Stage IV Breast Cancer
While many people know about breast cancer, most patient information focuses on early-stage breast cancers. For women with stage IV or metastatic breast cancer, it is a challenge to find good information about their disease. The goals of this book are to help these women understand their disease and to tell them about tests and treatments recommended by breast cancer experts.

The National Comprehensive Cancer Network® (NCCN®) is a not-for-profit alliance of 25 of the world’s leading cancer centers. Experts from NCCN have written treatment guidelines for doctors who treat stage IV breast cancer. These treatment guidelines suggest what the best practice is for cancer care. The information in this patient book is based on the guidelines written for doctors.

This book focuses on stage IV breast cancer. NCCN also offers books on the other stages of breast cancer and many other cancer types. Visit NCCN.org/patients for the full library of patient books as well as other patient and caregiver resources.
NCCN® aims to improve the care given to patients with cancer. NCCN staff work with experts to create helpful programs and resources for many stakeholders. Stakeholders include health providers, patients, businesses, and others. One resource is the series of books for patients called the NCCN Patient Guidelines®. Each book presents the best practice for a type of cancer.

The patient books are based on clinical practice guidelines written for cancer doctors. These guidelines are called the NCCN Guidelines®. Clinical practice guidelines list the best health care options for groups of patients. Many doctors use them to help plan cancer treatment for their patients.

Panels of experts create the NCCN Guidelines. Most of the experts are from the 25 NCCN Member Institutions. Panelists may include surgeons, radiation oncologists, medical oncologists, and patient advocates. Recommendations in the NCCN Guidelines are based on clinical trials and the experience of the panelists.

The NCCN Guidelines are updated at least once a year. When funded, the patient books are updated to reflect the most recent version of the NCCN Guidelines for doctors. For more information about the NCCN Guidelines, visit NCCN.org/clinical.asp.

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The NCCN Foundation supports the mission of the National Comprehensive Cancer Network® (NCCN®) to improve the care of patients with cancer. One of its aims is to raise funds to create a library of books for patients. Learn more about the NCCN Foundation at NCCN.org/foundation.

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Stage IV Breast Cancer

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Who should read this book?

This book is about treatments for metastatic breast cancer among women. Patients and those who support them—caregivers, family, and friends—may find this booklet helpful. It may help you discuss and decide with doctors what care is best. As you read through this book, you may find it helpful to create a list of questions to ask your doctors.

Does the whole book apply to me?

There is important information in this booklet for many situations. Thus, you will likely not get every test and treatment listed. Your treatment team can point out what applies to you and give you more information.

The recommendations in this book include what NCCN experts feel is the most useful based on science and their experience. However, these recommendations may not be right for you. Your doctors may suggest other tests or treatments based on your health and other factors. If your treatment team suggests other tests or treatments, feel free to ask them why.

Making sense of medical terms

In this book, many medical words are included that describe cancer, tests, and treatments. These are words that you will likely hear from your treatment team. Most of the information may be new to you, and it may be a lot to learn.

Don’t be discouraged as you read. Keep reading and review the information. Don’t be shy to ask your treatment team to explain a word or phrase that you do not understand.

Words that you may not know are defined in the text or in the Dictionary. Words in the Dictionary are underlined when first used on a page.

Acronyms are also defined when first used and in the Glossary. Acronyms are words formed from the first letters of other words. One example is MRI for magnetic resonance imaging.
Breast cancer basics
You’ve learned that you have breast cancer. It’s common to feel shocked and confused. Part 1 reviews some basics about breast cancer that may help you start to cope. These basics may also help you start planning for treatment.

Women’s breasts

Before puberty, breasts have a ring of darker skin called the areola. In the middle of the areola is the raised tip of the breast called the nipple. Under the nipple, small milk ducts branch into fatty tissue like early growth from a seedling. These immature ducts are supported by connective tissue called stroma.

Among girls, increases in female hormones during puberty cause their breasts to change. The stroma increases, the ducts grow and branch out like tree limbs, and lobules form at the ends of the ducts like leaves at the ends of twigs. Lobules are small sacs that make breast milk after a baby is born. Breast milk drains from the millions of leaf-like lobules into the milk ducts that connect to the nipple. See Figure 1 for a look inside women's breasts.

Breast cancer

Breast cancer is a disease of cells—the building blocks of tissue in the body. Almost all breast cancers are carcinomas. Carcinomas are cancers that start in cells that line the inner (ducts, lungs, or gut) or outer (skin) surfaces of the body. In the breast, carcinomas start in the cells lining either the ducts or lobules, but most breast cancers start in ductal cells.

Cells have a control center called the nucleus. The nucleus contains special molecules called chromosomes. Within chromosomes are coded instructions, called genes, for building new cells and
controlling how cells behave. Changes in genes, called mutations, cause normal breast cells to become cancer cells. Cancer cells don’t behave like normal cells in three key ways.

First, the changes in genes cause cancer cells to make too many copies of themselves. Normal cells divide and multiply when new cells are needed, but otherwise live in a resting state. Normal cells also die when old or damaged. In contrast, cancer cells make new cells that aren’t needed and don’t die quickly when old or damaged. Over time, cancer cells form a mass called the primary tumor.

The second way cancer cells differ from normal cells is that they can grow into surrounding tissues. If not treated, the primary tumor can extend beyond the walls of lobules or ducts into the stroma. Breast cancers that have grown into the stroma are called “invasive.”

Third, unlike normal cells, cancer cells can break off from the primary tumor and form secondary tumors. Secondary tumors may form in the breast or in other parts of the body. Breast cancer can spread to other body parts through blood or lymph vessels that are in the stroma.

Most often, breast cancer spreads through lymph. Lymph is a clear fluid that gives cells water and food. It also has white blood cells that fight germs. Lymph nodes filter lymph and remove the germs. Most of the lymph in the breast drains to the axillary lymph nodes found inside the armpit. See Figure 2. Once in the axillary nodes, cancer cells can multiply and form secondary tumors. Other nearby lymph nodes include those just inside the ribs near the breast bone (internal mammary nodes), those right below the collarbone (infraclavicular nodes), and those right above the collarbone (supraclavicular nodes).

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**Figure 1. Parts of the breast**

[Image: Breast anatomy diagram]

Derivative work of Breast Anatomy by Patrick J. Lynch and C. Carl Jaffe, MD available at commons.wikimedia.org/wiki/File:Breast_anatomy_normal_scheme.png under a Creative Commons Attribution 3.0 Unported license.

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**Figure 2. Axillary lymph nodes**

[Image: Axillary lymph nodes diagram]

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This book focuses on stage IV breast cancers. These breast cancers have spread beyond the breast and nearby lymph nodes to distant sites. Breast cancer that has spread to a distant site is called metastatic breast cancer. Metastases often occur in the bone, lung, brain, or liver.

### Review

- Inside of women’s breasts are milk ducts, lobules that can make milk, and fatty tissue called stroma.
- Breast cancer often starts in the milk ducts or lobules and then spreads into the stroma.
- Breast cancer can spread outside the breast through lymph or blood.
- Stage IV breast cancers have spread to distant sites outside the breast.
2

Treatment planning
You may have learned that you have metastatic breast cancer when first diagnosed or after treatment for an earlier stage of breast cancer. The next step is to plan treatment based on test results, your treatment wishes, and other factors.

Since there are different types of metastatic breast cancer, your doctor will want to know all about the cancer and you so that your treatment can be tailored to you. This is called personalized medicine. Part 2 describes the recommended tests for stage IV breast cancer.

**General health tests**

**Medical history**
Your medical history includes any health events in your life and any medications you’ve taken. Your doctors will want to know about all your illnesses, breast biopsies, any prior radiation therapy, and if you are pregnant. It may help to make a list of old and new medications while at home to bring to your doctor’s office. Since breast cancer and other health conditions can run in families, your doctors will ask about the medical history of your relatives.

**Physical exam**
A physical exam is a review of your body for signs of disease. During this exam, your doctor will listen to your lungs, heart, and gut. He or she will also look at and touch your breasts and nearby lymph nodes to see if they feel normal. Your breasts may be felt while you sit or stand up as well as when you recline. This is called a CBE (clinical breast exam). Besides your breasts, other parts of your body will be felt to see if organs are of normal size, are soft or hard, or cause pain when touched.
Blood tests

Doctors test blood to look for signs of disease. Blood is often removed from a vein in the inside of the elbow by a needle. The needle may bruise your skin and you may feel dizzy from the blood draw. Your blood will be sent to a lab for testing.

