Endocrine therapy will stop your body from making hormones or it will block what hormones do in the body. This can slow tumor growth or shrink the tumor for a period of time. Endocrine therapy can be local (surgery or ablation) or systemic (drug therapy). It is sometimes called hormone therapy. It is **not** the same as hormone replacement therapy used for menopause.

The goal of endocrine therapy is to reduce the amount of estrogen or progesterone in your body.

There is one type of surgical endocrine therapy that is used for premenopausal women:

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

There are 5 main types of endocrine therapy:

- **Ovarian ablation** permanently stops the ovaries from making hormones. Ablation uses extreme hot or cold to stop ovaries from working.
- **Ovarian suppression** temporarily stops the ovaries from making hormones. It is achieved with drugs called LHRH agonists. These drugs stop LHRH from being made, which stops the ovaries from making hormones. LHRH agonists include goserelin (Zoladex[®]) and leuprolide (Lupron Depot[®]).
- **Aromatase inhibitors** stop a type of hormone called androgen from changing into estrogen by an enzyme called aromatase. They do not affect estrogen made by the ovaries. Non-steroidal aromatase inhibitors include anastrozole (Arimidex[®]) and letrozole (Femara[®]). Exemestane (Aromasin[®]) is a steroidal aromatase inhibitor.
- **Anti-estrogens** prevent hormones from binding to receptors. Selective estrogen receptor modulators (SERMs) block estrogen from attaching to hormone receptors. They include tamoxifen and toremifene (Fareston[®]). Selective estrogen receptor degraders (SERDs) block and destroy estrogen receptors. Fulvestrant (Faslodex[®]) is a SERD.
- **Hormones** may treat breast cancer when taken in high doses. It is not known how hormones stop breast cancer from growing. They include ethinyl estradiol, fluoxymesterone, and megestrol acetate.

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

Menopause

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

When menstrual periods stop for 12 months or more, it is called postmenopause. If you don't get periods, a test using a blood sample may be needed to confirm your status. If you get menstrual periods, you are in premenopause.

Premenopause

In premenopause, your ovaries are the main source of estrogen and progesterone. Ovarian ablation or suppression help reduce hormone levels. For premenopause, ovarian ablation or suppression will be used with systemic therapy and/or an aromatase inhibitor.

Postmenopause

In postmenopause, your adrenal glands, liver, and body fat make small amounts of estrogen. Often in postmenopause, an aromatase inhibitor and a targeted therapy are used together.



Men with breast cancer

1 out of every 100 breast cancers occurs in men. Men with breast cancer are treated much like women. One important difference is treatment with endocrine therapy. The options are the same as for women in postmenopause. However, if men take aromatase inhibitors, they should also take a treatment to block testosterone. Aromatase inhibitors alone won't stop hormone-related cancer growth in men.

HER2-targeted therapy

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

HER2-targeted therapies include:

- Pertuzumab (Perjeta®)
- Trastuzumab (Herceptin®)
- Trastuzumab substitutes such as Kanjinti™, Ogivri®, Herzuma®, Ontruzant®, and Trazimera™
- Ado-trastuzumab emtansine (T-DM1) (Kadcyla®)
- Fam-trastuzumab deruxtecan-nxki (Enhertu®)
- Lapatinib (Tykerb®)
- Neratinib (Nerlynx®)

Most often, HER2-targeted therapy is given with chemotherapy. However, it might be used alone or in combination with endocrine therapy.

HER2-targeted therapies include:

- **HER2 antibodies** prevent growth signals from HER2 from outside the cell. They also increase the attack of immune cells on cancer cells. These drugs include trastuzumab (Herceptin®) and pertuzumab (Perjeta®).
- **HER2 inhibitors** stop growth signals from HER2 from within the cell. Lapatinib (Tykerb®) and neratinib (Nerlynx®) are examples of these drugs.

Treatment options by cell receptor type

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

- ✓ Endocrine therapy stops cancer growth caused by hormones. It is a standard treatment for hormone-positive cancers.
- ✓ CDK4/6 inhibitors and mTOR inhibitors are targeted therapies for hormone-positive, HER2- cancers.
- ✓ HER2-targeted therapy is a standard treatment for HER2+ cancers.
- ✓ Chemotherapy is often the first treatment for hormone-negative cancers.
- ✓ PARP inhibitors may be used to treat those with a *BRCA* mutation.

- **HER2 conjugates** deliver cell-specific chemotherapy. They attach to HER2s then enter the cell. Once inside, chemotherapy is released. Ado-trastuzumab emtansine (Kadcyla®) and fam-trastuzumab deruxtecan-nxki (Enhertu®) are included in this class.

Chemotherapy

Chemotherapy is a type of drug therapy used to treat cancer. Chemotherapy kills fast-growing cells throughout the body, including cancer cells and normal cells. All chemotherapy drugs affect the information inside genes called DNA (deoxyribonucleic acid). Genes tell cancer cells how and when to grow and divide. Chemotherapy disrupts the life cycle of cancer cells.

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

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

Did you know?

The terms “chemotherapy” and “systemic therapy” are often used interchangeably, but they are not the same. Chemotherapy, targeted therapy, and immunotherapy are all types of systemic therapy.

