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Treating Breast Cancer in Men

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. Weigh the benefits of each treatment option against the possible risks and side effects.

Local treatments

Some treatments are called *local therapies*, meaning they treat the tumor without affecting the rest of the body. These treatments are more likely to be useful for earlier stage (less advanced) cancers, although they might also be used in some other situations. Types of local therapy used for breast cancer include:

- Surgery for Breast Cancer in Men
- Radiation Therapy for Breast Cancer in Men

Systemic treatments

Breast cancer can also be treated using drugs, which can be given by mouth or directly into the bloodstream. These are called *systemic therapies* because they can reach cancer cells almost anywhere in the body. Depending on the type of breast cancer, several different types of drugs might be used, including:

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

Common treatment approaches

Most of the information about treating male breast cancer comes from doctors' experience with treating female breast cancer. Because so few men have breast cancer, it is hard for doctors to study the treatment of male breast cancer patients separately in clinical trials.

Treatment of Breast Cancer in Men, by Stage

Adjuvant therapy

Patients who have no detectable cancer after surgery are often given **treatment to help keep the cancer from coming back**. This is known as *adjuvant therapy*. Even in the early stages of breast cancer, cancer cells may break away from the main breast tumor and begin to spread. These cells can't be felt on a physical exam or seen on x-rays or other imaging tests, and they cause no symptoms. But they can become new tumors in nearby tissues and other organs (and bones). The goal of adjuvant therapy is to kill these hidden cells. Systemic therapy and radiation can both be used as adjuvant therapy.

Not every patient needs adjuvant therapy. Whether or not you are likely to benefit depends on the stage and characteristics of your cancer and what type of surgery you had. Generally, if the tumor is larger or the cancer has spread to lymph nodes, it is more likely to have spread through the bloodstream, and you are more likely to benefit. But other features may determine if you should consider adjuvant therapy.

Neoadjuvant therapy

Some patients are given **treatment before surgery to shrink the tumor** in the hope it will allow a less extensive operation to be done. This often involves the same treatments used for adjuvant therapy, only giving them (or starting them) before surgery and not after. This is called *neoadjuvant therapy*.

Neoadjuvant therapy also lowers the chance of the cancer coming back later, so many patients who get neoadjuvant therapy will not need adjuvant therapy, or will not need as much.

Who treats breast cancer?

Doctors on your cancer treatment team might 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 and other medicines to treat cancer

Many other specialists might be part of your treatment team as well, including physician assistants, nurse practitioners, nurses, psychologists, social workers, nutritionists, genetic counselors, 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 in Men
- Seeking a Second Opinion

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 stage of illness they may be in. 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 trained 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 and 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 in Men

- Surgery to remove breast cancer
- Surgery to remove nearby lymph nodes
- Chronic pain after breast surgery
- More information about Surgery

Most men with breast cancer have some type of surgery as part of their treatment. There are different types of breast surgery, and it 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)
- · 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 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:

Mastectomy

In this surgery, the entire breast is removed, including all of the breast tissue and sometimes other nearby tissues. Most men with breast cancer will undergo a mastectomy since men have a small amount of breast tissue. There are several types of mastectomies:

- In a **simple** or **total mastectomy**, the surgeon removes the entire breast, including the nipple, but does not remove underarm lymph nodes or muscle tissue from beneath the breast.
- In a **modified radical mastectomy**, the surgeon extends the incision to remove the entire breast and lymph nodes under the arm as well.
- If the tumor is large and growing into the chest muscles, the surgeon must do a radical mastectomy, a more extensive operation removing the entire breast, axillary lymph nodes, and the chest wall muscles under the breast. This is only needed if the cancer has grown into the pectoral muscles under the breast.

Breast-conserving surgery (BCS)

This surgery might also be called a **lumpectomy**, **quadrantectomy**, **partial mastectomy**, or **segmental mastectomy**. For this surgery, only the part of the breast containing the cancer is removed. The goal is to remove the cancer as well as some surrounding normal tissue. How much of the breast is removed depends on the size and location of the tumor and other factors.

BCS is commonly used to treat women with breast cancer. It is used much less often in men because most male breast cancers are located behind the nipple and many times have grown into the nipple, so they require more extensive surgery such as a mastectomy. If BCS is done, it is typically followed by radiation therapy.

Possible side effects of breast surgery

Aside from post-surgical pain, temporary swelling, and a change in the appearance of the breast, possible side effects of surgery include bleeding and infection at the surgical site, *hematoma* (buildup of blood in the wound), and *seroma* (buildup of clear fluid in the wound).

Surgery to remove nearby lymph nodes

To find out if the breast cancer has spread to axillary (underarm) lymph nodes, one or more of these lymph nodes may be removed and looked at in the lab. This is an important part of figuring out the stage¹ (extent) of the cancer.

Lymph nodes may be removed either as part of the surgery to remove the breast cancer or as a separate operation.

Two types of surgery can be used to remove the lymph nodes:

- Sentinel lymph node biopsy (SLNB): A procedure in which the surgeon removes only the lymph node(s) under the arm to which the cancer would likely spread first.
 Removing only one or a few lymph nodes lowers the risk of side effects from the surgery.
- Axillary lymph node dissection (ALND): A procedure in which the surgeon removes many lymph nodes from under the arm. 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.

Either of these procedures can usually be done at the same time as mastectomy or lumpectomy, but they might also be done in a second operation.

For a **sentinel lymph node biopsy**, the surgeon finds and removes the *sentinel node* (or nodes) — the first lymph node(s) into which a tumor drains, and the one(s) most likely to contain cancer cells if they have started to spread.

To do this, the surgeon injects a substance into the area around the tumor, into the skin over the tumor, or into the tissues just under the areola (the colored area around the nipple). This can be done with either:

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

Lymph vessels will carry these substances into the sentinel node(s) over the next few hours. The sentinel nodes can then be found by:

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

The doctor then makes an incision (cut) in the skin over the area in the armpit and removes the nodes. These nodes (often 2 or 3) are then looked at in the lab.

The lymph nodes can sometimes be checked for cancer during surgery. If cancer is found in the sentinel lymph node, the surgeon may go on to do a full ALND. If no cancer cells are seen in the lymph node at the time of the surgery, or if the sentinel node is not checked during surgery, the lymph node(s) will be examined more closely over the next several days. If cancer is found in the lymph node, the surgeon may recommend a full ALND at a later time.

If there are no cancer cells in the sentinel node(s), it's very unlikely that the cancer has spread to other lymph nodes, so no further lymph node surgery is needed. This lets you avoid some of the potential side effects of a full ALND.

A SLNB might not always be the best option for checking the lymph nodes. If an underarm lymph node looks or feels large or abnormal by touch or by a test like ultrasound, it may be checked by <u>fine needle aspiration (FNA)</u>². If cancer is found, a full ALND is typically recommended, so a SLNB is not needed.

SLNB is a complex technique that requires a great deal of skill. It should only be done by a surgical team experienced with this technique. If you are thinking about having this type of biopsy, ask your health care team if this is something they do regularly.

Possible side effects of lymph node surgery

As with other operations, pain, swelling, bleeding, and infection are possible.

Lymphedema: A possible long-term effect of removing axillary lymph nodes islymphedema (swelling) of the arm. This occurs because any excess fluid in the arms normally travels back into the bloodstream through the lymphatic system. Removing the lymph nodes sometimes blocks the drainage from the arm, causing this fluid to build up.

This side effect has not been well studied in men. In women the risk of lymphedema is

thought to be in the range of 20-30% after an ALND, and it is less common after a SLNB. Lymphedema seems to be more common if radiation is given after surgery. Sometimes this starts soon after surgery, but it can take a long time to develop. For some people, the swelling lasts for only a few weeks and then goes away. Other times, the swelling 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. For more information about ways to prevent or manage lymphedema after breast surgery, see Lymphedema³.

Limited arm and shoulder movement: You may also have limited movement in your arm and shoulder after surgery. This is more common after an ALND than a SLNB. Your doctor may give you exercises to ensure that you do not have permanent problems with movement (a frozen shoulder).

Some patients notice a rope-like structure that begins under the arm and can extend down toward the elbow. This, sometimes called *axillary web syndrome* or *lymphatic cording*. It is more common after an ALND than SLNB. Symptoms might 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 people seem to find physical therapy helpful.

Numbness: Numbness of the skin of the upper, inner arm is another common side effect because the nerve that controls sensation here travels through the lymph node area.

Chronic pain after breast surgery

Some patients have problems with nerve (neuropathic) pain in the chest wall, armpit, and/or arm after surgery that doesn't go away over time. This is called post-mastectomy pain syndrome (PMPS) because it was first described in women who had mastectomies, but it occurs after breast-conserving therapy, as well.