CBC test

A CBC (complete blood count) measures the number of white blood cells, red blood cells, and platelets. It is important to know if you have enough red blood cells to carry oxygen to your tissues, white blood cells to fight infections, and platelets to clot blood in open wounds. Your blood counts may be low because the cancer has spread into your bones or because of another health problem.

Liver function tests

Your liver is an organ in the upper right side of your abdomen. It does many important jobs, such as remove toxins from your blood. Liver function tests assess for chemicals that are made or processed by the liver. Levels that are too high or low may signal that the cancer has spread to the liver. One such chemical is ALP (alkaline phosphatase). High levels of ALP may mean that the cancer has spread to the bone or liver.
Imaging tests

Imaging tests make pictures of the insides of your body. The pictures can show how far the cancer has spread. Getting an imaging test is often easy. Depending on the test, you may need to stop taking some medicines, stop eating and drinking for a few hours, and remove metal objects from your body.

Chest diagnostic CT
A CT (computed tomography) of your chest is recommended. This test takes many x-rays from different angles to make detailed pictures. Before the test, a contrast dye that makes the pictures clearer may be injected into your vein. The dye may cause you to feel flushed or get hives. Rarely, serious allergic reactions occur. Tell your doctors if you have had bad reactions before. During the CT scan, you will need to lie face up on a table that moves through the CT machine. See Figure 3.

Brain MRI
MRI (magnetic resonance imaging) is very useful for viewing the brain. You may have an MRI if you have symptoms that suggest the cancer has spread to the brain. Symptoms of cancer in the brain include chronic headaches, seizures, loss of balance, difficulty walking, speech problems, changes in vision, weakness on one side of the body, and personality changes.

An MRI uses radio waves and powerful magnets to make pictures. Like CT, contrast may be used. You will need to lie face up on a table. A device will be put around your head to keep it still. The table will then be moved so that your head is inside the MRI machine. The scan is completed in several minutes.

Abdominal/pelvic diagnostic scans
CT and MRI scans can be used to see the insides of your abdomen. It is recommended that pictures of your abdomen be taken with one of these scans. Your doctor may also recommend a scan of your pelvis, too.

Bone scan
A bone scan can be used to see if the cancer has spread to your bones. For this scan, a radiotracer will be injected into your vein. The most common radiotracer used for bone scans is technetium. You will need to wait about 3 hours for the radiotracer to enter your bones. Next, a special camera will be used to take pictures while you lie still on a table. It takes 45 to 60 minutes to complete the pictures. Areas of bone damage use more radiotracer than healthy bone and thus appear as bright spots in the pictures. Bone damage can be caused by cancer as well as by other health problems.
Sodium fluoride PET/CT
Instead of a bone scan, PET (positron emission tomography) and CT scans can be used to image bones. However, PET/CT is recommended only when other tests don’t clearly show if cancer is present in the bones. Some cancer centers have an imaging machine that does both scans. At other centers, the scans are done with two machines.

Like a bone scan, PET also uses a radiotracer to see the activity of cells. The radiotracer used to image bone with PET is sodium fluoride. Sodium fluoride PET/CT is a costly test but shows areas of bone damage and repair better than a bone scan. It also has a shorter waiting time of 40 to 60 minutes for the radiotracer to be seen and a shorter scanning time of 15 to 20 minutes than a bone scan.

FDG PET/CT
Another type of PET used to see if breast cancer has spread is FDG (fluorodeoxyglucose) PET/CT. FDG is a radiotracer that is made of fluoride and a simple form of sugar (glucose). Cancer cells use more FDG than normal cells and thus show up as bright spots on pictures. For this test, you must fast for 4 hours or more. FDG PET/CT is most helpful when other imaging tests are unclear and may be helpful with finding breast cancer that has spread to lymph nodes or distant sites.

X-rays
X-rays of bones that hurt are recommended. Long and weight-bearing bones that aren’t normal on bone scan or PET/CT should also be x-rayed. During an x-ray, you must lie still on a table while the x-ray machine sends small amounts of radiation into your body. Images made from the x-rays are seen on a screen.

Biopsy
A biopsy removes small samples of tissue or fluid from the body for testing. The methods used to remove samples will depend on where the cancer has spread. A biopsy is recommended to confirm if the distant site has cancer, test for the type of cancer, and perform the receptor tests described next. If your doctor does not suggest a biopsy, ask why.

Tissue from the breast tumor was likely tested before if you have been treated for early stage-breast cancer. Expect that your doctor will want to biopsy your metastatic breast cancer. In a small number of cases, the biology of the tumor changes. Such changes can greatly impact your treatment options and response to treatment.
Cancer cell tests

Not all breast cancer cells are alike. Cancer cells can differ by the type of receptors they have. A receptor is a protein found in the membrane of cells or inside of cells. Substances bind to the receptors and start changes within the cell. The two types of receptors important for treatment planning are:

Hormone receptor test

Estrogen and progesterone are hormones that increase during puberty in girls causing their breasts to grow. For some breast cancers, the cancer cells have a high number of hormone receptors. When hormones attach to the receptors, the cancer cells grow and divide forming new cancer cells.

Testing for hormone receptors is important because for cancer fueled by hormones, there are drugs that stop hormones from causing cancer growth. IHC (immunochemistry) is the lab test that most pathologists use to see if cancer cells have hormone receptors. The cancer cells are stained to see the number of cells with hormone receptors. If at least 1 out of every 100 cancer cells stains positive, the cancer is called hormone receptor–positive. If fewer cancer cells stain positive for hormone receptors, the cancer is called hormone receptor–negative.

HER2 receptor tests

In normal breast cells, there are two copies of the gene that makes HER2 (human epidermal growth factor receptor 2). HER2 is found within the membrane of cells. This type of receptor is called a surface receptor. When HER2 is activated, it causes breast cancer cells to grow and divide. Some breast cancers have cells with more than two copies of the HER2 gene causing too many HER2 receptors to be made. Other breast cancers have cells with only two HER2 gene copies but still too many HER2 receptors are made.

With too many HER2 receptors, breast cancer cells grow and divide fast. However, there are drugs to stop these cancer cells from growing. Due to high costs and the side effects of these drugs, it is very important to have tests that correctly show HER2 status. Like for hormone receptors, IHC is used to count the number of HER2 receptors. An IHC score of 3+ means that the cancer cells have many HER2 receptors. Another test of HER2 is ISH (in situ hybridization). ISH counts the number of copies of the HER2 gene. If the cancer cells have too many HER2 genes or receptors, the cancer is called HER2 positive.

Test results

Some breast cancers have high numbers of hormone receptors, HER2 receptors, or both. Other breast cancers have normal numbers of estrogen, progesterone, and HER2 receptors. In these cases, the cancer is called triple-negative breast cancer. Be sure your treatment team explains your test results and how they will guide treatment. Always ask for a copy of your test results.
Genetic counseling

About 10 out of 100 breast cancers are due to changes in genes that are passed down from a parent to a child. This is called hereditary breast cancer. Using your age, medical history, and family history, your doctor will assess how likely you are to have hereditary breast cancer. If the likelihood is high, you should see a genetic counselor.

A genetic counselor is an expert in changes within genes that are related to disease. The counselor can tell you more about how likely you are to have hereditary breast cancer. He or she may suggest that you undergo genetic testing to look for changes in genes that increase your chances of developing breast cancer.

Hereditary breast cancer is most often caused by mutations in the BRCA1 and BRCA2 genes. Normal BRCA genes help to prevent tumor growth by fixing damaged cells and helping cells grow normally. Genetic testing can tell if you have a BRCA or another mutation. Your test results may be used to guide treatment planning.

Some abnormal changes in genes, called VUS (variants of unknown significance), are not fully understood by doctors. Your doctors may know of research that aims to learn more. If interested, ask your doctors.
Review

- Physical exams and blood tests look for signs of disease.
- Imaging tests allow your doctor to see how far the cancer has spread.
- Testing of hormone and HER2 receptors can help with treatment planning.
- Genetic counseling may help you decide whether to be tested for hereditary breast cancer.
Oncologists are cancer doctors trained to use systemic therapy to treat breast cancer. Systemic therapy is the use of drugs to treat cancer throughout the body. While metastatic breast cancer is unlikely to be cured, long-term cancer control is often possible with systemic therapy.

Some women with metastatic breast cancer live for years and even decades with a high quality of life. Part 3 describes the types of treatment used for metastatic breast cancer.

**Hormone therapy**

Estrogen and progesterone are hormones that cause some breast cancer cells to make more cancer cells. Estrogen is mostly made by the ovaries and made in small amounts by the adrenal glands, liver, and body fat. Progesterone is also mostly made by the ovaries. Blocking these hormones from working or lowering hormone levels can help stop breast cancer from growing. There are many types of hormone therapy used to treat early breast cancer.