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

Birth control during treatment

If you get pregnant during chemotherapy, radiation therapy, endocrine therapy, or systemic therapy, serious birth defects can occur. If you had menstrual periods before starting chemotherapy, use birth control without hormones. Condoms are an option. “The pill” is not. Speak to your doctor about preventing pregnancy while being treated for breast cancer.

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

Bone-targeted therapy

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

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

There are 3 drugs used to prevent bone loss and fractures:

- Zoledronic acid (Zometa®)
- Pamidronate (Aredia®)
- Denosumab (Prolia®)

There are 3 drugs used to treat bone metastases:

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

You will be screened for 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.

If you are at an increased risk for fracture, a baseline DEXA scan is recommended before starting endocrine therapy.

Zoledronic acid, pamidronate, and denosumab

Denosumab, pamidronate, and zoledronic acid are used to prevent bone loss (osteoporosis) and fractures caused by endocrine therapy. Denosumab and zoledronic acid are also used in those with metastatic breast cancer who have bone metastases to help prevent fractures or spinal cord compression. You might have blood tests to monitor kidney function, calcium levels, and magnesium levels. A calcium and vitamin D supplement will be recommended by your doctor.

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

Other targeted therapies

CDK4/6 inhibitors

Cyclin-dependent kinase (CDK) is a cell protein that helps cells grow and divide. For hormone-positive, HER2- cancer, taking a CDK4/6 inhibitor with endocrine therapy may help control cancer longer. CDK4/6 inhibitors include palbociclib (Ibrance[®]), ribociclib (Kisqali[®]), and abemaciclib (Verzenio[™]).

With all CDK4/6 regimens, premenopausal women must also receive ovarian ablation or suppression.

mTOR inhibitors

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

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

PARP inhibitors

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

PIK3CA inhibitor

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

Immunotherapy

Immunotherapy is a type of systemic treatment that increases the activity of your immune system. By doing so, it improves your body's ability to find and destroy cancer cells. Immunotherapy can be given alone or with other types of treatment. Atezolizumab (Tecentriq[™]) is an immunotherapy.

Clinical trials

Clinical trials study how safe and helpful tests and treatments are for people. Clinical trials find out how to prevent, diagnose, and treat a disease like cancer. Because of clinical trials, doctors find safe and helpful ways to improve your care and treatment for cancer.

Clinical trials have 4 phases.

- **Phase I trials** aim to find the safest and best dose of a new drug. Another aim is to find the best way to give the drug with the fewest side effects.
- **Phase II trials** assess if a drug works for a specific type of cancer.
- **Phase III trials** compare a new drug to a standard treatment.
- **Phase IV trials** evaluate a drug's safety and treatment results after it has been approved.

To join a clinical trial, you must meet the conditions of the study. Patients in a clinical trial often are alike in terms of their cancer and general health. This helps to ensure that any change is from the treatment and not because of differences between patients.

If you decide to join a clinical trial, you will need to review and sign a paper called an informed consent form. This form describes the study in detail, including the risks and benefits. Even after you sign a consent form, you can stop taking part in a clinical trial at any time.

Ask your treatment team if there is an open clinical trial that you can join. There may be clinical trials where you're getting treatment or at other treatment centers nearby. Discuss the



Finding a clinical trial

- Search the National Institutes of Health (NIH) database for clinical trials. It includes publicly and privately funded clinical trials, whom to contact, and how to enroll. Look for an open clinical trial for your specific type of cancer. Go to ClinicalTrials.gov.
- The National Cancer Institute's Cancer Information Service (CIS) provides up-to-date information on clinical trials. You can call, e-mail, or chat live. Call 1.800.4.CANCER (800.422.6237) or go to cancer.gov.

risks and benefits of joining a clinical trial with your care team. Together, decide if a clinical trial is right for you.

NCCN experts encourage patients to join a clinical trial when it is the best option for the patient.

Trouble eating

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

Advance care planning

Advance care planning is making decisions now about the care you would want to receive if you become unable to speak for yourself. Advance care planning is for everyone, not just for those who are very sick. It is a way to ensure your wishes are understood and respected.

Advance care planning starts with an honest discussion with your doctor. Ask your doctor about the course your cancer will take called a prognosis. Find out what you might expect if your cancer spreads. Discuss the medicines or therapies that will give you the best quality of life. Include family and friends in your advance care planning. Make your wishes clear. It is important that everyone understands what you want.

You don't have to know the exact details of your prognosis. Just having a general idea will help with planning. With this information, you can decide if there is a point you might want to stop cancer treatment. You can also decide what treatments you would want for symptom relief, such as radiation therapy, surgery, or medicine.

You can change your advance care plan at any time. It might be helpful to have this talk with

your doctor and/or friends and family more than once during your treatment. What you want today might change tomorrow. Making your wishes clear will ensure everyone knows what you want.

Treatment team

Treating metastatic breast cancer takes a team approach. 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 let them get to know you.

- **Your primary care doctor** handles medical care not related to your cancer. This person can help you express your feelings about treatments to your cancer care team.
- **A pathologist** reads tests and studies the cells, tissues, and organs removed during a biopsy or surgery.
- **A diagnostic radiologist** reads the results of x-rays and other imaging tests.
- **A surgical oncologist** or breast surgeon performs operations to remove cancer.
- **A medical oncologist** treats cancer in adults using systemic therapy. Often, this person will lead the overall treatment team and keep track of tests and exams done by other specialists. A medical oncologist will often coordinate your care. Ask who will coordinate your care.