PMPS is thought to be linked to damage done to the nerves in the armpit and chest during surgery. But the causes are not known. Between 20% and 30% of women develop symptoms of PMPS after surgery. It isn't clear how common this is in men after breast cancer surgery. It seems to be more common in younger patients, those who had a full ALND (not just a SLNB), and those who were treated with radiation after surgery. Because ALNDs are done less often now, PMPS is less common than it once was.

Symptoms of PMPS include:

- Pain and tingling in the chest wall, armpit, and/or arm
- Pain in the shoulder or surgical scar
- Numbness
- Burning or shooting pain
- A "pins and needles" sensation
- Severe itching

Most patients with PMPS say that their symptoms are not severe, but PMPS can cause you to not use your arm the way you should, and over time you could lose the ability to use it normally. Tell your doctor if you are having pain or other symptoms of PMPS. Nerve pain requires different treatment from other types of pain. See Cancer Pain for more information.

More information about Surgery

For more general information about surgery as a treatment for cancer, see <u>Cancer</u> <u>Surgery</u>⁵.

To learn about some of the side effects listed here and how to manage them, see Managing Cancer-related Side Effects⁶.

Hyperlinks

- 1. <u>www.cancer.org/cancer/types/breast-cancer-in-men/detection-diagnosis-staging/staging.html</u>
- 2. <u>www.cancer.org/cancer/types/breast-cancer-in-men/detection-diagnosis-staging/how-diagnosed.html</u>
- 3. www.cancer.org/cancer/managing-cancer/side-effects/swelling/lymphedema.html
- 4. www.cancer.org/cancer/managing-cancer/side-effects/pain.html
- 5. www.cancer.org/cancer/managing-cancer/treatment-types/surgery.html
- 6. www.cancer.org/cancer/managing-cancer/side-effects.html

References

Cheville AL. Chapter 39: Preserving and Restoring Function after Local Treatment. In: Harris JR, Lippman ME, Morrow M, Osborne CK, eds. *Diseases of the Breast.* 5th ed. Philadelphia: Wolters Kluwer Health; 2014.

Chung AP and Giuliano AE. Chapter 37: Sentinel Lymph Node Biopsy. In: Harris JR, Lippman ME, Morrow M, Osborne CK, eds. *Diseases of the Breast*. 5th ed. Philadelphia: Wolters Kluwer Health; 2014.

Cody III HS and Plitas G. Chapter 38: Axillary Dissection. In: Harris JR, Lippman ME, Morrow M, Osborne CK, eds. *Diseases of the Breast*. 5th ed. Philadelphia: Wolters Kluwer Health; 2014.

Doscher ME, Schreiber JE, Weichman KE, Garfein ES. Update on Post-mastectomy Lymphedema Management. *Breast J.* 2016 Sep;22(5):553-60.

Gärtner R, Jensen MB, Nielsen J, Ewertz M, Kroman N, Kehlet H. Prevalence of and factors associated with persistent pain following breast cancer surgery. *JAMA*. 2009 Nov 11;302(18):19851992.

Giuliano AE, Hunt KK, Ballman KV, et al. Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis. *JAMA*. 2011;305: 569-575.

Gnerlich JL, Deshpande AD, Jeffe DB et al. Poorer survival outcomes for male breast cancer compared with female breast cancer may be attributable to in-stage migration. *Ann Surg Oncol.* 2011;18(7):1837. Epub 2010 Dec 14.

Golshan M, Rusby J, Dominguez F, Smith BL. Breast conservation for male breast carcinoma. *Breast.* 2007;16(6):653.

Gradishar, W. J. (2018, March). Breast cancer in men. Retrieved April 09, 2018, from https://www.uptodate.com/contents/breast-cancer-in-men?search=breast cancer men&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1 #H13

Lawenda BD, Mondry TE, Johnstone PA. Lymphedema: A primer on the identification and management of a chronic condition in oncologic treatment. *CA Cancer J Clin*. 2009; 59:8–24.

McLaughlin. Chapter 40: Lymphedema. In: Harris JR, Lippman ME, Morrow M, Osborne CK, eds. *Diseases of the Breast*. 5th ed. Philadelphia: Wolters Kluwer Health; 2014.

Morrow M, Burstein HJ, Harris JR. Chapter 79: Malignant Tumors of the Breast. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and*

Rosenberg's Cancer: Principles and Practice of Oncology. 10th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2015.

Morrow M and Golshan M. Chapter 33: Mastectomy. In: Harris JR, Lippman ME, Morrow M, Osborne CK, eds. *Diseases of the Breast*. 5th ed. Philadelphia: Wolters Kluwer Health; 2014.

Morrow M and Harris JR. Chapter 35: Breast-Conserving Therapy. In: Harris JR, Lippman ME, Morrow M, Osborne CK, eds. *Diseases of the Breast*. 5th ed. Philadelphia: Wolters Kluwer Health; 2014.

Moskovitz AH, Anderson BO, Yeung RS, Byrd DR, Lawton TJ, Moe RE. Axillary web syndrome after axillary dissection. *Am J Surg.* 2001 May;181(5):434439.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: Breast Cancer. Version 3.2017. Accessed at www.nccn.org on January 18, 2018.

OJ Vilholm, S Cold, L Rasmussen and SH Sindrup. The postmastectomy pain syndrome: an epidemiological study on the prevalence of chronic pain after surgery for breast cancer. *British Journal of Cancer* (2008) 99, 604 – 610.

Shaitelman SF, Recent Progress in Cancer-Related Lymphedema Treatment and Prevention *CA Cancer J Clin.* 2015; 65(1): 55–81.

Wolff AC, Domchek SM, Davidson NE, Sacchini V, McCormick B. Chapter 91: Cancer of the Breast. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa: Elsevier; 2014.

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Radiation Therapy for Breast Cancer in Men

- When might radiation therapy be used?
- When will I get radiation therapy?
- Preparing for external beam radiation therapy
- Possible side effects of radiation therapy

More information about radiation therapy

Some men with breast cancer will need radiation, often in addition to other treatments. The recommendations for radiation therapy in men with breast cancer is largely taken from those for female breast cancer because not enough studies have been done in men. The need for radiation depends on what type of surgery you had or whether your cancer has spread to the lymph nodes or somewhere else in your body. Tumors that are large or involve the skin might also need radiation. You could have just one type of radiation, or a combination of different types.

Radiation therapy is treatment with high-energy rays (such as x-rays) or particles that destroy cancer cells. The most common type of radiation therapy for men with breast cancer is called *external beam radiation*. A machine focuses the radiation on the area affected by the cancer.

When might radiation therapy be used?

Not all men with breast cancer need radiation therapy, but it may be used in several situations:

- After breast-conserving surgery (BCS), to help lower the chance that the cancer will
 come back in the remaining breast tissue or nearby lymph nodes. Radiation is
 needed less often for men with breast cancer than it is for women, mainly because
 breast-conserving surgery (BCS) isn't done as much.
- After a mastectomy, especially if the cancer is larger than 5 cm (about 2 inches), attached to the skin, or if cancer is found in the lymph nodes.
- If cancer has spread to other parts of the body, such as the bones or brain.

Which areas need radiation depends on whether you had a mastectomy or breastconserving surgery (BCS) and whether or not the cancer has reached nearby lymph nodes.

- If you had a mastectomy and no lymph nodes had cancer, radiation is focused on the chest wall, the mastectomy scar, and anywhere drains had been placed after surgery.
- If you had BCS, you will most likely have radiation to the entire breast (called whole breast radiation), and an extra boost of radiation to the area in the breast where the cancer was removed (called the tumor bed) to help prevent it from coming back in that area. The boost is often given after the treatments to the whole breast have

- ended. It uses the same machine, with lower amounts of radiation, but the beams are aimed at the tumor bed.
- If cancer was found in the lymph nodes under the arm (axillary lymph nodes), this
 area may be given radiation, as well. In some cases, 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).

When will I get radiation therapy?

If you will need external radiation therapy after surgery, it is usually not started until your surgery site has healed, which is often a month or longer. If you are getting chemotherapy as well, radiation treatments are usually delayed until chemotherapy is complete.

Breast radiation is most often given 5 days a week (Monday thru Friday) for about 6 to 7 weeks.

Preparing for external beam radiation therapy

Before your treatment starts, the radiation team will carefully figure out the correct angles for aiming the radiation beams and the proper dose of radiation. They will make some ink marks or small tattoos on your skin to focus the radiation on the right area. Check with your health care team whether the marks they use will be permanent.

External radiation therapy is much like getting an x-ray, but the radiation is stronger. The procedure itself is painless. Each treatment lasts only a few minutes, but the setup time—getting you into place for treatment—usually takes longer.