**Antiestrogens**

Antiestrogens are drugs that stop the effect of estrogen on cancer cell growth. Tamoxifen and toremifene are antiestrogens that treat breast cancer by attaching to estrogen receptors and blocking estrogen from attaching. These drugs are also called SERMs (selective estrogen receptor modulators). Fulvestrant is an antiestrogen that also blocks and reduces the number of estrogen receptors. This drug is also called a SERD (selective estrogen receptor down-regulator).
Aromatase inhibitors
Aromatase inhibitors are drugs that lower estrogen levels in the body. These drugs work by blocking a protein that makes estrogen. However, they can’t stop the ovaries of premenopausal women from making estrogen. For this reason, these drugs are only used among postmenopausal women. Three drugs in this category are anastrozole, letrozole, and exemestane. In very special circumstances, exemestane is given with everolimus. Read Targeted therapy on page 22 for more information.

Hormones
Although not used often, some doctors prescribe high doses of hormones to treat breast cancer. Such hormones include megestrol acetate, fluoxymesterone, and ethinyl estradiol. It is not known how high doses of hormones stop breast cancer cells with hormone receptors from growing.

Ovarian ablation
The ovaries are the main source of estrogen and progesterone in premenopausal women. Removing them stops most of the hormones from being made. Surgery that removes both ovaries is called a bilateral oophorectomy. Radiation therapy to the ovaries also stops the ovaries from making estrogen and progesterone, but isn’t often used. Both treatments are forms of ovarian ablation.

Ovarian suppression
Ovarian suppression is when drugs are used to tell the ovaries to make less estrogen. Ovarian suppression is achieved with drugs called LHRH (luteinizing hormone-releasing hormone) agonists. LHRH is a hormone made in the brain that helps to regulate estrogen production in the ovaries. LHRH agonists stop LHRH from being made, which stops the ovaries from making more estrogen. Goserelin acetate and leuprolide are LHRH agonists and should be given as monthly injections under the skin.
Chemotherapy

Some chemotherapy drugs kill cancer cells by damaging their DNA (deoxyribonucleic acid) or disrupting the making of DNA. Other drugs interfere with cell parts that are needed for making new cells.

Many chemotherapy drugs work when cells are in an active growth phase. During the active growth phase, cells grow and divide to form a new cell. Chemotherapy drugs that disrupt the growth phase work well for cancer cells that are growing and dividing quickly. Other chemotherapy drugs work whether cells are in a growth or resting phase. Chemotherapy can kill both cancer and normal cells.

There are four classes of chemotherapy drugs used to treat metastatic breast cancer:

- Alkylating agents – (carboplatin, cisplatin, cyclophosphamide) damage DNA by adding a chemical to it.

Systemic drugs for stage IV breast cancer

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<th>Generic name</th>
<th>Brand name</th>
<th>Type of systemic therapy</th>
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<td>Ado-trastuzumab emtansine</td>
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Continues on page 21.
• Anthracyclines – (doxorubicin, epirubicin) damage and disrupt the making of DNA.

• Antimetabolites – (capecitabine, gemcitabine, fluorouracil, methotrexate) prevent the "building blocks" of DNA from being used.

• Microtubule inhibitors – (docetaxel, emtansine, eribulin, ixabepilone, paclitaxel, vinorelbine) stop a cell from dividing into two cells.

**Systemic drugs (Continued from page 20.)**

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Targeted therapy

Targeted therapy stops the action of molecules that start the growth of cancer cells. Targeted therapy is less likely to harm normal cells than chemotherapy. There are six targeted therapy drugs used to treat stage IV breast cancer:

**Trastuzumab and pertuzumab**
Both drugs are used to treat HER2-positive breast cancer. They work by attaching to the end of HER2 that is outside the cell, but each drug attaches to a different part of HER2. This stops HER2 from being activated. These two drugs also attract immune cells that help to kill the cancer cells.

**Ado-trastuzumab emtansine**
This drug is a combination of trastuzumab and the chemotherapy drug emtansine. If emtansine was given alone, it would affect any cell since it works when cells are growing or resting. However, since emtansine is attached to trastuzumab, it affects mostly HER2-positive cancer cells since the drug attaches to HER2 receptors. This drug was also made so that emtansine would not be released into the blood stream. Instead, emtansine is released inside of HER2-positive cancer cells.

**Lapatinib**
Lapatinib also treats HER2-positive breast cancer but stops the action of HER2 from within the cancer cell. Lapatinib works by attaching to the end of HER2

Supportive care for bone metastases

Your bones are at risk for injury and disease when breast cancer spreads to them. Such health problems include bone fractures, bone pain, and squeezing (compression) of the spinal cord. High levels of calcium in the blood, called hypercalcemia, may also occur. Denosumab (Xgeva™), zoledronic acid (Zometa®), and pamidronate (Aredia®) are drugs that may stop these problems from starting.

However, these drugs may cause damage to the jaw bone (called osteonecrosis). Some medications, including chemotherapy, may increase your chances for jaw osteonecrosis. Oral problems, such as periodontal disease and dental abscess, also may increase your risk. You should have a dental exam and get treatment for any dental problems before starting these drugs. It is recommended that you take these drugs with calcium and vitamin D.
that is inside the cancer cell. This blocks substances within the cell from attachimg to HER2 and starting cell growth.

**Bevacizumab**
Cancer cells need the food and oxygen in blood to grow. Thus, cancer cells send out signals for new blood vessels to grow into the tumor. These signals are called [VEGFs](https://www.nccn.org/) (vascular endothelial growth factor). Bevacizumab attaches to VEGF, which stops these signals from causing new blood vessels to form.

The U.S. FDA (Food and Drug Administration) has removed its approval of bevacizumab for stage IV breast cancer. However, NCCN experts agree that science has shown that adding bevacizumab to some chemotherapy agents slows cancer growth. However, bevacizumab with chemotherapy does not prolong life.

**Everolimus**
Inside of cells are [protein kinases](https://www.nccn.org/), called mTor. Protein kinases are molecules that move chemicals, called phosphates, from one molecule to another. The phosphate “turns on” the second molecule. Everolimus stops mTor from transferring the phosphate, which then stops the cell from receiving signals to grow. Everolimus is given with exemestane among women who meet very specific criteria. Ask your doctor for more information.
Review

- Three classes of drugs are used to treat metastatic breast cancer: hormone therapy, chemotherapy, and targeted therapy.
- Hormone therapy stops the growth of cancer cells that is caused by hormones.
- Chemotherapy damages, disrupts, or interferes with cell parts needed to make new cells.
- Targeted therapy stops the action of molecules that start the growth of cancer cells.
Part 4 is a guide to which treatment options are best for different types of metastatic breast cancer. Clinical trials are first discussed. Clinical trials are the preferred treatment option for all stages of breast cancer. The other treatment options that are presented are based on features of the cancer and other information about you. Treatment for metastatic breast cancer works best when it is tailored to you.

Clinical trials

New tests and treatments aren’t offered to the public as soon as they’re made. They need to be studied. A clinical trial is a type of research that studies a test or treatment. Clinical trials study how safe and helpful tests and treatments are. When found to be safe and helpful, they may become tomorrow’s standard of care. Because of clinical trials, the tests and treatments in this book are now widely used to help patients.

New tests and treatments go through a series of clinical trials to make sure they’re safe and work. Without clinical trials, there is no way to know if a test or treatment is safe or helpful. Clinical trials have four phases. Examples of the four phases for treatment are:

- Phase I trials – aim to find the best dose of a new 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 the standard treatment.

• Phase IV trials – test new drugs approved by the FDA in many patients with different types of cancer.

Joining a clinical trial has benefits. First, you’ll have access to the most current cancer care. Second, you will receive the best management of care. Third, the results of your treatment—both good and bad—will be carefully tracked. Fourth, you may help other patients with cancer.

Clinical trials have risks, too. Like any test or treatment, there may be side effects. Also, new tests or treatments may not help. Another downside may be that paperwork or more trips to the hospital are needed.

To join a clinical trial, you must meet the conditions of the study. Patients in a clinical trial are often alike in terms of their cancer and general health. This is to know that any progress is because of the treatment and not because of differences between patients. To join, you’ll need to review and sign a paper called an informed consent form. This form describes the study in detail, including the risks and benefits.

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. You can also find clinical trials through the websites listed in Part 6.

Recommended treatment

For metastatic breast cancer, the treatment approach often is to use one treatment regimen until it stops working and then use another. This allows long-term cancer control for many women. Which systemic therapy is first used is decided by many factors.

