Treating Breast Cancer

If you've been diagnosed with breast cancer, your cancer care team will discuss your treatment options with you. It's important that you think carefully about each of your choices and weigh the benefits of each treatment option against the possible risks and side effects.

Local treatments

Some treatments, like surgery and radiation, are **local**, meaning they treat the tumor without affecting the rest of the body.

Most women with breast cancer will have some type of surgery to remove the tumor. Depending on the type of breast cancer and how advanced it is, you might need other types of treatment as well, either before or after surgery, or sometimes both.

- Surgery for Breast Cancer
- Radiation for Breast Cancer

Systemic treatments

Drugs used to treat breast cancer are considered **systemic therapies** because they can reach cancer cells almost anywhere in the body. Some can be given by mouth, injected into a muscle, or put directly into the bloodstream. Depending on the type of breast cancer, different types of drug treatment might be used, including:

- Chemotherapy for Breast Cancer
- Hormone Therapy for Breast Cancer
- Targeted Drug Therapy for Breast Cancer
- Immunotherapy for Breast Cancer

Common treatment approaches

Typically, treatment is based on the type of breast cancer and its stage. Other factors, including your overall health, menopause status, and personal preferences are also taken into account.

- Treatment of Breast Cancer by Stage
- Treatment of Triple-negative Breast Cancer
- Treatment of Inflammatory Breast Cancer
- Treating Breast Cancer During Pregnancy

Who treats breast cancer?

Based on your treatment options, you might have different types of doctors on your treatment team. These doctors could include:

- A **breast surgeon** or **surgical oncologist:** a doctor who uses surgery to treat breast cancer
- A **radiation oncologist:** a doctor who uses radiation to treat cancer
- A **medical oncologist:** a doctor who uses chemotherapy, hormone therapy, immunotherapy, and other medicines to treat cancer
- A **plastic surgeon:** a doctor who specializes in reconstructing or repairing parts of the body

You might have many other specialists on your treatment team as well, including physician assistants (PAs), nurse practitioners (NPs), nurses, psychologists, nutritionists, social workers, patient/nurse navigators, and other health professionals.

- Health Professionals Associated with Cancer Care

Making treatment decisions

It’s important to discuss all of your treatment options, including their goals and possible side effects, with your doctors to help make the decision that best fits your needs. It’s also very important to ask questions if there's anything you’re not sure about.

If time permits, it is often a good idea to seek a second opinion. A second opinion can give you more information and help you feel more confident about the treatment plan

you choose.

- Questions to Ask Your Doctor About Breast Cancer
- Breast Reconstruction Surgery
- Seeking a Second Opinion

Connect with a breast cancer survivor

Reach To Recovery

The American Cancer Society Reach To Recovery® program connects people facing breast cancer – from diagnosis through survivorship – with trained volunteers who are breast cancer survivors. Our volunteers provide one-on-one support through our website and mobile app to help those facing breast cancer cope with diagnosis, treatment, side effects, and more.

Thinking about taking part in a clinical trial

Clinical trials are carefully controlled research studies that are done to get a closer look at promising new treatments or procedures. Clinical trials are one way to get state-of-the art cancer treatment. In some cases they may be the only way to get access to newer treatments. They are also the best way for doctors to learn better methods to treat cancer. Still, they're not right for everyone.

If you would like to learn more about clinical trials that might be right for you, start by asking your doctor if your clinic or hospital conducts clinical trials.

- Clinical Trials

Considering complementary and alternative methods

You may hear about alternative or complementary methods that your doctor hasn’t mentioned to treat your cancer or relieve symptoms. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

Complementary methods refer to treatments that are used along with your regular medical care. Alternative treatments are used instead of a doctor’s medical treatment. Although some of these methods might be helpful in relieving symptoms or helping you feel better, many have not been proven to work. Some might even be harmful.

Be sure to talk to your cancer care team about any method you are thinking about

using. They can help you learn what is known (or not known) about the method, which can help you make an informed decision.

- Complementary and Integrative Medicine

Help getting through cancer treatment

People with cancer need support and information, no matter what part of their journey they may be on. Knowing all of your options and finding the resources you need will help you make informed decisions about your care.

Whether you are thinking about treatment, getting treatment, or not being treated at all, you can still get supportive care to help with pain or other symptoms. Communicating with your cancer care team is important so you understand your diagnosis, what treatment is recommended, and ways to maintain or improve your quality of life.

Different types of programs and support services may be helpful, and can be an important part of your care. These might include nursing or social work services, financial aid, nutritional advice, rehab, or spiritual help.

The American Cancer Society also has programs and services – including rides to treatment, lodging, and more – to help you get through treatment. Call our National Cancer Information Center at 1-800-227-2345 and speak with one of our caring, trained cancer helpline specialists.

- Palliative Care
- Programs & Services

Choosing to stop treatment or choosing no treatment at all

For some people, when treatments have been tried and are no longer controlling the cancer, it could be time to weigh the benefits and risks of continuing to try new treatments. Whether or not you continue treatment, there are still things you can do to help maintain or improve your quality of life.

Some people, especially if the cancer is advanced, might not want to be treated at all. There are many reasons you might decide not to get cancer treatment, but it’s important to talk to your doctors as you make that decision. Remember that even if you choose not to treat the cancer, you can still get supportive care to help with pain or other symptoms.

- If Cancer Treatments Stop Working

The treatment information given here is not official policy of the American Cancer Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor. Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask your cancer care team any questions you may have about your treatment options.

Surgery for Breast Cancer

- Surgery to remove breast cancer
- Surgery to remove nearby lymph nodes
- Wire localization to guide surgery
- Breast reconstruction after surgery
- Surgery for advanced breast cancer
- More information about Surgery

Most women with breast cancer have some type of surgery as part of their treatment. There are different types of breast surgery, and they may be done for different reasons, depending on the situation. For example, surgery may be done to:

- Remove as much of the cancer as possible (breast-conserving surgery or mastectomy)
- Find out whether the cancer has spread to the lymph nodes under the arm (sentinel lymph node biopsy or axillary lymph node dissection)
- Restore the breast's shape after the cancer is removed (breast reconstruction)
- Relieve symptoms of advanced cancer

Your doctor may recommend a certain operation based on your breast cancer features and your medical history, or you may have a choice about which type of surgery to have. It's important to know your options so you can talk about them with your doctor and make the choice that is right for you.

Surgery to remove breast cancer

There are two main types of surgery to remove breast cancer:

- Breast-conserving surgery is surgery to remove the cancer as well as some surrounding normal tissue. Only the part of the breast containing the cancer is removed. How much breast is removed depends on where and how big the tumor is, as well as other factors. This surgery is also called a lumpectomy, quadrantectomy, partial mastectomy, or segmental mastectomy.
- Mastectomy is a surgery in which the entire breast is removed, including all of the breast tissue and sometimes other nearby tissues. There are several different types of mastectomies. Some women may also have both breasts removed in a **double mastectomy**.

Choosing between breast-conserving surgery and mastectomy

Many women with early-stage cancers can choose between having breast-conserving surgery (BCS) and mastectomy. The main advantage of BCS is that a woman keeps most of her breast. But most often, she will also need radiation. Women who have mastectomy for early-stage cancers are less likely to need radiation.

For some women, mastectomy may be a better option or the only option, because of the type of breast cancer, the large size of the tumor, previous treatment with radiation, or certain other factors.

Some women might worry that having a less extensive surgery might raise the risk of the cancer coming back. But studies of thousands of women over more than 20 years show that when BCS is done with radiation, survival is the same as having a mastectomy, in people with early-stage cancer who are candidates for both types of surgery.

Surgery to remove nearby lymph nodes

To find out if the breast cancer has spread to underarm (axillary) lymph nodes, one or more of these lymph nodes will be removed and looked at in the lab. This is important to figuring out the stage (how big and where it has spread) of the cancer. Lymph nodes may be removed either as part of the surgery to remove the breast cancer or as a separate operation.

The two main types of surgery to remove lymph nodes are:

- **Sentinel lymph node biopsy (SLNB)** is a procedure in which the surgeon injects a dye and then removes only the lymph node(s) under the arm that have taken up the dye. These lymph nodes are where the cancer would likely spread first. Removing only one or a few lymph nodes lowers the risk of side effects that can happen after an axillary lymph node dissection (below), such as arm swelling that is also known as lymphedema[1].
- **Axillary lymph node dissection (ALND)** is a procedure that does not use a dye and in which the surgeon removes many (usually less than 20) underarm lymph nodes. ALND is not done as often as it was in the past, but it might still be the best way to look at the lymph nodes in some situations.

To learn more about these procedures, see Lymph Node Surgery for Breast Cancer.

Wire localization to guide surgery

Sometimes, if the cancer in your breast can't be felt, is hard to find, and/or is difficult to get to, the surgeon might use a mammogram or ultrasound to guide a wire to the right spot. This is called **wire localization** or **needle localization**. If a mammogram is used you may hear the term **stereotactic wire localization**. Rarely, an MRI might be used if using the mammogram or ultrasound is not successful.

After medicine is injected into your breast to numb the area, a mammogram or ultrasound is used to guide a thin hollow needle to the abnormal area. Once the tip of the needle is in the right spot, a thin wire is put in through the center of the needle. A small hook at the end of the wire keeps it in place. The needle is then taken out. Once in the operating room, the surgeon uses the wire as a guide to find the part of the breast to be removed.

The surgery done as part of the wire localization may be enough to count as breast-conserving surgery if all of the cancer is taken out and the margins are negative. If cancer cells are found at or near the edge of the removed tissue (also called a **positive or close margin**), more surgery may be needed.

It should be noted that a wire-localization procedure is sometimes used to perform a surgical biopsy[2] of a suspicious area in the breast to find out if it is cancer or not.

There are other ways a surgeon can be guided to the tumor, but these techniques are newer and not used in every facility.

Breast reconstruction after surgery

Many woman having surgery for breast cancer might have the option of breast reconstruction. A woman having a mastectomy might want to consider having the breast mound rebuilt to restore the breast's appearance after surgery. In some breast-conserving surgeries, a woman may consider having fat grafted[3] into the affected breast to correct any dimples left from the surgery. The options will depend on each woman's situation.

There are several types of reconstructive surgery, but your options depend on your medical situation and personal preferences. You may have a choice between having breast reconstruction at the same time as the breast cancer surgery (**immediate reconstruction**) or at a later time (**delayed reconstruction**).

If you are thinking about having reconstructive surgery, it's a good idea to discuss it with your breast surgeon and a plastic surgeon **before** your mastectomy or BCS. This gives the surgical team time to plan out the treatment options that might be best for you, even if you wait and have the reconstructive surgery later.

To learn about different breast reconstruction options, see Breast Reconstruction Surgery[4].

Surgery for advanced breast cancer

Although surgery is very unlikely to cure breast cancer that has spread to other parts of the body, it can still be helpful in some situations, either as a way to slow the spread of the cancer, or to help prevent or relieve symptoms from it. For example, surgery might be used:

- When the breast tumor is causing an open wound in the breast (or chest)
- To treat a small number of areas of cancer metastases[5] in a certain part of the body, such as the brain
- When an area of cancer is pressing on the spinal cord or in a bone that weakens it or causes it to break
- To treat a blockage in the liver
- To provide relief of pain or other symptoms

If your doctor recommends surgery for advanced breast cancer, it's important that you understand if it's to try to cure the cancer or to prevent or treat symptoms.

More information about Surgery

For more general information about surgery as a treatment for cancer, see Cancer Surgery[6].

To learn about some of the side effects listed here and how to manage them, see Managing Cancer-related Side Effects[7].

Hyperlinks

1. www.cancer.org/cancer/managing-cancer/side-effects/swelling/lymphedema.html
2. www.cancer.org/cancer/types/breast-cancer/screening-tests-and-early-detection/breast-biopsy/surgical-breast-biopsy.html
3. www.cancer.org/cancer/types/breast-cancer/reconstruction-surgery/breast-reconstruction-options/breast-reconstruction-using-your-own-tissues-flap-procedures.html
4. www.cancer.org/cancer/types/breast-cancer/reconstruction-surgery.html
5. www.cancer.org/cancer/managing-cancer/advanced-cancer/what-is.html
6. www.cancer.org/cancer/managing-cancer/treatment-types/surgery.html
7. www.cancer.org/cancer/managing-cancer/side-effects.html

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Last Revised: January 11, 2023

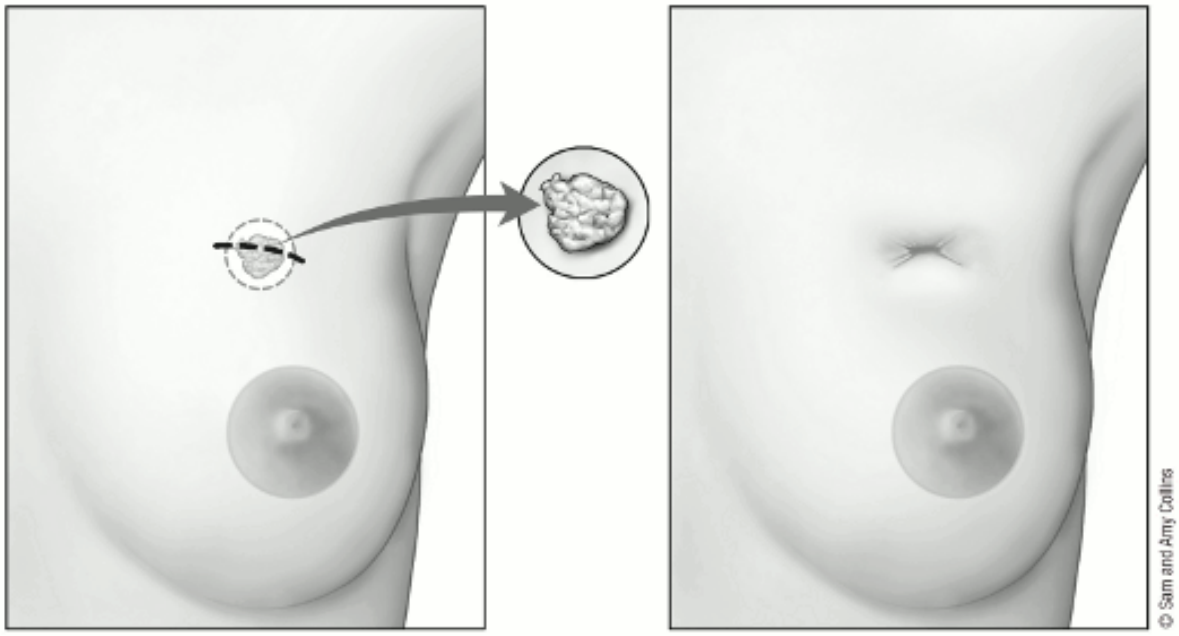
Breast-conserving Surgery (Lumpectomy)

Breast-conserving surgery (BCS) removes the cancer while leaving as much normal breast as possible. Usually, some surrounding healthy tissue and lymph nodes also are removed. Breast-conserving surgery is sometimes called**lumpectomy, quadrantectomy, partial mastectomy**, or**segmental mastectomy**depending on how much tissue is removed.

What you should know before having breast-conserving surgery

- How much of the breast is removed depends on the size and location of the tumor, your breast size, and other factors.
- Breast-conserving surgery allows a woman to keep most of her breast, but makes it likely she will also need radiation.
- After BCS, most women will have radiation therapy. Some women might also get other treatments, such as hormone therapy or chemotherapy.

- Choosing BCS plus radiation over mastectomy does not affect a woman's chances of long-term survival.
- If you think you want breast reconstruction[1], talk to your doctor **before** your breast cancer surgery.
- Not all women with breast cancer can have BCS. Talk to your doctor to find out whether BCS is an option for you.
- Side effects of BCS may include pain, a scar and/or dimple where the tumor was removed, a firm or hard surgical scar, and sometimes lymphedema[2], a type of swelling, in the arm.



The tumor is removed with a rim of normal breast tissue.

Postoperative appearance depends on the amount of tissue removed, but there will be a small scar and often an indentation in the breast.

Lumpectomy/partial mastectomy

Who can have breast-conserving surgery?

Breast-conserving surgery (BCS) is a good option for many women with early-stage cancers. The main advantage is that a woman keeps most of her breast. However, most women will also need radiation therapy, given by a **radiation oncologist** (a doctor who specializes in radiation). Women who have their entire breast removed (mastectomy) for early-stage cancers are less likely to need radiation, but they may be referred to a

radiation oncologistfor evaluation because each patient's cancer is unique.

BCS might be a good option if you:

- Are concerned about losing a breast
- Are willing to have radiation therapy and are able to get to the appointments (if you need help getting to and from your appointments see Road To Recovery[3]).
- Have not already had that breast treated with radiation therapy or BCS
- Have only one area of cancer in the breast, or multiple areas in one quadrant (multifocal) that are close enough to be removed together without changing the look of the breast too much
- Have a tumor smaller than 5 cm (2 inches), that is also small relative to the size of the breast
- Are not pregnant or, if pregnant, will not need radiation therapy immediately (to avoid risking harm to the fetus)
- Do not have a gene mutation (change) such as a *BRCA* or *ATM* mutation, which might increase your chance of a second breast cancer
- Do not have certain serious connective tissue diseases such as scleroderma or Sjögren's syndrome, which may make you very sensitive to the side effects of radiation therapy
- Do not have inflammatory breast cancer[4]
- Do not have positive margins (see Was all the cancer removed? below)

Recovering from breast-conserving surgery

This type of surgery is typically done in an outpatient surgery center, and an overnight stay in the hospital usually is not needed. Most women should be able to function after going home and can often return to their regular activities within 2 weeks. Some women may need help at home depending on how extensive their surgery was.

Ask a member of your health care team to show you how to care for your surgery site and affected arm. Usually, you and your caregiver(s) will get written instructions about care after surgery. These instructions might include:

- How to care for the surgery site and dressing
- How to care for your drain, if you have one (This is a plastic or rubber tube coming out of the surgery site that removes the fluid that collects during healing.)
- How to tell if an infection is starting

- Tips on bathing and showering after surgery
- When to call the doctor or nurse
- When to start using your arm again and how to do arm exercises to prevent stiffness
- When you can start wearing a bra again
- The use of medicines, including pain medicines and possibly antibiotics
- Any restrictions on activity
- What to expect regarding sensations or numbness in the breast and arm
- What to expect regarding feelings about body image
- When to see your doctor for a follow-up appointment
- Referral to a Reach To Recovery volunteer. Through our Reach To Recovery program[5], a specially trained volunteer who has had breast cancer can provide information, comfort, and support.

Possible side effects of breast-conserving surgery

As with all operations, bleeding and infection at the surgery site are possible. Other side effects of breast-conserving surgery can include:

- Pain or tenderness or a "tugging" sensation in the breast
- Temporary swelling of the breast
- Hard scar tissue and/or a dimple that forms at the surgical site
- Swelling of the breast from a collection of fluid (seroma) that might need to be drained
- Change in the shape of the breast
- Neuropathic (nerve) pain (sometimes described as burning or shooting pain) in the chest wall, armpit, and/or arm that doesn't go away over time. This can also happen in mastectomy patients and is called post-mastectomy pain syndrome[6] or PMPS.
- If axillary lymph nodes are also removed, other side effects such as lymphedema[7] may occur.

Was all the cancer removed?

During BCS, the surgeon will try to remove all the cancer, plus some surrounding normal tissue. This can sometimes be difficult depending on where the cancer is located in your breast.

After surgery, a doctor, called a pathologist, will look closely at the tissue that was removed in the lab. If the pathologist finds no invasive cancer cells at any of the edges of the removed tissue, it is said to have **negative** or clear margins. For women with DCIS, at least 2mm (0.08 inches) of normal tissue between the cancer and the edge of the removed tissue is preferred. If DCIS cancer cells are found near the edges of the tissue (within the 2mm), it is said to have a **close** margin. If cancer (invasive or DCIS) cells are found at the edge of the tissue, it is said to have a **positive** margin.

Having a **positive** margin means that some cancer cells may still be in the breast after surgery, so the surgeon often needs to go back and remove more tissue. This operation is called a **re-excision**. If cancer cells are still found at the edges of the removed tissue after the second surgery, a mastectomy might be needed.

Breast reconstruction surgery after breast-conserving surgery

Before your surgery, talk to your breast surgeon about how breast-conserving surgery might change the look of your breast. The larger the portion of breast removed, the more likely it is that you will see a change in the shape of the breast afterward. If your breasts look very different after surgery, it may be possible to have some type of reconstructive surgery[8] or to have the size of the unaffected breast reduced to make the breasts more symmetrical (even). It may even be possible to have this done during the initial surgery. It's very important to talk with your doctor (and possibly a plastic surgeon) **before** the cancer surgery to get an idea of how your breasts are likely to look afterward, and to learn about your options.

Treatment after breast-conserving surgery

Most women will need radiation therapy to the breast after breast-conserving surgery. Sometimes, to make it easier to aim the radiation, small metallic-like clips (which will show up on x-rays) may be placed inside the breast during surgery to mark the area where the cancer was removed.

Many women will have hormone therapy after surgery to help lower the risk of the cancer coming back. Some women might also need chemotherapy after surgery. If so, radiation therapy and hormone therapy are usually delayed until the chemotherapy is completed.

Hyperlinks

1. www.cancer.org/cancer/types/breast-cancer/reconstruction-surgery.html
2. www.cancer.org/cancer/managing-cancer/side-effects/swelling/lymphedema.html
3. www.cancer.org/support-programs-and-services/road-to-recovery.html
4. www.cancer.org/cancer/types/breast-cancer/about/types-of-breast-cancer/inflammatory-breast-cancer.html
5. www.cancer.org/support-programs-and-services/reach-to-recovery.html
6. www.cancer.org/cancer/managing-cancer/side-effects/pain/post-mastectomy-pain-syndrome.html
7. www.cancer.org/cancer/managing-cancer/side-effects/swelling/lymphedema.html
8. www.cancer.org/cancer/types/breast-cancer/reconstruction-surgery.html

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Last Revised: October 27, 2021

Mastectomy

Mastectomy is breast cancer surgery that removes the entire breast.