Possible side effects of radiation therapy

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

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

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:

- Radiation to the breast or chest wall 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 can cause lymphedema, 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. Modern radiation therapy equipment allows doctors to better focus the radiation beams, so these problems are rare today.
- A very rare complication of radiation to the breast or chest wall is the development of another cancer called an angiosarcoma.

More information about radiation therapy

To learn more about how radiation is used to treat cancer, see Radiation Therapy1.

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

Hyperlinks

- 1. <u>www.cancer.org/cancer/managing-cancer/treatment-types/radiation.html</u>
- 2. www.cancer.org/cancer/managing-cancer/side-effects.html

References

Jain S and Gradishar WJ. Chapter 61: Male Breast Cancer. In: Harris JR, Lippman ME, Morrow M, Osborne CK, eds. *Diseases of the Breast*. 5th ed. Philadelphia, Pa:

Lippincott-Williams & Wilkins; 2014.

Jardell P, Vignot S, Cutuli B, et al. Should Adjuvant Radiation Therapy Be Systematically Proposed for Male Breast Cancer? A Systematic Review. *Anticancer Research*. 2018 (38): 23-31.

Khan A and Haffty BG. Chapter 42: Postmastectomy Radiation Therapy. In: Harris JR, Lippman ME, Morrow M, Osborne CK, eds. *Diseases of the Breast*. 5th ed. Philadelphia: Wolters Kluwer Health; 2014.

Morrow M, Burstein HJ, Harris JR. Chapter 79: Malignant Tumors of the Breast. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology.* 10th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2015.

Morrow M and Harris JR. Chapter 35: Breast-Conserving Therapy. In: Harris JR, Lippman ME, Morrow M, Osborne CK, eds. *Diseases of the Breast*. 5th ed. Philadelphia: Wolters Kluwer Health; 2014.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: Breast Cancer. Version 3.2017. Accessed at www.nccn.org on January 18 2018.

Whelan T, MacKenzie R, Julian J, et al. Randomized trial of breast irradiation schedules after lumpectomy for women with lymph node-negative breast cancer. *J Natl Cancer Inst.* 2002;94:1143–1150.

Wolff AC, Domchek SM, Davidson NE, Sacchini V, McCormick B. Chapter 91: Cancer of the Breast. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa: Elsevier; 2014.

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Chemotherapy for Breast Cancer in Men

- When is chemotherapy used?
- Which chemotherapy drugs are used for breast cancer?
- How is chemotherapy given?
- Possible side effects of chemotherapy

More information about chemotherapy

Chemotherapy (chemo) is treatment with cancer-killing 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. Occasionally, chemo might be given directly into the spinal fluid which surrounds the brain and spinal cord.

When is chemotherapy used?

Not all men with breast cancer will need chemo, but there are several situations in which chemo might be recommended:

- After surgery (adjuvant chemotherapy): When treatment is given to patients who have no evidence of cancer after surgery, it is called adjuvant therapy. Adjuvant chemo is used to try to kill any cancer cells that might have been left behind or have spread but can't be seen, even on imaging tests¹. 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. Radiation and hormone therapy can also be used as adjuvant treatments.
- Before surgery (neoadjuvant chemotherapy): Neoadjuvant therapy is like adjuvant therapy, except you get the treatments (or at least start them) before surgery instead of after. Neoadjuvant chemo can be used 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 at the time of diagnosis (called *locally advanced cancers*). Also, by giving chemo before the tumor is removed, doctors can better 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 have spread but can't be seen. Just like adjuvant chemo, neoadjuvant chemo can lower the risk of breast cancer coming back. In terms of survival and the chances of cancer coming back, there is no difference between getting chemo before or after surgery.
- For advanced breast cancer: Chemo can also be used as the main treatment for men whose cancer has either already spread beyond the breast and underarm area when it is diagnosed, or if it spreads after initial treatments. The length of treatment depends on how well the chemo is working and how well you tolerate treatment.

Sometimes it's not clear if chemotherapy will be helpful. There are tests available, such as Oncotype DX and MammaPrint, that can help determine which men will most likely

benefit from chemo after breast surgery. See <u>How is Breast Cancer in Men Classified?</u>² for more information.

Which chemotherapy drugs are used for breast cancer?

In most cases (especially as adjuvant or neoadjuvant treatment), chemo is most effective when combinations of drugs are used. Today, doctors use many different combinations, and it's not clear that any single combination is clearly the best.

The most common drugs used for adjuvant and neoadjuvant chemo include:

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

Most often, combinations of 2 or 3 of these drugs are used.

Chemo drugs useful in treating breast cancer that has spread include:

- Taxanes, such as paclitaxel (Taxol), docetaxel (Taxotere), and albumin-bound paclitaxel (Abraxane)
- Anthracyclines (Doxorubicin, pegylated liposomal doxorubicin, and Epirubicin)
- Platinum agents (cisplatin, carboplatin)
- Vinorelbine (Navelbine)
- Capecitabine (Xeloda)
- Gemcitabine (Gemzar)
- Ixabepilone (Ixempra) Albumin-bound paclitaxel (nab-paclitaxel or Abraxane)
- Eribulin (Halaven)

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

For cancers that are <u>HER2-positive</u>³ one or more drugs that target HER2 may be used with chemo. See <u>Targeted Therapy for Breast Cancer in Men</u> for more information about these drugs.

How is chemotherapy 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, chemotherapy clinic, or in a hospital.

Often, a slightly larger and sturdier IV is required in the vein system to administer chemo. They are known as <u>central venous catheters</u>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.

Many different kinds of CVCs are available. The 2 most common types are the port and the PICC line. For breast cancer patients, the central line is typically placed on the opposite side of the breast that had surgery.

Doctors give chemo in cycles, with each period of treatment followed by a rest period. Chemo begins on the first day of each cycle, but the schedule varies depending on the drugs used. For example, with some drugs, the chemo is given only on the first day of the cycle. With others, it is given every day for 14 days, or weekly for 2 weeks. Then, at the end of the cycle, the schedule of chemo repeats to start the next cycle.

Cycles are most often 2 or 3 weeks long, but they vary according to the specific drug or combination of drugs. Some drugs are given more often. Adjuvant and neoadjuvant chemo is often given for a total of 3 to 6 months, depending on what drugs are used. Treatment is often longer for advanced breast cancer, and is based 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 agents closer together can lower the chance that the cancer will come back and improve survival in some patients. This usually means giving the same chemo that is normally given, but giving it every 2 weeks instead of every 3 weeks. A drug (growth factor) to help boost the white blood cell count is given after the chemo to make sure the white blood cell count returns to normal in time for the next cycle. This approach can be used for both adjuvant and neoadjuvant chemo. It can lead to more problems with low blood counts, though, so it isn't for everyone.

Possible side effects of chemotherapy

Chemo drugs attack cells that are dividing quickly, which is why they work against cancer cells. But other cells in the body, such as those in the bone marrow, the lining of

the mouth and intestines, and the hair follicles, also divide quickly. These cells are likely to be affected by chemo too, which can lead to side effects. Some men have many side effects while other men may have few.

The side effects of chemotherapy depend on the type of drugs, the amount taken, and the length of treatment. Some of the most common possible side effects include:

- Hair loss
- Mouth sores
- Loss of appetite (or increased appetite)
- Nausea and vomiting
- Low blood cell counts

Chemo can 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 or other reasons)

These side effects are usually short-term and go away after treatment is finished. Let your cancer care team know if you have any side effects, because there are often ways to lessen them. For example, drugs can be given to help prevent or reduce nausea and vomiting.

Several other side effects are also possible. Some of these are only seen with certain chemotherapy drugs. Ask your cancer care team about the possible side effects of the specific drugs you are getting.

Nerve damage (neuropathy): Many drugs used to treat breast cancer, including the taxanes (docetaxel and paclitaxel), platinum agents (carboplatin, cisplatin), vinorelbine, erubulin, and ixabepilone, can damage nerves outside the brain and spinal cord. This can sometimes lead to symptoms (mainly in the hands and feet) such as numbness, pain, burning or tingling sensations, sensitivity to cold or heat, or weakness. In most cases this goes away once treatment is stopped, but it might last a long time in some men.

Heart damage: Doxorubicin, epirubicin, and some other drugs may cause permanent heart damage (called *cardiomyopathy*). The risk is highest if the drug is used for a long time or in high doses. Most doctors check your heart function with a test like a MUGA or echocardiogram(an ultrasound of the heart) before starting one of these drugs. They

also carefully control the doses and watch for symptoms of heart problems, and may repeat the heart test to monitor heart function 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. Damage from these drugs happens more often if other drugs that can cause heart damage (such as those that target HER2) are used also, so doctors are more cautious when these drugs are used together.