Next, the NCCN treatment recommendations are listed by hormone receptor status—hormone receptor–positive, hormone therapy–refractory, and hormone receptor–negative tumors. Hormone therapy-refractory tumors are those that didn’t respond during three hormone regimens given one right after the other.
Hormone receptor–positive tumors

<table>
<thead>
<tr>
<th>Hormone therapy</th>
<th>Menopausal status</th>
<th>Treatment options</th>
</tr>
</thead>
</table>
| None in past year | Premenopausal      | • Ovarian ablation or suppression + aromatase inhibitor  
|                  |                   | • Ovarian ablation or suppression + antiestrogen, or  
|                  |                   | • SERMs alone |
|                  | Postmenopausal    | • Aromatase inhibitor, or  
|                  |                   | • Antiestrogen |
| Took in past year | Premenopausal      | • Ovarian ablation or suppression + aromatase inhibitor  
|                  |                   | • Ovarian ablation or suppression + antiestrogen, or  
|                  |                   | • Ovarian ablation or suppression + hormones |
|                  | Postmenopausal    | • Aromatase inhibitor, or  
|                  |                   | • Antiestrogen  
|                  |                   | • Hormones |

This chart lists the treatment options for tumors that are hormone receptor–positive. Many of these cancers first spread only to the bone or to limited areas. **Hormone therapy** often works well for these cancers. However, if the cancer is quickly spreading within internal organs, such as the liver or lungs, you may be first given **chemotherapy** to quickly control the cancer growth and then be given hormone therapy. Options for hormone therapy are based on whether you had this treatment in the past year and your menopausal status.

**Menopause** is the point in time when you won’t have another menstrual period again. When a woman hasn’t had a period in one or more years, she’s often considered **postmenopausal**. Breast cancer doctors also define postmenopausal as when the ovaries make low amounts of estrogen. If you get menstrual periods, you are **premenopausal**. If you don’t get periods, the amount of estrogen or **FSH** (follicle-stimulating hormone) in your blood may need to be tested to confirm your menopausal status. If you have been taking **LHRH agonists**, it isn’t possible to know your menopausal status until you’re off the drugs for awhile.

If you are premenopausal, you may have **ovarian ablation or suppression** to lower the levels of **hormones** in your body. Thus, you will become postmenopausal. Next, you should receive hormone therapy that is given to postmenopausal women. If you haven’t had hormone therapy in the past year, a second option is to take a **SERM**.

If you are postmenopausal, an **aromatase inhibitor** is often first given if you’ve had no hormone therapy in the past year. The other option is **antiestrogens**—SERMs or **SERD**. If you took hormone therapy in the past year, the next hormone therapy you will take depends on what you took before. Options include an aromatase inhibitor, an antiestrogen, or a hormone.
Next steps: You should stay on hormone therapy until the tumor doesn’t respond to three back-to-back hormone regimens or cancer in the internal organs causes symptoms. At this point, chemotherapy may be given. Read *Hormone therapy–refractory tumors* for more information.
Hormone therapy–refractory tumors

<table>
<thead>
<tr>
<th>HER2 status</th>
<th>Treatment options</th>
</tr>
</thead>
<tbody>
<tr>
<td>HER2 negative</td>
<td>• Chemotherapy</td>
</tr>
<tr>
<td>HER2 positive</td>
<td>• Trastuzumab and pertuzumab with paclitaxel or docetaxel, or</td>
</tr>
<tr>
<td></td>
<td>• Trastuzumab ± chemotherapy</td>
</tr>
</tbody>
</table>

This chart is for women with hormone receptor–positive tumors that haven’t responded to three back-to-back hormone regimens. Treatment options are based on HER2 status. Chemotherapy is an option for HER2-negative tumors. Chemotherapy regimens for HER2-negative tumors are listed in Part 5. If the cancer grows on the first regimen, a second regimen may be given.

If the cancer is HER2-positive, targeted therapy may be used with chemotherapy or given alone. Preferred first-line treatment for HER2-positive disease is trastuzumab and pertuzumab with paclitaxel or docetaxel. Otherwise, trastuzumab with or without chemotherapy may be given. If the cancer grows during either of these regimens, treatment for HER2-positive breast cancer should be continued. Ado-trastuzumab emtansine is preferred but other regimens listed in Part 5 may be given.

Next steps: If the cancer doesn’t shrink during three back-to-back regimens, stopping cancer treatment and receiving supportive care may be your best option. Supportive care is also recommended if your general health becomes poor. Supportive care is used to relieve symptoms from the cancer or treatments and does not treat the cancer.
### Hormone receptor–negative tumors

<table>
<thead>
<tr>
<th>HER2 status</th>
<th>Area with cancer</th>
<th>Treatment options</th>
</tr>
</thead>
<tbody>
<tr>
<td>HER2 negative</td>
<td>Bones, supportive soft tissue, or internal organs without symptoms</td>
<td>• Hormone therapy, or&lt;br&gt;• Chemotherapy</td>
</tr>
<tr>
<td>Internal organs with symptoms</td>
<td>• Chemotherapy</td>
<td></td>
</tr>
<tr>
<td>HER2 positive</td>
<td>Bones, supportive soft tissue, or internal organs without symptoms</td>
<td>• Hormone therapy,&lt;br&gt;• Trastuzumab and pertuzumab with paclitaxel or docetaxel, or&lt;br&gt;• Trastuzumab ± chemotherapy</td>
</tr>
<tr>
<td>Internal organs with symptoms</td>
<td>• Trastuzumab and pertuzumab with paclitaxel or docetaxel, or&lt;br&gt;• Trastuzumab ± chemotherapy</td>
<td></td>
</tr>
</tbody>
</table>

This chart lists the treatment for tumors that tested hormone receptor–negative. Treatment options are based on HER2 status and where the cancer has spread. Areas of cancer spread include bones, supportive soft tissue, and internal organs.

Examples of supportive soft tissue include muscle, fat, and nerves. Examples of internal organs include the liver, brain, and lungs. When cancer spreads throughout an organ, the organ won’t work as well and symptoms will appear.

For either HER2 status, hormone therapy is an option for cancer in the bones, soft tissues, and internal organs that isn’t causing symptoms. This may seem wrong since, in other NCCN books, only women with hormone receptor–positive cancer were recommended to have hormone therapy. Hormone therapy is now recommended because sometimes a metastasis is hormone receptor–positive and the tests are wrong.

Hormone therapy is especially recommended if test results were negative but the cancer acts like it is hormone receptor–positive. Signs of hormone receptor–positive cancer include a long disease-free period after initial treatment, few sites of recurrence, and breast cancer in older women.

Another reason to have hormone therapy is that it has fewer side effects than chemotherapy. Since chemotherapy does not cure metastatic cancer, treatments with the fewest side effects that can still control cancer growth are recommended. The options for hormone therapy are listed under Hormone receptor–positive tumors.

Chemotherapy is an option for all hormone receptor–negative, HER2-negative cancers. Chemotherapy regimens for HER2-negative tumors are listed in Part 5. If the cancer grows on the first regimen, a second regimen may be given.

If the cancer is HER2 positive, targeted therapy may be used with chemotherapy or given alone. Trastuzumab and pertuzumab with paclitaxel or docetaxel is the preferred treatment option for HER2–positive disease. Otherwise, trastuzumab with or without chemotherapy may be given.
If the cancer grows during either of these regimens, ado-trastuzumab emtansine is preferred as the next treatment option. Other options are trastuzumab with another chemotherapy regimen or trastuzumab with lapatinib. Chemotherapy regimens for HER2–positive tumors are listed in Part 5.

Next steps: If the cancer doesn’t respond to three back-to-back regimens, stopping cancer treatment and receiving supportive care may be your best option. Supportive care is also recommended if your general health becomes poor. Supportive care is used to relieve symptoms from the cancer or treatments and does not treat the cancer.

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**Review**

- Clinical trials give women access to new tests and treatments. They are the preferred treatment for metastatic breast cancer.

- Other treatment recommendations are based on features of the cancer and facts about you.

- For metastatic breast cancer, the treatment approach often is to use one treatment regimen until it stops working and then use another. This allows long-term cancer control for many women.
Receiving cancer treatment
Part 5 describes how treatments are given so you will better know what to expect during treatment. Some side effects of treatments are also listed. However, ask your treatment team for a complete list of common and rare side effects. Part 5 also describes the tests recommended for checking treatment results and how often these tests may be given.

### External radiation therapy

Radiation therapy is given after chemotherapy is finished. It is okay to take trastuzumab during radiation therapy. If you didn’t have chemotherapy, radiation therapy follows surgery. If you are pregnant, you may have radiation after your baby is born.