A mastectomy might be done:

- When a woman cannot be treated with breast-conserving surgery (lumpectomy), which saves most of the breast.
- If a woman chooses mastectomy over breast-conserving surgery for personal reasons.
- For women at very high risk of getting a second breast cancer who sometimes choose to have a double mastectomy (the removal of both breasts).

Types of mastectomies

There are several different types of mastectomies, based on how the surgery is done

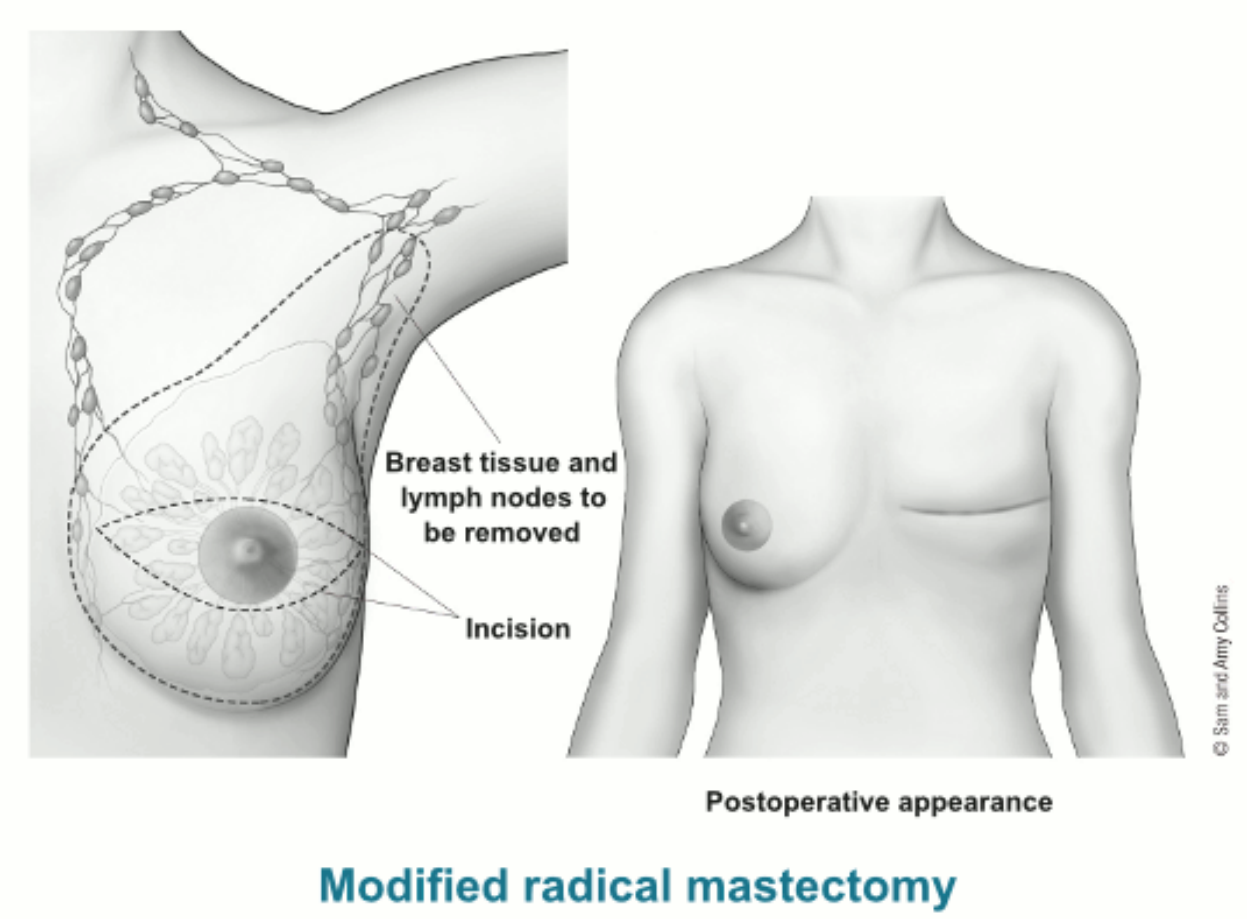
and how much tissue is removed.

Simple (or total) mastectomy

In this procedure, the surgeon removes the entire breast, including the nipple, areola, fascia (covering) of the pectoralis major muscle (main chest muscle), and skin. A few underarm lymph nodes might be removed as part of a sentinel lymph node biopsy depending on the situation. Most women, if they are hospitalized, can go home the next day.

Modified radical mastectomy

A modified radical mastectomy combines a simple mastectomy with the removal of the lymph nodes under the arm (called an axillary lymph node dissection).



Radical mastectomy

This extensive surgery is rarely done now. The surgeon removes the entire breast, axillary (underarm) lymph nodes, and the pectoral(chest wall) muscles under the breast. This surgery was once very common, but less extensive surgery (such as the modified radical mastectomy) has been found to be just as effective and with fewer side effects. This operation might be done if the tumor is growing into the pectoral muscles.

Skin-sparing mastectomy

In this procedure, most of the skin over the breast is left place. Only the breast tissue, nipple, and areola are removed. The amount of breast tissue removed is the same as with a simple mastectomy. Implants or tissue from other parts of the body can be used during the surgery to reconstruct the breast[1].

Many women prefer a skin-sparing mastectomy because it offers the advantage of less scar tissue and a reconstructed breast that seems more natural. But it may not be suitable for larger tumors or those that are close to the surface of the skin.

The risk of local cancer recurrence with this type of mastectomy is the same as with other types of mastectomies.

Experts recommended that skin-sparing mastectomies be done by a team of breast surgeons with a lot of experience in this procedure.

Nipple-sparing mastectomy

A nipple-sparing mastectomy is similar to a skin-sparing mastectomy in that the breast tissue is removed and the breast skin is saved. But in this procedure, the nipple and areola are left in place. This can be followed by breast reconstruction. The surgeon often removes the breast tissue under the nipple and areola during the procedure to check for cancer cells. If cancer is found in this tissue, the nipple and areola must be removed.

This type of mastectomy is more often an option for women who have a small, early-stage cancer, away (more than 2cm) from the nipple and areola, with no signs of cancer in the skin or the nipple.

As with any surgery, there are risks. After the surgery, the nipple may not have a good blood supply, causing the tissue to shrink or become deformed. Because the nerves are also cut, there often may be little or no feeling left in the nipple. If a woman has larger breasts, the nipple may look out of place after the breast is reconstructed. As a result, many doctors feel that this surgery is best done in women with small to medium sized

breasts. This procedure leaves fewer scars you can see, but it also has a risk of leaving behind more breast tissue than other forms of mastectomy. This could result in a higher risk of cancer developing than for a skin-sparing or simple mastectomy. However, improvements in technique have helped lower this risk and the risk of cancer coming back in the same area is about the same as with other types of mastectomies. Most experts consider nipple-sparing mastectomy to be an acceptable treatment for breast cancer in certain cases.

As with a skin-sparing mastectomy, experts also recommended that this type of mastectomy be done by a team of breast surgeons with a lot of experience with this procedure.

Double mastectomy

When both breasts are removed, it is called a **double (or bilateral) mastectomy**. Double mastectomy is sometimes done as a risk-reducing (or preventive) surgery for women at very high risk for getting breast cancer, such as those with a *BRCA* gene mutation. Most of these mastectomies are simple mastectomies, but some may be nipple-sparing. There are other situations where a double mastectomy might be done as part of a women's breast cancer treatment plan. This is done after careful consideration and discussion between the patient and their cancer care team.

Who might get a mastectomy?

Many women with early-stage cancers can choose between breast-conserving surgery (BCS) and mastectomy. You may prefer mastectomy as a way to "take out all the cancer as quickly as possible." But the fact is that in most cases, mastectomy does not give you any better chance of long-term survival compared to BCS. Studies of thousands of women over more than 20 years show that when BCS is done along with radiation, the outcome is the same as having a mastectomy.

Mastectomy might be recommended if you:

- Are unable to have radiation therapy
- Would prefer more extensive surgery instead of having radiation therapy
- Have had the breast treated with radiation therapy in the past
- Have already had BCS with re-excision(s) that did not completely remove the cancer
- Have two or more areas of cancer in different quadrants of the same breast (multicentric) that are not close enough to be removed together without changing

the look of the breast too much
- Have a tumor larger than 5 cm (2 inches) across, or a tumor that is large relative to your breast size
- Are pregnant and would need radiation therapy while still pregnant (risking harm to the fetus)
- Have a genetic factor such as a *BRCA* mutation, which might increase your chance of a second cancer
- Have a serious connective tissue disease such as scleroderma or lupus, which may make you especially sensitive to the side effects of radiation therapy
- Have inflammatory breast cancer

For women who are worried about breast cancer coming back, it is important to understand that having a mastectomy instead of breast-conserving surgery plus radiation **only**lowers your risk of developing a second breast cancer in the same breast. It does not lower the chance of the cancer coming back in other parts of the body, including the opposite breast.

Breast reconstruction surgery after mastectomy

After having a mastectomy a woman might want to consider having the breast mound rebuilt to restore the breast's appearance. This is called breast reconstruction[2]. Although each case is different, most mastectomy patients can have reconstruction. Reconstruction can be done at the same time as the mastectomy or sometime later.

If you are thinking about having reconstructive surgery, it's a good idea to discuss it with your surgeon and a plastic surgeon before your mastectomy. This allows the surgical teams to plan the treatment that's best for you, even if you wait and have the reconstructive surgery later. Insurance companies typically cover breast reconstruction, but you should check with your insurance company so you know what is covered.

Going flat

Some women choose not to have reconstructive surgery[3]. Wearing a breast prosthesis (breast form) is an option for women who want to have the shape of a breast under their clothes without having surgery. Some women are also comfortable with just 'going flat[4]'. Going flat involves a procedure called **aesthetic flat closure** or **flat closure**. A flat closure means the extra fat, skin, and other tissue in the breast area are removed and the leftover tissue is tightened and smoothed out to flatten the chest wall.

Recovering from a mastectomy

In general, women having a mastectomy stay in the hospital for 1 or 2 nights and then go home. How long it takes to recover from surgery depends on what procedures were done, and some women may need help at home. Most women should be fairly functional after going home and can often return to their regular activities within about 4 weeks. Recovery time is longer if breast reconstruction was also done, and it can take months to return to full activity after some procedures.

Ask your health care team how to care for your surgery site and arm. Usually, you and your caregivers will get written instructions about care after surgery. These instructions typically cover:

- How to care for the surgery site and dressing
- How to care for your drain, if you have one (this is a plastic or rubber tube coming out of the surgery site attached to a soft rubber ball that collects the fluid that occurs during healing)
- How to tell if an infection is starting
- Bathing and showering after surgery
- When to call the doctor or nurse
- When to start using your arm again and how to do arm exercises to prevent stiffness
- When you can start wearing a bra again
- When to begin using a prosthesis and what type to use
- Use of medicines, including pain medicines and possibly antibiotics
- Any restrictions on activity
- What to expect regarding sensations or numbness in the breast and arm
- What to expect regarding feelings about body image
- When to see your doctor for a follow-up appointment
- Referral to a Reach To Recovery volunteer. Through our Reach To Recovery program[5], a specially trained volunteer who has had breast cancer and can provide information, comfort, and support.

Possible side effects of mastectomy

Bleeding and infection at the surgery site are possible with all operations. The side effects of mastectomy can depend on the type of mastectomy you have (complex surgeries tend to have more side effects). Side effects can include:

- Pain or tenderness at the surgery site
- Swelling at the surgery site
- Buildup of blood in the wound (hematoma)
- Buildup of clear fluid in the wound (seroma)
- Limited arm or shoulder movement
- Numbness in the chest or upper arm
- Neuropathic (nerve) pain (sometimes described as burning or shooting pain) in the chest wall, armpit, and/or arm that doesn't go away over time. It is also called post-mastectomy pain syndrome or PMPS[6].
- If axillary lymph nodes are also removed, other side effects such as lymphedema[7] may occur.

Treatment after mastectomy

Some women might get other treatments after a mastectomy, such as hormone therapyto help lower the risk of the cancer coming back. Some women might also need chemotherapy, or targeted therapyafter surgery. If so, radiation therapy and/or hormone therapy is usually delayed until the chemotherapy is completed. Talk to your doctor about what to expect.

Hyperlinks

1. www.cancer.org/cancer/types/breast-cancer/reconstruction-surgery/breast-reconstruction-options.html
2. www.cancer.org/cancer/types/breast-cancer/reconstruction-surgery.html
3. www.cancer.org/cancer/types/breast-cancer/reconstruction-surgery/breast-reconstruction-alternatives.html
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Last Revised: December 20, 2023

Lymph Node Surgery for Breast Cancer

If breast cancer spreads, it typically goes first to nearby lymph nodes[1] under the arm. It can also sometimes spread to lymph nodes near the collarbone or near the breastbone (the front center of the chest). Knowing if the cancer has spread to your lymph nodes helps doctors find the best way to treat your cancer.

If you have been diagnosed with breast cancer, it's important to find out how far the cancer has spread[2]. To help find out if the cancer has spread outside the breast, one or more of the lymph nodes under the arm (axillary lymph nodes) are removed and checked in the lab. This is an important part of staging. If the lymph nodes have cancer cells, there is a higher chance that cancer cells have also spread to other parts of the body. More imaging tests might be done if this is the case.

Lymph node removal can be done in different ways, depending on whether any lymph nodes are enlarged, how big the breast tumor is, and other factors.

Biopsy of an enlarged lymph node

If any of the lymph nodes under the arm or around the collarbone are swollen, they may be checked for cancer with a needle biopsy[3], either a fine needle aspiration (FNA) or a core needle biopsy. Less often, the enlarged node is removed with surgery. If cancer is found in the lymph node, more nodes will need to be removed (see below).

Types of lymph node surgery

Even if the nearby lymph nodes are not enlarged, they will still need to be checked for cancer. This can be done in two ways:

- Most often, a **sentinel lymph node biopsy (SLNB)** is done, during which only a few lymph nodes are removed.
- In some cases, an **axillary lymph node dissection (ALND)**, which removes more lymph nodes, might be needed.

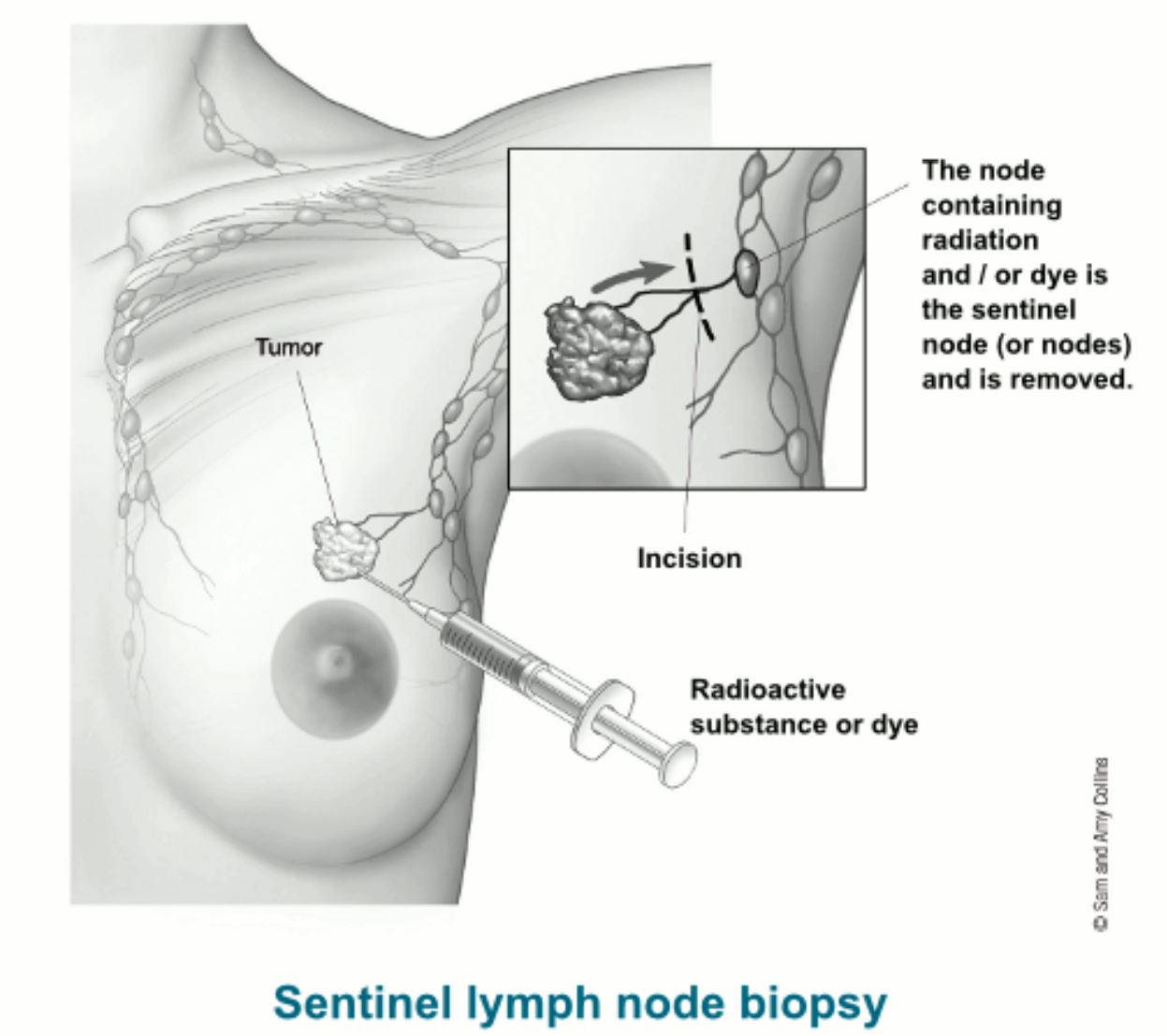
Lymph node surgery is often done as part of the main surgery to remove the breast cancer, but sometimes it might be done as a separate operation.

Sentinel lymph node biopsy

In a sentinel lymph node biopsy (SLNB), the surgeon finds and removes the first lymph node(s) to which a cancer is likely to spread (called the **sentinel nodes**). To do this, a substance is injected into the tumor, the area around it, or the area around the nipple. This can be done with either:

- A radioactive substance and/or a blue dye, OR
- A liquid containing coated iron oxide particles

Lymph vessels will carry these substances along the same path that the cancer would likely take. The first lymph node(s) the substance travels to will be the sentinel node(s).



Sentinel lymph node biopsy

After the substance has been injected, the sentinel node(s) can be found by:

- Using a special machine to detect either radioactivity or iron oxide particles in the nodes
- Looking for nodes that have turned blue (or brown, if iron oxide particles are used)

Sometimes, both methods are used.

The surgeon cuts the skin over the lymph node area and removes the affected node(s).

The few removed lymph nodes are then checked closely in the lab for cancer cells by a pathologist. Sometimes, this is done during the surgery. Because there is a chance that

other lymph nodes in the same area will also have cancer if cancer is found in the sentinel lymph node(s), the surgeon may go ahead with an axillary dissection (ALND) to remove more lymph nodes while you are still on the operating table. If no cancer cells are seen in the node(s) at the time of the surgery, or if they are not checked by a pathologist at the time of the surgery, they will be examined more closely over the next several days.

If cancer is found in the sentinel node(s) later, the surgeon may recommend an ALND at a later time to check more nodes for cancer. Studies have shown, however, that in some cases it may be safe to leave the rest of the lymph nodes behind. This is based on certain factors, such as the size of the breast tumor, what type of surgery is used to remove the tumor, and what treatment is planned after surgery, among other things.

Based on the studies that have looked at this, skipping the ALND may be an option for:

- Women with breast tumors 5 cm (about 2 inches) across or smaller who have no more than 2 positive sentinel lymph nodes, are having breast-conserving surgery followed by radiation, and did not get any chemotherapy before surgery.
- Women who have lymph nodes with a very small amount of cancer (no more than 2 mm) and are having a mastectomy.

If there is no cancer in the sentinel node(s), it's very unlikely that the cancer has spread to other lymph nodes, so no further lymph node surgery will be needed.

SLNB is often considered for women with early-stage breast cancer and is typically not used for women with inflammatory breast cancer. It might be used for women with locally advanced breast cancer in certain instances, such as after neoadjuvant treatment.