- **A palliative care specialist** is an expert in the treatment of symptoms caused by the cancer with the goal of improving a patient's quality of life and easing suffering.
- **Advanced practice providers** are an important part of any team. These are registered nurse practitioners and physician assistants who monitor your health and provide care.
- **Oncology nurses** provide your hands-on care, like giving systemic therapy, managing your care, answering questions, and helping you cope with side effects.
- **Nutritionists** can provide guidance on what foods or diet are most suitable for your particular condition.
- **Psychologists and psychiatrists** are mental health experts that can help manage issues such as depression, anxiety, or other mental health conditions that can affect how you feel.

Depending on your diagnosis, your team might include:

- **An anesthesiologist** who gives anesthesia, a medicine so you do not feel pain during surgery or procedures
- **An interventional radiologist** who performs needle biopsies of tumors and sometimes performs ablation therapies or places ports for treatment
- **A radiation oncologist** who prescribes and plans radiation therapy to treat cancer
- **A plastic surgeon** who performs breast reconstruction for those undergoing mastectomy, if desired.

- **An occupational therapist** who helps people with the tasks of daily living
- **A physical therapist** who helps people move with greater comfort and ease

You know your body better than anyone. Help other team members understand:

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

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

Review

- Metastatic breast cancer is treatable. The goal of treatment is to prevent or slow the spread of cancer and to relieve any pain or discomfort.
- Local therapy focuses on a certain area. It includes surgery, ablation, and radiation therapy.
- Systemic therapy works throughout the body. It includes endocrine therapy, chemotherapy, and targeted therapy.
- Treatment for metastatic breast cancer is usually a combination of systemic therapies. Local therapy might be used with systemic therapy.
- Targeted therapies can block the ways cancer cells grow, divide, and move in the body.
- Those who want to have children in the future should be referred to a fertility specialist before starting chemotherapy and/or endocrine therapy to discuss the options.
- A clinical trial is a type of research that studies a treatment to see how safe it is and how well it works. It might be an option as a treatment for your disease.
- Supportive care is health care that relieves symptoms caused by cancer or cancer treatment and improves quality of life.

4

Hormone positive with HER2-

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

When doctors diagnose breast cancer, they look for 3 types of receptors:

- Estrogen
- Progesterone
- HER2

In hormone-positive cancer, hormone receptors for estrogen and/or progesterone are found. In HER2- breast cancer, tests are negative for

HER2. This cancer is sometimes written as ER+ and/or PR+ with HER2-. Treatment is endocrine therapy that might be used alone or with another systemic therapy. Since HER2 is negative, HER2-targeted therapy will not be used.

Treatment

If bone disease is present, you will be treated with calcium, vitamin D, and either denosumab (Xgeva®), zoledronic acid (Zometa®), or pamidronate (Aredia®). You should go to the dentist before starting any of these bone-targeted drugs.

Treatment is based on if:

- You are in visceral crisis
- You had endocrine therapy and if yes, then how long ago and what type

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

Guide 2

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

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

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

Visceral crisis

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

Guide 3 Systemic therapy for HER-

Preferred options

- Anthracyclines (doxorubicin or liposomal doxorubicin)
- Taxanes such as paclitaxel
- Anti-metabolites (capecitabine or gemcitabine)
- Microtubule inhibitors (vinorelbine or eribulin)
- For *BRCA1* or *BRCA2* mutations, olaparib or talazoparib
- For *BRCA1* or *BRCA2* mutation, platinum (carboplatin or cisplatin)
- For *NTRK* fusion, larotrectinib or entrectinib
- For MSI-H/dMMR, pembrolizumab

Other recommended

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

Used in some cases

- AC (doxorubicin with cyclophosphamide)
- EC (epirubicin with cyclophosphamide)
- CMF (cyclophosphamide with methotrexate and fluorouracil)
- Docetaxel with capecitabine
- GT (gemcitabine with paclitaxel)
- Gemcitabine with carboplatin
- Paclitaxel with bevacizumab
- Carboplatin with paclitaxel or albumin-bound paclitaxel

No visceral crisis

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

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

Guide 4**HER2- and postmenopause or premenopause with ovarian ablation/suppression****Preferred first-line therapy options**

- Aromatase inhibitor with CDK4/6 inhibitor (abemaciclib, palbociclib, or ribociclib)
- ER down-regulator (fulvestrant) alone or with non-steroidal aromatase inhibitor (anastrozole, letrozole)
- Fulvestrant with CDK4/6 inhibitor (abemaciclib, palbociclib, or ribociclib)
- Non-steroidal aromatase inhibitor (anastrozole, letrozole)
- Select estrogen receptor modulator (tamoxifen or toremifene)
- Steroidal aromatase inactivator (exemestane)

Preferred second-line and next-line options

- Aromatase inhibitor with CDK4/6 inhibitor (abemaciclib, palbociclib, or ribociclib) if CDK4/6 inhibitor not used before
- For *PIK3CA* mutation, alpelisib and fulvestrant
- Everolimus with endocrine therapy (exemestane, fulvestrant, tamoxifen)
- Non-steroidal aromatase inhibitor (anastrozole, letrozole)
- Steroidal aromatase inactivator (exemestane)
- ER down-regulator (fulvestrant)
- Select estrogen receptor modulator (tamoxifen or toremifene)