The most common type of radiation therapy used for breast cancer is **EBRT** (external beam radiation therapy). This type of therapy uses a machine outside the body to deliver radiation. Radiation beams are aimed at the tumor with help from ink marks or tiny tattoos on the skin.

Before EBRT, pictures (images) of the breast region should be taken with a **CT** scan. See page 12 for information on CT scans. Imaging the region and designing the radiation treatment before EBRT is called **simulation**. Your doctors will use the images to decide the radiation dose and to shape the radiation beams. Beams are shaped with computer software...
and hardware added to the radiation machine. The beams are shaped so that normal tissue is spared.

There are other methods that can be used to spare normal tissue. Moreover, there are ways to protect your heart if radiation will be given in that area. Ask your doctor what methods will be used for your treatment. Some methods are:

- Directing the beam not toward the heart,
- Lying face down during treatment,
- Holding your breath at times during treatment,
- Use of devices that keep you from moving during treatment,
- EBRT machines that give treatment only when the tumor is in the right spot, and
- EBRT machines that deliver very precise radiation beams. 3D machines deliver beams matched to the shape of the tumor. IMRT (intensity-modulated radiation therapy) uses small radiation beams of different strengths based on the thickness of the tissue.

You will be alone while a technician operates the EBRT machine from a nearby room. An EBRT machine is shown in Figure 7. He or she will be able to see, hear, and speak with you at all times. As treatment is given, you may hear noises. A session can take between 15 to 30 minutes. Radiation therapy is often given 5 days a week for 5 to 7 weeks but may be done quicker for some women.

Figure 7. EBRT machine

Radiation is delivered using an EBRT machine.
Hormone therapy

Bilateral oophorectomy
There are two types of surgery that can remove your ovaries. Your doctor will recommend which type of surgery you should have. Before either surgery, you will be asked to stop eating, drinking, and taking some medicines for a short period of time.

Open surgery removes your ovaries through one large cut in your abdomen while you’re under general anesthesia. After this surgery, you may stay in the hospital for a couple of days. Laparoscopic surgery removes your ovaries through several small cuts. Local or general anesthesia may be used. After this surgery, you may leave the hospital the same day or the day after. After either surgery, you will have some pain, swelling, and scars. The pain and swelling will lessen over time.

Radiation therapy
Radiation therapy uses high-energy rays to destroy cells in your ovaries. It is given for 15 to 30 minutes each day over a few days. You may feel sick and have diarrhea. It'll take some time after treatment for your ovaries to stop working and stop making hormones. In the meantime, you should use birth control to prevent pregnancy.

Drug therapy
Goserelin and leuprolide are drugs used to shut down the ovaries. These drugs are given as monthly injections under the skin. The antiestrogens—tamoxifen, toremifene, and fulvestrant—are pills that are taken every day during the course of treatment. The aromatase inhibitors—anastrozole, letrozole, and exemestane—are also pills that are taken every day. Antiestrogens and aromatase inhibitors may work better if taken at the same time each day.

Menopausal symptoms
For many women, hormone therapy causes symptoms of menopause. Menopausal symptoms include hot flashes, vaginal discharge or dryness, sleep problems, weight gain, hair thinning, fatigue, and changes in mood. You may have different symptoms from other women.

Tamoxifen also has two rare but more serious side effects: 1) cancer of the uterus; and 2) blood clots. For most women with breast cancer, the benefits of taking tamoxifen far outweigh the risks. Aromatase inhibitors don’t cause cancer and very rarely cause blood clots. However, they can weaken your bones (called osteoporosis) and cause bone fractures. Checking your bone health with regular bone mineral density tests can show bone weakness before fractures occur. Your doctor can order medicine to strengthen your bones if necessary.
Chemotherapy

Before starting chemotherapy, your doctor may ask you to stop taking some of your medicines, vitamins, or both. Some of these treatments can cause chemotherapy to not work as well or may cause health problems while on chemotherapy. You may also have to change what you drink and eat. If you smoke, it’s important that you stop.

Chemotherapy drugs for metastatic breast cancers are liquids that are injected into a vein or are made as pills to be swallowed. The injection may be one fast shot of drugs into a vein or may be a slow drip called an infusion. Chemotherapy can also be given through a needle surgically placed in the chest or the arm.

You may receive one or more chemotherapy drugs. When only one drug is used, it is called a single agent. However, drugs differ in the way they work, so often more than one drug is used. A combination regimen is the use of two or more chemotherapy drugs.

Chemotherapy is given in cycles of treatment days followed by days of rest. The cycles vary in length depending on which drugs are used. Giving chemotherapy in cycles gives your body a chance to recover after receiving chemotherapy.

You will need to go to a chemotherapy center to receive the drugs. How long your visit will be depends on which drugs you will get. It can take a few minutes or a few hours to finish a dose of chemotherapy.

The reactions to chemotherapy differ among women. Some women have many side effects. Other women have few. Some side effects can be very serious while others can be unpleasant but not serious.

Side effects of chemotherapy depend on the drug type, amount taken, length of treatment, and the person. In general, side effects are caused by the death of fast-growing cells. These cells are found in the hair follicles, gut, mouth, and blood. Thus, common side effects of chemotherapy include low blood cell counts, not feeling hungry, nausea, vomiting, diarrhea, hair loss, and mouth sores.

During chemotherapy cycles, you may be given other drugs to help you feel your best. You may be given drugs to fight nausea and vomiting. You may also receive filgrastim to increase the number of white blood cells to normal levels.

If you’re still premenopausal, chemotherapy may cause menopause. Even if menstrual periods return after chemotherapy, you may still be unable to have babies. However, don’t depend on chemotherapy for birth control. You may become pregnant while on chemotherapy, which can cause birth defects. If you had menstrual periods before chemotherapy, use birth control but not birth control with hormones (eg, “the pill”).

The recommended regimens for HER2-negative and HER2–positive tumors are listed on the next pages. They are divided by “preferred” and “other” regimens by NCCN experts based on how well they work, side effects, and treatment schedules.
## Chemotherapy regimens | HER2–negative tumors

<table>
<thead>
<tr>
<th>Preferred single agents</th>
<th>Length of a cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doxorubicin</td>
<td>7 or 21 days</td>
</tr>
<tr>
<td>Pegylated liposomal doxorubicin</td>
<td>28 days</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>7 or 21 days</td>
</tr>
<tr>
<td>Capecitabine</td>
<td>21 days</td>
</tr>
<tr>
<td>Gemcitabine</td>
<td>28 days</td>
</tr>
<tr>
<td>Vinorelbine</td>
<td>7 days</td>
</tr>
<tr>
<td>Eribulin</td>
<td>21 days</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other single agents</th>
<th>Length of a cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>28 days</td>
</tr>
<tr>
<td>Carboplatin</td>
<td>21 to 28 days</td>
</tr>
<tr>
<td>Docetaxel</td>
<td>21 or 56 days</td>
</tr>
<tr>
<td>Albumin-bound paclitaxel</td>
<td>21 or 28 days</td>
</tr>
<tr>
<td>Cisplatin</td>
<td>21 days</td>
</tr>
<tr>
<td>Epirubicin</td>
<td>21 days</td>
</tr>
<tr>
<td>Ixabepilone</td>
<td>21 days</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Combination regimens</th>
<th>Length of a cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAF/FAC (cyclophosphamide/doxorubicin/fluorouracil)</td>
<td>21 (FAC) or 28 (CAF) days</td>
</tr>
<tr>
<td>FEC (fluorouracil/epirubicin/cyclophosphamide)</td>
<td>28 days</td>
</tr>
<tr>
<td>AC (doxorubicin/cyclophosphamide)</td>
<td>21 days</td>
</tr>
<tr>
<td>EC (epirubicin/cyclophosphamide)</td>
<td>21 days</td>
</tr>
<tr>
<td>CMF (cyclophosphamide/methotrexate/fluorouracil)</td>
<td>28 days</td>
</tr>
<tr>
<td>Docetaxel/capecitabine</td>
<td>21 days</td>
</tr>
<tr>
<td>GT (gemcitabine/paclitaxel)</td>
<td>21 days</td>
</tr>
<tr>
<td>Gemcitabine/carboplatin</td>
<td>21 days</td>
</tr>
<tr>
<td>Paclitaxel/bevacizumab</td>
<td>28 days</td>
</tr>
</tbody>
</table>
### Chemotherapy regimens | HER2–positive tumors