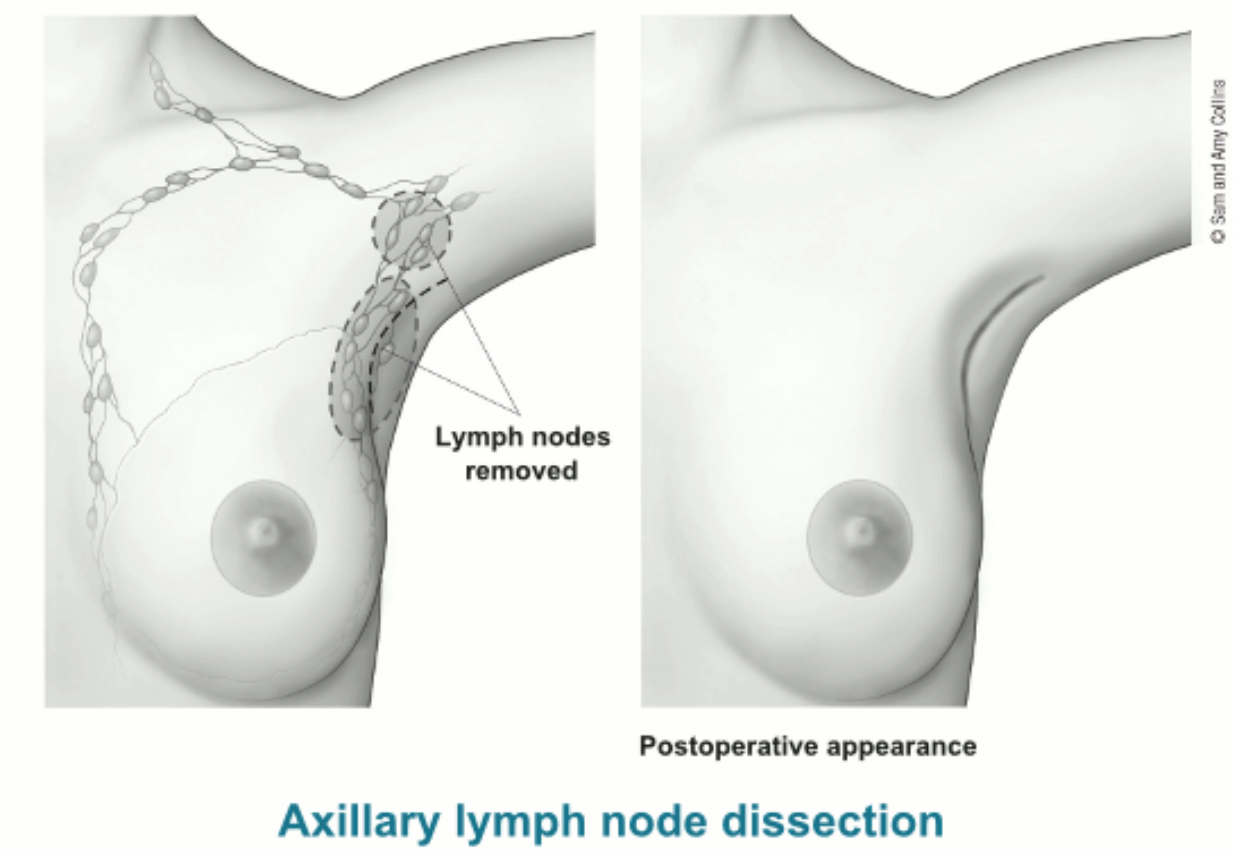
Although SLNB has become a common procedure, it requires a great deal of skill. It should be done only by a surgeon who has experience with this technique. If you are offered this type of biopsy, ask your surgeon if they do them regularly.

Axillary lymph node dissection (ALND)

In this procedure, anywhere from about 10 to 40 (though usually less than 20) lymph nodes are removed from the area under the arm (axilla) and checked for cancer spread. ALND is usually done at the same time as a mastectomy or breast-conserving surgery (BCS), but it can be done in a second operation. ALND may be needed:

- If a previous SLNB has shown 3 or more of the underarm lymph nodes have cancer

cells
- If swollen underarm or collarbone lymph nodes can be felt before surgery or seen on imaging tests and a FNA or core needle biopsy shows cancer
- If the cancer has grown large enough to extend outside the lymph node(s)
- If the SLNB is positive for cancer cells after chemotherapy was given to shrink the tumor before surgery

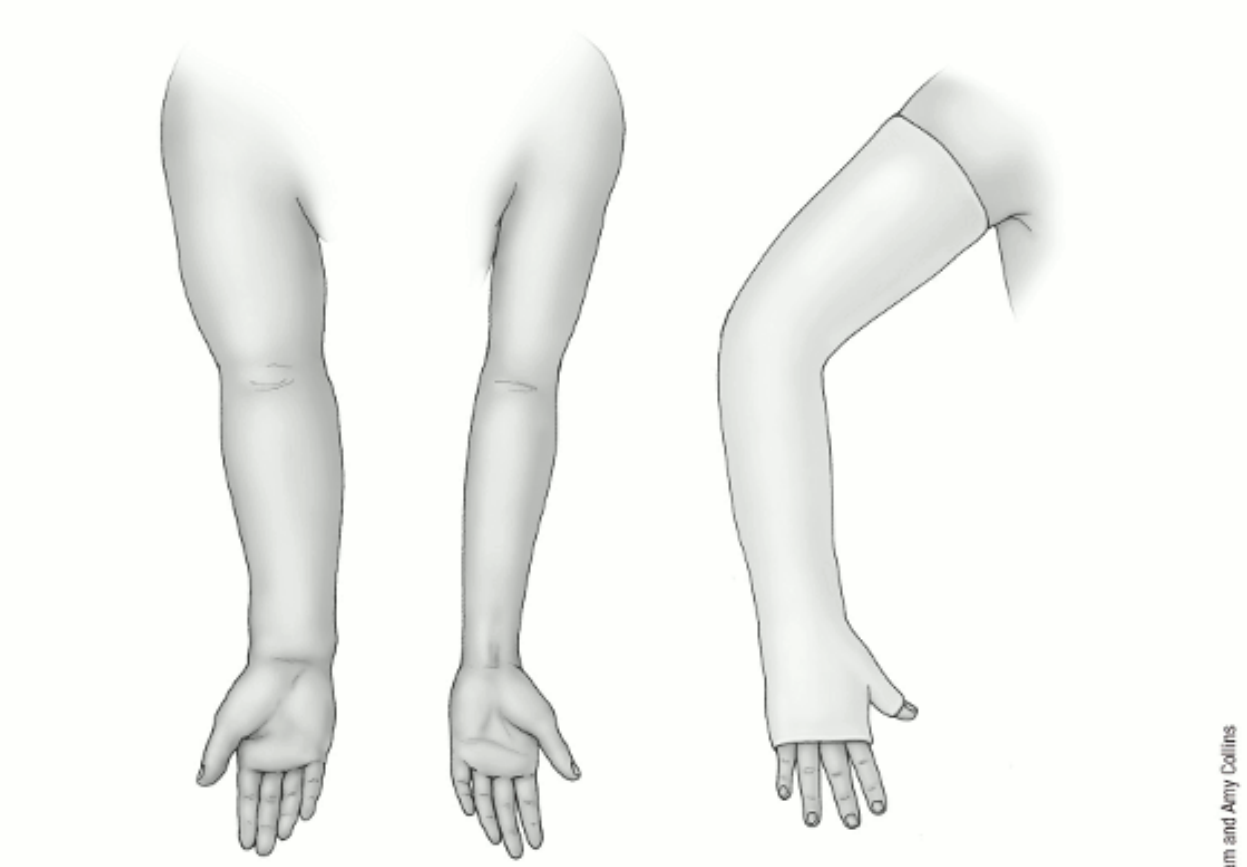


Side effects of lymph node surgery

After lymph node surgery, pain[4], swelling, bleeding, blood clots, and infection[5] are possible.

Lymphedema

A possible long-term effect of lymph node surgery is swelling in the arm or chest called lymphedema[6]. Because any excess fluid in the arms normally travels back into the bloodstream through the lymph system, removing the lymph nodes sometimes blocks drainage from the arm, causing this fluid to build up.



Left, an arm showing lymphedema swelling beside an unaffected arm. Right, a compression garment used to help control lymphedema.

Lymphedema is less common after a sentinel lymph node biopsy (SLNB) than an axillary lymph node dissection (ALND). The risk is thought to be in the range of 5% to 17% in women who have a SLNB and around 20% to 30% in women who have an ALND. It may be more common if radiation is given after surgery or in women who are obese. Sometimes the swelling lasts for only a few weeks and then goes away. But in some women, it lasts a long time. If your arm is swollen, tight, or painful after lymph node surgery, be sure to tell someone on your cancer care team right away.

Limited arm and shoulder movement

You might also have **limited movement in your arm and shoulder** after surgery. This is more common after ALND than SLNB. Your doctor may advise exercises to help keep you from having long-lasting problems (a frozen shoulder).

Some women notice a rope-like structure that begins under the arm and can extend down toward the elbow. This is sometimes called **axillary web syndrome** or **lymphatic**

cording. It is more common after ALND than SLNB. Symptoms may not appear for weeks or even months after surgery. It can cause pain and limit movement of the arm and shoulder. This often goes away without treatment, although some women may find physical therapy helpful.

Numbness

Numbness of the skin on the upper, inner arm is a common side effect because the nerve that controls sensation (feeling) here travels through the lymph node area.

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1. www.cancer.org/cancer/diagnosis-staging/lymph-nodes-and-cancer.html
2. www.cancer.org/cancer/types/breast-cancer/understanding-a-breast-cancer-diagnosis/stages-of-breast-cancer.html
3. www.cancer.org/cancer/diagnosis-staging/tests/biopsy-and-cytology-tests.html
4. www.cancer.org/cancer/managing-cancer/side-effects/pain.html
5. www.cancer.org/cancer/managing-cancer/side-effects/infections.html
6. www.cancer.org/cancer/managing-cancer/side-effects/swelling/lymphedema.html

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Last Revised: January 3, 2023

Exercises After Breast Cancer Surgery

This information was developed with assistance from the Oncology Section of the American Physical Therapy Association.

Women with breast cancer often are treated with some kind of surgery which can include:

- Surgical breast biopsy
- Lymph node removal
- Breast- conserving surgery (lumpectomy)
- Mastectomy
- Breast reconstruction

Any of these can affect how well you can move your shoulder and arm or go about your daily activities, like dressing, bathing, and combing your hair. Pain and stiffness can cause weakness and limit movement of your arm and shoulder.

Exercises can help get movement back

No matter what type of surgery you have, it's important to do exercises afterward to get the arm and shoulder moving again. Exercises help decrease side effects of your surgery and help you get back to your usual activities.

If you've had radiation therapy after surgery, exercises are even more important to help keep your arm and shoulder flexible. Radiation may affect your arm and shoulder long after treatment is finished. Because of this, it's important to develop a regular habit of doing exercises to maintain arm and shoulder mobility after radiation treatments for breast cancer.

It's very important to talk with your doctor before starting any exercises so that you can decide on a program that's right for you. Your doctor might suggest you see a physical therapist or occupational therapist, or a cancer exercise specialist certified by the American College of Sports Medicine. These health professionals are specially trained to design an exercise program just for you. You might need this kind of help if you do not have full use of your arm within 3 to 4 weeks of surgery.

Some exercises should not be done until drains and sutures (stitches) are removed, but others can be done soon after surgery. The exercises that increase your shoulder and arm motion can usually be started in a few days. Exercises to help make your arm stronger are added later.

Here are some of the more common exercises that women do after breast surgery. Talk to your doctor or therapist about which of these are right for you and when you should start doing them. Do not start any of these exercises without talking to your doctor first.

The week after surgery

The tips and exercises listed below should be done for the first 3 to 7 days after surgery. **Do not do them until you get the OK from your doctor.**

- Use your affected arm (on the same side as your surgery) as you normally would when you comb your hair, bathe, get dressed, and eat. Be sure to ask your doctor if you can lift heavier items.
- Raise your arms up to shoulder height, or whatever height you can without pulling on your drains, and lower them again a few times. Repeat this 3 or 4 times a day. These exercises help move lymph fluid out of your arm and help restore movement.
- You can exercise your affected arm while it's raised. There are a few ways to do this. With your arm raised, open and close your hand 15 to 25 times. Next, bend and straighten your elbow several times. You can also bend your elbow and touch the shoulder on the same side a few times, then the shoulder on the opposite side a few times.
- Practice deep breathing exercises (using your diaphragm) at least 6 times a day. Lie down on your back and take a slow, deep breath. Breathe in as much air as you can while trying to expand your chest and abdomen (push your belly button away from your spine). Relax and breathe out. Repeat this 4 or 5 times. This exercise will help maintain normal movement of your chest, making it easier for your lungs to work. Do deep breathing exercises often.

General guidelines for these exercises

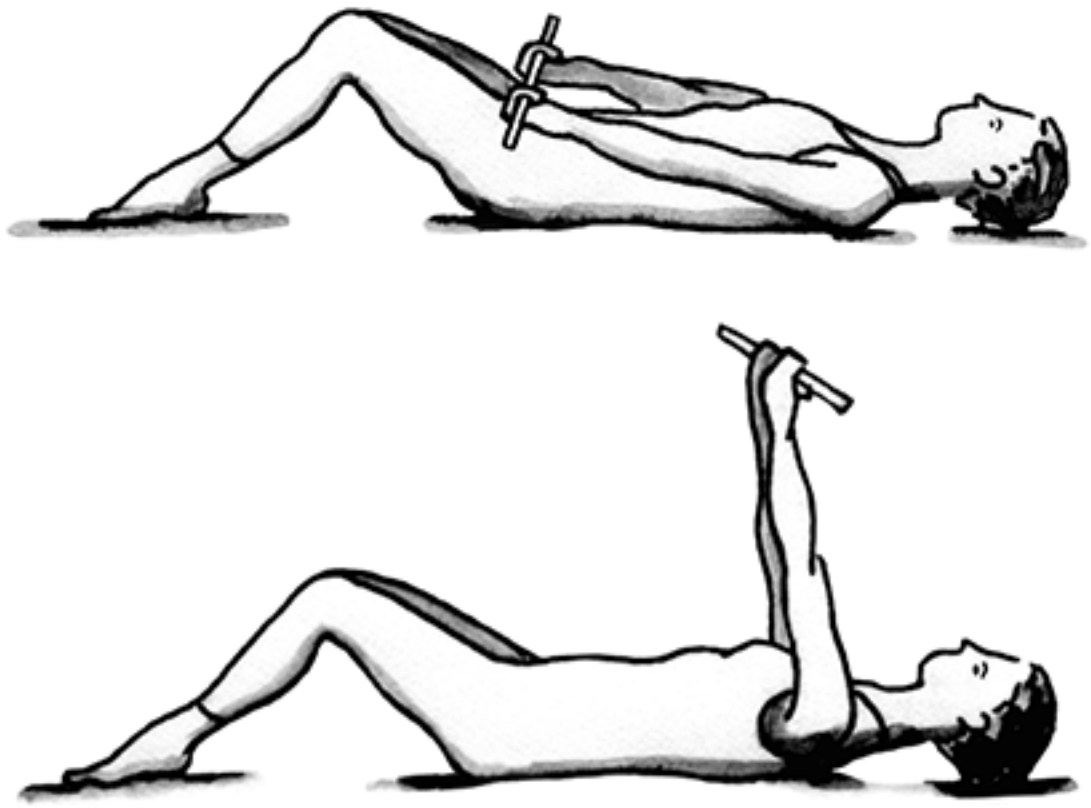
The exercises described here can be done as soon as your doctor says it's OK. They're usually started a week or more after surgery. Be sure to talk to your doctor before trying any of them. Here are some things to keep in mind after breast surgery:

- You might feel some tightness in your chest and armpit after surgery. This is normal, and the tightness should decrease as you do your exercises. If it doesn't, call your doctor.
- Many women have burning, tingling, numbness, or soreness on the back of the arm and/or on the chest wall. This is because the surgery can irritate some of your nerves. These feelings might increase a few weeks after surgery. But keep doing your exercises unless you notice unusual swelling or tenderness. (If this happens, let your doctor know about it right away.) Sometimes rubbing or stroking the area with your hand or a soft cloth can help make the area less sensitive.

- It may be helpful to exercise after a warm shower when muscles are warm and relaxed.
- Wear comfortable, loose clothing when doing the exercises.
- Do the exercises slowly until you feel a gentle stretch. Hold each stretch at the end of the motion and slowly count to 5. It's normal to feel some pulling as you stretch the skin that has been shortened because of the surgery. Do not bounce or make any jerky movements when doing any of the exercises. You should not feel pain as you do them, only gentle stretching.
- Do each exercise 5 to 7 times. Try to do each exercise correctly. Tell your cancer care team if you have trouble doing them . You may need to be referred to a physical or occupational therapist.
- Do the exercises twice a day until you get back your normal flexibility. Continuing to do some exercises during the months after surgery can help you keep moving.
- Be sure to take deep breaths, in and out, as you do each exercise.
- The exercises are set up so that you start them first lying down, then sitting, and finish them standing up.

Here are some of the more common exercises that women do after breast surgery. Talk to your doctor or therapist about which of these are right for you and when you should start doing them. Do not start any of these exercises without talking to your doctor first.

Wand exercise



This exercise helps increase your ability to move your shoulders forward. You will need a broom handle, yardstick, or other stick-like object to use as the wand in this exercise. Do these exercises on a bed or the floor. Lie on your back with your knees bent and your feet flat.

- Hold the wand across your belly in both hands with your palms facing up.
- Lift the wand up over your head as far as you can. Use your unaffected arm to help lift the wand until you feel a stretch in your affected arm.
- Hold for 5 seconds.
- Lower arms and repeat 5 to 7 times.

Elbow winging

This exercise helps increase the movement in the front of your chest and shoulder. It may take many weeks of regular exercise before your elbows will get close to the bed or floor. Do these exercises on a bed or the floor. Lie on your back with your knees bent and your feet flat.

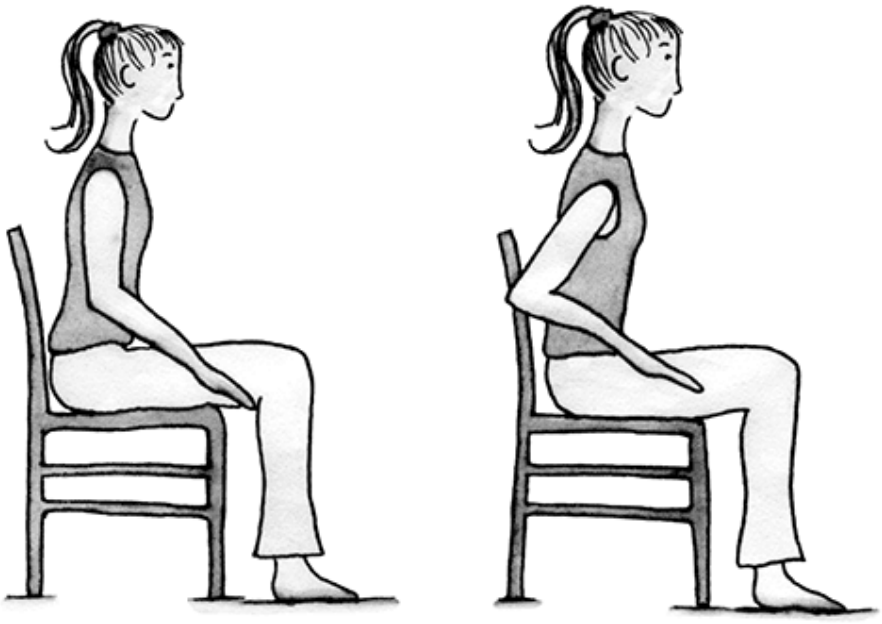
- Clasp your hands behind your neck with your elbows pointing toward the ceiling.
- Move your elbows apart and down toward the bed or floor.
- Repeat 5 to 7 times.

Shoulder blade stretch

This exercise helps increase your shoulder blade movement.

- Sit in a chair very close to a table with your back against the back of the chair.
- Place the unaffected arm on the table with your elbow bent and palm down. Do not move this arm during the exercise.
- Place the affected arm on the table, palm down, with your elbow straight.
- Without moving your trunk, slide the affected arm forward, toward the opposite side of the table. You should feel your shoulder blade move as you do this.
- Relax your arm and repeat 5 to 7 times.

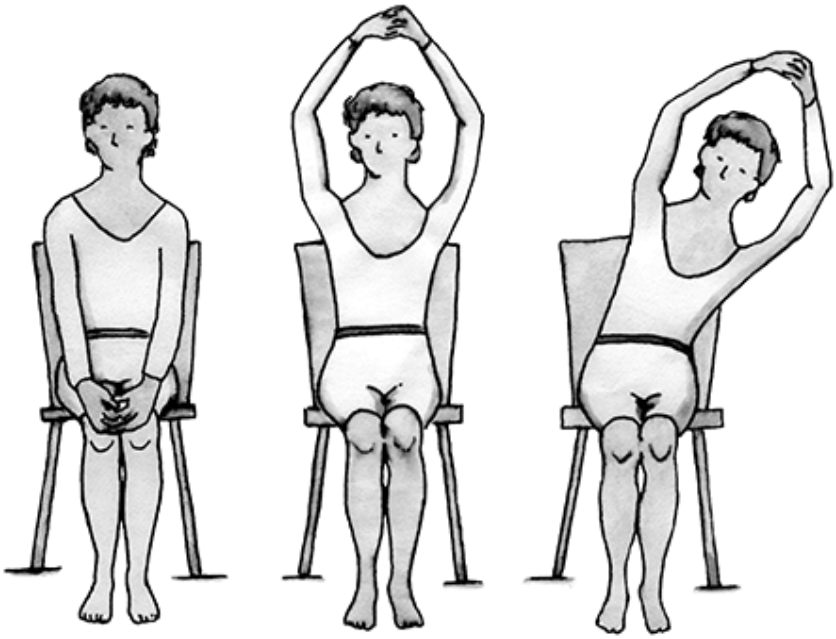
Shoulder blade squeeze



This exercise also helps increase shoulder blade movement and improve posture.

- Sit in a chair in front of a mirror. Face straight ahead. Do not rest against the back of the chair.
- Your arms should be at your sides with your elbows bent.
- Squeeze your shoulder blades together, bringing your elbows behind you toward your spine. Elbows will move with you, but don't force the motion with your elbows. Keep your shoulders level as you do this. Do not lift your shoulders up toward your ears.
- Return to the starting position and repeat 5 to 7 times.

Side bends



This exercise helps increase movement of your trunk and body.