Hand-foot syndrome: Certain chemo drugs, such as capecitabine and liposomal doxorubicin, 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, uncomfortable, or even painful. The skin may blister and peel. 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 early symptoms come up, so that the drug dose can be changed or other medications can be given .

Chemo brain: There is very little research on chemo brain in men, but many women who are treated for breast cancer report a slight decrease in mental functioning. There may be some long-lasting problems with concentration and memory. Although many women have linked this to chemo, it also has been seen in women who did not get chemo as a part of their treatment. Also, most women do function well after chemotherapy. In studies of chemo brain as a side effect of treatment, the symptoms most often go away within a few years. Even though most research was done in women, there's no reason to expect any differences in men being treated for breast cancer.

Increased risk of leukemia: Very rarely, certain chemo drugs can cause diseases of the bone marrow such as myelodysplastic syndrome or even acute myeloid leukemia, a cancer of white blood cells. When this happens it is usually within 10 years of treatment. For most men though, chemo's benefits of helping to prevent breast cancer from coming back or extending life are likely to far exceed the risk of this serious but rare complication.

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

Fatigue is often another common (but often overlooked) problem for those who have had chemo. This may last up to several years. It can often be helped, so it is important

to let your doctor or nurse know about it. Exercise, naps, and conserving energy may be recommended. If there are problems with sleep, these can be treated. Sometimes there is 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 Chemotherapy⁷.

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

Hyperlinks

- 1. <u>www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/imaging-radiology-tests-for-cancer.html</u>
- 2. <u>www.cancer.org/cancer/types/breast-cancer-in-men/detection-diagnosis-staging/classifying.html</u>
- 3. www.cancer.org/cancer/types/breast-cancer-in-men/detection-diagnosis-staging/classifying.html
- 4. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/tubes-lines-ports-catheters.html</u>
- 5. www.cancer.org/cancer/types/myelodysplastic-syndrome.html
- 6. www.cancer.org/cancer/types/acute-myeloid-leukemia.html
- 7. www.cancer.org/cancer/managing-cancer/treatment-types/chemotherapy.html
- 8. www.cancer.org/cancer/managing-cancer/side-effects.html

References

Callahan RD and Ganz PA. Chapter 52: Long-Term and Late Effects of Primary Curative Intent Therapy: Neurocognitive, Cardiac, and Secondary Malignancies. In: Harris JR, Lippman ME, Morrow M, Osborne CK, eds. *Diseases of the Breast*. 5th ed. Philadelphia: Wolters Kluwer Health; 2014.

Citron ML, Berry DA, Cirrincione C, et al: Randomized trial of dose-dense versus conventionally scheduled and sequential versus concurrent combination chemotherapy as postoperative adjuvant treatment of node-positive primary breast cancer: First report of Intergroup Trial C9741/Cancer and Leukemia Group B Trial 9741. *J Clin Oncol*

21:1431–1439, 2003.

Dang C and Hudis CA. Chapter 44: Adjuvant Systemic Chemotherapy in Early Breast Cancer. In: Harris JR, Lippman ME, Morrow M, Osborne CK, eds. *Diseases of the Breast*. 5th ed. Philadelphia: Wolters Kluwer Health; 2014.

Giordano SH, Perkins GH, Broglio K, Garcia SG, Middleton LP, Buzdar AU, Hortobagyi GN. Adjuvant systemic therapy for male breast carcinoma. *Cancer*. 2005 Dec 1;104(11):2359-64.

Giordano SH. A review of the diagnosis and management of male breast cancer. *Oncologist.* 2005;10: 471–479.

Jain S and Gradishar WJ. Chapter 61: Male Breast Cancer. In: Harris JR, Lippman ME, Morrow M, Osborne CK, eds. *Diseases of the Breast*. 5th ed. Philadelphia, Pa: Lippincott-Williams & Wilkins; 2014.

Losurdo A et al. Controversies in clinicopathological characteristics and treatment strategies of male breast cancer: A review of the literature. *Critical Reviews in Oncology/Hematology* 113 (2017) 283–291.

Morrow M, Burstein HJ, Harris JR. Chapter 79: Malignant Tumors of the Breast. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology.* 10th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2015.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: Breast Cancer. Version 3.2017. Accessed at www.nccn.org on January 18, 2018.

PDQ Adult Treatment Editorial Board. Male Breast Cancer Treatment (PDQ®): Health Professional Version. 2017 Dec 15. In: PDQ Cancer Information Summaries [Internet]. Bethesda (MD): National Cancer Institute (US); 2002-. Available from: https://www-ncbi-nlm-nih-gov.ezproxyhost.library.tmc.edu/books/NBK65792/. Accessed Jan 10, 2018.

Osborne CK. Chapter 53: Adjuvant Systemic Therapy Treatment Guidelines. In: Harris JR, Lippman ME, Morrow M, Osborne CK, eds. *Diseases of the Breast*. 5th ed. Philadelphia: Wolters Kluwer Health; 2014.

Untch M, Möbus V, Kuhn W, et al. Intensive dose-dense compared with conventionally scheduled preoperative chemotherapy for high-risk primary breast cancer. *J Clin Oncol.* 2009 Jun 20;27(18):29382945. Epub 2009 Apr 13.

Wolff AC, Domchek SM, Davidson NE, Sacchini V, McCormick B. Chapter 91: Cancer of the Breast. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa: Elsevier; 2014.

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Hormone Therapy for Breast Cancer in Men

- What types of drugs are used in hormone therapy?
- Orchiectomy (castration)
- Possible side effects of hormone therapy
- More information about hormone therapy

Hormone therapy (sometimes called endocrine therapy) is a way to treat cancer by using hormones or drugs or other treatments that affect hormones. Hormone therapy is a form of systemic therapy, meaning it can reach nearly all parts of the body.

Hormone therapy can be used after surgery (adjuvant therapy) to help lower the risk of cancer coming back, or before surgery (neoadjuvant treatment). It can also be used to treat cancer that has spread, or cancer that has come back after treatment (recurred).

Some breast cancers grow in response to the hormones estrogen or progesterone. Estrogen and progesterone are usually thought of as female hormones, but men have them in their bodies, too, just at lower levels.

About 9 of 10 breast cancers in men are hormone receptor-positive, meaning they are estrogen receptor (ER)-positive, progesterone receptor (PR)-positive, or both. This makes them more likely to respond to hormone treatments. Hormone therapy does not help people whose tumors are both ER- and PR-negative.

What types of drugs are used in hormone therapy?

Several approaches to blocking the effects of estrogen or lowering estrogen levels are used to treat breast cancer in women. Although many of these may work in men as well, they often haven't been studied well, if at all.

Tamoxifen and toremifene

These drugs are known as **selective estrogen receptor modulators (SERMs)**. They block estrogen receptors on breast cancer cells, which can help keep the cells from growing. Both of these drugs are taken daily as pills.

Tamoxifenis the best studied hormone drug for breast cancer in men and is most often used first. If tamoxifen doesn't work (or stops working), other hormone drugs may be tried, but this is largely based on how well they work in women with breast cancer.

Large studies of women with early-stage, hormone receptor-positive cancers have shown that taking tamoxifen after surgery for 5 years reduces the chances of the cancer coming back by about half. Taking it for 10 years may help even more. Studies in men with breast cancer have been smaller, but they have also found that taking tamoxifen after surgery for early-stage breast cancer can lower the chance of the cancer coming back and improve survival.

Tamoxifen can also be used to treat metastatic breast cancer.

Toremifene (Fareston) works like tamoxifen, but it's not used as often and is only approved to treat metastatic breast cancer. It is not likely to work if tamoxifen has already been used and has stopped working.

The most common **side effects** of tamoxifen and toremifene are:

- Hot flashes
- Sexual problems
- Fatigue

Some men with cancer spread to the bones may have a **tumor flare** with pain and swelling in the muscles and bones. This usually goes away quickly, but rarely a man 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:

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 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 post-menopausal women.
 The risk in men is not clear. Tell your doctor if you have a sudden severe headache, confusion, or trouble speaking or moving.

Tamoxifen may also increase the risk of **heart attacks** in some people, although this link is not clear.

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 (degraded).

Fulvestrant (Faslodex) is used to treat metastatic breast cancer, most often after other hormone drugs (like tamoxifen and often an aromatase inhibitor) have stopped working. It is given by injection into the buttocks every 2 weeks for a month, then monthly.

Elacestrant (Orserdu) can be used to treat advanced, ER-positive, HER2-negative breast cancer when the cancer cells have an *ESR1* gene mutation, and the cancer has grown after at least one other type of hormone therapy. This drug is taken daily as pills.