<table>
<thead>
<tr>
<th>Preferred first-line treatment</th>
<th>Length of a cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pertuzumab + trastuzumab + docetaxel</td>
<td>21 days</td>
</tr>
<tr>
<td>Pertuzumab + trastuzumab + paclitaxel</td>
<td>21 days</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other first-line treatment</th>
<th>Length of a cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trastuzumab + paclitaxel ± carboplatin</td>
<td>21 or 28 days</td>
</tr>
<tr>
<td>Trastuzumab + docetaxel</td>
<td>21 days</td>
</tr>
<tr>
<td>Trastuzumab + vinorelbine</td>
<td>7 days</td>
</tr>
<tr>
<td>Trastuzumab + capecitabine</td>
<td>21 days</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Second-line treatment</th>
<th>Length of a cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ado-trastuzumab emtansine (preferred)</td>
<td>21 days</td>
</tr>
<tr>
<td>Lapatinib + capecitabine</td>
<td>21 days</td>
</tr>
<tr>
<td>Trastuzumab + capecitabine</td>
<td>21 days</td>
</tr>
<tr>
<td>Trastuzumab + lapatinib</td>
<td>7 or 21 days</td>
</tr>
<tr>
<td>Trastuzumab + other agents</td>
<td>Depends on agents</td>
</tr>
</tbody>
</table>
Targeted therapy

Trastuzumab
Allergic reactions are common with the first or second dose of trastuzumab. You may need to take medicine for allergies. You may also have a mild flu-like response to the first dose of trastuzumab that includes fever, chills, headache, muscle aches, and nausea. This response is less common with the second and third doses. Other side effects may include damage to the heart and rarely to the lungs.

Ado-trastuzumab emtansine
Ado-trastuzumab emtansine is given by infusion. It takes about 90 minutes to get the first dose and 30 minutes for later doses. It is given every three weeks. Common side effects include headache, nausea, tiredness, diarrhea or constipation, nosebleeds, and pain in your muscles, joints, or bones. Other side effects may include damage to the heart, liver, or lungs.

Pertuzumab
Pertuzumab is given by infusion. It takes about 60 minutes to get the first dose and about 30 to 60 minutes for later doses. Pertuzumab is given every three weeks. Common side effects of pertuzumab are diarrhea, nausea, and feeling tired and weak. Less common side effects include skin rash, low white blood counts, mouth sores, and hair loss. It is not yet clear if pertuzumab damages the heart although similar drugs do.

Lapatinib
Lapatinib is made as a pill that is taken every day one hour before or after a meal. Common side effects include diarrhea and skin rash. Your hands and feet may become red, swollen, numb, and painful. Less common side effects include fatigue, vomiting, headaches, shortness of breath, and heartburn. Other side effects include heart, liver, and lung problems.

Lapatinib
Lapatinib is given by infusion. It takes about 90 minutes to get the first dose and 30 minutes for later doses. It is given every three weeks. Common side effects of lapatinib are high blood pressure, diarrhea, and feeling tired and weak. You might also have nosebleeds, shortness of breath, nausea, and vomiting. Rare but serious effects include stroke, heart attack, kidney damage, holes in the intestine, and bleeding within the body.

Everolimus
Everolimus is a pill that is taken around the same time every day. Common side effects include diarrhea, tiredness, mouth sores, skin rash, cough, and low blood counts. Serious side effects include other cancers, lung problems, infections, and kidney failure.
Checking treatment results

While being treated for stage IV breast cancer, testing of treatment results is recommended. Testing should occur on a regular basis to check if the treatment is working and not causing serious side effects. The recommended schedule of tests is in the table below.

Different types of tests are used to check treatment results. Some of these tests were recommended for treatment planning in Part 2. Your doctor will ask you about any new or worse symptoms. He or she will also perform a physical exam and measure your body weight. Your state of general health will be rated using a performance status scale. There are two scales commonly used: ECOG (Eastern Cooperative Oncology Group) Performance Scale and the KPS (Karnofsky Performance Status Scale). For either scale, your doctor will choose a score that best represents your health.

Blood samples will need to be drawn to perform three tests. CBC is used to assess the extent of cancer growth within bones. Liver functioning tests are used to assess the extent of cancer growth within the liver and other organs.

Your blood may also be tested for proteins that can indicate whether or not treatment is working. These proteins are called tumor markers. Examples of tumor markers include CEA (carcinoembryonic antigen), CA 15-3 (cancer antigen 15-3), and CA 27.29 (cancer antigen 27.29). Rising levels of tumor markers across a series of tests suggest that treatment isn’t working.

Three imaging tests may be used to check treatment results. CT, PET/CT, and bone scans can show larger or new areas of cancer. PET/CT scans may be used less often because of a lack of standards that detect cancer growth.

The best way to find cancer growth is to repeat tests on a regular schedule. A suggested schedule of tests that was used in research studies has been listed. This schedule may be changed to fit your situation. Testing should be done if there are signs of cancer growth or when starting a new treatment despite when testing was last done.

Testing schedule

<table>
<thead>
<tr>
<th>Test name</th>
<th>During hormone therapy</th>
<th>During chemotherapy</th>
<th>After cancer progression</th>
<th>Before new treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td>Every 2–3 months</td>
<td>Before each cycle</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Physical exam</td>
<td>Every 2–3 months</td>
<td>Before each cycle</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Weight</td>
<td>Every 2–3 months</td>
<td>Before each cycle</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Performance status</td>
<td>Every 2–3 months</td>
<td>Before each cycle</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>CBC</td>
<td>Every 2–3 months</td>
<td>Before each cycle</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Liver function</td>
<td>Every 2–3 months</td>
<td>Before each cycle</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Tumor markers</td>
<td>Maybe</td>
<td>Maybe</td>
<td>Maybe</td>
<td>Maybe</td>
</tr>
<tr>
<td>CT scan</td>
<td>Every 2–6 months</td>
<td>Every 2–4 cycles</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Bone scan</td>
<td>Every 4–6 months</td>
<td>Every 4 cycles</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>PET/CT scan</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Maybe</td>
<td>Maybe</td>
</tr>
</tbody>
</table>
Review

- The most common type of radiation therapy used for breast cancer is EBRT.
- Hormone therapy for metastatic breast cancer includes surgery, radiation therapy, or drugs.
- Recommended chemotherapy regimens are based on whether the cancer is HER2-positive or HER2-negative.
- There are 6 targeted therapy drugs used for metastatic breast cancer.
- Testing during treatment should occur on a regular basis to check if treatment is working and not causing serious side effects.
Making treatment decisions
Having metastatic breast cancer can be very stressful. Besides dealing with the fear that comes with having a life-threatening disease, you have to learn about tests and treatments. You will need to decide whether to accept your doctors’ treatment plan or seek another opinion.

Parts 2 through 5 gave the recommendations of the breast cancer experts from NCCN. Part 6 aims to help you make treatment decisions that affect both your physical and emotional quality of life.

Get a treatment plan

Learning you have cancer starts an unplanned journey. A treatment plan is like having a roadmap for your journey. It is a written course of action through treatment and beyond. It can help you, your loved ones, and your treatment team.

Parts of a treatment plan
A treatment plan addresses all cancer care needs while respecting your beliefs, wishes, and values. It is likely to change and expand as you go through treatment. The plan will include the role of your doctors and how you can help yourself. A treatment plan often has the following parts:

Cancer information
Cancer can greatly differ even when people have a tumor in the same organ. Test results that describe the cancer are reported in the treatment plan. Such test results include the cancer site, cell type, cancer stage, and other features of the cancer. Read Parts 2 and 5 for the tests used for metastatic breast cancer.
Your treatment team
Excellent care for metastatic breast cancer will include a team approach. When you see your medical oncologist for the first time, ask who is on your treatment team. Also ask to have the names and contact information of your health care providers included in the treatment plan.

Having a nurse on your treatment team can be very helpful, especially for questions about treatment. If you undergo ovarian ablation, your surgeon or radiation oncologist should be on your team. Your primary care doctor can also act on your behalf and treat health problems better if informed about your cancer care. However, don’t hesitate to tell your oncologist your feelings. Ask for a referral to a social worker to help with any emotional and social issues. Also ask for an expert in palliative care so that any pain or other symptoms can be addressed.

Cancer treatment
There is no single treatment practice that is best for all patients. There is often more than one treatment option along with clinical trial options. Clinical trials study how well a treatment works and its safety. Treatment planning takes many factors into account, such as:

- Location of the cancer,
- Your general health,
- Treatment side effects,
- Costs of treatment,
- Changes to your life,
- What you want from treatment, and
- Your feelings about side effects.

A guide to treatment options can be found in Part 4. The cancer treatment that you agree to have should be reported in the treatment plan. It is also important to note the goal of treatment and the chance of a good treatment response. In addition, all known side effects should be listed and the time required for treatment should be noted. Read Part 5 to learn about the side effects of treatment.