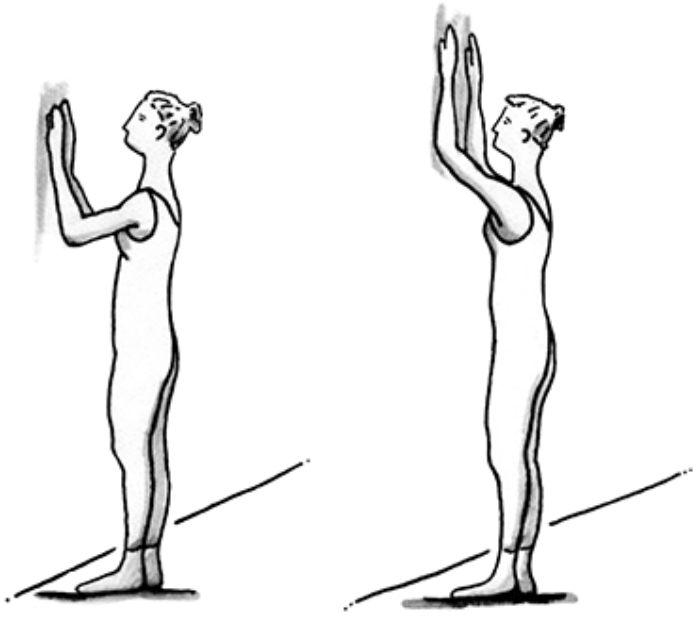
- Sit in a chair and clasp your hands together in front of you. Lift your arms slowly over your head, straightening your arms.
- When your arms are over your head, bend your trunk to the right keeping your arms overhead.
- Return to the starting position and bend to the left.
- Repeat 5 to 7 times.

Chest wall stretch

This exercise helps stretch your chest.

- Stand facing a corner with your toes about 8 to 10 inches from the corner.
- Bend your elbows and put your forearms on the wall, one on each side of the corner. Your elbows should be as close to shoulder height as possible.
- Keep your arms and feet in place and move your chest toward the corner. You will feel a stretch across your chest and shoulders.
- Return to the starting position and repeat 5 to 7 times.
- The picture shows stretching both sides at the same time, but you may find it more comfortable to stretch one arm at a time.
- Be sure you keep your shoulders dropped far away from your ears as you do this stretch. Keep your ears over your shoulders to avoid making your neck sore.

Shoulder stretch



This exercise helps increase your mobility in your shoulder.

- Stand facing the wall with your toes about 8 to 10 inches from the wall.
- Put your hands on the wall. Use your fingers to "climb the wall," reaching as high as you can until you feel a stretch.
- Return to the starting position and repeat 5 to 7 times.
- The picture shows both arms going up at the same time, but you might find it easier to raise one arm at a time.
- Be sure you keep your shoulders dropped far away from your ears as you raise your arms. Keep your ears over your shoulders to avoid making your neck sore.

Things to keep in mind after breast surgery

Start exercising slowly and do more as you are able. Stop exercising and talk to your doctor right away if you:

- Get weaker, start losing your balance, or start falling
- Have pain that gets worse
- Have new heaviness, aching, tightness, or other strange sensations in your arm
- Have unusual swelling or swelling that gets worse
- Have headaches, dizziness, blurred vision, new numbness, or tingling in your arms or chest

It's important to exercise to keep your muscles working as well as possible, but it's also important to be safe. Talk with your doctor about the right kind of exercises for you and ask about seeing a lymphedema[1] specialist who can help with safe exercise. Then set goals for increasing your level of physical activity.

Other kinds of exercise

Exercise to help **improve aerobic (heart-lung) capacity** is also important for women who have had breast cancer. There's evidence that fitness and weight loss may even help lower the risk that some types of cancer will come back after treatment. Ask your doctor about fitness exercises during and after breast cancer treatment.

Other exercises are designed to help **reduce your risk of lymphedema[2]**, or swelling in the arm, on the side where you had surgery. The exercises shown here are mainly designed to help regain range of motion (flexibility) in your arm and shoulder. Ask your doctor about your lymphedema risk and if you should use exercises to help reduce that risk.

Strengthening exercises are now recommended as part of regular exercise programs to improve health. These are not started until 4 to 6 weeks after surgery, and must be tailored to your general health, medical condition, and fitness. Strength building starts by using small hand weights, and is increased slowly over time. Again, this is best discussed with your doctor or physical therapist. It's probably best to start a strengthening program in a supervised setting with a cancer exercise trainer or physical therapist to be sure you're doing the exercises properly.

Hyperlinks

1. www.cancer.org/cancer/managing-cancer/side-effects/swelling/lymphedema.html
2. www.cancer.org/cancer/managing-cancer/side-effects/swelling/lymphedema.html

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Last Revised: October 27, 2021

Radiation for Breast Cancer

Radiation therapy is treatment with high-energy rays (or particles) that destroy cancer cells. Some women with breast cancer will need radiation, in addition to other treatments.

Depending on the breast cancer's stage[1] and other factors, radiation therapy can be used in several situations:

- After breast-conserving surgery(BCS), to help lower the chance that the cancer will come back in the same breast or nearby lymph nodes.

- After a mastectomy, especially if the cancer was larger than 5 cm (about 2 inches), if cancer is found in many lymph nodes, or if certain surgical margins, such as the skin or muscle, have cancer cells.
- **If cancer has spread to other parts of the body**, such as the bones, spinal cord, or brain.

Types of radiation therapy for breast cancer

The main types of radiation therapy that can be used to treat breast cancer are:

- External beam radiation therapy
- Brachytherapy

External beam radiation therapy (EBRT)

EBRT[2] **is the most common type of radiation therapy for women with breast cancer**. A machine outside the body focuses the radiation on the area affected by the cancer.

Which areas need radiation depends on whether you had a mastectomy or breast-conserving surgery (BCS) and if the cancer has reached nearby lymph nodes.

- If you had a mastectomy and no lymph nodes had cancer cells, radiation will be focused on the chest wall, the mastectomy scar, and the places where any drains exited the body after surgery.
- If you had BCS, you will most likely have radiation to the entire breast (called **whole breast radiation**). An extra **boost** of radiation to the area in the breast where the cancer was removed (called the **tumor bed**) is often given if there is a high risk of the cancer coming back. The boost is often given after the treatments to the whole breast have ended. It uses the same machine, with lower amounts of radiation aimed at the tumor bed. Most women don't notice different side effects from boost radiation than from whole breast radiation.
- If cancer was found in the lymph nodes under the arm (axillary lymph nodes), this area may be given radiation, as well. Sometimes, the area treated might also include the nodes above the collarbone (supraclavicular lymph nodes) and the nodes beneath the breast bone in the center of the chest (internal mammary lymph

nodes).

If you will need external beam radiation therapy after surgery, it is usually not started until your surgery site has healed, which often takes a month or longer. If you are getting chemotherapy as well, radiation treatments are usually delayed until chemotherapy is done. Some treatments after surgery, like hormone therapy or HER2 targeted therapy, can be given at the same time as radiation.

Types and schedules of external beam radiation for breast cancer

Whole breast radiation

Radiation to the entire affected breast is called **whole breast radiation.**

- The standard schedule for getting whole breast radiation is 5 days a week (Monday through Friday) for about 6 to 7 weeks.
- Another option is **hypofractionated radiation therapy** where the radiation is also given to the whole breast, but in larger daily doses (Monday through Friday) using fewer treatments (typically for only 3 to 4 weeks). For women who have had breast-conserving surgery (BCS) and whose cancer has not spread to underarm lymph nodes, this schedule has been shown to be just as good at keeping the cancer from coming back in the same breast as giving the radiation over longer periods of time. It might also lead to fewer short-term side effects.

Accelerated partial breast irradiation

After whole breast radiation or even after surgery alone, most breast cancers tend to come back very close to the area where the tumor was removed (tumor bed). For this reason, some doctors are using **accelerated partial breast irradiation** (APBI) in selected women to give larger doses over a shorter time to only one part of the breast (the tumor bed) compared to the entire breast (whole breast radiation). Since more research is needed to know if these newer methods will have the same long-term results as standard radiation, not all doctors use them. There are several different types of accelerated partial breast irradiation:

- **Intraoperative radiation therapy (IORT):** In this approach, a single large dose of radiation is given to the area where the tumor was removed (tumor bed) in the operating room right after BCS (before the breast incision is closed). IORT requires

special equipment and is not widely available.

- **3D-conformal radiotherapy (3D-CRT):** In this technique, the radiation is given with special machines so that it is better aimed at the tumor bed. This spares more of the surrounding normal breast tissue. Treatments are given twice a day for 5 days or daily for 2 weeks.
- **Intensity-modulated radiotherapy (IMRT):** IMRT is like 3D-CRT, but it also changes the strength of some of the beams in certain areas. This gets stronger doses to certain parts of the tumor bed and helps lessen damage to nearby normal body tissues.
- **Brachytherapy:** See brachytherapy below.

Women who are interested in these approaches may want to ask their doctor about taking part in clinical trials[3] of accelerated partial breast irradiation.

Chest wall radiation

If you had a mastectomy and none of the lymph nodes had cancer, radiation will be given to the entire chest wall, the mastectomy scar, and the areas of any surgical drains. It is typically given every day, 5 days a week, for 6 weeks.

Lymph node radiation

Whether or not you have had BCS or a mastectomy, if cancer was found in the lymph nodes under the arm (axillary lymph nodes), this area may be given radiation. In certain cases, the lymph nodes above the collarbone (supraclavicular lymph nodes) and behind the breastbone in the center of the chest (internal mammary lymph nodes) will also get radiation along with the underarm nodes. It is typically given daily 5 days a week for 6 weeks at the same time as the radiation to the breast or chest wall is given.

Possible side effects of external beam radiation

The main short-term side effects of external beam radiation therapy to the breast are:

- Swelling in the breast
- Skin changes in the treated area similar to a sunburn (redness, skin peeling, darkening of the skin)
- Fatigue

Your health care team may advise you to avoid exposing the treated skin to the sun because it could make the skin changes worse. Most skin changes get better within a few months. Changes to the breast tissue usually go away in 6 to 12 months, but it can take longer.

External beam radiation therapy can also cause side effects later on:

- Some women may find that radiation therapy causes the breast to become smaller and the skin to become firmer or swollen.
- Radiation may affect your options for breast reconstruction later on. It can also raise the risk of problems with appearance and healing if it's given after reconstruction, especially tissue flap procedures.
- Women who have had breast radiation may not be able to breastfeed from the radiated breast.
- Radiation to the breast can sometimes damage some of the nerves to the arm. This is called **brachial plexopathy** and can lead to numbness, pain, and weakness in the shoulder, arm, and hand.
- Radiation to the underarm lymph nodes might causelymphedema[4], a type of pain and swelling in the arm or chest.
- In rare cases, radiation therapy may weaken the ribs, which could lead to a fracture.
- In the past, parts of the lungs and heart were more likely to get some radiation, which could lead to long-term damage of these organs in some women. Modern radiation therapy equipment focuses the radiation beams better than older machines, so these problems are rare today.
- A very rare complication of radiation to the breast is the development of another cancer called an angiosarcoma[5].

Brachytherapy

Brachytherapy[6], also known as **internal radiation**, is another way to deliver radiation therapy. Instead of aiming radiation beams from outside the body, a device containing radioactive seeds or pellets is placed into the breast tissue for a short time in the area where the cancer had been removed (tumor bed).

For certain women who had breast-conserving surgery (BCS), brachytherapy can be used by itself (instead of radiation to the whole breast) as a form of accelerated partial

breast irradiation. Tumor size, location, and other factors may limit who can get brachytherapy.

Types of brachytherapy

Intracavitary brachytherapy

This is the most common type of brachytherapy for women with breast cancer. A device is put into the space left from BCS and is left there until treatment is complete. There are several different devices available, most of which require surgical training for proper placement. They all go into the breast as a small catheter (tube). The end of the device inside the breast is then expanded like a balloon so that it stays securely in place for the entire treatment. The other end of the catheter sticks out of the breast. For each treatment, one or more sources of radiation (often pellets) are placed down through the tube and into the device for a short time and then removed. Treatments are typically given twice a day for 5 days in an outpatient setting. After the last treatment, the device is deflated and removed.

Interstitial brachytherapy

In this approach, several small, hollow tubes called catheters are inserted into the breast around the area where the cancer was removed and are left in place for several days. Radioactive pellets are inserted into the catheters for short periods of time each day and then removed. This method of brachytherapy has been around longer (and has more evidence to support it), but it is not used as much.

Early studies of intracavitary brachytherapy as the only radiation after BCS have had promising results as far as having at least equal cancer control compared with standard whole breast radiation, but may have more complications including poor cosmetic results. Studies of this treatment are being done and more follow-up is needed.

Possible side effects of intracavitary brachytherapy

As with external beam radiation, intracavitary brachytherapy can have side effects, including:

- Redness and/or bruising at the treatment site
- Breast pain
- Infection
- Damage to fatty tissue in the breast

- Weakness and fracture of the ribs in rare cases
- Fluid collecting in the breast (seroma)

More information about radiation therapy

To learn more about how radiation is used to treat cancer, see Radiation Therapy[7].

To learn about some of the side effects listed here and how to manage them, see Managing Cancer-related Side Effects[8].

Hyperlinks

1. www.cancer.org/cancer/types/breast-cancer/understanding-a-breast-cancer-diagnosis/stages-of-breast-cancer.html
2. www.cancer.org/cancer/managing-cancer/treatment-types/radiation/external-beam-radiation-therapy.html
3. www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html
4. www.cancer.org/cancer/managing-cancer/side-effects/swelling/lymphedema.html
5. www.cancer.org/cancer/types/breast-cancer/about/types-of-breast-cancer/angiosarcoma-of-the-breast.html
6. www.cancer.org/cancer/managing-cancer/treatment-types/radiation/internal-radiation-therapy-brachytherapy.html
7. www.cancer.org/cancer/managing-cancer/treatment-types/radiation.html
8. www.cancer.org/cancer/managing-cancer/side-effects.html

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Last Revised: October 27, 2021

Chemotherapy for Breast Cancer

Chemotherapy (chemo) uses anti-cancer drugs that may be given intravenously (injected into your vein) or by mouth. The drugs travel through the bloodstream to reach cancer cells in most parts of the body. Sometimes, if cancer spreads to the spinal fluid, which surrounds and cushions the brain and spinal cord, chemo may be given directly into in this area (called intrathecal chemotherapy).

When is chemotherapy used for breast cancer?

Not all women with breast cancer will need chemo, but there are several situations in which chemo may be recommended.

After surgery (adjuvant chemotherapy)

Adjuvant chemo might be given to try to kill any cancer cells that might have been left behind or have spread but can't be seen, even on imaging tests[1]. These cells are considered microscopic because they can't be seen by the naked eye. If these cells were allowed to grow, they could form new tumors in other places in the body. Adjuvant chemo can lower the risk of breast cancer coming back. Sometimes it is not clear if chemotherapy will be helpful. There are tests available, such as Oncotype DX, that can help determine which women will most likely benefit from chemo after breast surgery. See Breast Cancer Gene Expression Tests[2] for more information.

Before surgery (neoadjuvant chemotherapy)

Neoadjuvant chemo might be given to try to shrink the tumor so it can be removed with less extensive surgery. Because of this, neoadjuvant chemo is often used to treat

cancers that are too big to be removed by surgery when first diagnosed, have many lymph nodes involved with cancer, or are inflammatory breast cancers .

If after neoadjuvant chemo, cancer cells are still found when surgery is done (also called residual disease), you might be offered more chemotherapy (adjuvant chemotherapy) to reduce the chances of the cancer coming back (recurrence).

Some other reasons you might get neoadjuvant chemo:

- By giving chemo before the tumor is removed, doctors can see how the cancer responds to it. If the first set of chemo drugs doesn't shrink the tumor, your doctor will know that other drugs are needed. It should also kill any cancer cells that might have spread but can't be seen by the naked eye or on imaging tests. Just like adjuvant chemo, neoadjuvant chemo can lower the risk of breast cancer coming back.
- Some people with early-stage cancer who get neoadjuvant chemo might live longer if the cancer completely goes away with that treatment. This can be seen most often in women who have triple-negative breast cancer or HER2-positive breast cancer.
- Getting chemo before surgery can also give some people extra time to get genetic testing or plan reconstructive surgery.

Keep in mind that not all women with breast cancer are good candidates for neoadjuvant chemo.

For metastatic breast cancer

Chemo can be used as the main treatment for women whose cancer has spread outside the breast and underarm area to distant organs like the liver or lungs. Chemo can be given either when breast cancer is diagnosed or after initial treatments. The length of treatment depends on how well the chemo is working and how well you tolerate it.

Chemotherapy drugs used for breast cancer

In most cases, chemo has the greatest effect when more than one drug is used at a time. Often, combinations of 2 or 3 drugs are used. Doctors use many different combinations, and it's not clear that any particular drug combination is the best.

Adjuvant and neoadjuvant chemo drugs

- Anthracyclines, such as doxorubicin (Adriamycin) and epirubicin (Ellence)
- Taxanes, such as paclitaxel (Taxol) and docetaxel (Taxotere)
- 5-fluorouracil (5-FU) or capecitabine (Xeloda)
- Cyclophosphamide (Cytoxan)
- Carboplatin (Paraplatin)

Chemo drugs for breast cancer that has spread (metastatic breast cancer)

- Taxanes: Paclitaxel (Taxol), docetaxel (Taxotere), and albumin-bound paclitaxel (Abraxane)
- Ixabepilone (Ixempra)
- Eribulin (Halaven)
- Anthracyclines: Doxorubicin (Adriamycin), liposomal doxorubicin (Doxil), and epirubicin (Ellence)
- Platinum agents (Cisplatin, carboplatin)
- Vinorelbine (Navelbine)
- Capecitabine (Xeloda)
- Gemcitabine (Gemzar)
- Antibody drug conjugates (Ado-trastuzumab emtansine [Kadcyla], Fam-trastuzumab deruxtecan [Enhertu], Sacituzumab govitecan [Trodelvy])

Although drug combinations are often used to treat early breast cancer, advanced breast cancer often is treated with single chemo drugs. Still, some combinations, such as paclitaxel plus gemcitabine, are commonly used to treat metastatic breast cancer.

For cancers that are HER2-positive[3], one or more drugs that target HER2 may be used with chemo. (See Targeted Therapy for Breast Cancer for more information about these drugs.)

How is chemotherapy for breast cancer given?

Chemo drugs for breast cancer are typically given into a vein (IV), either as an injection over a few minutes or as an infusion over a longer period of time. This can be done in a doctor's office, infusion center, or in a hospital setting.

Often, a slightly larger and sturdier IV is required in the vein system to administer

chemo. These are known as central venous catheters[4] (CVCs), central venous access devices (CVADs), or central lines. They are used to put medicines, blood products, nutrients, or fluids right into your blood. They can also be used to take out blood for testing.

There are many different kinds of CVCs. The most common types are the port and the PICC line. For breast cancer patients, the central line is typically placed on the side opposite of the breast cancer. If a woman has breast cancer in both breasts, the central line will most likely be placed on the side that had fewer lymph nodes removed or involved with cancer.

Chemo is given in cycles, followed by a rest period to give you time to recover from the effects of the drugs. Chemo cycles are most often 2 or 3 weeks long. The schedule varies depending on the drugs used. For example, with some drugs, chemo is given only on the first day of the cycle. With others, it is given one day a week for a few weeks or every other week. Then, at the end of the cycle, the chemo schedule repeats to start the next cycle.

Adjuvant and neoadjuvant chemo is often given for a total of 3 to 6 months, depending on the drugs used. The length of treatment for metastatic (Stage 4) breast cancer depends on how well it is working and what side effects you have.

Dose-dense chemotherapy

Doctors have found that giving the cycles of certain chemo drugs closer together can lower the chance that the cancer will come back and improve survival for some women with breast cancer. For example, a drug that would normally be given every 3 weeks might be given every 2 weeks. This can be done for both neoadjuvant and adjuvant treatment. It can lead to more problems with low blood cell counts, so it's not an option for all women. For example, a chemo combination sometimes given this way is doxorubicin (Adriamycin) and cyclophosphamide (Cytoxan) every 2 weeks, followed by paclitaxel (Taxol) every 2 weeks.

Possible side effects of chemo for breast cancer

Chemo drugs can cause side effects, depending on the type and dose of drugs given, and the length of treatment. Some of the most common possible side effects[5] include:

- Hair loss
- Nail changes
- Mouth sores

- Loss of appetite or weight changes
- Nausea and vomiting
- Diarrhea
- Fatigue
- Hot flashes and/or vaginal dryness from menopause caused by chemo (see Menstrual changes and fertility issues below)
- Nerve damage (see Nerve damage below)

Chemo can also affect the blood-forming cells of the bone marrow, which can lead to:

- Increased chance of infections (from low white blood cell counts)
- Easy bruising or bleeding (from low blood platelet counts)
- Fatigue (from low red blood cell counts and other reasons)

These side effects usually go away after treatment is finished. There are often ways to lessen these side effects. For example, drugs can be given to help prevent or reduce nausea and vomiting.

Other side effects are also possible. Some of these are more common with certain chemo drugs. Ask your cancer care team about the possible side effects of the specific drugs you are getting.

Menstrual changes and fertility issues

For younger women, changes in menstrual periods are a common side effect of chemo. Premature menopause (not having any more menstrual periods) and infertility (not being able to become pregnant) may occur and could be permanent. If this happens, there is an increased risk of heart disease, bone loss, and osteoporosis. There are medicines that can treat or help prevent bone loss.