The most common side effects of these drugs are **hot flashes**, **nausea**, **muscle or joint pain**, **headache**, and **pain at the injection site**. Elacestrant can also increase cholesterol and fat levels in the blood.

Aromatase inhibitors

This group of drugs includes **anastrozole (Arimidex)**, **letrozole (Femara)**, and **exemestane (Aromasin)**. These drugs stop estrogen production by blocking an enzyme (aromatase) in fat tissue that converts male hormones from the adrenal glands into estrogen.

Aromatase inhibitors are taken daily as pills. They have been very effective in treating breast cancer in women, but they have not been well-studied in men. Still, some doctors use them to treat advanced breast cancer in men, often combined with a **luteinizing hormone-releasing hormone (LHRH) analog** to turn off hormone production by the testicles (discussed below). These drugs are generally used if tamoxifen stops working.

The main side effects are thinning of the bones and pain in muscles and joints.

Luteinizing hormone-releasing hormone (LHRH) analogs and anti-androgens

In men, **LHRH analogs** such as leuprolide (Lupron) and goserelin (Zoladex) affect the pituitary gland, which regulates testosterone production in the testicles. These drugs cause the pituitary gland to turn off production of testosterone by the testicles, leading to lower testosterone levels. They are given as shots either monthly or every few months. These drugs may be used by themselves, or combined with aromatase inhibitors or anti-androgens to treat advanced breast cancer in men.

Anti-androgens such as flutamide and bicalutamide work by blocking the effect of male hormones on breast cancer cells. These drugs are taken daily as pills.

Megestrol

Megestrol(Megace) is a progesterone-like drug. It is unclear how it stops cancer cells from growing, but it appears to compete for hormone receptor sites in the cells. This is an older drug that is usually reserved for men who are no longer responding to other forms of hormone therapy. Megestrol may **increase the risk for blood clots** and **frequently causes weight gain** by increasing appetite.

Orchiectomy (castration)

Surgical removal of the testicles (orchiectomy) is another way to regulate hormones that might affect breast cancer growth. Removing the testicles greatly lowers the levels of testosterone and other androgens (male hormones). Most male breast cancers have androgen receptors that may cause the cells to grow. Androgens can also be converted into estrogens in the body.

Orchiectomy shrinks most male breast cancers, and it may help make other treatments like tamoxifen more likely to work.

This was once a common treatment for breast cancer in men, but it is now used less often because medicines such as LHRH analogs can now be used to lower androgen levels.

Possible side effects of hormone therapy

Although some of these drugs have unique side effects (see descriptions above), in general they can cause **loss of sexual desire**, **trouble getting erections**, **weight gain**, **hot flashes**, and **mood swings**. Be sure to discuss any such side effects with

your cancer care team because there may be ways to treat them.

More information about hormone therapy

To learn more about how hormone therapy is used to treat cancer, see <u>Hormone Therapy</u>¹.

To learn about some of the side effects listed here and how to manage them, see Managing Cancer-related Side Effects².

Hyperlinks

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

References

Cardoso F, et al. Characterization of male breast cancer: results of the EORTC 10085/TBCRC/BIG/NABCG International Male Breast Cancer Program. *Annals of Oncology* 0: 1–13, 2017.

Davies C, Pan H, Godwin J, et al. Long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years after diagnosis of oestrogen receptor-positive breast cancer: ATLAS, a randomised trial. *Lancet.* 2013;381:805-816. Erratum in: *Lancet.* 2013 Mar 9;381(9869):804.

Dimitrov NV, Colucci P, Nagpal S. Some aspects of the endocrine profile and management of hormone-dependent male breast cancer. *Oncologist.* 2007;12-798–807.

Di Lauro L, Vici P, Del Medico P, Laudadio L, Tomao S, Giannarelli D, Pizzuti L, Sergi D, Barba M, Maugeri-Saccà M. Letrozole combined with gonadotropin-releasing hormone analog for metastatic male breast cancer. *Breast Cancer Res Treat.* 2013 Aug;141(1):119-23. Epub 2013 Aug 28.

Giordano SH. A review of the diagnosis and management of male breast cancer. *Oncologist.* 2005;10: 471–479.

Giordano SH, Perkins GH, Broglio K, Garcia SG, Middleton LP, Buzdar AU, Hortobagyi GN. Adjuvant systemic therapy for male breast carcinoma. *Cancer*. 2005 Dec

1;104(11):2359-64.

Gray RG, Rea D, Handley K, et al. Long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years in 6,953 women with early breast cancer. *J Clin Oncol* (Meeting Abstracts) June 2013 vol. 31 no. 18_suppl 5.

Jain S and Gradishar WJ. Chapter 61: Male Breast Cancer. In: Harris JR, Lippman ME, Morrow M, Osborne CK, eds. *Diseases of the Breast*. 5th ed. Philadelphia, Pa: Lippincott-Williams & Wilkins; 2014.

Losurdo A et al. Controversies in clinicopathological characteristics and treatment strategies of male breast cancer: A review of the literature. *Critical Reviews in Oncology/Hematology* 113 (2017) 283–291.

PDQ Adult Treatment Editorial Board. Male Breast Cancer Treatment (PDQ®): Health Professional Version. 2017 Dec 15. In: PDQ Cancer Information Summaries [Internet]. Bethesda (MD): National Cancer Institute (US); 2002-. Available from: https://www-ncbi-nlm-nih-gov.ezproxyhost.library.tmc.edu/books/NBK65792/. Accessed Jan 10, 2018.

Stearns V and Davidson NE. Chapter 45: Adjuvant Chemo Endocrine Therapy. In: Harris JR, Lippman ME, Morrow M, Osborne CK, eds. *Diseases of the Breast.* 5th ed. Philadelphia: Wolters Kluwer Health; 2014.

Zagouri F, Sergentanis TN, Chrysikos D, Zografos E, Rudas M, Steger G, Zografos G, Bartsch R. Fulvestrant and male breast cancer: a case series. *Ann Oncol.* 2013 Jan;24(1):265-6.

Zagouri F, Sergentanis TN, Koutoulidis V, Sparber C, Steger GG, Dubsky P, Zografos GC, Psaltopoulou T, Gnant M, Dimopoulos MA, Bartsch R. Aromatase inhibitors with or without gonadotropin-releasing hormone analogue in metastatic male breast cancer: a case series. *Br J Cancer*. 2013 Jun 11;108(11):2259-63. Epub 2013 May 30.

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Targeted Drug Therapy for Breast Cancer in Men

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

As researchers have learned more about changes in cancer cells that cause them to grow out of control, they've developed new types of drugs that target some of these cell changes. These targeted drugs work differently from chemotherapy (chemo) drugs.

Targeted drugs sometimes work even when chemo drugs do not. Some targeted drugs can help other types of treatment work better. Targeted drugs also tend to have different side effects than chemo.

Several targeted drugs have been approved for use in treating breast cancer, although using these drugs in men is often based largely on how well they work in women.

Targeted therapy for HER2-positive breast cancer

In some men with breast cancer, the cancer cells have too much of a growth-promoting protein known as HER2 (or HER2/neu) on their surface. These cancers, known as HER2-positive breast cancers, tend to grow and spread more aggressively.

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 names¹): 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 also available. It is given as a subcutaneous (under the skin)

shot over a few minutes.

Pertuzumab (Perjeta): This 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).

For people getting both of these monoclonal antibodies as part of their treatment, a combination of **trastuzumab**, **pertuzumab**, **and hyaluronidase** (**Phesgo**) is also available as a single injection. It is given as a subcutaneous (under the skin) shot over several minutes.

Margetuximab (Margenza): This 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 or TDM-1): This antibody-drug conjugate 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 men 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 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 2 other anti-HER2 targeted drugs have been tried. This drug is given in a vein (IV).

Fam-trastuzumab deruxtecan can also be used to treat <u>HER2-low</u>² 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, typically along with the chemo drug capecitabine or with certain hormone therapy drugs.

Neratinib (Nerlynx): This kinase inhibitor is a pill taken daily. Neratinib is used to treat early-stage breast cancer after completing one year of trastuzumab, 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 pills, 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 typically given along with trastuzumab and the chemo drug capecitabine.

Side effects of HER2 targeted drugs

The side effects of HER2 targeted drugs are often mild, but some can be serious. Discuss what you can expect with your doctor.