Your treatment plan may change because of new information. You may change your mind about treatment, tests may find new results, or how well the treatment is working may change. Any of these changes may require a new plan.
Becoming a “cancer patient”

Hearing, “You have cancer” is likely to be life-changing.

Some challenges may include managing doctor visits, figuring out how to care for your kids, missing work, and feeling a loss of control. Some people try to keep their life as normal as they can. Others change their life a lot. However, being a patient can feel like having a new job. It’s a job that requires much time and energy. This can be hard.

Use your strengths, talents, and resources to help you cope. Maintain warm relationships with family and friends. Accept the support offered to you and reach out for more help if you need it. Most people would be happy to hear what you need. Make a list for them of things that would help you.

If you are a person of faith, your personal beliefs and faith community can help. There are also professionals in mental health, social work, and pastoral services who are able to assist you. You can also start attending support groups for women with metastatic breast cancer. Visit the websites listed on page 52 for more information.
Stress and symptom control
You will find that living with metastatic breast cancer is complex and brings many physical and emotional challenges. Cancer or its treatment can cause bothersome symptoms. Also, the stress of having cancer can also cause symptoms. Helping you to be comfortable and stay active are key goals of the treatment plan. There are ways to treat many symptoms, so tell your treatment team about any symptoms you have. Some of the challenges you may face are addressed next.

You may have already lost some nights of sleep. This is common. The stress of learning that you have metastatic breast cancer and worrying about the future takes its toll. You may lose more sleep while waiting to have treatment and then worry about whether the treatment will work. Getting less sleep can affect your mood, conversations, and ability to do things. If possible, allow yourself to rest, let people do things for you, and talk with your doctor about sleep medication. Behavioral sleep medicine—a type of talk therapy—may also help.

Feelings of anxiety and depression are common among patients with cancer. You may feel anxious before testing and while waiting for the results. Likewise, you may have a passing depression during a hard part of treatment. Feeling distressed may be a minor problem or it may be more serious. Serious or not, tell your treatment team so that you can get help if needed. Help can include support groups, talk therapy, or medication. Some people also feel better by exercising, talking with loved ones, or relaxing. Your treatment team has information to help you.

Having cancer may cause you to feel helpless, fearful, alone, or overwhelmed. There are ways to manage this stress. At your cancer center, cancer navigators, social workers, and other experts can help. There may also be helpful community resources, such as support groups and wellness centers.

Financial stress is common. You may be unemployed or miss work during treatment. You may have too little or no health insurance. Talk with your treatment team about work, insurance, or money problems. They will include information in the treatment plan to help you control your finances.

Advance care
Talking with your doctor about your prognosis can help with treatment planning. When cancer can’t be cured, a care plan for the end of life can be made. However, such talks often happen too late or not at all. Your doctor may delay these talks for fear that you may lose hope, become depressed, or have a shorter survival. Studies suggest that these fears are wrong. Instead, there are many benefits to advance care planning. It is useful for:

- Knowing what to expect,
- Making the most of your time,
- Lowering the stress of caregivers,
- Having your wishes followed,
- Having a better quality of life, and
- Getting good care.

Advance care planning starts with an honest talk between you and your doctors. 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 at what point you’d want to stop cancer treatment, if at all. You can also decide what treatments you’d want for symptom relief, such as surgery or drugs.

Another part of the planning involves hospice care. Hospice care doesn’t include treatment to fight the cancer but rather to reduce symptoms caused by cancer. Hospice care may be started because you aren’t interested in more cancer treatment, no other cancer treatment is available, or because you may be too sick for cancer treatment. Hospice care allows you to have the best quality of life possible. Care is
Treatment decisions

Decide your role

You can choose to have hospice care at home or at a hospice center.

An advance directive describes the treatment you’d want if you weren’t able to make your wishes known. It also can name a person whom you’d want to make decisions for you. It is a legal paper that your doctors have to follow. It can reveal your wishes about life-sustaining machines, such as feeding tubes. It can also include your treatment wishes if your heart or lungs were to stop working. If you already have an advance directive, it may need to be updated to be legally valid.

Decide your role

The role patients want in treatment planning differs. Some patients want to be involved as little as possible. Others want to know everything and share decision making with their doctors. These two roles are described as passive and active. Tell your treatment team which role you want or if you want a role somewhere in the middle.

Passive role

In a passive role, a person often doesn’t seek out information, speak up for him/herself, or think through treatment options. This may be due to a high level of stress. It may be hard to hear or know what others are saying. Stress, pain, and drugs can limit your ability to make good decisions. You may want a passive role because you don’t know much about cancer. However, you should know that with help from your treatment team and other patients, you may learn enough to take part in treatment decisions.

Active role

In an active role, a person often searches for all information, prepares for all outcomes, and speaks up for him/herself. He or she may take the lead or share in decision making. Taking this role may make you feel more certain and hopeful. You’ll likely get the treatment you want, at the place you want, and by the doctors you want.

There are four key steps to shared decision making. First, know what you want from treatment. Do you want cancer control or symptom relief? What challenges are you willing to accept to meet your goal? Second, know your test results. This information can pinpoint what’s important for you on websites and in books and brochures. Test results can also clarify which treatments are needed. Third, strive to have helpful talks with your doctor. Prepare questions before your visit and ask questions if your doctor isn’t clear. You can also record your
talks and get copies of your medical records. Fourth, accept help from others, especially other women with metastatic breast cancer. An active role doesn’t mean going through it alone. Others can help you be active by finding information, taking notes, asking questions, and helping you talk through your options.

Get a 2nd opinion

The time around a cancer diagnosis is very stressful. People with cancer often want to get treated as soon as possible. They want treatment before it spreads farther. While cancer can’t be ignored, there is time to think about and choose which treatment plan is best for you.

You may wish to have another doctor review your test results and the treatment plan your doctor has recommended. This is called getting a 2nd opinion. Breast cancer is a serious disease, and new information may have been published about which treatments are most effective and safe. You may completely trust your doctor, but a 2nd opinion on which treatment is right for you can help.

Copies of the pathology report, a DVD of the imaging tests, and other test results need to be sent to the doctor giving the 2nd opinion. Some people feel uneasy asking for copies from their doctors. However, a 2nd opinion is a normal part of cancer care.

When doctors have cancer, most will talk with more than one doctor before choosing their treatment. What's more, some health plans require a 2nd opinion. If your health plan doesn’t cover the cost of a 2nd opinion, you have the choice of paying for it yourself. Choosing your cancer treatment is a very important decision. It can affect your length and quality of life.

Caring for caregivers

No one experiences cancer alone.

Having cancer can affect your loved ones, especially those who provide care. This care can take many forms. It can range from giving emotional support to giving medical services in the home. Caregivers often take on extra duties to keep life normal for the family. They also play a central role in explaining what is happening to you to others, like friends and doctors.

It is natural for caregivers to focus on you. Don’t feel guilty. However, caregivers need to meet their own needs as well. Cancer treatment can last from months to years. Caregivers often get too tired from the physical and mental challenges related to the cancer. It isn't easy, but caregivers need to take care of themselves. If they don’t, they won’t be able to take good care of anyone.
Questions about testing to ask your doctor

Ask your doctors questions:

1. What blood tests and imaging tests do you recommend for me?
2. My first breast cancer was years ago. Should I get a biopsy of my metastatic disease? If no, why not?
3. Where will the tests take place?
4. How long will the tests take and will any test hurt?
5. What if I am pregnant?
6. How do I prepare for testing?
7. Should I bring a list of my medications?
8. Should I bring someone with me?
9. How soon will I know the results and who will explain them to me?
10. I want a copy of all the test results including the pathology report. Who will give them to me?
11. Who will talk with me about the next steps? When?
Questions about **treatment** to ask your doctor

**Ask your doctors questions:**

1. What treatments do you recommend?
2. How do my age, health, and other factors affect my treatment choices?
3. What are the benefits of these treatments?
4. What are the risks of these treatments?
5. What are the short-term and long-term side effects of this treatment?
6. Will the treatment prevent me from enjoying daily activities?
7. What can I do to prepare for treatment?
8. How is the treatment given?
9. How soon should I start treatment?
10. How much will the treatment cost? How can I find out how much my health insurance will cover?
11. Why do you believe this treatment is the best option for me?
12. If this treatment doesn’t work, or makes me feel too sick, what are my other options?
13. I would like to get a second opinion. Will you help me to do this?
Websites

The goal of this book is to inform you of treatment recommendations by NCCN experts. In doing so, short descriptions of the tests and treatments were included. More information about these tests and treatments can be found on the internet. Visit the websites of NCCN Member Institutions listed on page 62.