Used in some cases

- Megestrol acetate
- Flouxymesterone
- Ethinyl estradiol
- Abemaciclib
- For *BRCA1* or *BRCA2* mutations, olaparib or talazoparib
- For *PIK3CA* mutation, alpelisib and fulvestrant
- For *NTRK* fusion, larotrectinib or entrectinib
- For MSI-H/dMMR, pembrolizumab

Monitoring

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

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

Every treatment has side effects. Cancer treatment can be toxic and harmful to your body. Treatment should help you in some way, but not at the risk of your overall health. When treatment is not helping and it is making you sick, then it might be time to consider stopping or changing treatment. Sometimes, your cancer

and body stop responding to treatment. This is called resistance.

Disease progression

Disease progression is defined in a few ways. It can be a worsening of symptoms, the growth or spread of cancer as shown on imaging tests, a decline in performance status, an unexplained weight loss, an increase in tumor markers, or a visceral crisis.

Treatment is based on if cancer progressed while:

- On endocrine therapy or
- In visceral crisis

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

Guide 5 Progression: ER+ and/or PR+ with HER2-			
Progression or unacceptable toxicity on first-line endocrine therapy	If not endocrine-resistant, consider: another line of endocrine therapy alone or with targeted therapy (See Guide 4)	➔	If no change after up to 3 lines of endocrine therapy alone or visceral disease with symptoms, then try systemic therapy (See Guide 3)
		➔	Consider ending systemic therapy and continue supportive care
For visceral crisis: progression or unacceptable toxicity on first-line systemic therapy	Another line of systemic therapy (See Guide 3)	➔	Continue systemic therapy until progression
		➔	Consider ending systemic therapy and continue supportive care

Progression or toxicity on endocrine therapy

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

After 3 rounds of endocrine therapy

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

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

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

Visceral crisis and progression or toxicity

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

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

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

At some point you may wish to stop treatment. Systemic therapy has side effects. When performance status is poor, the side effects of systemic therapy might affect your quality of life. Even if you stop systemic therapy, supportive care will continue.

Review

- ▶ Hormone-positive with HER2-negative (HER2-) metastatic breast cancer is treated with endocrine therapy. Another systemic therapy might be added.
- ▶ If you are in premenopause, then systemic therapy will be given with ovarian ablation or suppression.
- ▶ You will continue therapy until disease progression or there is an unacceptable toxicity. An unacceptable toxicity is one that puts your overall health at risk.
- ▶ At some point you may wish to stop treatment. Systemic therapy has side effects. Even if you stop systemic therapy, supportive care will continue.
- ▶ In a visceral crisis, cancer in the internal organs causes severe symptoms.
- ▶ Supportive care is always given.
- ▶ Your wishes about treatment are always important.

A preferred treatment option is proven to be more effective.