The 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) people, 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). 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, 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 people. 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

In about 9 out of 10 men with breast cancer, the breast cancer cells have proteins (receptors) on the outside that can attach to hormones, like estrogen or progesterone, to help them grow. These are called **hormone receptor-positive (HR-positive) breast cancers**. Sometimes they are called estrogen receptor-positive (ER-positive) or progesterone receptor-positive (PR-positive) breast cancers. These cancers are commonly treated with hormone therapy. 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 can be used to treat men with hormone receptor-positive, HER2-negative breast cancer. There are different ways to use these drugs:

- For men 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.
- Any of these drugs can be given along with an aromatase inhibitor (AI) or fulvestrant to treat advanced breast cancer.
- Abemaciclib can also be used by itself in men with advanced breast cancer who
 have previously been treated with hormone therapy and chemotherapy.

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

The most common side effects of CDK4/6 inhibitors are 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.

PI3K inhibitor

Alpelisib (Piqray) is a targeted drug known as a *PI3K inhibitor*. It blocks a form of the PI3K protein in cancer cells, which can help stop them from growing.

This drug can be used along with the hormone drug fulvestrant to treat both men and postmenopausal 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 high blood sugar levels, signs of kidney, liver, or pancreatic problems, diarrhea, rash, 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.

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 stool 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, skin rash, and changes in certain blood tests.

mTOR inhibitor

Everolimus (Afinitor) is a targeted drug known as an *mTOR inhibitor*. It 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, this drug seems to help hormone therapy drugs work better.

This drug is approved to treat advanced hormone receptor-positive, HER2-negative, breast cancer in women who have gone through menopause. It is meant to be used with exemestane (Aromasin) in these women if their cancers have grown while they were being treated with either letrozole or anastrozole (or if the cancer started growing shortly after treatment with these drugs was stopped).

Everolimus is also being studied for use for earlier stage breast cancer and combined with other treatments. Although most of the people with breast cancer in studies of everolimus are women, some studies have included men.

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

Common **side effects of everolimus** include mouth sores, diarrhea, nausea, fatigue, 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 periodically while you are on this drug. It can also increase your risk of serious infections, so your doctor will watch you closely for infection while you are on treatment.

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 men with BRCA mutations

Olaparib (Lynparza) and talazoparib (Talzenna) are drugs known as *PARP inhibitors*. PARP proteins normally help repair damaged DNA inside cells. 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.

Olaparib and talazoparib can be used to treat metastatic, HER2-negative breast cancer in patients with a *BRCA* mutation who have already gotten chemotherapy (and hormone therapy if the cancer is hormone receptor-positive).

Only a portion of men with breast cancer have a <u>mutated BRCA</u> gene that they are born <u>with</u>³, and which is in all the cells of the body (as opposed to the gene change being acquired and 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 one of these drugs.

These drugs come in pills that are taken once or twice a day.

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 the chemo 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 reaction) 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 <u>Targeted Cancer</u> <u>Therapy</u>⁶.

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

Hyperlinks

- 1. <u>www.cancer.org/cancer/managing-cancer/treatment-types/biosimilar-drugs/list.html</u>
- 2. <u>www.cancer.org/cancer/types/breast-cancer-in-men/detection-diagnosis-staging/classifying.html</u>
- 3. <u>www.cancer.org/cancer/types/breast-cancer-in-men/causes-risks-prevention/what-causes.html</u>
- 4. www.cancer.org/cancer/types/myelodysplastic-syndrome.html
- 5. www.cancer.org/cancer/types/acute-myeloid-leukemia.html
- 6. www.cancer.org/cancer/managing-cancer/treatment-types/targeted-therapy.html
- 7. www.cancer.org/cancer/managing-cancer/side-effects.html

References

Bardia A, Mayer IA, Diamond JR, et al. Efficacy and Safety of Anti-Trop-2 Antibody Drug Conjugate Sacituzumab Govitecan (IMMU-132) in Heavily Pretreated Patients With Metastatic Triple-Negative Breast Cancer. *J Clin Oncol*. 2017;35(19):21412148. doi:10.1200/JCO.2016.70.8297.

Baselga J, Campone M, Piccart M, et al. Everolimus in postmenopausal hormone-receptor-positive advanced breast cancer. *N Engl J Med.* 2012;366: 520529.

Baselga J, Cortés J, Kim SB, et al. Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer. *N Engl J Med*. 2012 Jan 12;366(2):109-19. Epub 2011 Dec 7.

Blackwell KL, Burstein HJ, Storniolo AM, et al. Randomized study of lapatinib alone or in combination with trastuzumab in women with ErbB2-positive, trastuzumab-refractory metastatic breast cancer. *J Clin Oncol.* 2010 Mar 1;28(7):1124-1130. Epub 2010 Feb 1.

Burstein HJ, Sun Y, Dirix LY, et al. Neratinib, an irreversible ErbB receptor tyrosine kinase inhibitor, in patients with advanced ErbB2-positive breast cancer. *J Clin Oncol.* 2010 Mar 10;28(8):1301-7. Epub 2010 Feb 8.

Dickler MN et al. MONARCH 1, A Phase II Study of Abemaciclib, a CDK4 and CDK6 Inhibitor, as a Single Agent, in Patients with Refractory HRp/HER2_ Metastatic Breast

Cancer. Clin Cancer Res; 23(17); 5218-5224.

Finn RS, Crown JP, Lang I, et al. The cyclin-dependent kinase 4/6 inhibitor palbociclib in combination with letrozole versus letrozole alone as first-line treatment of oestrogen receptor-positive, HER2-negative, advanced breast cancer (PALOMA-1/TRIO-18): a randomised phase 2 study. *Lancet Oncol.* 2015;16(1):25-35.

Finn RS, Martin M, Rugo HS, et al. Palbociclib and letrozole in advanced breast cancer. *N Engl J Med.* 2016;375(20):1925-1936.

Gao et al. *Sci. Signal.* 2013 & Cerami et al. *Cancer Discov.* 2012. Accessed at http://www.cbioportal.org/results/cancerTypesSummary?case_set_id=all&gene_list=PIK 3CA&cancer_study_list=5c8a7d55e4b046111fee2296 on May 29, 2019.

Hortobagyi GN, Stemmer SM, Burris HA, et al. Ribociclib as first-line therapy for HR-positive, advanced breast cancer. *N Engl J Med.* 2016;375(18):1738-1748;(suppl).

Hortobagyi GN, Stemmer SM, Burris HA, et al. Updated results from MONALEESA-2, a phase III trial of first-line ribociclib + letrozole in hormone receptor-positive, HER2-negative advanced breast cancer. Poster presented at: American Society of Clinical Oncology Annual Meeting; June 2-6, 2017; Chicago, IL. Abstract 1038.

Morrow M, Burstein HJ, Harris JR. Chapter 79: Malignant Tumors of the Breast. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology.* 10th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2015.

Mukohara T. PI3K mutations in breast cancer: prognostic and therapeutic implications. *Breast Cancer (Dove Med Press)*. 2015;7: 111–123.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: Breast Cancer. Version 3.2017. Accessed at www.nccn.org on January 18, 2018.

Verma S, Miles D, Gianni L, et al. Trastuzumab emtansine for HER2-positive advanced breast cancer. *N Engl J Med.* 2012 Nov 8;367(19):1783-91. Epub 2012 Oct 1.

Sledge GW, Toi M, Neven P, et al. MONARCH 2: Abemaciclib in Combination With Fulvestrant in Women With HR+/HER2 Advanced Breast Cancer Who Had Progressed While Receiving Endocrine Therapy. Journal of Clinical Oncology 2017 35:25, 2875-2884.

Wolff AC, Domchek SM, Davidson NE, Sacchini V, McCormick B. Chapter 91: Cancer of the Breast. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa: Elsevier; 2014.

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Immunotherapy for Breast Cancer in Men

- Immune checkpoint inhibitors
- More information about immunotherapy

Immunotherapy is the use of medicines to stimulate a person's own immune system to recognize and destroy cancer cells more effectively. Immunotherapy can be used to treat some types of breast cancer.

Immune checkpoint inhibitors

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 "checkpoints," which are proteins 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 to 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 cells called *T cells* that normally help keep these cells 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 cancer¹ (that makes the

PD-L1 protein) that:

- has come back (recurred) locally but can't be removed by surgery and hasn't been treated with chemotherapy this time OR
- has spread to other parts of the body and has not been treated with chemotherapy this time.

This drug is given as an intravenous (IV) infusion, typically every 3 or 6 weeks.

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 safeguards 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 Immunotherapy².

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u>³.

Hyperlinks

- 1. <u>www.cancer.org/cancer/types/breast-cancer-in-men/detection-diagnosis-staging/classifying.html</u>
- 2. www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy.html
- 3. www.cancer.org/cancer/managing-cancer/side-effects.html

References

Jagsi R, King TA, Lehman C, Morrow M, Harris JR, Burstein HJ. Chapter 79: Malignant Tumors of the Breast. In: DeVita VT, Lawrence TS, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology.* 11th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2019.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: Breast Cancer. Version 2.2019. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf on July 22, 2019.