Even if your periods stop while you are on chemo, you may still be able to get pregnant. Getting pregnant while on chemo could lead to birth defects and interfere with treatment. If you have not gone through menopause before treatment and are sexually active, it's important to discuss using birth control with your doctor. It is not a good idea for women with hormone receptor-positive breast cancer[6] to take hormonal birth control (like birth control pills), so it's important to talk with both your oncologist and your gynecologist (or family doctor) about what options would be best for you. When women have finished treatment (like chemo), they can safely go on to have children, but it's not safe to get pregnant while being treated.

If you think you might want to have children after being treated for breast cancer, talk with your doctor soon after being diagnosed and before you start treatment. For some women, adding medicines, like monthly injections with a luteinizing hormone-releasing hormone (LHRH) analog, along with chemo, can help them have a successful pregnancy after cancer treatment. To learn more, see Female Fertility and Cancer[7].

If you are pregnant when you get breast cancer, you still can be treated. Certain chemo drugs can be taken safely during the last 2 trimesters of pregnancy. More details can be found in Treating Breast Cancer During Pregnancy.

Heart damage

Even though it is not common, doxorubicin, epirubicin, and some other chemo drugs can cause permanent heart damage (called cardiomyopathy). The risk is highest if the drug is used for a long time or in high doses. Damage from these drugs also happens more often if other drugs that can cause heart damage (such as those that target HER2) are used. Other heart failure risk factors, such as family history of heart problems, high blood pressure, and diabetes can also put you at risk if you receive one of these drugs.

Most doctors will check your heart function with a test like an echocardiogram (an ultrasound of the heart; also called an ECHO) or a MUGA scan before starting one of these drugs. They also carefully control the doses, watch for symptoms of heart problems, and may regularly repeat heart tests during treatment. If the heart function begins to worsen, treatment with these drugs will be temporarily or permanently stopped. Still, in some people, signs of damage might not appear until months or years after treatment stops.

Nerve damage (neuropathy)

Many drugs used to treat breast cancer, including taxanes (docetaxel, paclitaxel, and protein-bound paclitaxel), platinum agents (carboplatin, cisplatin), vinorelbine, eribulin, and ixabepilone, can damage nerves in the hands, arms, feet, and legs. This can sometimes lead to symptoms in those areas like numbness, pain, burning or tingling sensations, sensitivity to cold or heat, or weakness. In most cases these symptoms go away once treatment is stopped, but in some women it might last a long time or may become permanent. There are medicines that could help with these symptoms.

Hand-foot syndrome

Certain chemo drugs, such as capecitabine (Xeloda) and liposomal doxorubicin (Doxil), can irritate the palms of the hands and the soles of the feet. This is called hand-foot

syndrome. Early symptoms include numbness, tingling, and redness. If it gets worse, the hands and feet can become swollen and uncomfortable or even painful. The skin may blister, leading to peeling or even open sores. There is no specific treatment, although some creams or steroids given before chemo may help. These symptoms gradually get better when the drug is stopped or the dose is lowered. The best way to prevent severe hand-foot syndrome is to tell your doctor when symptoms first come up, so that the drug dose can be changed or other medicines can be given.

Chemo brain

Many women who are treated with chemotherapy for breast cancer report a slight decrease in mental functioning. They may have some problems with concentration and memory, which may last a long time. Although many women have linked this to chemo, it also has been seen in women who did not get chemo as part of their treatment. Still, most women function well after treatment. In studies that have found chemo brain to be a side effect of treatment, the symptoms most often last for a few years.

Increased risk of leukemia

Very rarely, certain chemo drugs, such as doxorubicin (Adriamycin), can cause diseases of the bone marrow, such as myelodysplastic syndromes[8] or even acute myeloid leukemia[9], a cancer of white blood cells. If this happens, it is usually within 10 years after treatment. For most women, the benefits of chemo in helping prevent breast cancer from coming back or in extending life are far likely to exceed the risk of this rare but serious complication.

Feeling unwell or tired (fatigue)

Many women do not feel as healthy after chemo as they did before. There is often a residual feeling of body pain or achiness and a mild loss of physical functioning. These changes may be very subtle and happen slowly over time.

Fatigue is another common problem for women who have received chemo. This may last a few months up to several years. It can often be helped, so it’s important to let your doctor or nurse know about it. Exercise, naps, and conserving energy may be recommended. If you have sleep problems, they can be treated. Sometimes fatigue can be a sign of depression, which may be helped by counseling and/or medicines.

More information about chemotherapy

For more general information about how chemotherapy is used to treat cancer,

see Chemotherapy[10].

To learn about some of the side effects listed here and how to manage them, see Managing Cancer-related Side Effects[11].

Hyperlinks

1. www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/imaging-radiology-tests-for-cancer.html
2. www.cancer.org/cancer/types/breast-cancer/understanding-a-breast-cancer-diagnosis/breast-cancer-gene-expression.html
3. www.cancer.org/cancer/types/breast-cancer/understanding-a-breast-cancer-diagnosis/breast-cancer-her2-status.html
4. www.cancer.org/cancer/managing-cancer/making-treatment-decisions/tubes-lines-ports-catheters.html
5. www.cancer.org/cancer/managing-cancer/side-effects.html
6. www.cancer.org/cancer/types/breast-cancer/understanding-a-breast-cancer-diagnosis/breast-cancer-hormone-receptor-status.html
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8. www.cancer.org/cancer/types/myelodysplastic-syndrome.html
9. www.cancer.org/cancer/types/acute-myeloid-leukemia.html
10. www.cancer.org/cancer/managing-cancer/treatment-types/chemotherapy.html
11. www.cancer.org/cancer/managing-cancer/side-effects.html

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Last Revised: October 27, 2021

Hormone Therapy for Breast Cancer

Some types of breast cancer are affected by hormones, like estrogen and progesterone. The breast cancer cells have receptors (proteins) that attach to estrogen and progesterone, which helps them grow. Treatments that stop these hormones from attaching to these receptors are called **hormone or endocrine therapy.**

Hormone therapy can reach cancer cells almost anywhere in the body and not just in the breast. It's recommended for women with tumors that are hormone receptor-positive. It does not help women whose tumors don't have hormone receptors (these tumors are called hormone receptor-negative).

When is hormone therapy used for breast cancer?

Hormone therapy is often used after surgery (as adjuvant therapy) to help reduce the risk of the cancer coming back. Sometimes it is started before surgery (as neoadjuvant therapy).

It is usually taken for at least 5 years. Treatment longer than 5 years might be offered to women whose cancers have a higher chance of coming back. A test called the Breast Cancer Index[1] might be used to help decide if a woman will benefit from more than 5 years of hormone therapy.

Hormone therapy can also be used to treat cancer that has come back after treatment or that has spread to other parts of the body.

How does hormone therapy work?

About 2 out of 3 breast cancers are hormone receptor-positive. Their cells have receptors (proteins) for estrogen (ER-positive cancers) and/or progesterone (PR-positive cancers) which help the cancer cells grow and spread.

There are several types of hormone therapy for breast cancer. Most types of hormone therapy either lower estrogen levels in the body or stop estrogen from helping breast cancer cells grow.

Drugs that block estrogen receptors

These drugs work by stopping estrogen from fueling breast cancer cells to grow.

Selective estrogen receptor modulators (SERMs)

These drugs block estrogen from connecting to the cancer cells and telling them to grow and divide. While they have anti-estrogen effects in breast cells, they act like an estrogen in other tissues, like the uterus and the bones.

These drugs are pills, taken by mouth.

Tamoxifen

Tamoxifen can be used to treat women with breast cancer who have or have not gone through menopause.

This drug can be used in several ways:

- In women at high risk of breast cancer, tamoxifen can be used to help lower the risk of developing breast cancer.
- For women who have been treated with breast-conserving surgery for ductal carcinoma in situ (DCIS) that is hormone receptor-positive, taking tamoxifen for 5 years lowers the chance of the DCIS coming back in the same breast. It also lowers the chance of getting an invasive breast cancer or another DCIS in both breasts.
- For women with hormone receptor-positive invasive breast cancer treated with surgery, tamoxifen can help lower the chances of the cancer coming back and improve the chances of living longer. It can also lower the risk of a new cancer developing in the other breast. Tamoxifen can be started either after surgery (adjuvant therapy) or before surgery (neoadjuvant therapy). When given after surgery, it is usually taken for 5 to 10 years. This drug is used mainly for women with early-stage breast cancer who have not yet gone through menopause. If you have gone through menopause, aromatase inhibitors (see below) are often used instead.
- For women with hormone-positive breast cancer that has spread to other parts of the body, tamoxifen can often help slow or stop the growth of the cancer, and might even shrink some tumors.

Toremifene (Fareston)

Toremifene is a SERM that works in a similar way, but it is used less often and is only approved to treat post-menopausal women with metastatic breast cancer. It is not likely to work if tamoxifen has already been used and has stopped working.

Side effects of tamoxifen and toremifene

The most common side effects of tamoxifen and toremifene are:

- Hot flashes
- Vaginal dryness or discharge
- Changes in the menstrual cycle

When tamoxifen treatment starts, a small number of women with cancer that has spread to the bones might have a **tumor flare** (thetumor gets bigger for a short time) which can cause bone pain. This usually goes away quickly, but rarely a woman may also develop a high calcium level in the blood that is hard to control. If this happens, the treatment may need to be stopped for a time.

Rare, but more serious side effects are also possible:

- If a woman has gone through menopause, SERMs can increase her risk of developing endometrial cancer[2] and uterine sarcoma[3]. Tell your doctor right away about any unusual vaginal bleeding (a common symptom of this cancer). Most uterine bleeding is not from cancer, but this symptom always needs quick attention.
- **Blood clots** are another uncommon, but serious side effect. They usually form in the legs (called **deep vein thrombosis** or DVT), but sometimes a piece of clot in the leg may break off and end up blocking an artery in the lungs (**pulmonary embolism** or PE). Call your doctor or nurse right away if you develop pain, redness, or swelling in your lower leg (calf), shortness of breath, or chest pain, because these can be symptoms of a DVT or PE. Rarely, tamoxifen has been associated with **strokes** in postmenopausal women, so tell your doctor if you have severe headaches, confusion, or trouble speaking or moving.
- **Eye problems** such as cataracts can sometimes happen when taking tamoxifen. It is important to tell your doctor right away if you are having any new trouble with your eyesight.
- **Bones can be affected.** Depending on a woman's menopausal status, tamoxifen can have different effects on the bones. In pre-menopausal women, tamoxifen can cause some bone thinning, but in post-menopausal women it often strengthens bones to some degree. The benefits of taking these drugs outweigh the risks for

almost all women with hormone receptor-positive breast cancer.

Selective estrogen receptor degraders (SERDs)

Like SERMs, these drugs attach to estrogen receptors. But SERDs bind to the receptors more tightly and cause them to be broken down. These drugs have anti-estrogen effects throughout the body.

SERDs are used most often in women who are past menopause. When given to pre-menopausal women, they need to be combined with a luteinizing-hormone releasing hormone (LHRH) agonist to turn off the ovaries (see Ovarian suppression below).

Fulvestrant (Faslodex)

Fulvestrant can be used:

- Alone to treat advanced breast cancer that has not been treated with other hormone therapy.
- Alone to treat advanced breast cancer after other hormone drugs (like tamoxifen and often an aromatase inhibitor) have stopped working.
- In combination with a CDK 4/6 inhibitor or PI3K inhibitor to treat metastatic breast cancer as initial hormone therapy or after other hormone treatments have been tried.

It is given as 2 injections into the buttocks (bottom). For the first month, the 2 shots are given 2 weeks apart. After that, they are given once a month.

Elacestrant (Orserdu)

This drug can be used to treat advanced, ER-positive, HER2-negative breast cancer when the cancer cells have an *ESR1* gene mutation[4], and the cancer has grown after at least one other type of hormone therapy.

Elacestrant is taken daily as pills.

Side effects of fulvestrant and elacestrant

Common short-term side effects of these drugs can include:

- Hot flashes and/or night sweats
- Headache
- Nausea
- Feeling tired
- Loss of appetite
- Muscle, joint, or bone pain
- Injection site pain

Elacestrant can also increase cholesterol and fat levels in the blood.

Drugs that lower estrogen levels

Because estrogen stimulates hormone receptor-positive breast cancers to grow, lowering the estrogen level can help slow the cancer's growth or help prevent it from coming back.

Aromatase inhibitors (AIs)

Aromatase inhibitors (AIs) are drugs that stop most estrogen production in the body. Before menopause, most estrogen is made by the ovaries. But in women whose ovaries aren't working, either because they have gone through menopause or because of certain treatments, estrogen is still made in body fat by an enzyme called aromatase. AIs work by preventing aromatase from making estrogen.

These drugs are useful for women who have gone through menopause, although they can also be used in pre-menopausal women when they are combined with ovarian suppression (see below).

These AIs are pills taken every day to treat breast cancer:

- Letrozole (Femara)
- Anastrozole (Arimidex)
- Exemestane (Aromasin)

Possible side effects of AIs

The most common side effects of AIs are:

- Hot flashes
- Vaginal dryness
- Bone and joint pain
- Muscle pain

AIs tend to have side effects different from tamoxifen. They don't cause uterine cancers and very rarely cause blood clots. They can, however, cause **muscle pain and joint stiffness and/or pain**. The joint pain may be similar to a feeling of having arthritis in many different joints at one time. Options for treating this side effect include, stopping the AI and then switching to a different AI, taking a medicine called duloxetine (Cymbalta), or routine exercise with nonsteroidal anti-inflammatory drugs (NSAIDs). But the muscle and joint pain has led some women to stop treatment. If this happens, most doctors recommend using tamoxifen to complete 5 to 10 years of hormone treatment.

Because AIs drastically lower the estrogen level in women after menopause, they can also cause **bone thinning**, sometimes leading to osteoporosis and even fractures. If you are taking an AI, your bone density may be tested regularly and you may also be given bisphosphonates (zoledronic acid [Zometa] for example) or denosumab (Xgeva, Prolia), to strengthen your bones.

Ovarian suppression

For pre-menopausal women, removing or shutting down the ovaries (ovarian suppression), which are the main source of estrogen, is effectively making them post-menopausal. This may allow some other hormone therapies, such as AIs, to be used. Ovarian suppression along with tamoxifen or an AI might be recommended for women whose breast cancer is at high risk of coming back.

There are several ways to remove or shut down the ovaries to treat breast cancer:

- **Oophorectomy:** Surgery to remove the ovaries. This is permanent and is also called ovarian ablation.
- **Luteinizing hormone-releasing hormone (LHRH) agonists:** These drugs, also called **LHRH analogs**, are used more often than oophorectomy. They stop the signal that the body sends to the ovaries to make estrogen, which causes temporary menopause. Common LHRH drugs include goserelin (Zoladex) and leuprolide (Lupron). They can be used alone or with other hormone drugs (tamoxifen, aromatase inhibitors, fulvestrant) as hormone therapy in pre-menopausal women.

- **Chemotherapy drugs:** Some chemo drugs can damage the ovaries of pre-menopausal women so they no longer make estrogen. Ovarian function can return months or years later in some women, but in others the damage to the ovaries is permanent and leads to menopause.

All of these methods can cause symptoms of menopause, including hot flashes, night sweats, vaginal dryness, and mood swings.

Hormone therapy after surgery for breast cancer

After surgery, hormone therapy can be given to reduce the risk of the cancer coming back. Taking an AI, either alone or after tamoxifen, has been shown to work better than taking just tamoxifen for 5 years.

These hormone therapy schedules are known to be helpful for women who are **post-menopausal when diagnosed**:

- Tamoxifen for 2 to 3 years, followed by an AI for 2 to 3 years (5 years total of treatment)
- Tamoxifen for 2 to 3 years, followed by an AI for 5 years (7 to 8 years of treatment)
- Tamoxifen for 4½ to 6 years, followed by an AI for 5 years (9½ to 11 years of treatment)
- Tamoxifen for 5 to 10 years
- An AI for 5 to 10 years
- An AI for 2 to 3 years, followed by tamoxifen for 2 to 3 years (5 years total of treatment)
- For women who are unable to take an AI, tamoxifen for 5 to 10 years is an option

For most post-menopausal women whose cancers are hormone receptor-positive, most doctors recommend taking an AI at some point during adjuvant (after surgery) therapy. Standard treatment is to take these drugs for about 5 years, or to take in sequence with tamoxifen for 5 to 10 years. For women at a higher risk of recurrence, hormone treatment for longer than 5 years may be recommended. Tamoxifen is an option for some women who cannot take an AI. Taking tamoxifen for 10 years is considered more effective than taking it for 5 years, but you and your doctor will decide the best schedule of treatment for you.

These therapy schedules are known to be helpful forwomen who are **pre-menopausal when diagnosed**:

- Tamoxifen (with or without ovarian suppression) for 5 to 10 years.
- Tamoxifen (with or without ovarian suppression) for 5 years followed by an AI for 5 years if you have gone through menopause.
- An AI plus some sort of ovarian suppression (see above) for 5 to 10 years.

If you have early-stage breast cancer and had not gone through menopause when you were first diagnosed, your doctor might recommend taking tamoxifen first, and then taking an AI later if you go through menopause during treatment. Another option is ovarian suppression by getting a drug called a luteinizing hormone-releasing hormone (LHRH) agonist, which turns off the ovaries, along with an AI. **Pre-menopausal women should not take an AI alone for breast cancer treatment because it is unsafe and can increase hormone levels.**

If cancer comes back or has spread

Tamoxifen, AIs, elacestrant, and fulvestrant can be used to treat more advanced hormone-positive breast cancers, especially in post-menopausal women. They are often continued for as long as they are helpful. Pre-menopausal women might be offered tamoxifen alone or an AI in combination with an LHRH agonist for advanced disease.

Less common types of hormone therapy

Some other types of hormone therapy that were used more often in the past, but are rarely given now include:

- Megestrol acetate (Megace), a progesterone-like drug
- Androgens (male hormones), like testosterone
- Estradiol (a form of estrogen)

These might be options if other forms of hormone therapy are no longer working, but they can often cause side effects.

More information about hormone therapy

To learn more about how hormone therapy is used to treat cancer, see Hormone Therapy[5].

To learn about some of the side effects listed here and how to manage them, see Managing Cancer-related Side Effects[6].

Hyperlinks

1. www.cancer.org/cancer/types/breast-cancer/understanding-a-breast-cancer-diagnosis/breast-cancer-gene-expression.html
2. www.cancer.org/cancer/types/endometrial-cancer.html
3. www.cancer.org/cancer/types/uterine-sarcoma.html
4. www.cancer.org/cancer/types/breast-cancer/understanding-a-breast-cancer-diagnosis/other-breast-cancer-gene-protein-blood-tests.html
5. www.cancer.org/cancer/managing-cancer/treatment-types/hormone-therapy.html
6. www.cancer.org/cancer/managing-cancer/side-effects.html

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Last Revised: January 31, 2023

Targeted Drug Therapy for Breast Cancer

Targeted drug therapy uses medicines that are directed at (target) proteins on breast cancer cells that help them grow, spread, and live longer. Targeted drugs work to destroy cancer cells or slow down their growth. They have side effects different from chemotherapy.

Some targeted therapy drugs, for example, monoclonal antibodies, work in more than one way to control cancer cells and may also be considered immunotherapy because they boost the immune system.

Like chemotherapy, these drugs enter the bloodstream and reach almost all areas of the body, which makes them useful against cancers that have spread to distant parts of the body. Targeted drugs sometimes work even when chemo drugs do not. Some targeted drugs can help other types of treatment work better.

Several types of targeted therapy drugs can be used to treat breast cancer.

- Targeted therapy for HER2-positive breast cancer
- Targeted therapy for hormone receptor-positive breast cancer
- Targeted therapy for women with BRCA gene mutations
- Targeted therapy for triple-negative breast cancer
- More information about targeted therapy

Targeted therapy for HER2-positive breast cancer

In about 15% to 20% of breast cancers, the cancer cells make too much of a growth-promoting protein known as HER2[1]. These cancers, known as HER2-positive breastcancers, tend to grow and spread more aggressively than HER2-negative breast cancers. Different types of drugs have been developed that target the HER2 protein.

Monoclonal antibodies

Monoclonal antibodies are man-made versions of immune system proteins (antibodies) that are designed to attach to a specific target. In this case, they attach to the HER2 protein on cancer cells, which can help stop the cells from growing.

Trastuzumab (Herceptin, other brand names[2]): Trastuzumab can be used to treat

both early-stage and advanced breast cancer. This drug is often given with chemo, but it might also be used alone (especially if chemo alone has already been tried). When started before (neoadjuvant) or after (adjuvant) surgery to treat early breast cancer, this drug is usually given for 6 months to a year. For advanced breast cancer, treatment is often given for as long as the drug is helpful. This drug is given into a vein (IV).

Another form of trastuzumab, called **trastuzumab and hyaluronidase injection (Herceptin Hylecta),** is given as a subcutaneous (under the skin) shot over a few minutes.

Pertuzumab (Perjeta): This HER2 monoclonal antibody can be given with trastuzumab and chemo, either before or after surgery to treat early-stage breast cancer, or to treat advanced breast cancer. This drug is given into a vein (IV).

Trastuzumab, pertuzumab, and hyaluronidase injection (Phesgo): This is a combination of these drugs given as a subcutaneous (under the skin) shot over several minutes.

Margetuximab (Margenza): This HER2 monoclonal antibody can be used along with chemo to treat advanced breast cancer, typically after at least 2 other drugs that target HER2 have been tried. This drug is given into a vein (IV).

Antibody-drug conjugates

An antibody-drug conjugate (ADC) is a monoclonal antibody linked to a chemotherapy drug. In this case, the anti-HER2 antibody acts like a homing signal by attaching to the HER2 protein on cancer cells, bringing the chemo directly to them.