5

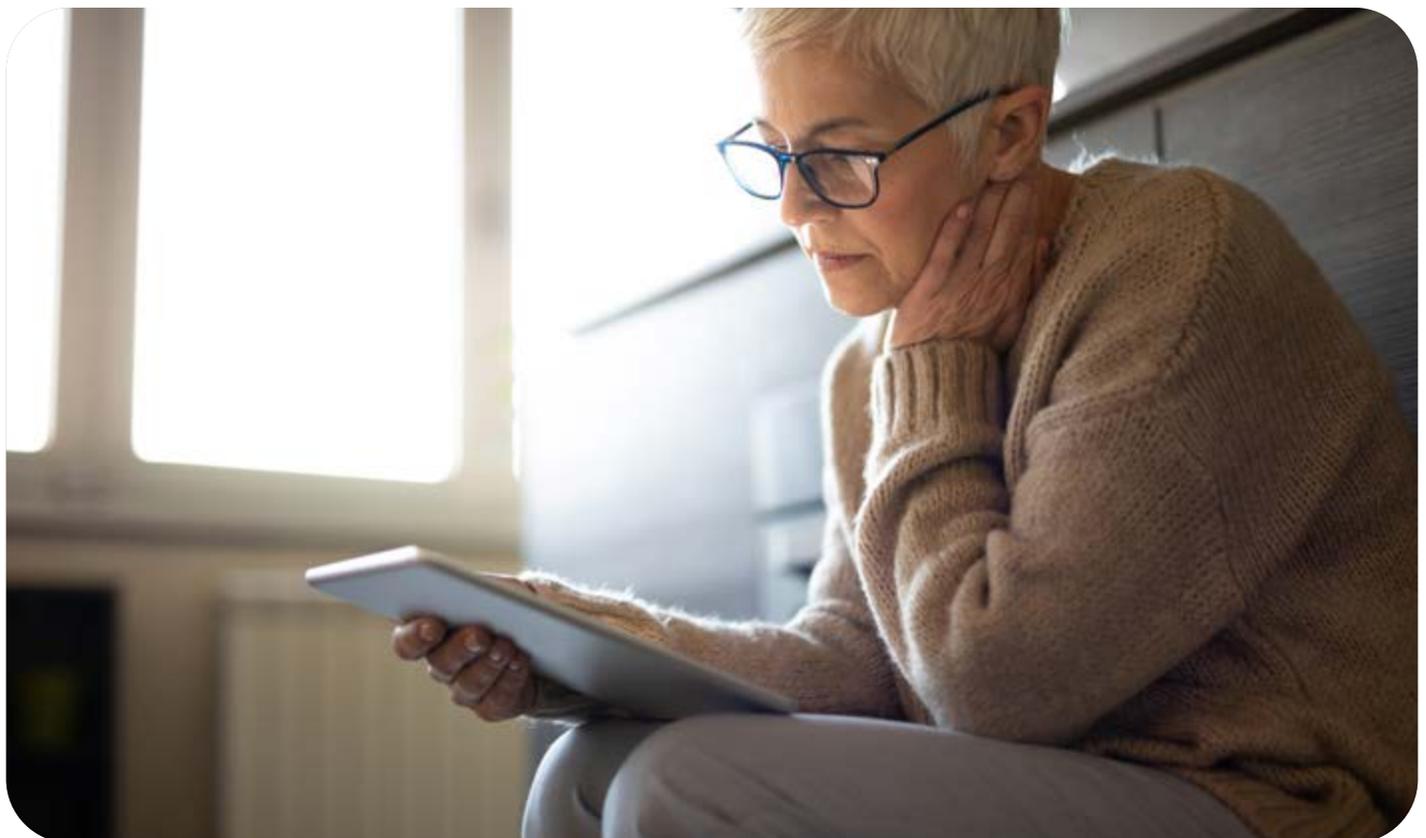
Hormone positive with HER2+

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

When doctors diagnose breast cancer, they look for 3 types of receptors:

- Estrogen
- Progesterone
- HER2

In hormone-positive with HER2-positive (HER2+) cancer, receptors for estrogen, progesterone, and HER2 are found. This

cancer is sometimes written as ER+ and/or PR+ with HER2+.

Treatment

Treatment is usually a combination of endocrine and systemic therapies that target hormone receptors and HER2.

If bone disease is present, you will be treated with calcium, vitamin D, and either denosumab (Xgeva®), zoledronic acid (Zometa®), or pamidronate (Aredia®). You should go to the dentist before starting any of these bone-targeted drugs.

Guide 6

Systemic therapy options: ER+ and/or PR+ with HER2+

Systemic therapy and HER2-targeted therapy with

- Pertuzumab and trastuzumab with taxane (preferred)
- Ado-trastuzumab emtansine (T-DM1)
- Fam-trastuzumab deruxtecan-nxki
- Trastuzumab with chemotherapy
- [See Guide 7](#) for more details

Endocrine therapy alone (aromatase inhibitor, fulvestrant, or tamoxifen)

Endocrine therapy alone or with HER2-targeted therapy (if premenopausal, consider ovarian ablation or suppression) ([See Guide 8](#))

Other HER2-targeted therapies ([See Guide 7](#))

Treatment options are as follows:

- For general treatment options, [see Guide 6 and 7](#).
- For options that don't include endocrine therapy, [see Guide 7](#).
- Treatment usually starts with a combination of endocrine therapy and HER2-targeted therapy, as found in [Guide 8](#).
- If you are in premenopause, then ovarian ablation or suppression are recommended with endocrine and HER2-targeted therapy. [See Guide 8](#).

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

Guide 7 Systemic therapy for HER+

Preferred options

- Pertuzumab, trastuzumab, and docetaxel
- Pertuzumab, trastuzumab, and paclitaxel

Other recommended

- Ado-trastuzumab emtansine (T-DM1)
- Fam-trastuzumab deruxtecan-nxki
- Trastuzumab and paclitaxel with or without carboplatin
- Trastuzumab and docetaxel
- Trastuzumab and vinorelbine
- Trastuzumab and capecitabine
- Lapatinib and capecitabine
- Trastuzumab and lapatinib (without cytotoxic therapy)
- Trastuzumab with other agents
- Neratinib and capecitabine
- For *BRCA1* or *BRCA2* mutations, olaparib or talazoparib
- For *NTRK* fusion, larotrectinib or entrectinib
- For MSI-H/dMMR, pembrolizumab

Monitoring

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

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

Every treatment has side effects. Cancer treatment can be toxic and harmful to your body. Treatment should help you in some way, but not at the risk of your overall health. When treatment is not helping and it is making you sick, then it might be time to consider stopping or changing treatment. Sometimes, your cancer and body stop responding to treatment. This is called resistance.

Guide 8

HER2+ and postmenopause or premenopause with ovarian ablation/suppression

Aromatase inhibitor alone or with

- Trastuzumab
- Lapatinib
- Lapatinib and trastuzumab

Fulvestrant alone or with trastuzumab

Tamoxifen alone or with trastuzumab

Disease progression

Disease progression is defined in a few ways. It can be a worsening of symptoms, the growth or spread of cancer as shown on imaging tests, a decline in performance status, an unexplained weight loss, an increase in tumor markers, or a visceral crisis.

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

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

Most people will be able to have many lines of systemic therapy. You will be monitored throughout treatment. For treatment options, see [Guide 9](#).

Cancer progresses on first-line endocrine therapy

First-line therapy is the first treatment tried. If cancer progresses while on first-line endocrine therapy, then you will likely switch to a different endocrine therapy for second-line. See [Guide 8](#).