Schmidt P, Adams S, Rugo HS, Scheeweiss A, Barrios CH, Iwata H, et al. Atezolizumab and Nab-Paclitaxel in Advanced Triple-Negative Breast Cancer. *N Engl J Med.* 2018 Nov 29;379(22):2108-2121. doi: 10.1056/NEJMoa1809615. Epub 2018 Oct 20.

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Treatment of Breast Cancer in Men, by Stage

- Stage 0 (ductal carcinoma in situ)
- Stage I
- Stage II
- Stage III

- Stage IV (metastatic)
- Recurrent cancer

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 the ER, 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 physician.

Because there have been few <u>clinical trials</u>¹ on treatment of male breast cancer, most doctors base their treatment recommendations on their experience with the disease and on the results of studies of breast cancer in women. With some minor variations, breast cancer in men is treated the same way as breast cancer in women.

The <u>stage (extent) of your breast cancer</u>² 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 <u>other factors</u>³ can also be important, such as:

- If the cancer cells contain hormone receptors (that is, if the cancer is ER-positive or PR-positive)
- If the cancer cells have large amounts of the HER2 protein (that is, if the cancer is HER2-positive)
- Your overall health and personal preferences
- How fast the cancer is growing (measured by grade or other measures)

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

Stage 0 (ductal carcinoma in situ)

Stage 0 cancer means that the cancer is limited to the inside of the milk duct and is a non-invasive cancer. Stage 0 breast tumors include ductal carcinoma in situ (DCIS).

It is treated with <u>surgery</u> to remove the cancer. Most often in males, a mastectomy is done. If breast-conserving surgery is done, it is followed by <u>radiation therapy</u> to the remaining breast tissue.

Sometimes DCIS can contain an area of invasive cancer. The chance that an area of DCIS contains invasive cancer goes up with tumor size and how fast the cancer is growing. If there is concern of invasive cancer, the lymph nodes under the arm may be

checked for spread, most often with a sentinel lymph node biopsy. If cancer cells are found in the sentinel lymph node, it means the tumor must contain some invasive cancer, and the man will be treated based on his invasive cancer stage.

Stage I

These cancers are still relatively small and either have not spread to the lymph nodes (N0) or there is a tiny area of cancer spread in the sentinel lymph node (N1mi).

The main treatment for stage I breast cancer is to remove it with surgery. This is usually done by mastectomy, but breast-conserving surgery (BCS) might occasionally be an option. If breast-conserving surgery is done, it is usually followed by radiation therapy.

The lymph nodes under the arm will be checked for cancer spread, either with an axillary lymph node dissection (ALND) or sentinel node biopsy (SLNB). If the sentinel lymph node contains cancer, a full ALND may be needed, depending on the size of the cancer in the lymph node as well as what other treatment is planned.

Hormone therapy, chemotherapy (chemo) and/or targeted therapy may be recommended as adjuvant (after surgery) therapy, based on the tumor size and results of lab tests. Hormone therapy with tamoxifen is usually recommended for hormone receptor-positive tumors. Adjuvant chemo is commonly used for tumors larger than 1 cm (about 1/2 inch) across and some smaller tumors that may be more likely to spread (based on features such as grade or a high growth rate). Men with HER2-positive tumors may also receive targeted therapy with trastuzumab (Herceptin).

Stage II

These cancers tend to be larger than stage I cancers and/or have spread to a few nearby lymph nodes.

Systemic (drug) therapy is often recommended for men with stage II breast cancer. Some systemic therapies are given before surgery (neoadjuvant therapy), and others are given after surgery (adjuvant therapy). Neoadjuvant treatments may be an option for men with large tumors, because they can shrink the tumor before surgery, possibly enough to make breast-conserving surgery (BCS) an option. The lymph nodes under the arm will be checked for cancer spread, either with an axillary lymph node dissection (ALND) or sentinel lymph node biopsy. If the sentinel lymph node contains cancer, a full ALND may be needed, depending on the size of the cancer in the lymph node as well as what other treatment is planned.

Radiation therapy may be given after surgery if the tumor is large or if it is found to have spread to several lymph nodes. Radiation therapy lowers the risk of the cancer coming back (recurrence).

The drugs used will depend on the man's age and the tumor's hormone-receptor status and HER2 status. They may include:

Chemotherapy: Chemo can be given before or after surgery.

HER2 targeted drugs: If the cancer is HER2-positive, HER2 targeted drugs are started along with chemo. Both trastuzumab (Herceptin) and pertuzumab (Perjeta) may be used as a part of neoadjuvant treatment. Then trastuzumab is continued after surgery for a total of one year of treatment.

Hormone therapy: If the cancer is hormone receptor-positive, hormone therapy with tamoxifen is typically used for 5 years after surgery.

Stage III

This stage includes more advanced tumors (large or growing into nearby skin or muscle) and cancers with spread to many nearby lymph nodes.

Most often, these cancers are treated with chemo before surgery (neoadjuvant chemo). For HER2-positive tumors, the targeted drug trastuzumab is given as well, sometimes along with pertuzumab. This is usually followed by a mastectomy. Most men with this stage need a full axillary lymph node dissection (ALND). Often, radiation therapy is recommended after surgery. Adjuvant hormone therapy with tamoxifen is given for at least 5 years if the tumor is hormone receptor-positive. Men with HER2-positive cancers will probably also receive trastuzumab to complete one year of treatment. Adjuvant hormone therapy can typically be taken at the same time as trastuzumab.

Another option for stage III cancers is to treat with surgery first. This usually means a mastectomy with an ALND. Surgery is usually followed by adjuvant chemo. Trastuzumab is given with chemo if the tumor is HER2 positive, and then it is continued to complete one year of treatment. Radiation is recommended after surgery and chemo. Adjuvant hormone therapy is given to men with hormone receptor-positive breast cancers for at least 5 years.

Stage IV (metastatic)

Stage IV cancers have spread beyond the breast and nearby lymph nodes to other

parts of the body. Breast cancer most commonly spreads to the bones, liver, and lungs. As the cancer progresses, it may spread to the brain, but it can affect any organ and tissue.

Systemic (drug) therapy is the main treatment for stage IV breast cancer in men. Depending on many factors, this may be hormone therapy, chemo, targeted therapy, immunotherapy, or some combination of these treatments.

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

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

If your doctor recommends such local treatments, it is important that you understand their goal, whether it is to try to cure the cancer or to prevent or treat symptoms.

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

Treatment to relieve symptoms depends on where the cancer has spread. For example, pain from bone metastases may be treated with external beam radiation therapy and/or bisphosphonates or denosumab (Xqeva). For more information, see Bone Metastases⁴.

Advanced <u>triple-negative breast cancer</u>⁵ (TNBC) that makes the PD-L1 protein may be treated first with the immunotherapy drug atezolizumab along with albumin-bound paclitaxel (Abraxane). Another option might be treatment with the immunotherapy drug pembrolizumab (Keytruda) along with chemotherapy. The PD-L1 protein is found in about 1 out of 5 TNBCs.

Advanced cancer that progresses during treatment

Treatment for advanced breast cancer can often shrink or slow the growth of the cancer (sometimes for many years), but after a time it may stop working. Further treatment at this point depends on several factors, including previous treatments, where the cancer is located, and a man's age, general health, and desire to continue getting treatment.

Progression while on hormone therapy: For hormone receptor-positive cancers that

were being treated with hormone therapy, switching to another type of hormone therapy is sometimes helpful. Another option might be a hormone drug along with a targeted therapy drug. If this isn't helpful, chemo is usually the next step.

Progression while on chemotherapy: For cancers that are 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.

For breast cancers that are considered <u>HER2-low</u>⁶ and have spread to distant sites after trying chemotherapy, the antibody-drug conjugate fam-trastuzumab deruxtecan (Enhertu) might be an option.

For advanced hormone receptor-positive, HER2-negative breast cancer or for <u>triple-negative breast cancer</u>⁷ in which at least 2 other chemo treatments have been tried, the <u>antibody-drug conjugate</u> sacituzumab govitecan (Trodelvy) might be an option.

Progression while getting HER2 drugs: HER2-positive cancers that no longer respond to trastuzumab may respond to other drugs that target the HER2 protein (sometimes along with chemo or hormone therapy drugs). Some options might include:

- Pertuzumab (Perjeta) with chemo and trastuzumab
- Ado-trastuzumab emtansine (Kadcyla)
- Fam-trastuzumab deruxtecan (Enhertu)
- Margetuximab (Margenza) with chemo
- Lapatinib (Tykerb) and the 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 advanced breast cancer, if you are in otherwise good health, you may want to think about taking part in a <u>clinical</u> <u>trial</u>⁸ testing newer treatments. You can also read about living with later-stage cancer in Advanced Cancer, Metastatic Cancer, and Bone Metastasis⁹.