Ado-trastuzumab emtansine (Kadcyla): This antibody-drug conjugate connects the HER2 antibody to the chemo drug emtansine, which is similar to paclitaxel. It is used by itself to treat early-stage breast cancer after surgery (when chemo and trastuzumab were given before surgery, and there was cancer still present at the time of surgery), or to treat advanced breast cancer in women who have already been treated with trastuzumab and chemo. This drug is given in a vein (IV).

Fam-trastuzumab deruxtecan (Enhertu): This antibody-drug conjugate connects the HER2 antibody to a chemo drug deruxtecan, which is similar to irinotecan. It can be used by itself to treat breast cancer that can’t be removed with surgery or that has spread (metastasized) to another part of the body, typically after at least 1 other anti-HER2 targeted drug has been tried. This drug is given in a vein (IV).

Fam-trastuzumab deruxtecan can also be used to treat HER2-low breast cancers that

can’t be removed with surgery or that has spread to another part of the body, typically after chemotherapy has been tried or if the cancer recurs within 6 months of finishing adjuvant chemotherapy.

Kinase inhibitors

HER2 is a type of protein known as a kinase. Kinases are proteins in cells that normally relay signals (such as telling the cell to grow). Drugs that block kinases are called **kinase inhibitors**.

Lapatinib (Tykerb): This drug is a pill taken daily. Lapatinib is used to treat advanced breast cancer. It is typically given along with trastuzumab and the chemo drug capecitabine.

Neratinib (Nerlynx): This kinase inhibitor is a pill taken daily. Neratinib is used to treat early-stage breast cancer after a woman has been treated with trastuzumab for one year, and it is usually given for one year. It can also be given along with the chemo drug capecitabine to treat people with metastatic disease, typically after at least 2 other anti-HER2 targeted drugs have been tried.

Tucatinib (Tukysa): This kinase inhibitor is taken as a pill, typically twice a day. Tucatinib is used to treat advanced breast cancer, after at least one other anti-HER2 targeted drug has been tried. It is usually given along with trastuzumab and the chemo drug capecitabine.

Side effects of HER2 targeted drug therapy

The side effects of HER2 targeted drugs are often mild, but some can be serious. Discuss what you can expect with your doctor. **If you are pregnant, you should not take these drugs.** They can harm and even cause death to the fetus. If you could become pregnant, talk to your doctor about using effective birth control while taking these drugs.

Monoclonal antibodies and antibody-drug conjugates can sometimes cause **heart damage** during or after treatment. This can lead to **congestive heart failure**. For most (but not all) women, this effect lasts a short time and gets better when the drug is stopped. The risk of heart problems is higher when these drugs are given with certain chemo drugs that also can cause heart damage, such as doxorubicin (Adriamycin) and epirubicin (Ellence). Other factors that can increase your risk of heart problems are being older than 50, being overweight or obese, having heart problems, and taking medicines for high blood pressure.

Because these drugs can cause heart damage, doctors often check your heart function (with an echocardiogram or a MUGA scan) before treatment, and regularly while you are taking the drug. Let your doctor know if you develop symptoms such as **shortness of breath**, a **fast heartbeat**, **leg swelling**, and **severe fatigue**.

Lapatinib, neratinib, tucatinib, and the combination of pertuzumab with trastuzumab can cause **severe diarrhea**, so it's very important to let your health care team know about any changes in bowel habits as soon as they happen.

Lapatinib and tucatinib can also cause **hand-foot syndrome**, in which the hands and feet become sore and red, and may blister and peel.

Lapatinib, neratinib, and tucatinib can cause **liver problems**. Your doctor will do blood tests to check your liver function during treatment. Let your health care team know right away if you have possible signs or symptoms of liver problems, such as itchy skin, yellowing of the skin or the white parts of your eyes, dark urine, or pain in the right upper belly area.

Fam-trastuzumab deruxtecan (Enhertu) can cause **serious lung disease** in some women. In some cases this might even be life threatening. It's very important to let your doctor or nurse know right away if you're having symptoms such as coughing, wheezing, trouble breathing, or fever.

Targeted therapy for hormone receptor-positive breast cancer

About 3 of 4 breast cancers are hormone (estrogen or progesterone) receptor-positive. For women with these cancers, treatment with hormone therapy is often helpful. Certain targeted therapy drugs can make hormone therapy even more effective, although these targeted drugs might also add to the side effects.

CDK4/6 inhibitors

Palbociclib (Ibrance), **ribociclib (Kisqali)**, and **abemaciclib (Verzenio)** are drugs that block proteins in the cell called cyclin-dependent kinases (CDKs), particularly CDK4 and CDK6. Blocking these proteins in hormone receptor-positive breast cancer cells helps stop the cells from dividing. This can slow cancer growth.

These drugs are approved to treat some hormone receptor-positive, HER2-negative breast cancers.

There are different ways to use these drugs.

- Any of these drugs can be given along with an aromatase inhibitor (AI) or fulvestrant to women with advanced breast cancer who have gone through menopause.
- Any of these drugs can be given with fulvestrant or an aromatase inhibitor to women with advanced breast cancer who are still having regular periods (premenopausal) or are almost in menopause (perimenopausal). These women, however, must also be on medicines, such as luteinizing hormone-releasing hormone (LHRH) analogs, that stop the ovaries from making estrogen or have their ovaries removed with surgery.
- Abemaciclib can also be used by itself in women with advanced breast cancer who have previously been treated with hormone therapy and chemotherapy.
- For women with early-stage breast cancer that has spread to the lymph nodes and has a high chance of coming back after surgery, abemaciclib can be given as adjuvant treatment along with tamoxifen or an AI. It is typically given for 2 years.

These drugs are taken as pills, typically once or twice a day.

The most common **side effects of CDK4/6 inhibitors** include low blood cell counts and fatigue. Nausea and vomiting, mouth sores, hair loss, diarrhea, and headache are less common side effects. Very low white blood cell counts can increase the risk of serious infection. A rare but possible life-threatening side effect is inflammation of the lungs, also called interstitial lung disease or pneumonitis.

mTOR inhibitor

Everolimus (Afinitor) blocks mTOR, a protein in cells that normally helps them grow and divide. Everolimus may also stop tumors from developing new blood vessels, which can help limit their growth. When used for treating breast cancer , it seems to help hormone therapy drugs work better.

This drug is used for women who have gone through menopause and have advanced hormone receptor-positive, HER2-negative breast cancer. It is used with the aromatase inhibitor exemestane (Aromasin) for women whose cancers have grown while being treated with either letrozole or anastrozole (or if the cancer started growing shortly after treatment with these drugs was stopped). It might also be used with fulvestrant, a hormone therapy drug.

Everolimus is taken as a pill, typically once a day.

Common **side effects of everolimus** include mouth sores, rash, diarrhea, nausea,

feeling weak or tired, low blood counts, shortness of breath, and cough. Everolimus can also increase blood lipids (cholesterol and triglycerides) and blood sugars, so your doctor will check your blood work regularly while you are taking this drug. It can also increase your risk of serious infections, so your doctor will watch you closely for infection.

PI3K inhibitor

Alpelisib (Piqray) blocks a form of the PI3K protein in cancer cells. This can help stop them from growing.

This drug can be used along with the hormone drug fulvestrant to treat women with advanced hormone receptor-positive, HER2-negative breast cancer with a *PIK3CA* gene mutation that has grown during or after treatment with an aromatase inhibitor. (The *PIK3CA* gene is the gene that tells the cell to make the PI3K protein.) Your doctor will test your blood or tumor for this mutation before starting treatment with this drug.

This drug is taken as a pill, typically once a day.

Side effects of alpelisib can include skin rash, high blood sugar levels, signs of kidney, liver, or pancreatic problems, diarrhea, low blood counts, nausea and vomiting, fatigue, decreased appetite, mouth sores, weight loss, low calcium levels, blood clotting problems, and hair loss.

Very severe skin reactions, such as rashes with peeling and blistering, are possible and should be reported to a doctor. People with a history of severe skin reactions should tell their doctor before taking alpelisib. Your cancer care team might recommend that you take an antihistamine medicine to help prevent the rash and may also check your blood sugar levels regularly.

AKT inhibitor

Capivasertib (Truqap) blocks forms of the AKT protein, which is part of a signaling pathway inside cells (including cancer cells) that can help them grow. Other proteins in this pathway include the PI3K and PTEN proteins.

This drug can be used along with the hormone drug fulvestrant to treat advanced hormone receptor-positive, HER2-negative breast cancer, if the cancer cells have changes in any of the *PIK3CA*, *AKT1*, or *PTEN* genes, and if the cancer has grown during or after treatment with hormone therapy. Your doctor will test your blood or tumor for these mutations before starting treatment with this drug.

This drug is taken as pills, typically twice a day for 4 days, followed by 3 days off each week.

Side effects of capivasertib can include:

- High blood sugar levels: Your cancer care team will check your blood sugar levels before and during your treatment.
- Diarrhea (which may be severe): Tell your cancer team right away if start to have loose stools or diarrhea.
- Skin rash or other skin reactions: Very severe skin reactions, such as rashes with peeling and blistering, are possible and should be reported to a doctor.

Other possible side effects can include nausea, vomiting, mouth sores, and changes in certain blood tests.

Antibody-drug conjugate

An antibody-drug conjugate (ADC) is a monoclonal antibody joined to a chemotherapy drug. The antibody acts like a homing signal by attaching to a specific protein on cancer cells, bringing the chemo directly to them.

Sacituzumab govitecan (Trodelvy): In the case of this ADC, the monoclonal antibody part attaches to the Trop-2 protein on breast cancer cells and brings the chemo directly to them. (Some breast cancer cells have too much Trop-2, which helps them grow and spread quickly.)

This ADC can be used to treat advanced hormone receptor-positive, HER2-negative breast cancer, in people who have already received hormone therapy and at least 2 chemo regimens.

This drug is given into a vein (IV) weekly for 2 weeks, followed by one week off, then restarted.

Some common **side effects** of this drug include nausea, vomiting, diarrhea, constipation, feeling tired, rash, loss of appetite, hair loss, low red blood cell counts, and belly pain. Serious side effects can include very low white blood cell counts (with an increased risk of infection), severe diarrhea, and infusion reactions (similar to an allergic reaction) when the drug is infused. Medicines are normally given before each treatment to lower the chances of vomiting and infusion reactions.

Targeted therapy for women with *BRCA* gene mutations

Olaparib (Lynparza) and **talazoparib (Talzenna)** are drugs known as *PARP inhibitor*s. PARP proteins normally help repair damaged DNA inside cells[3]. The *BRCA* genes (*BRCA1* and *BRCA2*) also help repair DNA (in a slightly different way), but mutations in one of those genes can stop this from happening. PARP inhibitors work by blocking the PARP proteins. Because tumor cells with a mutated *BRCA* gene already have trouble repairing damaged DNA, blocking the PARP proteins often leads to the death of these cells. These drugs are pills and are taken once or twice a day. They can be used in different ways to treat breast cancer.

- Olaparib can be given to women with a BRCA mutation with early-stage HER2-negative breast cancer after surgery who have been treated with chemotherapy (before or after surgery) and are at high risk of the cancer recurring. It is typically given for one year. When given in this way, it can help some women live longer.
- Olaparib and talazoparib can be used to treat advanced or metastatic, HER2-negative breast cancer in women with a *BRCA* mutation who have already had chemotherapy. If the cancer is hormone receptor-positive, olaparib can also be used in women who have already received hormone therapy.

Only a small portion of women with breast cancer are born with a mutated *BRCA* gene,[4]which is in all the cells of the body. This is different from the gene change happening after you are born which is found only in the cancer cells. If you are not known to have a *BRCA* mutation, your doctor will test your blood to be sure you have one before starting treatment with these drugs.

Side effects can include nausea, vomiting, diarrhea, fatigue, loss of appetite, taste changes, low red blood cell counts (anemia), low platelet counts, and low white blood cell counts. Rarely, some people treated with a PARP inhibitor have developed a blood cancer, such as myelodysplastic syndrome[5] or acute myeloid leukemia (AML)[6].

Targeted therapy for triple-negative breast cancer

In triple-negative breast cancer (TNBC), the cancer cells don’t have estrogen or progesterone receptors and they make very little or none of the HER2 protein.

Antibody-drug conjugate

An antibody-drug conjugate (ADC) is a monoclonal antibody joined to a chemotherapy drug. The antibody acts like a homing signal by attaching to a specific protein on cancer

cells, bringing the chemo directly to them.

Sacituzumab govitecan (Trodelvy): In the case of this ADC, the monoclonal antibody part attaches to the Trop-2 protein on breast cancer cells and brings a chemo drug, similar to irinotecan, directly to them. (Some breast cancer cells have too much Trop-2, which helps them grow and spread quickly.)

This antibody-drug conjugate can be used by itself to treat advanced TNBC, after at least 2 other chemo regimens have been tried. This drug is given in a vein (IV) weekly for 2 weeks, followed by one week off, then restarted.

Some common **side effects** of this drug include nausea, vomiting, diarrhea, constipation, feeling tired, rash, loss of appetite, hair loss, low red blood cell counts, and belly pain. Serious side effects can include very low white blood cell counts (with an increased risk of infection), severe diarrhea, and infusion reactions (similar to an allergic rection) when the drug is infused. Medicines are normally given before each treatment to lower the chances of vomiting and infusion reactions.

More information about targeted therapy

To learn more about how targeted drugs are used to treat cancer, see Targeted Cancer Therapy[7].

To learn about some of the side effects listed here and how to manage them, see Managing Cancer-related Side Effects[8].

Hyperlinks

1. www.cancer.org/cancer/types/breast-cancer/understanding-a-breast-cancer-diagnosis/breast-cancer-her2-status.html
2. www.cancer.org/cancer/types/breast-cancer/understanding-a-breast-cancer-diagnosis/breast-cancer-her2-status.html
3. www.cancer.org/cancer/managing-cancer/treatment-types/biosimilar-drugs/list.html
4. www.cancer.org/cancer/understanding-cancer/genes-and-cancer.html
5. www.cancer.org/cancer/types/breast-cancer/risk-and-prevention/breast-cancer-risk-factors-you-cannot-change.html
6. www.cancer.org/cancer/types/myelodysplastic-syndrome.html

7. www.cancer.org/cancer/types/acute-myeloid-leukemia.html
8. www.cancer.org/cancer/managing-cancer/treatment-types/targeted-therapy.html
9. www.cancer.org/cancer/managing-cancer/side-effects.html

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Last Revised: January 22, 2024

Immunotherapy for Breast Cancer

Immunotherapy is the use of medicines to boost a person's own immune system to recognize and destroy cancer cells more effectively. Immunotherapy typically works on specific proteins involved in the immune system to enhance the immune response. These drugs have side effects different from those of chemotherapy.

Some immunotherapy drugs, for example, monoclonal antibodies, work in more than one way to control cancer cells and may also be considered targeted therapy because they block a specific protein on the cancer cell to keep it from growing.

Immunotherapy is used to treat some types of breast cancer.

Immune checkpoint inhibitors for breast cancer

An important part of the immune system is its ability to keep itself from attacking normal cells in the body. To do this, it uses proteins (or "checkpoints") on immune cells that

need to be turned on (or off) to start an immune response. Breast cancer cells sometimes use these checkpoints to avoid being attacked by the immune system. Drugs that target these checkpoint proteins, help restore the immune response against breast cancer cells.

PD-1 inhibitor

Pembrolizumab (Keytruda) for breast cancer

Pembrolizumab (Keytruda) is a drug that targets PD-1 (a protein on immune system T cells that normally helps keep them from attacking other cells in the body). By blocking PD-1, these drugs boost the immune response against breast cancer cells. This can often shrink tumors.

It can be used with chemotherapy to treat triple-negative breast cancer:

- Before and after surgery for stage 2 or 3 cancers
- That has come back (recurred) locally but can't be removed by surgery
- That has spread to other parts of the body.

This drug is given as an intravenous (IV) infusion, typically every 3 or 6 weeks. In certain situations, your doctor might test your cancer cells for the PD-L1 protein to show that the cancer is more likely to respond to treatment with pembrolizumab.

Possible side effects of immune checkpoint inhibitors

Side effects of these drugs can include fatigue, cough, nausea, skin rash, poor appetite, constipation, and diarrhea.

Other, more serious side effects occur less often.

Infusion reactions: Some people might have an infusion reaction while getting these drugs. This is like an allergic reaction, and can include fever, chills, flushing of the face, rash, itchy skin, feeling dizzy, wheezing, and trouble breathing. It's important to tell your doctor or nurse right away if you have any of these symptoms while getting these drugs.

Autoimmune reactions: These drugs remove one of the protections on the body's immune system. Sometimes the immune system starts attacking other parts of the body, which can cause serious or even life-threatening problems in the lungs, intestines, liver, hormone-making glands, kidneys, or other organs.

It's very important to report any new side effects to your health care team quickly. If serious side effects do occur, treatment may need to be stopped and you may get high doses of corticosteroids to suppress your immune system.

More information about immunotherapy

To learn more about how drugs that work on the immune system are used to treat cancer, see Cancer Immunotherapy[1].

To learn about some of the side effects listed here and how to manage them, see Managing Cancer-related Side Effects[2].

Hyperlinks

1. www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy.html
2. www.cancer.org/cancer/managing-cancer/side-effects.html

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Last Revised: October 27, 2021

Treatment of Breast Cancer by Stage

This information is based on AJCC Staging systems prior to 2018 which were primarily based on tumor size and lymph node status. Since the updated staging system for breast cancer now also includes estrogen receptor (ER), progesterone receptor (PR), and HER2 status, the stages may be higher or lower than previous staging systems. Whether or not treatment strategies will change with this new staging system are yet to be determined. You should discuss your stage and treatment options with your doctor.

The stage[1] of your breast cancer is an important factor in making decisions about your treatment options. In general, the more the breast cancer has spread, the more treatment you will likely need. But other factors can also be important, such as:

- If the cancer cells have hormone receptors[2] (that is, if the cancer is ER-positive or PR-positive)
- If the cancer cells have large amounts of theHER2 protein[3] (that is, if the cancer is HER2-positive)
- If the cancer cells have a certain gene mutation (change)
- Your overall health and personal preferences
- If you have gone through menopause or not
- How fast the cancer is growing (measured by grade or other measures) and if it is affecting major organs like the lungs or liver

Talk with your doctor about how these factors can affect your treatment options.

Stage 0 [4]

Stage 0 cancers are limited to the inside of the milk duct and are non-invasive (does not invade nearby tissues). Ductal carcinoma in situ (DCIS) is a stage 0 breast tumor. Lobular carcinoma in situ (LCIS) used to be categorized as stage 0, but this has been changed because it is not cancer. Still, it does indicate a higher risk of breast cancer. See Lobular Carcinoma in Situ (LCIS) for more information.

- Treatment of Ductal Carcinoma in Situ (DCIS)

Stages I-III

Treatment for stages I to III breast cancer usually includes surgery and radiation therapy, often with chemo or other drug therapies either before (neoadjuvant) or after (adjuvant) surgery. Stage I: These breast cancers are still relatively small and either have not spread to the lymph nodes or have only a tiny area of cancer spread in the sentinel lymph node (the first lymph node to which cancer is likely to spread). Stage II: These breast cancers are larger than stage I cancers and/or have spread to a few nearby lymph nodes. Stage III: These tumors are larger or are growing into nearby tissues (the skin over the breast or the muscle underneath), or they have spread to many nearby lymph nodes.

- Treatment of Breast Cancer Stages I-III

Stage IV (metastatic breast cancer)

Stage IV cancers have spread beyond the breast and nearby lymph nodes to other parts of the body.

- Treatment of Stage IV (Metastatic) Breast Cancer

Recurrent breast cancer

Cancer is called recurrent when it comes back after primary treatment. Recurrence can be local (in the same breast or in the surgery scar), regional (in nearby lymph nodes), or in a distant area. Treatment for recurrent breast cancer depends on where the cancer comes back and what treatments you've had before.

- Treatment of Recurrent Breast Cancer

Hyperlinks

1. www.cancer.org/cancer/types/breast-cancer/understanding-a-breast-cancer-diagnosis/stages-of-breast-cancer.html
2. www.cancer.org/cancer/types/breast-cancer/understanding-a-breast-cancer-diagnosis/breast-cancer-hormone-receptor-status.html
3. www.cancer.org/cancer/types/breast-cancer/understanding-a-breast-cancer-diagnosis/breast-cancer-her2-status.html
4. www.cancer.org/cancer/types/breast-cancer/non-cancerous-breast-conditions/lobular-carcinoma-in-situ.html

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Last Revised: September 18, 2019

Treatment of Ductal Carcinoma in Situ (DCIS)

Ductal carcinoma in situ (DCIS) means the cells that line the milk ducts of the breast have become cancer, but they have not spread into surrounding breast tissue.

DCIS is considered non-invasive or pre-invasive breast cancer. DCIS can't spread outside the breast, but it is often treated because if left alone, some DCIS cells can continue to undergo abnormal changes that cause it to become invasive breast cancer (which can spread).

In most cases, a woman with DCIS can choose between breast-conserving surgery (BCS) and simple mastectomy. But sometimes, if DCIS is throughout the breast, a mastectomy might be a better option. There are clinical studies being done to see if observation instead of surgery might be an option for some women.

Breast-conserving surgery (BCS)

In breast-conserving surgery (BCS), the surgeon removes the tumor and a small amount of normal breast tissue around it. Lymph node removal is not usually needed with BCS. It might be done after the first surgery if an area of invasive cancer is found. The chances an area of DCIS contains invasive cancer goes up with tumor size and how fast the cancer is growing. If lymph nodes are removed, this is usually done as a sentinel lymph node biopsy (SLNB).