Endocrine therapy might be given with HER2-targeted therapy. At some point, this cancer becomes resistant to endocrine therapy and only systemic therapy with HER2-targeted therapy will be used. See [Guide 7](#).

After 3 rounds of endocrine therapy

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

Guide 9

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

First-line endocrine therapy	Consider another line of endocrine therapy alone (See Guide 8) or with HER2-targeted therapy (See Guide 7)	➔	If no change after up to 3 lines of endocrine therapy alone or with HER2-targeted therapy or visceral disease with symptoms, then try systemic therapy with HER2-targeted therapy until progression	➔	Consider ending HER2-targeted therapy and continue supportive care
Systemic therapy with HER2-targeted therapy	Another line of systemic therapy with HER2-targeted therapy (See Guide 7)	➔	Continue HER2-targeted therapy until progression	➔	Consider ending HER2-targeted therapy and continue supportive care

Cancer progresses on systemic therapy with HER2-targeted therapy

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

Continue HER2-targeted therapy until disease progression. [See Guide 7.](#)

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

After multiple lines of systemic therapy

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

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

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

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

Review

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

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Hormone negative with HER2+

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In hormone-negative cancer, there are no receptors for estrogen (ER-) and progesterone (PR-). When HER2 receptors are found, it is HER2-positive (HER2+). This cancer is sometimes written as ER- and/or PR- with HER2+. Together, you and your doctor will choose a treatment plan that is best for you.

When doctors diagnose breast cancer, they look for 3 types of receptors:

- Estrogen
- Progesterone
- HER2

In hormone-negative with HER2-positive (HER2+) cancer, there are no receptors for estrogen and progesterone. This means that tests are negative for estrogen (ER-) and progesterone (PR-). In HER2+ breast cancer, tests are positive for HER2. This cancer is sometimes written as ER- and PR- with HER2+.

Treatment

Treatment is systemic therapy with HER2-targeted therapy. Endocrine therapy is not used in ER-.

If bone disease is present, you will be treated with calcium, vitamin D, and either denosumab (Xgeva®), zoledronic acid (Zometa®), or pamidronate (Aredia®). You should go to the dentist before starting any of these bone-targeted drugs.

- For general systemic treatment options, see [Guide 10](#).
- For more specific HER2+ treatment options, see [Guide 11](#).

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

Guide 10

Systemic therapy options: ER- and/or PR- with HER2+

Systemic therapy and HER2-targeted therapy with one of the following:

- Pertuzumab, trastuzumab, and taxane (preferred)
- Ado-trastuzumab emtansine (T-DM1)
- Fam-trastuzumab deruxtecan-nxki for third-line only
- Trastuzumab and chemotherapy
- Other HER2-targeted therapy

Monitoring

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

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

Every treatment has side effects. Cancer treatment can be toxic and harmful to your body. Treatment should help you in some way, but not at the risk of your overall health. When treatment is not helping and it is making you sick, then it might be time to consider stopping or changing treatment. Sometimes, your cancer and body stop responding to treatment. This is called resistance.

Guide 11 Systemic therapy for HER+

Preferred options

- Pertuzumab, trastuzumab, and docetaxel
- Pertuzumab, trastuzumab, and paclitaxel

Other recommended

- Ado-trastuzumab emtansine (T-DM1)
- Fam-trastuzumab deruxtecan-nxki
- Trastuzumab and paclitaxel with or without carboplatin
- Trastuzumab and docetaxel
- Trastuzumab and vinorelbine
- Trastuzumab and capecitabine
- Lapatinib and capecitabine
- Trastuzumab and lapatinib (without cytotoxic therapy)
- Trastuzumab with other agents
- Neratinib and capecitabine
- For *BRCA1* or *BRCA2* mutations, olaparib or talazoparib
- For *NTRK* fusion, larotrectinib or entrectinib
- For MSI-H/dMMR, pembrolizumab

Disease progression

Disease progression is defined in a few ways. It can be a worsening of symptoms, the growth or spread of cancer as shown on imaging tests, a decline in performance status, an unexplained weight loss, an increase in tumor markers, or a visceral crisis.

When this cancer progresses, treatment is another line of systemic therapy with HER2-targeted therapy. You will have a different therapy than before. There are many options. Most people will be able to have many lines of systemic therapy. Systemic therapy is used to prevent the growth and spread, and to relieve pain and discomfort in metastatic breast cancer. [See Guide 10 and 11.](#)

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

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

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

After multiple lines of systemic therapy

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

Review

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

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Triple-negative breast cancer

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In triple-negative breast cancer (TNBC), receptors for estrogen, progesterone, and HER2 are not found. This means that the breast cancer cells have tested negative for HER2, estrogen hormone receptors, and progesterone hormone receptors. Together, you and your doctor will choose a treatment plan that is best for you.

When doctors diagnose breast cancer, they look for 3 types of receptors:

- Estrogen
- Progesterone
- HER2

These are what cause breast cancer to grow and what are usually targeted in treatment. In triple-negative breast cancer (TNBC), receptors for estrogen, progesterone, and HER2 are not found. It is sometimes written as ER- and/or PR- with HER2-.

Treatment

TNBC is more aggressive and difficult to treat. It is more likely to spread and return after treatment.