American Cancer Society
www.cancer.org/Cancer/BreastCancer/index

Breastcancer.org
www.breastcancer.org

Cancer Support Community
www.cancersupportcommunity.org

Komen Foundation
ww5.komen.org

Living Beyond Breast Cancer
www.lbbc.org

Metastatic Breast Cancer Network
www.mbcn.org

National Cancer Institute
www.cancer.gov/cancertopics/types/breast

National Coalition for Cancer Survivorship
www.canceradvocacy.org

NCCN
http://www.nccn.org/patients/guidelines/cancers.aspx

Review

• Having a treatment plan is like having a roadmap for your journey.

• Getting a 2nd opinion may help you feel more at peace about your treatment plan.

• Ask your doctors questions about testing and treatment.

• More information on the tests and treatments described in this book can be found on the internet.
Glossary

Dictionary

Acronyms
abdomen
The belly area between the chest and pelvis.

access port
A small device implanted under the skin that allows access to veins; sometimes called a port-a-cath.

adrenal gland
A small organ on top of each kidney that makes hormones.

alkaline phosphatase (ALP)
A protein found in most tissues of the body.

alkylating agents
Cancer drugs that damage coded instructions in cells by adding a chemical to it.

allergic reaction
Symptoms caused when the body is trying to rid itself of invaders.

anthracyclines
Cancer drugs that damage and disrupt the making of DNA.

antiestrogen
A drug that stops estrogen from attaching to cells.

antimetabolites
Cancer drugs that prevent the “building blocks” of DNA from being used.

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 nodes
Lymph nodes that are under the armpit.

bilateral oophorectomy
Surgical removal of both ovaries.

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

bone mineral density
A test that measures the strength of bones.

bone scan
A test that uses radioactive material to assess for bone damage.

BRCA1 or BRCA2 genes
Coded information within cells that help to prevent tumor growth by fixing damaged cells and helping cells grow normally. Abnormal changes within these genes increases the chances of developing breast and ovarian cancer.

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

clinical breast exam
A physical exam of the breasts by a health professional to feel for disease or changes in the body.

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

complete blood count (CBC)
A test of the number of blood cells.

computed tomography (CT)
A test that uses x-rays from many angles to make a picture of the insides of the body.

contrast
A dye put into the body to make clearer pictures during imaging tests.

dental abscess
Pus trapped in the tissues near the jaw.

deoxyribonucleic acid (DNA)
A very thin and long molecule that contains genetic code. Also called the “blueprint of life.”

duct
A hollow tube through which breast milk travels to the nipple.
**estrogen**
A hormone that develops female body traits. Cancer cells may use this hormone to grow.

**external beam radiation therapy (EBRT)**
Treatment with radiation received from a machine outside the body.

**follicle-stimulating hormone (FSH)**
A hormone made by the ovaries.

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

**general anesthesia**
A controlled loss of wakefulness from drugs.

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

**hereditary breast cancer**
Breast cancer caused by abnormal coded information in cells that is passed from parent to child.

**hives**
Itchy, swollen, and red skin caused by the body ridding itself of an invader.

**hormone**
Chemical in the body that activates cells or organs.

**hormone receptor**
A protein in cell membranes that bind with hormones.

**hormone receptor–negative**
Cancer cells that don’t use hormones to grow.

**hormone receptor–positive**
Cancer cells that use hormones to grow.

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

**hormone therapy–refractory**
A lack of response to three hormone regimens given one right after the other.

**hospice care**
A care team that offers services to relieve the physical, emotional, social, and spiritual burdens of a life-ending illness.

**hot flashes**
A health condition of intense body heat and sweat for short periods.

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

**human epidermal growth factor receptor 2 (HER2)-negative**
Cancer cells with normal numbers of HER2 receptors.

**human epidermal growth factor receptor 2 (HER2)-positive**
Cancer cells with too many HER2 receptors.

**hypercaldemia**
High levels of calcium in the blood.

**imaging test**
A test that makes pictures of the insides of the body.

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

**in situ hybridization (ISH)**
A lab test of that counts the number of copies of a gene.

**infusion**
A method of giving drugs slowly through a needle into a vein.

**infraclavicular**
The area right below the collarbone.

**internal mammary**
The area along the breastbone.

**invasive breast cancer**
Cancer cells have grown into the supporting tissue of the breast.

**laparoscopic surgery**
Removal of tissues through several small cuts.

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

**lobule**
A gland in the breast that makes breast milk.

**local anesthesia**
A controlled loss of feeling in a small area of the body from drugs.
luteinizing hormone-releasing hormone (LHRH)
A hormone made in the brain that helps regulate estrogen production 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 history
All health events and medications taken to date.

medical oncologist
A doctor who’s an expert in cancer drugs.

menopause
The point in time when you won’t have another menstrual period.

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

metastatic breast cancer
Cancer that has spread to distant sites in the body; a term used to refer to stage IV cancer.

microtubule inhibitors
Cancer drugs that stop a cell from dividing into two cells.

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

no evidence of disease (NED)
A period where tests show no signs of disease.

open surgery
Removal of tissues through one large cut.

osteonecrosis
Death of bone tissue.

osteoporosis
A disease that causes bones to become thin and weakened.

ovarian ablation
Methods used to stop the ovaries from making estrogen.

ovarian suppression
Methods used to lower the amount of estrogen made by the ovaries.

palliative care
Treatment for symptoms of a disease. Also sometimes called supportive care.

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

pelvis
The area between the hip bones.

performance status
A rating of general health.

periodontal disease
A disease of the gums in the mouth.

physical exam
A review of the body by a health expert for signs of disease.

peripherally inserted central catheter (PICC line)
A thin, flexible tube inserted through the skin into a vein then guided to a larger vein to give chemotherapy.

positron emission tomography (PET)
Use of radioactive material to see the shape and function of body parts.

primary diagnosis
The first diagnosis of breast cancer.

primary tumor
The first mass of cancer cells in the body.

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

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

protein kinase
A molecule that move chemicals, called phosphates, from one molecule to another.

puberty
The time when teens sexually develop.
radiotracer
A substance with radioactive material that is used to make pictures of body parts.

receptor
A protein within cells to which substances can attach.

recurrence
The return of cancer after a disease-free period.

regression
Decreases in the tumor size or spread of cancer.

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 or unpleasant physical or emotional response to treatment.

spinal cord compression
Painful squeezing of the bundle of nerves in the spine.

stroma
Supportive tissue in the breast.

supportive care
Treatment for symptoms of a disease. Also sometimes called palliative care.

supraclavicular
The area right above the collarbone.

systemic therapy
Treatment of cancer throughout the body.

treatment breaks
Short breaks in treatment that allow for rests or for special events like weddings or vacations.

treatment plan
A written course of action through cancer treatment.

triple-negative breast cancer
Breast cancer that is not hormone-positive or HER2-positive.

tumor markers
Proteins in the blood that are measured to assess if cancer treatment is working.

vascular endothelial growth factor (VEGF)
A molecule that binds to cells that form blood vessels.
Acronyms

CBC
complete blood count

CT
computed tomography

DNA
deoxyribonucleic acid

EBRT
external beam radiation therapy

FSH
follicle-stimulating hormone

IHC
immunohistochemistry

IMRT
intensity-modulated radiation therapy

ISH
in situ hybridization

LHRH
luteinizing hormone-releasing hormone

MRI
magnetic resonance imaging

PET
positron emission tomography

VEGF
vascular endothelial growth factor

NCCN Abbreviations and Acronyms

NCCN®
National Comprehensive Cancer Network®

NCCN Patient Guidelines®
NCCN Guidelines for Patients®

NCCN Guidelines®
NCCN Clinical Practice Guidelines in Oncology®
The same authoritative sources referenced by physicians and other health care professionals are available for patients:

- Caring for Adolescents and Young Adults
- Chronic Myelogenous Leukemia
- Colon Cancer
- Esophageal Cancer
- Lung Cancer Screening
- Malignant Pleural Mesothelioma
- Melanoma
- Multiple Myeloma
- Non-Small Cell Lung Cancer
- Ovarian Cancer
- Pancreatic Cancer
- Prostate Cancer
- Stage 0 Breast Cancer
- Stages I and II Breast Cancer
- Stage III Breast Cancer
- Stage IV Breast Cancer

Available at NCCN.org/patients
To request a printed copy, e-mail: patientguidelines@nccn.org
State Fundraising Notices

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For disclosures, visit www.nccn.org/about/disclosure.aspx
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