If BCS is done, it is usually followed by radiation therapy. This lowers the chance of the cancer coming back in the same breast (either as more DCIS or as an invasive cancer). BCS without radiation therapy is not a standard treatment, but it might be an option for older women, women with other significant health problems, or women who had small areas of low-grade DCIS that were removed with large enough cancer-free surgical margins.

Many women with early-stage breast cancer, like DCIS, can choose between breast-conserving surgery (BCS) and mastectomy. The main advantage of BCS is that a woman keeps most of her breast. Some women might worry that having less extensive surgery might raise their risk of the cancer coming back. But studies following thousands of women for more than 20 years show that when BCS is done with radiation in women with early-stage cancer , survival is the same as having a mastectomy.

Mastectomy

Simple mastectomy (removal of the entire breast) may be needed if the area of DCIS is very large, if the breast has several separate areas of DCIS in different quadrants (multicentric), or if BCS cannot remove the DCIS completely (that is, the BCS specimen and re-excision specimens still have cancer cells in or near the surgical margins). If a mastectomy is needed for any of the reasons stated above, many doctors will do a SLNB along with the mastectomy because there is a higher chance that invasive cancer might be found. If an area of invasive cancer is found in the tissue removed during a mastectomy, the doctor won’t be able to go back and do SLNB later, and as a result may have to do a full axillary lymph node dissection (ALND) instead.

Women having a mastectomy for DCIS typically don’t need radiation therapy and may

choose to have breast reconstruction[1] right away or later.

Hormone therapy after breast surgery

If the DCIS is hormone receptor-positive (estrogen or progesterone), treatment with tamoxifen (for any woman) or an aromatase inhibitor, such as exemestane or anastrozole, (for women past menopause) for 5 years after surgery can lower the risk of another DCIS or invasive cancer developing in either breast. If you have hormone receptor-positive DCIS, discuss the reasons for and against hormone therapy with your doctor.

Hyperlinks

1. www.cancer.org/cancer/types/breast-cancer/reconstruction-surgery.html

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Last Revised: October 27, 2021

Treatment of Breast Cancer Stages I-III

The stage[1] of your breast cancer is an important factor in making decisions about your treatment.

Most women with breast cancer in stages I, II, or III are treated with surgery, often followed by radiation therapy. Many women also get some kind of systemic drug therapy (medicine that travels to almost all areas of the body). In general, the more the breast cancer has spread, the more treatment you will likely need. But your treatment options are affected by your personal preferences and other information about your breast cancer, such as:

- If the cancer cells have hormone receptors.[2] That is, if the cancer is estrogen receptor (ER)-positive or progesterone receptor (PR)-positive.
- If the cancer cells have large amounts of the HER2 protein[3] (that is, if the cancer is HER2-positive)
- How fast the cancer is growing (measured by grade[4] or Ki-67[5])
- Your overall health
- If you have gone through menopause or not

Talk with your doctor about how these factors can affect your treatment options.

What type of drug treatment(s) might I get?

Most women with breast cancer in stages I, II, or III will get some kind of systemic therapy as part of their treatment. This might include:

- Chemotherapy
- Hormone therapy (tamoxifen, an aromatase inhibitor, or one followed by the other)
- Targeted drugs, such as trastuzumab (Herceptin), pertuzumab (Perjeta), or abemaciclib (Verzenio)
- Immunotherapy
- Some combination of these

The types of drugs that might work best depend on the tumor's hormone receptor status, HER2 status, and other factors.

Treating stage I breast cancer

These breast cancers are still fairly small and either have not spread to the lymph nodes or have spread to only a tiny area in the sentinel lymph node (the first lymph node to which cancer is likely to spread).

Local therapy (surgery and radiation therapy)

Surgery is the main treatment for stage I breast cancer. These cancers can be treated with either breast-conserving surgery (BCS; sometimes called lumpectomy or partial mastectomy) or mastectomy. The nearby lymph nodes will also need to be checked, either with a sentinel lymph node biopsy (SLNB) or an axillary lymph node dissection (ALND).

Some women can have breast reconstruction[6] at the same time as the surgery to remove the cancer. But if you will need radiation therapy after surgery, it is better to wait to get reconstruction until after the radiation is complete.

If BCS is done, radiation therapy is usually given after surgery to lower the chance of the cancer coming back in the breast and to also help people live longer.

In a separate group, women who are at least 65 years old may consider BCS **without** radiation therapy if ALL of the following are true:

- The tumor was 3 cm (a little more than 1 inch) or less across and it has been removed completely.
- None of the lymph nodes removed contained cancer.
- The cancer is ER-positive or PR-positive, and hormone therapy will be given.

Radiation therapy given to women with these characteristics still lowers the chance of the cancer coming back, but it has not been shown to help them live longer.

If you had a mastectomy, you are less likely to need radiation therapy, but it might be given depending on the details of your specific cancer. You should discuss if you need radiation treatment with your doctor. You might be sent to a doctor who specializes in radiation (a radiation oncologist) for evaluation.

Systemic therapy (chemo and other drugs)

If a woman has a hormone receptor-positive (ER-positive or PR-positive) breast cancer, most doctors will recommend hormone therapy (tamoxifen or an aromatase inhibitor, or one followed by the other) as an adjuvant (after surgery) treatment, no matter how small the tumor is. Women with tumors larger than 0.5 cm (about ¼ inch) across may be more likely to benefit from it. Hormone therapy is typically given for at least 5 years.

If the tumor is larger than 0.5 cm (about 1/4 inch) across, chemo after surgery (adjuvant chemotherapy) is sometimes recommended. A woman's age when she is diagnosed may help in deciding if chemo should be offered or not. Some doctors may suggest chemo for smaller tumors as well, especially if they have any unfavorable features (a cancer that is growing fast; hormone receptor-negative, HER2-positive; or having a high score on a gene panel such as Oncotype DX[7]).

After surgery, some women with HER2-positive cancers will be treated with trastuzumab (with or without pertuzumab) for up to 1 year.

Many women with HER2-positive cancers will be treated with neoadjuvant (before surgery) chemo and trastuzumab (with or without pertuzumab) followed by surgery and more trastuzumab (with or without pertuzumab) for up to 1 year. If after neoadjuvant therapy, residual cancer is found during surgery, trastuzumab may be changed to a different drug, called ado-trastuzumab emtansine, which is given every 3 weeks for 14 doses.

For women with a BRCA mutation and hormone-positive, HER2-negative breast cancer who received neoadjuvant chemotherapy but still have residual cancer at the time of surgery, the targeted drug olaparib might be given after surgery. It is usually given for one year. When given this way, it can help some women live longer.

Treating stage II breast cancer

Stage II breast cancers are larger than stage I cancers and/or have spread to a few nearby lymph nodes.

Local therapy (surgery and radiation therapy)

Stage II cancers are treated with either breast-conserving surgery (BCS; sometimes called lumpectomy or partial mastectomy) or mastectomy. The nearby lymph nodes will also be checked, either with a sentinel lymph node biopsy (SLNB) or an axillary lymph node dissection (ALND).

Women who have BCS are treated with radiation therapy after surgery. Women who have a mastectomy are typically treated with radiation if the cancer is found in the lymph nodes. Some patients who have a SLNB that shows cancer in a few lymph nodes might not have the rest of their lymph nodes removed to check for more cancer. In these patients, radiation may be discussed as a treatment option after mastectomy.

If you were initially diagnosed with stage II breast cancer and were given a systemic treatment such as chemotherapy or hormone therapy before surgery, radiation therapy might be recommended if cancer is found in the lymph nodes during mastectomy. A **radiation oncologist** may talk with you to see if radiation would be helpful.

If chemotherapy is also needed after surgery, the radiation will be delayed until the chemo is done.

In some women, breast reconstruction can be done during the surgery to remove the cancer. But if you will need radiation after surgery, it is better to wait to get reconstruction until after the radiation is complete.

Systemic therapy (chemo and other drugs)

Systemic therapy (drugs that travel to almost every part of the body) is recommended for some women with stage II breast cancer. Some systemic therapies are given before surgery (neoadjuvant therapy), and others are given after surgery (adjuvant therapy). For some women, systemic therapy will be started before surgery and then continued after surgery. Neoadjuvant treatments are a good option for women with large tumors, because they can shrink the tumor before surgery, possibly enough to make BCS an option.

Neoadjuvant treatment is also a preferable option for women with triple-negative breast cancer (TNBC) or HER2-positive breast cancer because the treatment given after surgery is often chosen depending on how much cancer is still in the breast and/or lymph nodes at the time of surgery. Some women with early-stage cancer who get neoadjuvant treatment might live longer if the cancer completely goes away with that treatment.

To help decide which women with stage II hormone receptor-positive, HER2-negative breast cancer will benefit from chemotherapy, a gene panel test such as Oncotype DX[8] may be done on the tumor sample.

The drugs used will depend on the woman’s menopause status, as well as tumor test results. Treatment might include:

- **Chemotherapy:** Chemo can be given before and/or after surgery.
- **HER2 targeted drugs:** Some women with HER2-positive cancers will be treated with adjuvant (after surgery) chemotherapy with trastuzumab with or without pertuzumab for up to 1 year. Many women with HER2-positive cancers will be treated first with trastuzumab (with or without pertuzumab) followed by surgery and then more trastuzumab (with or without pertuzumab) for up to a year. If after neoadjuvant therapy, residual cancer is found at the time of surgery, the targeted drug, ado-trastuzumab emtansine, may be used instead of trastuzumab. It is given every 3 weeks for 14 doses. For women with hormone receptor-positive cancer found in the lymph nodes after completing 1 year of trastuzumab, the doctor might also recommend additional treatment with an oral targeted drug called neratinib for 1 year.
- **Hormone therapy:** If the cancer is hormone receptor-positive, hormone therapy (tamoxifen, an aromatase inhibitor (AI), or one followed by the other) is typically used. It can be started before surgery, but because it continues for at least 5 years, it needs to be given after surgery as well.
- **Targeted drug therapy**: For women with early-stage breast cancer that is hormone receptor-positive, HER2-negative, has cancer in the lymph nodes, and has a high chance of coming back, the targeted drug abemaciclib can be given after surgery along with tamoxifen or an AI. It is a pill typically given for 2 years twice a day. For women who have a BRCA mutation with a hormone receptor-positive, HER2-negative tumor who still have cancer in the tissue removed at surgery after neoadjuvant chemo, the targeted drug olaparib might be given for one year to help lower the chance of the cancer recurring. When given this way, it can help some women live longer.
- **Immunotherapy:** Women with TNBC might get the immunotherapy drug, pembrolizumab, before surgery and then again after surgery. See Treatment of Triple-negative Breast Cancer for more details.

Treating stage III breast cancer

In stage III breast cancer, the tumor is large (more than 5 cm or about 2 inches across) or growing into nearby tissues (the skin over the breast or the muscle underneath), or the cancer has spread to many nearby lymph nodes.

If you have inflammatory breast cancer: Stage III cancers also include some inflammatory breast cancers that have not spread beyond nearby lymph nodes. These

cancers are treated slightly different from other stage III breast cancers. You can find more details in Treatment of Inflammatory Breast Cancer.

There are two main approaches to treating stage III breast cancer:

Starting with neoadjuvant therapy

Most often, these cancers are treated with neoadjuvant (before surgery) chemotherapy. For HER2-positive tumors, the targeted drug trastuzumab is given as well, often along with pertuzumab (Perjeta). This may shrink the tumor enough for a woman to have breast-conserving surgery (BCS). If the tumor doesn't shrink enough, a mastectomy is done. Nearby lymph nodes will also need to be checked. A sentinel lymph node biopsy (SLNB) is often not an option for stage III cancers, so an axillary lymph node dissection (ALND) is usually done.

Often, radiation therapy is needed after surgery. If breast reconstruction is planned, it is usually delayed until after radiation therapy is done. For some, additional chemo is given after surgery as well.

After surgery, some women with HER2-positive cancers will be treated with trastuzumab (with or without pertuzumab) for up to a year. Many women with HER2-positive cancers will be treated first with trastuzumab (with or without pertuzumab) followed by surgery and then more trastuzumab (with or without pertuzumab) for up to a year. If after neoadjuvant therapy, any residual cancer is found at the time of surgery, ado-trastuzumab emtansine may be used instead of trastuzumab. It is given every 3 weeks for 14 doses. For women with hormone receptor-positive cancer that is in the lymph nodes, who have completed a year of trastuzumab, the doctor might also recommend additional treatment with an oral targeted drug called neratinib for a year.

Women with hormone receptor-positive (ER-positive or PR-positive) breast cancers will also get adjuvant hormone therapy which can typically be taken at the same time as trastuzumab.

For women with hormone receptor-positive, HER2-negative breast cancer that is in the lymph nodes, and has a high chance of coming back, abemaciclib can be given after surgery along with tamoxifen or an AI. It is a pill typically given twice a day for 2 years.

For women who have a BRCA mutation and hormone receptor-positive, HER2-negative breast cancer and still have cancer in the tissue removed at surgery after neoadjuvant chemo, the targeted drug olaparib might be given for one year to help lower the chance of the cancer recurring. When given this way, it can help some women live longer.

Neoadjuvant treatment is a preferable option for women with stage III TNBC or HER2-positive breast cancer because the treatment given after surgery is chosen depending on how much cancer is still in the breast and/or lymph nodes at the time of surgery. Some women with stage III cancer who get neoadjuvant treatment might live longer if the cancer goes away completely with that treatment.

Women with TNBC might get the immunotherapy drug, pembrolizumab, before surgery and then again after surgery. See Treatment of Triple-negative Breast Cancer for more details.

Starting with surgery

Surgery first is an option for some women with stage III cancers. Because these tumors are fairly large and/or have grown into nearby tissues, this usually means getting a mastectomy. For women with fairly large breasts, BCS may be an option if the cancer hasn't grown into nearby tissues. SLNB may be an option for some patients, but most will need an ALND. Surgery is usually followed by adjuvant chemotherapy, and/or hormone therapy, and/or targeted drug therapy, and/or HER2-positive treatment (trastuzumab, pertuzumab, or neratinib) depending on the traits of the cancer cells. Radiation is recommended after surgery.

Hyperlinks

1. www.cancer.org/cancer/types/breast-cancer/understanding-a-breast-cancer-diagnosis/stages-of-breast-cancer.html
2. www.cancer.org/cancer/types/breast-cancer/understanding-a-breast-cancer-diagnosis/breast-cancer-hormone-receptor-status.html
3. www.cancer.org/cancer/types/breast-cancer/understanding-a-breast-cancer-diagnosis/breast-cancer-her2-status.html
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8. www.cancer.org/cancer/types/breast-cancer/understanding-a-breast-cancer-

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Last Revised: April 12, 2022

Treatment of Stage IV (Metastatic) Breast Cancer

Stage IV cancers have spread (metastasized) beyond the breast and nearby lymph nodes to other parts of the body. When breast cancer spreads, it most commonly goes to the bones, liver, and lungs. It may also spread to the brain or other organs.

For women with stage IV breast cancer, systemic drug therapies are the main treatments. These may include:

- Hormone therapy
- Chemotherapy (chemo)
- Targeted drugs
- Immunotherapy
- Some combination of these

Surgery and/or radiation therapy may be useful in certain situations (see below).

Treatment can often shrink tumors (or slow their growth), improve symptoms, and help some women live longer. These cancers are considered incurable.

Systemic (drug) treatments for stage IV breast cancer

Treatment often continues until the cancer starts growing again or until side effects become unacceptable. If this happens, other drugs might be tried. The types of drugs used for stage IV breast cancer depend on the hormone receptor status, the HER2 status of the cancer, and sometimes gene mutations that might be found.

Hormone receptor-positive cancers

Women with hormone (estrogen or progesterone) receptor-positive cancers are sometimes treated first with hormone therapy (tamoxifen or an aromatase inhibitor).

This may be combined with a targeted drug such as a CDK4/6 inhibitor.

If the initial hormone therapy stops working, another type can be tried, often along with a targeted drug such everolimus, a PI3K inhibitor such as alpelisib (Piqray) or an AKT inhibitor such as capivasertib (Truqap), if the cancer cells have certain gene changes. (See “Advanced cancer that progresses during treatment” below.)

Women who haven’t yet gone through menopause are often treated with tamoxifen or with medicines that keep the ovaries from making hormones along with other drugs.

Hormone receptor-negative cancers

Chemo is the main treatment for women with hormone (estrogen and progesterone) receptor-negative cancers, because hormone therapy isn’t helpful for these cancers.

HER2-positive cancers

The first therapy given is usually chemotherapy in combination with trastuzumab (Herceptin, other names[1]) and pertuzumab (Perjeta), both HER2 targeted drugs. If the cancer grows, other options might include:

- An antibody-drug conjugate
- A kinase inhibitor with an anti-HER2 drug or with a chemo drug or both
- Other HER2 targeted drugs with chemo

Hormone therapy might be added to these drug combinations if the cancer is also hormone-receptor positive.

HER2-low cancers

For breast cancers that are considered HER2-low[2] and have spread to distant sites, the antibody-drug conjugate fam-trastuzumab deruxtecan (Enhertu) might be an option.

HER2-negative cancers in women with a *BRCA* gene mutation

These women are typically treated with a targeted drug called a PARP inhibitor, such as olaparib or talazoparib. Chemotherapy drugs and hormone drugs are also very helpful in treating these cancers.

Triple-negative breast cancer (TNBC)

An immunotherapy drug along with chemotherapy might be used in people with advanced triple-negative breast cancer whose tumor makes the PD-L1 protein. The PD-L1 protein is found is about 1 in 5 women with triple-negative breast cancer. For women with TNBC and a *BRCA* mutation, drugs called PARP inhibitors (like olaparib or talazoparib) may be considered.

For breast cancers in which the cancer cells show high levels of gene changes called microsatellite instability **(MSI)** or changes in any of the mismatch repair **(MMR)** genes (*MLH1, MSH2, MSH6*, or *PMS2*), immunotherapy with the drug pembrolizumab might be used. Pembrolizumab might also be an option for TNBC that has other gene or protein changes.

For TNBC that does not have any specific gene or protein changes, chemo alone or the antibody-drug conjugate sacituzumab govitecan (Trodelvy) might be an option.

You can find more treatment details in Treatment for Triple-negative Breast Cancer.

Local or regional treatments for stage IV breast cancer

Although systemic drugs are the main treatment for stage IV breast cancer, local and regional treatments such as surgery, radiation therapy, or regional chemotherapy are sometimes used as well. These can help treat breast cancer in a specific part of the body, but they are very unlikely to get rid of all of the cancer. These treatments are more likely to be used to help prevent or treat symptoms or complications from the cancer.

Radiation therapy and/or surgery may also be used in certain situations, such as:

- When the breast tumor is causing an open or painful wound in the breast (or chest)
- To treat a small number of metastases in a certain area, such as the brain
- To help prevent or treat bone fractures
- When a cancer is pressing on the spinal cord
- To treat a blood vessel blockage in the liver
- To provide relief of pain or other symptoms anywhere in the body

In some cases, regional chemo (where drugs are delivered directly into a certain area, such as into the fluid around the brain and spinal cord, called intrathecal chemo) may be useful as well.

If your doctor recommends such local or regional treatments, it is important that you

understand the goal—whether it is to try to cure the cancer or to prevent or treat symptoms.

Relieving symptoms of advanced breast cancer

Treatment to relieve symptoms depends on where the cancer has spread. For example, pain from bone metastases may be treated with radiation therapy, drugs called bisphosphonates such as pamidronate (Aredia) or zoledronic acid (Zometa), or the drug denosumab (Xgeva). For more, see treatment of bone metastases[3].

Advanced cancer that progresses during treatment

Treatment for advanced breast cancer can often shrink the cancer or slow its growth (sometimes for many years), but after a time, it tends to stop working. Further treatment options at this point depend on several factors, including previous treatments, where the cancer is located, a woman's menopause status, general health, desire to continue getting treatment, and whether the hormone receptor status and HER2 status have changed on the cancer cells.

Progression during hormone therapy

For hormone receptor-positive (ER-positive or PR-positive) cancers that were being treated with hormone therapy, switching to another type of hormone therapy and/or adding a targeted drug sometimes helps. For example:

- If either letrozole (Femara) or anastrozole (Arimidex) was given first, using exemestane, possibly with the targeted drug everolimus (Afinitor), may be an option.
- Another option might be using elacestrant (Orserdu), fulvestrant (Faslodex), or a different aromatase inhibitor, sometimes along with a targeted drug known as a CDK4/6 inhibitor.
- If the cancer has a *PIK3CA* gene mutation and has grown while being treated with an aromatase inhibitor, fulvestrant with the targeted drug alpelisib (Piqray) might be considered.
- If the cancer has a *PIK3CA*, *AKT1*, or *PTEN* gene mutation, fulvestrant with the targeted drug capivasertib (Truqap) might be an option.

If the cancer is no longer responding to any hormone drugs, chemotherapy immunotherapy, or PARP inhibitors might be options depending on specific features of

the cancer or any gene changes that might be present.

Progression during chemotherapy

If the cancer is no longer responding to one chemo regimen, trying another may be helpful. Many different drugs and combinations can be used to treat breast cancer. However, each time a cancer progresses during treatment, it becomes less likely that further treatment will have an effect. Sometimes, other options include adding an immunotherapy drug to the chemo or using a PARP inhibitor alone depending on specific features of the cancer or any gene changes that might be present.