Since there are no HER2 receptors, HER2-targeted therapy is not an option. And since there are no estrogen or progesterone hormone receptors, endocrine therapy is not an option. Without any of these receptors it is more challenging to treat. Treatment is usually systemic therapy. Multiple lines of

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

If bone disease is present, you will be treated with calcium, vitamin D, and either denosumab (Xgeva®), zoledronic acid (Zometa®), or pamidronate (Aredia®). You should go to the dentist before starting any of these bone-targeted drugs.

HER2- systemic treatment options are found in [Guide 12](#).

Monitoring

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

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

Every treatment has side effects. Cancer treatment can be toxic and harmful to your body. Treatment should help you in some way, but not at the risk of your overall health. If treatment is not helping and it is making you sick, then it might be time to consider stopping treatment. Sometimes, your cancer and body stop responding to treatment. This is called resistance.

Guide 12 Systemic therapy for HER-

Preferred options

- Anthracyclines (doxorubicin or liposomal doxorubicin)
- Taxanes such as paclitaxel
- Anti-metabolites (capecitabine or gemcitabine)
- Microtubule inhibitors (vinorelbine or eribulin)
- For *BRCA1* or *BRCA2* mutations, olaparib or talazoparib
- For *BRCA1* or *BRCA2* mutation, platinum (carboplatin or cisplatin)
- For *NTRK* fusion, larotrectinib or entrectinib
- For MSI-H/dMMR, pembrolizumab
- For PD-L1 expression of more than 1%, atezolizumab with albumin-bound paclitaxel

Other recommended

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

Used in some cases

- AC (doxorubicin with cyclophosphamide)
- EC (epirubicin with cyclophosphamide)
- CMF (cyclophosphamide with methotrexate and fluorouracil)
- Docetaxel with capecitabine
- GT (gemcitabine with paclitaxel)
- Gemcitabine with carboplatin
- Paclitaxel with bevacizumab
- Carboplatin with paclitaxel or albumin-bound paclitaxel

Disease progression

Disease progression is defined in a few ways. It can be a worsening of symptoms, the growth or spread of cancer as shown on imaging tests, a decline in performance status, an unexplained weight loss, an increase in tumor markers, or a visceral crisis.

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

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

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

Review

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

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Making treatment decisions

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- 60 Questions to ask your doctors
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It's important to be comfortable with the cancer treatment you choose. This choice starts with having an open and honest conversation with your doctor.

It's your choice

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

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

Some things that may play a role in your decisions:

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

Think about what you want from treatment. Discuss openly the risks and benefits of specific treatments and procedures. Weigh options and share concerns with your doctor. If you take the time to build a relationship with your doctor, it

will help you feel supported when considering options and making treatment decisions.

Second opinion

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

Things you can do to prepare:

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

Support groups

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

Questions to ask your doctors

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

Questions to ask about options

1. What will happen if I do nothing?
2. How do my age, overall health, and other factors affect my options?
3. What if I am pregnant? What if I'm planning to get pregnant in the near future?
4. Which option is proven to work best?
5. Does any option offer long-term cancer control? Are my chances any better for one option than another? Less time-consuming? Less expensive?
6. What are the possible complications and side effects?
7. Is surgery an option? Why or why not?
8. How do you know if treatment is working? How will I know if treatment is working?
9. What are my options if my treatment stops working?
10. What can be done to prevent or relieve the side effects of treatment?
11. Are there any life-threatening side effects of this treatment? How will I be monitored?
12. Can I stop treatment at any time? What will happen if I stop treatment?
13. Are there any clinical trials that I should consider for my condition?

Questions to ask about treatment

1. What are my treatment choices? What are the benefits and risks?
2. Which treatment do you recommend and why?
3. How long do I have to decide?
4. Will I have to go to the hospital or elsewhere for treatment? How often? How long is each visit? Will I have to stay overnight in the hospital or make travel plans?
5. Do I have a choice of when to begin treatment? Can I choose the days and times of treatment? Should I bring someone with me?
6. How much will the treatment hurt? What will you do to make me comfortable?
7. How much will this treatment cost me? What does my insurance cover? Are there any programs to help me pay for treatment?
8. Will I miss work or school? Will I be able to drive?
9. What type of home care will I need? What kind of treatment will I need to do at home?
10. When will I be able to return to my normal activities?
11. Which treatment will give me the best quality of life? Which treatment will extend my life? By how long?
12. I would like a second opinion. Is there someone you can recommend? Who can help me gather all of my records for a second opinion?

Questions to ask about clinical trials

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

Websites

American Cancer Society

cancer.org/cancer/breast-cancer.html

Breast Cancer Alliance

breastcanceralliance.org

Breastcancer.org

breastcancer.org

Breast Cancer Trials

breastcancertrials.org

DiepCFoundation

diepcfoundation.org

FORCE: Facing Our Risk of Cancer Empowered

facingourrisk.org

Living Beyond Breast Cancer (LBBC)

lbbc.org

National Cancer Institute (NCI)

cancer.gov/types/breast

Sharsheret

sharsheret.org

Young Survival Coalition (YSC)

youngsurvival.org



Finding a clinical trial

- Search the National Institutes of Health (NIH) database for clinical trials. It includes publicly and privately funded clinical trials, whom to contact, and how to enroll. Look for an open clinical trial for your specific type of cancer. Go to [ClinicalTrials.gov](https://clinicaltrials.gov).
- The National Cancer Institute's Cancer Information Service (CIS) provides up-to-date information on clinical trials. You can call, e-mail, or chat live. Call 1.800.4.CANCER (800.422.6237) or go to cancer.gov.