Recurrent cancer

For some men, 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.** If cancer is found in the opposite breast but nowhere else in the body, it is not a recurrence—it's a new cancer that requires its own treatment.

Treating local recurrence: This includes cancer coming back in the breast or in the chest wall (near the mastectomy scar). If a patient has a local recurrence and no evidence of distant metastases, it might still be cured. Treatment depends on what other treatments have been given already. The treatment for local recurrence may be additional surgery followed by radiation therapy. If the area has already been treated with radiation, it might not be possible to give more radiation to the area without damaging nearby tissues.

Hormone therapy, chemo, trastuzumab, or some combination of these may be used after surgery and/or radiation therapy.

For people with <u>triple-negative breast cancer</u>¹⁰ that has come back locally, cannot be removed with surgery, and makes the PD-L1 protein, immunotherapy with the drug pembrolizumab along with chemotherapy might be an option. If at least 2 other drug regimens have already been tried, the <u>antibody-drug conjugate</u> sacituzumab govitecan (Trodelvy) might be an option as well.

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. This may be followed by radiation treatments aimed at the area.

Systemic treatment (such as hormone therapy, chemo, targeted therapy, or some combination of these) may be used after surgery and/or radiation therapy.

Treating distant recurrence: Men who have a recurrence in places such as the bones, lungs, brain, etc., are often treated the same way as those found to have stage IV breast cancer with spread to these organs when they were first diagnosed (see above). The only difference is that treatment may be affected by the previous treatments a man has had.

Recurrent breast cancer can sometimes be hard to treat. If you are in otherwise good health, you may want to think about taking part in a <u>clinical trial</u>¹¹ testing a newer treatment.

If your cancer comes back, see <u>Understanding Recurrence</u>¹² for more general information on how to manage and cope with this phase of your treatment.

You can also read about treatments for metastatic cancer in <u>Advanced Cancer</u>, Metastatic Cancer, and Bone Metastasis¹³.

Hyperlinks

- 1. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html</u>
- 2. <u>www.cancer.org/cancer/types/breast-cancer-in-men/detection-diagnosis-staging/staging.html</u>
- 3. <u>www.cancer.org/cancer/types/breast-cancer-in-men/detection-diagnosis-staging/classifying.html</u>
- 4. www.cancer.org/cancer/managing-cancer/advanced-cancer/bone-metastases.html
- 5. <u>www.cancer.org/cancer/types/breast-cancer-in-men/detection-diagnosis-staging/classifying.html</u>
- 6. <u>www.cancer.org/cancer/types/breast-cancer-in-men/detection-diagnosis-staging/classifying.html</u>
- 7. www.cancer.org/cancer/types/breast-cancer-in-men/detection-diagnosis-staging/classifying.html
- 8. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html</u>
- 9. www.cancer.org/cancer/managing-cancer/advanced-cancer.html
- 10. <u>www.cancer.org/cancer/types/breast-cancer-in-men/detection-diagnosis-staging/classifying.html</u>
- 11. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html</u>
- 12. www.cancer.org/cancer/survivorship/long-term-health-concerns/recurrence.html
- 13. <u>www.cancer.org/cancer/managing-cancer/advanced-cancer.html</u>

References

¹⁴Jain S and Gradishar WJ. Chapter 61: Male Breast Cancer. In: Harris JR, Lippman ME, Morrow M, Osborne CK, eds. *Diseases of the Breast*. 5th ed. Philadelphia, Pa: Lippincott-Williams & Wilkins; 2014.

Morrow M, Burstein HJ, Harris JR. Chapter 79: Malignant Tumors of the Breast. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology.* 10th ed. Philadelphia, Pa:

Lippincott Williams & Wilkins; 2015.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: Breast Cancer. Version 3.2017. Accessed at www.nccn.org on January 18, 2018.

Wolff AC, Domchek SM, Davidson NE, Sacchini V, McCormick B. Chapter 91: Cancer of the Breast. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa: Elsevier; 2014.

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Questions to Ask Your Doctor About Breast Cancer in Men

- When you're told you have breast cancer
- When deciding on a treatment plan
- If you need surgery
- During treatment
- After treatment

It's important to be able to have frank, open discussions with your cancer care team. They want to answer all of your questions, so that you can make informed treatment and life decisions.

Here are some questions that you can use to help better understand your cancer and your treatment options. Don't be afraid to take notes and tell the doctors or nurses when you don't understand what they're saying. You might want to bring another person with you when you see your doctor and have them take notes to help you remember what was said.

Not all of these questions will apply to you, but they should help get you started. Be sure to write down some questions of your own. For instance, you might want more information about recovery times or you may want to ask about nearby or online support groups where you can talk with other men going through similar situations. You may also want to ask if you qualify for any <u>clinical trials</u>¹.

Keep in mind that doctors aren't the only ones who can give you information. Other health care professionals, such as nurses and social workers, can answer some of your questions. To find out more about speaking with your health care team, see
The Doctor-Doctor

When you're told you have breast cancer

- Exactly what type of breast cancer do I have?
- How big is the cancer? Where exactly is it?
- Has the cancer spread to my lymph nodes or other organs?
- What's the stage of the cancer? What does that mean?
- Will I need any other tests before we can decide on treatment?
- Do I need to see any other doctors or health professionals?
- What is the hormone receptor status of my cancer? What does this mean?
- What is the HER2 status of my cancer? What does this mean?
- How do these factors affect my treatment options and long-term outlook (prognosis)?
- What are my chances of survival, based on my cancer as you see it?
- Should I think about genetic testing? What would the pros and cons of testing be?
- How do I get a copy of my pathology report?
- If I'm concerned about the costs and insurance coverage for my diagnosis and treatment, who can help me?

When deciding on a treatment plan

- What treatments are appropriate for me? What do you recommend? Why?
- How long will treatment last? What will it involve? Where will it be done?
- What risks or side effects should I expect?
- Should I think about taking part in a clinical trial?
- What should I do to get ready for treatment?
- How much experience do you have treating this type of cancer?
- Should I get a second opinion³? How do I do that?
- What would the goal of the treatment be?
- How soon do I need to start treatment?
- How will treatment affect my daily activities? Can I still work fulltime?
- Will I lose my hair? If so, what can I do about it?
- What are the chances the cancer will come back (recur) after this treatment?

- What would we do if the treatment doesn't work or if the cancer comes back?
- What if I have transportation problems getting to and from treatment?

If you need surgery

- Is breast-conserving surgery (lumpectomy) an option for me? Why or why not?
- What are the pros and cons of breast-conserving surgery versus mastectomy?
- How many surgeries like mine have you done?
- Will you have to take out lymph nodes? If so, would you advise a sentinel lymph node biopsy? Why or why not?
- What side effects might lymph node removal cause?
- How long will I be in the hospital?
- Will I have stitches or staples at the surgery site? Will there be a drain (tube) coming out of the site?
- How do I care for the surgery site? Will I need someone to help me?
- What will the scar look like?
- Do I need to stop taking any medications or supplements before surgery?
- When should I call your office if I'm having side effects?

During treatment

Once treatment begins, you'll need to know what to expect and what to look for. Not all of these questions may apply to you, but asking the ones that do may be helpful.

- How will we know if the treatment is working?
- Is there anything I can do to help manage side effects?
- What symptoms or side effects should I tell you about right away?
- How can I reach you on nights, holidays, or weekends?
- Will I need to change what I eat during treatment?
- Are there any limits on what I can do?
- Can I exercise during treatment? If so, what kind of exercise should I do, and how often?
- Can you suggest a mental health professional I can see if I start to feel overwhelmed, depressed, or distressed?
- Will I need special tests, such as imaging scans or blood tests? How often?

After treatment

- What are the chances my cancer might come back? What will we do if that happens?
- What type of follow-up will I need after treatment?
- Will I need a special diet after treatment?
- Are there any limits on what I can do?
- Am I at risk for lymphedema?
- What can I do to reduce my risk for lymphedema?
- What should I do if I notice swelling in my arm?
- What other symptoms should I watch for? What kind of exercise should I do now?
- What type of follow-up will I need after treatment?
- How often will I need to have follow-up exams, blood tests, or imaging tests?
- How will we know if the cancer has come back? What should I watch for?

Hyperlinks

- 1. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html</u>
- 2. <u>www.cancer.org/cancer/managing-cancer/finding-care/the-doctor-patient-relationship.html</u>
- 3. www.cancer.org/cancer/managing-cancer/finding-care/seeking-a-second-opinion.html

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