Progression while being treated with HER2 drugs

HER2-positive cancers that no longer respond to trastuzumab (Herceptin) might respond to other drugs that target the HER2 protein. Options for women with HER2-positive cancers might include:

- Pertuzumab (Perjeta) with chemo and trastuzumab
- Ado-trastuzumab emtansine (Kadcyla)
- Fam-trastuzumab deruxtecan (Enhertu)
- Margetuximab (Margenza) with chemo
- Lapatinib (Tykerb) and the oral chemo drug capecitabine
- Lapatinib and an aromatase inhibitor (for hormone receptor-positive cancers)
- Neratinib (Nerlynx) and the chemo drug capecitabine (this combination can be helpful for cancers that have spread to the brain)
- Tucatinib (Tukysa), trastuzumab, and the chemo drug capecitabine (this combination can be helpful for cancers that have spread to the brain)

Because current treatments are very unlikely to cure metastatic breast cancer, if you are in otherwise good health, you may want to think about taking part in a clinical trial[4] testing a newer treatment.

Hyperlinks

1. www.cancer.org/cancer/managing-cancer/treatment-types/biosimilar-drugs/list.html

2. www.cancer.org/cancer/types/breast-cancer/understanding-a-breast-cancer-diagnosis/breast-cancer-her2-status.html
3. www.cancer.org/cancer/managing-cancer/advanced-cancer/bone-metastases.html
4. www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html

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Last Revised: November 28, 2023

Treatment of Recurrent Breast Cancer

For some women, breast cancer may come back after treatment – sometimes years later. This is called a recurrence. **Recurrence can be local (in the same breast or in the surgery scar), regional (in nearby lymph nodes), or in a distant area**. Cancer that is found in the opposite breast without any cancer elsewhere in the body is not a recurrence—it is a new cancer that requires its own treatment.

Treating local recurrence

For women whose breast cancer has recurred locally, treatment depends on their initial treatment.

- If you had breast-conserving surgery (lumpectomy), a local recurrence in the breast is usually treated with mastectomy.
- If the initial treatment was mastectomy, recurrence near the mastectomy site is treated by removing the tumor whenever possible. This is often followed by radiation therapyif not given before.

In either case, hormone therapy, targeted therapy (like trastuzumab), immunotherapy, chemotherapy, or some combination of these may be used after surgery and/or radiation therapy. These drugs might also be used if surgery or radiation are not options.

Treating regional recurrence

When breast cancer comes back in nearby lymph nodes (such as those under the arm or around the collar bone), it is treated by removing those lymph nodes, if possible. This may be followed by radiation aimed at the area if it was not given before. Systemic treatment (such as chemo, targeted therapy, or hormone therapy) may be considered after surgery as well.

Treating distant recurrence

In general, women whose breast cancer comes back in other parts of the body, such as the bones, lungs, or brain, are treated the same way as those found to have stage IV

breast cancer in these organs when they were first diagnosed. See Treating Stage IV (Metastatic) Breast Cancer. The only difference is that treatment may or may not include treatments or drugs a woman has already had.

Recurrent breast cancer can sometimes be hard to treat. If you are in otherwise good health, you might want to think about taking part in a clinical trial[1] testing a newer treatment.

Should your cancer come back, see Understanding Recurrence[2]for more on how to manage and cope with this phase of your treatment.

Hyperlinks

1. www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html
2. www.cancer.org/cancer/survivorship/long-term-health-concerns/recurrence.html

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Last Revised: October 27, 2021

Treatment of Triple-negative Breast Cancer

Triple-negative breast cancer (TNBC) doesn't have estrogen or progesterone receptors and also makes too little or none of the HER2 protein. Because the cancer cells don't have these proteins, hormone therapy and drugs that target HER2 are not helpful, so chemotherapy (chemo) is the main **systemic** treatment option. And even though TNBC tends to respond well to chemo initially, it also tends to come back (recur) more frequently than other breast cancers.

Stages I-III triple-negative breast cancer

Surgery first: If the early-stage TNBC tumor is small enough to be removed by surgery, then breast-conserving surgery or a mastectomy with a check of the lymph nodes may be done In certain cases, such as with a large tumor or if the lymph nodes are found to have cancer, radiation may follow surgery. You might also be given chemo after surgery (adjuvant chemotherapy) to reduce the chances of the cancer coming back. For women who have a *BRCA* mutation and at surgery are found to have:

- A tumor larger than 2cm but no bigger than 5cm OR
- 1 to 3 axillary (underarm) lymph nodes with cancer

the targeted drug olaparib (Lynparza) might be given for a year after adjuvant chemo. When given this way, it can help some women live longer.

Surgery second: Chemo is often given before surgery (neoadjuvant chemotherapy) by itself or with pembrolizumab(Keytruda) to shrink a large tumor and/or lymph nodes with cancer. If cancer is still found in the tissue removed by surgery after neoadjuvant chemo has been given, your doctor may recommend:

- an oral chemo drug called capecitabine (Xeloda) for 18 to 24 weeks. This might help some women live longer.
- more pembrolizumab after surgery (adjuvant treatment) to reduce the chances of the cancer coming back.

- the targeted drug olaparib for one year for women who have a BRCA mutation to help lower the chance of the cancer recurring. When given this way, it can help some women live longer.

Stage IV triple-negative breast cancer

Chemo is often used first when the cancer has spread to other parts of the body (stage IV). Common chemo drugs used include anthracyclines, taxanes, capecitabine, gemcitabine, eribulin, and others. Chemo drugs might be used alone or in combination.

For women with TNBC who have a ***BRCA mutation*** and whose cancer no longer responds to common breast cancer chemo drugs, other platinum chemo drugs (like cisplatin or carboplatin) or targeted drugs called PARP inhibitors (such as olaparib [Lynparza] or talazoparib [Talzenna]), may be considered.

For advanced TNBC in which the cancer cells have the **PD-L1 protein**, the first treatment may be immunotherapy (pembrolizumab) plus chemo . The PD-L1 protein is found in about 1 out of 5 TNBCs.

For advanced TNBC in which at least 2 other drug treatments have already been tried, the antibody-drug conjugate sacituzumab govitecan (Trodelvy) might be an option.

For advanced TNBC in which the cancer cells show high levels of gene changes called microsatellite instability **(MSI)** or changes in any of the mismatch repair **(MMR)** genes (MLH1, MSH2, MSH6, and PMS2), immunotherapy with the drug pembrolizumab might be used. Pembrolizumab might also be an option for TNBC that has a **high tumor mutational burden (TMB-H)** which is a measure of the number of gene mutations (changes) inside the cancer cells. Cells that have many gene mutations (a high TMB) might be more likely to be recognized as abnormal and attacked by the body's immune system.

Surgery and radiation may also be options in certain situations.

See Treatment of Stage IV (Metastatic) Breast Cancer for more information.

Recurrent triple-negative breast cancer

If TNBC comes back (recurs) locally, cannot be removed with surgery, and makes the

PD-L1 protein, immunotherapy with the drug pembrolizumab along with chemotherapy is an option. Other treatments might be options as well, depending on the situation.

If the cancer recurs in other parts of the body, options might include chemotherapy or the antibody-drug conjugate sacituzumab govitecan (Trodelvy).

Regardless of the stage of the cancer, participation in a clinical trial[1] of new treatments for TNBC is also a good option because TNBC is uncommon and tends to have a poor prognosis (outcome) compared to other types of breast cancer, and because these studies often allow patients to have access to drugs not available for standard treatment.

Hyperlinks

1. www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html

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Last Revised: April 12, 2022

Treatment of Inflammatory Breast Cancer

Inflammatory breast cancer (IBC) is an uncommon type of invasive breast cancer that typically makes the skin on the breast look red and feel warm. It also may give the breast skin a thick, pitted appearance that looks a lot like an orange peel. These changes are caused by cancer cells blocking lymph vessels in the skin.

Because inflammatory breast cancer has reached these lymph vessels and has caused changes in the skin, it is considered to be at least a stage III breast cancer when it is diagnosed. IBC that has spread to other parts of the body is considered stage IV. These

cancers typically grow quickly and can be challenging to treat.

Regardless of the stage of the cancer, participation in a clinical trial[1] of new treatments for IBC is also a good option because IBC is rare, has a poor prognosis (outcome), and these studies often allow access to drugs not available for standard treatment.

Treating stage III inflammatory breast cancer

IBC that has not spread outside the breast or to nearby lymph nodes is stage III. Treatment usually starts with chemotherapy (chemo) to try to shrink the tumor. If the cancer is HER2-positive, targeted therapy is given along with the chemo. This is typically followed by surgery (mastectomy and lymph node dissection) to remove the cancer. Radiation therapy often follows surgery. Sometimes, more chemo may be given after surgery but before radiation. If the cancer is hormone receptor-positive , hormone therapy is given as well (usually after all chemo has been given). Combining these treatments has improved survival significantly over the years.

Chemotherapy (possibly along with targeted therapy)

Using chemo before surgery is called **neoadjuvant** or **preoperative** treatment. Most women with IBC will receive two types of chemo drugs (although not always at the same time):

- An anthracycline, such as doxorubicin (Adriamycin) or epirubicin (Ellence)
- A taxane, such as paclitaxel (Taxol) or docetaxel (Taxotere)

Other chemo drugs may be used as well.

If the cancer is HER2-positive (the cancer cells make too much of a protein called HER2), the targeted therapy drug trastuzumab (Herceptin) is usually given, sometimes along with another targeted drug, pertuzumab (Perjeta). These drugs can lead to heart problems when given with an anthracycline, so one option is to give the anthracycline first (without trastuzumab or pertuzumab), followed by treatment with a taxane and trastuzumab (with or without pertuzumab).

For IBC that is triple-negative[2], the immunotherapy drug pembrolizumab can be given with chemo before surgery (neoadjuvant treatment) and then continued by itself after surgery (adjuvant treatment).

For women who have:

- a BRCA mutation AND
- triple-negative or HER2-negative IBC AND
- residual cancer in the tissue removed by surgery after neoadjuvant chemo

the targeted drug olaparib (Lynparza) might be given to lower the risk of the cancer recurring. It is typically given for one year. When given this way, olaparib can help some women live longer.

Surgery and further treatments

If the cancer improves with chemo, surgery is typically the next step. The standard operation is a modified radical mastectomy, where the entire breast and the lymph nodes under the arm are removed. Because IBC affects so much of the breast and skin, breast-conserving surgery (partial mastectomy or lumpectomy) and skin-sparing mastectomy are not options. It isn't clear that sentinel lymph node biopsy (where only one or a few nodes are removed) is reliable in IBC, so it is also not an option.

If the cancer does not respond to chemo (and the breast is still very swollen and red), surgery cannot be done. Either other chemo drugs will be tried, or the breast may be treated with radiation. Then if the cancer responds (the breast shrinks and is no longer red), surgery may be an option.

If breast radiation isn't given before surgery, it is given after surgery, even if no cancer is thought to remain. This is called **adjuvant** radiation. It lowers the chance that the cancer will come back. Radiation is usually given 5 days a week for 6 weeks, but in some cases a more intense treatment (twice a day) can be used instead. Depending on how much tumor was found in the breast after surgery, radiation might be delayed until further chemo and/or targeted therapy (such as trastuzumab) is given. If breast reconstruction is to be done, it is usually delayed until after the radiation therapy that most often follows surgery.

Treatment after surgery often includes additional (adjuvant) systemic treatment. This can include chemo, targeted therapy, hormone therapy (tamoxifen or an aromatase inhibitor) if the cancer cells have hormone receptors, the oral chemo drug capecitabine (Xeloda) if the cancer is triple-negative, the PARP inhibitor olaparib (Lynparza) if the woman has a BRCA mutation,and/or trastuzumab, pertuzumab or ado-trastuzumab emtansine if the cancer is HER2-positive.

Treating stage IV inflammatory breast cancer

Patients with metastatic (stage IV) IBC are treated with systemic therapy. This may include:

- Chemotherapy
- Hormonal therapy (if the cancer is hormone receptor-positive)
- Targeted therapy with a drug that targets HER2 (if the cancer is HER2-positive)
- Immunotherapy if the cancer makes a protein called PD-L1
- Targeted drug therapy with a PARP inhibitor called olaparib if the woman has a *BRCA* mutation

One or more of these treatments might be used. Many times, a targeted drug is given along with chemotherapy or with hormone therapy. Surgery and radiation may also be options in certain situations. See Treatment of Stage IV (Metastatic) Breast Cancer for more information.

Hyperlinks

1. www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html
2. www.cancer.org/cancer/types/breast-cancer/understanding-a-breast-cancer-diagnosis/breast-cancer-her2-status.html

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Last Revised: April 12, 2022

Treating Breast Cancer During Pregnancy

If you are diagnosed with breast cancer while pregnant, your treatment options will be more complicated because you will want to get the best treatment for your cancer while also protecting the baby. The type and timing of treatment will need to be planned carefully and coordinated between your cancer care team and your obstetrician.

When treating a pregnant woman with breast cancer, the goal is the same as when treating a non-pregnant woman: to cure the cancer whenever possible, or to control it and keep it from spreading if it can't be cured. But the extra concern of protecting a growing fetus may make treatment more complicated.

Is it safe to have breast cancer treatment during pregnancy?

If you are pregnant and have breast cancer, you might have hard choices to make, so get expert help and be sure you know all your options. Pregnant women can safely get treatment for breast cancer, although the types of treatment used and the timing of treatment might be affected by the pregnancy. If you are pregnant and have been diagnosed with breast cancer, your treatment recommendations will depend on:

- The size of the tumor
- Where the tumor is located
- If the cancer has spread and if so, how far
- How far along you are in the pregnancy
- Your overall health
- Your personal preferences

It is generally safe to have surgery for breast cancer while you're pregnant. Chemotherapy seems to be safe for the baby if given in the second or third trimester of pregnancy, but it isn't safe in the first trimester. Other breast cancer treatments, such as hormone therapy, targeted therapy, and radiation therapy, are more likely to harm the baby and are not usually given during pregnancy.

Treatment choices can become complicated if there is a conflict between the best known treatment for the mother and the well-being of the baby. For example, if a woman is found to have breast cancer early in her pregnancy and needs chemotherapy right away, she may be advised to think about ending the pregnancy. A counselor or psychologist should also be part of your health care team to help give you the emotional support you may need.

Some older studies found that ending a pregnancy in order to have cancer treatment

didn't improve a woman's prognosis (outlook). Even though there were flaws in these studies, ending the pregnancy is no longer routinely recommended when breast cancer is found. Still, this option may be discussed when looking at all the treatment choices available, especially for metastatic (stage IV) or aggressive cancers that may need treatment right away, such as inflammatory breast cancer[1].

Breast cancer surgery during pregnancy

Surgery to remove the cancer in the breast and nearby lymph nodes is a major part of treatment for any woman with early breast cancer, and generally is safe in pregnancy.

Options for breast cancer surgery might include:

- Removing the entire breast (mastectomy)
- Removing just the part containing the cancer (lumpectomy or breast-conserving surgery [BCS])

The type of surgery a woman might have depends on the extent of her cancer and when the cancer is diagnosed during the pregnancy.

Checking lymph nodes for cancer spread

In addition to removing the tumor in the breast, one or morelymph nodes in the underarm area (axillary lymph nodes) also need to be removed to check if the cancer has spread. One way to do this is an axillary lymph node dissection (ALND). This is often the standard procedure for pregnant women with breast cancer and removes many of the lymph nodes under the arm. Another procedure, called a sentinel lymph node biopsy (SLNB), might be an option depending on how far along you are in pregnancy and your cancer stage. SLNB allows the doctor to remove fewer nodes, but there are concerns about the effects the SLNB dye might have on the baby. Because of these concerns, most experts recommend that SLNB only be used in certain situations such as later in pregnancy, and that the blue dye not be used during the procedure.

Is anesthesia safe during pregnancy?

Surgery for breast cancer generally carries little risk to the baby. But there are certain times in pregnancy when anesthesia (the drugs used to make you sleep for surgery) may be risky for the baby.

Your surgeon and anesthesiologist, along with a high-risk obstetrician (OB), will need to

work together to decide the best time during pregnancy to operate. If the surgery is done later in the pregnancy, your obstetrician may be there just in case there are any problems with the baby during surgery. Together, your doctors will decide which anesthesia drugs and techniques are the safest for both you and the baby.

Treatment after surgery

Depending on the cancer's stage[2], you may need more treatment such as chemotherapy, radiation therapy, hormone therapy, and/or targeted therapy after surgery to help lower the risk of the cancer coming back[3]. This is called **adjuvant treatment**. In some cases, this treatment can be put off until after delivery.

Chemotherapy

Chemotherapy (chemo) may be used after surgery (as adjuvant treatment) for some earlier stages of breast cancer. It also can be used by itself for more advanced cancers.

Chemo is not given during the first 3 months (first trimester) of pregnancy. Because a lot of the baby's development occurs during this time, the safety of chemo hasn't been studied in the first trimester. The risk of miscarriage (losing the baby) is also the greatest during this time.

For many years, it was thought that all chemo would harm an unborn baby no matter when it was given. But studies have shown that certain chemo drugs (such as doxorubicin, cyclophosphamide, fluorouracil, and the taxanes) used during the second and third trimesters (months 4 through 9 of pregnancy) don't raise the risk of birth defects, stillbirths, or health problems shortly after birth, though they may increase the risk of early delivery. Researchers still don't know if these children will have any long-term effects.

If you have early breast cancer and you need chemo after surgery (adjuvant chemo), it will usually be delayed until at least your second trimester. If you are already in the third trimester when the cancer is found, chemo may be delayed until after birth. The birth may be induced (brought on) a few weeks early in some women. These same treatment plans may also be used for women with more advanced cancer.

Chemo is generally not recommended after 35 weeks of pregnancy or within 3 weeks of delivery because it can lower the mother's blood cell counts[4]. This could cause bleeding and increase the chances of infection during birth. Holding off on chemo for the last few weeks before delivery allows the mother's blood counts to return to normal before childbirth.

Treatments that typically are on hold until after delivery

Some treatments for breast cancer can harm the baby and are not safe during pregnancy. If these treatments are needed, they are usually scheduled after the baby is born.

Radiation therapy: Radiation therapy to the breast is often used after breast-conserving surgery (lumpectomy) to help reduce the risk of the cancer coming back. The high doses of radiation used for this can harm the baby any time during pregnancy. This may cause miscarriage, birth defects, slow fetal growth, or a higher risk of childhood cancer. Because of this, doctors don't use radiation treatment during pregnancy.

For some women whose cancer is found later in the pregnancy, it may be possible to have a lumpectomy during pregnancy and then wait until after the baby is born to get radiation therapy. But this treatment approach has not been well-studied. Waiting too long to start radiation can increase the chance of the cancer coming back.

Hormone therapy: Hormone therapy is often used as treatment after surgery or as treatment for advanced breast cancer in women with hormone receptor-positive (estrogen or progesterone) breast cancer. Hormone therapy drugs used for breast cancer include tamoxifen, anastrozole, letrozole, and exemestane.

Hormone therapy should not be given during pregnancy because it can affect the baby. It should be delayed until after the woman has given birth.

Targeted therapy: Drugs that target HER2, such as trastuzumab (Herceptin), pertuzumab (Perjeta), ado-trastuzumab emtansine (Kadcyla) and lapatinib (Tykerb), are important in treating HER2-positive breast cancers. In women who aren't pregnant, trastuzumab is used as a part of treatment after surgery, pertuzumab can be used with trastuzumab before surgery, and all of these drugs can be useful in treating advanced cancer. But based on studies of women who were treated during pregnancy, none of these drugs are considered safe for the baby if taken during pregnancy.

Everolimus (Afinitor) and palbociclib (Ibrance) are also targeted drugs that can be used with hormone therapy to treat advanced breast cancer. Again, these and other targeted drugs are thought to be unsafe to use during pregnancy.

Can I breastfeed during cancer treatment?

Most doctors recommend that women who have just had babies and are about to be

treated for breast cancer should stop (or not start) breastfeeding. Many chemo, hormone, and targeted therapy drugs can enter breast milk and be passed on to the baby. Breastfeeding isn't recommended if you are being treated with systemic drugs and sometimes shouldn't be restarted for months after treatment has ended, Sometimes, if a woman has hormone-positive breast cancer, she might be given drugs to stop the production of breast milk.

If breast surgery is planned, stopping breastfeeding will help reduce blood flow to the breasts and make them smaller. This can help with the operation. It also helps reduce the risk of infection in the breast and can help avoid breast milk collecting in biopsy or surgery areas.

If you have questions, such as when it might be safe to start breastfeeding, talk with your health care team. If you plan to start breastfeeding after you've stopped for a while, plan ahead. Breastfeeding (lactation) experts can give you extra help if you need it.

Does pregnancy affect survival rates for breast cancer?

Pregnancy can make it harder to find, diagnose, and treat breast cancer. Most studies have found that the outcomes among pregnant and non-pregnant women with breast cancer are about the same for cancers found at the same stage.

Some doctors believe that ending the pregnancy may help slow the course of more advanced breast cancers, and they may recommend that for some women with advanced breast cancer. It's hard to do research in this area, and good, unbiased studies don't exist. Ending the pregnancy makes treatment simpler, but so far no evidence shows that ending the pregnancy improves a woman's overall survival or cancer outcome.

Studies have not shown that the treatment delays that are sometimes needed during pregnancy have an effect on breast cancer outcome, either. But this, too, has proven to be a difficult area to study. Finally, there are no reports showing that breast cancer itself can harm the baby.

Hyperlinks

1. www.cancer.org/cancer/types/breast-cancer/about/types-of-breast-cancer/inflammatory-breast-cancer.html

2. www.cancer.org/cancer/types/breast-cancer/understanding-a-breast-cancer-diagnosis/stages-of-breast-cancer.html
3. www.cancer.org/cancer/survivorship/long-term-health-concerns/recurrence.html
4. www.cancer.org/cancer/managing-cancer/side-effects/low-blood-counts.html

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Last Revised: October 27, 2021

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