Words to know

areola

A darker, circular area of skin on the breast surrounding the nipple.

aromatase inhibitor

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.

bilateral oophorectomy

A surgery that removes both ovaries.

biopsy

Removal of small amounts of tissue or fluid to be tested for disease.

cancer stage

Rating of the growth and spread of tumors.

carcinoma

Cancer that starts in cells that form the lining of organs and structures in the body.

clinical trial

Research on a test or treatment to assess its safety or how well it works.

complete blood count (CBC)

A lab test that includes the number of blood cells.

computed tomography (CT)

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

connective tissue

Supporting and binding tissue that surrounds other tissues and organs.

contrast

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

duct

A tube in the breast that drains breast milk.

endocrine therapy

Treatment that stops the making or action of hormones in the body. Also called hormone therapy.

estrogen

A hormone that develops female body traits.

estrogen receptor

A protein inside of cells that binds with estrogen.

fertility

The ability to become pregnant and have a baby.

gene

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

genetic counseling

Discussion with a health expert about the risk for a disease caused by changes in genes.

hereditary breast cancer

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

hormone

Chemical in the body that activates cells or organs.

hormone receptor–negative (HR-) cancer

Cancer cells that don't use hormones to grow.

hormone receptor–positive (HR+) cancer

Cancer cells that use hormones to grow.

human epidermal growth factor receptor 2 (HER2)

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

immunohistochemistry (IHC)

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

invasive breast cancer

Cancer cells have grown into the supporting tissue of the breast.

kinase inhibitor

A cancer drug that blocks the transfer of phosphates.

liver function test

A test that measures chemicals made or processed by the liver.

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.

lymph node

Small groups of special disease-fighting cells located throughout the body.

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's an expert in cancer drugs.

menopause

The point in time when menstrual periods end.

metastasis

The spread of cancer beyond the breast and nearby lymph nodes to distant sites like bone, lung, liver, or brain.

mutation

An abnormal change in the instructions in cells for making and controlling cells.

noninvasive breast cancer

Cancer cells have not grown into the supporting tissue of the breast.

ovarian ablation

Methods used to stop the ovaries from making hormones.

ovarian suppression

Methods used to lower the amount of hormones made by the ovaries.

pathologist

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

performance status

A rating of general health.

premenopause

The state of having regular menstrual periods.

positron emission tomography (PET)

Use of radioactive material to see the shape and function of body parts.

postmenopause

The state of the end of menstrual periods.

primary tumor

The first mass of cancer cells in the body.

progesterone

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

prognosis

The expected pattern and outcome of a disease based on tests.

radiation therapy (RT)

The use of high-energy rays to destroy cancer cells.

selective estrogen receptor down-regulator (SERD)

Cancer drug that blocks the effect of estrogen.

selective estrogen receptor modulators (SERM)

Cancer drug that blocks the effect of estrogen.

side effect

An unhealthy physical or emotional response to treatment.

supportive care

Treatment for the symptoms or health conditions caused by cancer or cancer treatment.

systemic therapy

Treatment of cancer throughout the body.

triple-negative breast cancer (TNBC)

Breast cancer that is not hormone-positive or HER2-positive.

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

NCCN Cancer Centers

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

Fred & Pamela Buffett Cancer Center
Omaha, Nebraska
800.999.5465 • nebraskamed.com/cancer

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

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

Dana-Farber/Brigham and
Women's Cancer Center
Massachusetts General Hospital
Cancer Center
Boston, Massachusetts
877.332.4294
dfbwcc.org
massgeneral.org/cancer

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

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

Huntsman Cancer Institute
at the University of Utah
Salt Lake City, Utah
877.585.0303
huntsmancancer.org

Fred Hutchinson Cancer
Research Center/Seattle
Cancer Care Alliance
Seattle, Washington
206.288.7222 • seattlecca.org
206.667.5000 • fredhutch.org

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

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

Mayo Clinic Cancer Center
Phoenix/Scottsdale, Arizona
Jacksonville, Florida
Rochester, Minnesota
800.446.2279 • Arizona
904.953.0853 • Florida
507.538.3270 • Minnesota
mayoclinic.org/departments-centers/mayo-clinic-cancer-center

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

Moffitt Cancer Center
Tampa, Florida
800.456.3434 • moffitt.org

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

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

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
888.226.4343 • stjude.org
901.683.0055 • westclinic.com

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

UC San Diego Moores Cancer Center
La Jolla, California
858.657.7000 • cancer.ucsd.edu

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

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

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

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

The University of Texas
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Houston, Texas
800.392.1611 • mdanderson.org

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

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Dallas, Texas
214.648.3111 • utswmed.org/cancer

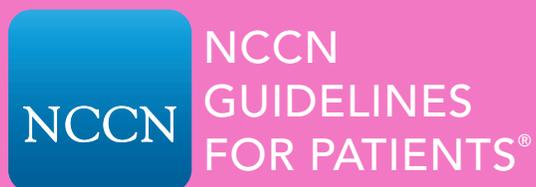
Vanderbilt-Ingram Cancer Center
Nashville, Tennessee
800.811.8480 • vicc.org

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

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Breast Cancer Metastatic

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