

TREATMENT UPDATE:

Metastatic Triple-Negative Breast Cancer (TNBC)

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Treatment Update: Metastatic Triple-Negative Breast Cancer (TNBC)

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Each year in the United States, there are nearly 290,000 diagnoses of breast cancer. In recent years, the number of effective treatments for breast cancer has increased.

Breast cancer is not just one disease. There are several different subtypes, each with unique features. Doctors are able to tailor treatments according to the characteristics of these specific subtypes.

Anyone can be diagnosed with breast cancer, with men representing about 1% of all breast cancer cases. This booklet is for anyone facing a breast cancer diagnosis. Your health care team will tailor a treatment plan that best fits your situation.

Types of Breast Cancer

Hormones and other chemical messengers in the bloodstream can attach to specialized proteins (called receptors) and fuel the growth of cancer cells. These receptors may lie within or on the surface of cancer cells.



There are three main subtypes of breast cancer, based on the presence or absence of specific receptors:

- **Hormone receptor (HR) positive.** Cancers that have receptors for estrogen (ER-positive) and/or progesterone (PR-positive) are considered hormone-positive. Nearly two-thirds of ER-positive cancers are also PR-positive.
- **HER2-positive.** This type of breast cancer contains an overabundance of a protein called human epidermal growth factor receptor 2 (HER2). About half of HER2-positive cancers are also HR-positive.
- **Triple-negative (TNBC).** Breast cancer that does not have receptors for estrogen or progesterone and does not contain an overabundance of the HER2 protein.

The focus of this booklet is treatment approaches for TNBC that has spread beyond the breast and axillary lymph nodes. TNBC accounts for approximately 15 percent of breast cancer cases.

Diagnostic Tests

There are a number of tests that can help diagnose metastatic TNBC, including:

- **Bone scan.** Using a radioactive tracer, a bone scan is used to look for the spread of cancer to the bones.
- **Computerized tomography (CT) scan.** Using x-rays taken from different angles, CT scans produce a detailed, 3-dimensional image that shows tumors in areas outside of the breast, such as the bone, lungs and liver.
- **Magnetic Resonance Imaging (MRI).** This test uses magnetic waves to produce detailed images of the body, including the presence and size of tumors.

- **Positron emission tomography (PET) scan.** Using a small amount of a radioactive sugar substance, PET scans produce images that can detect the spread of cancer beyond the breast. PET scans are often used in combination with CT scans.
- **Serum chemistry blood tests.** These tests look for abnormal levels of proteins in the blood, which can be an indicator of metastatic cancer.
- **Tumor markers.** Tumor markers are proteins manufactured by tumors and shed into the blood. The presence or absence of tumor markers as measured by a blood test may help guide treatment options in certain patients.
- **X-ray.** Using a small amount of radiation, a chest x-ray can be used to look for cancer that has spread from the breast to the lungs.

A biopsy is often performed after a diagnosis of TNBC. In a biopsy, tissue is extracted through a special needle and analyzed under a microscope by a pathologist, a doctor who examines laboratory samples of body tissue for diagnostic purposes. In cases of metastatic TNBC, biopsy results can evaluate the features of the cancer and guide treatment approaches.



Treatment Options

Chemotherapy

Because TNBC does not have receptors for estrogen or progesterone and does not contain an overabundance of the HER2 protein, many drugs that work for hormone receptor-positive tumors are not an effective treatment option. However, TNBC often responds well to chemotherapy.

The most common chemotherapies used to treat TNBC include:

- **Anthracyclines**, such as doxorubicin (Adriamycin), pegylated liposomal doxorubicin (Doxil, Caelyx) and epirubicin (Ellence).
- **Antimetabolites**, such as capecitabine (Xeloda) and gemcitabine (Gemzar).
- **Antimicrotubule agents**, such as ixabepilone (Ixempra), eribulin (Halaven) and vinorelbine (Navelbine).
- **Antitumor antibiotics**, such as mitoxantrone (Novantrone).
- **Platinum agents**, such as cisplatin (Platinol) and carboplatin (Paraplatin).
- **Taxanes**, such as paclitaxel (Taxol), docetaxel (Taxotere) and albumin-bound paclitaxel (Abraxane).

Chemotherapy can be given as a single drug or as a combination of drugs. Multiple courses of treatment are often given, with breaks between each course. If one treatment approach does not work or stops working, a different chemotherapy (or combination of chemotherapies) is often used. The chemotherapies used for the treatment of metastatic TNBC are generally given intravenously.

Antibody-drug conjugate

In April 2021, the U.S. Food and Drug Administration (FDA) approved sacituzumab govitecan-hziy (Trodelyv) for the treatment of metastatic TNBC that has been treated with at least two prior therapies. Sacituzumab govitecan-hziy works by linking a chemotherapy with an antibody (an immune system protein) that seeks out cancer cells. It is given intravenously.

Immunotherapy

Our immune system works constantly to keep us healthy. It recognizes and fights against danger, such as infections, viruses and growing cancer cells. In general terms, immunotherapy uses our own immune system as a treatment against cancer.

Immunotherapy is a newer approach for the treatment of metastatic breast cancer. The immunotherapy pembrolizumab (Keytruda), in combination with chemotherapy, is approved by the FDA for the treatment of TNBC. Pembrolizumab targets PD-1, a protein that can prevent the body's immune system from attacking tumors.



The Importance of Clinical Trials

Clinical trials are the standard by which we measure the worth of new treatments and the quality of life of individuals as they receive those treatments. For this reason, doctors and researchers urge people with cancer to take part in clinical trials.

Your doctor can guide you in making a decision about whether a clinical trial is right for you. Here are a few things that you should know:

- Often, people who take part in clinical trials gain access to and benefit from new treatments.
- Before you participate in a clinical trial, you will be fully informed as to the risks and benefits of the trial, including any possible side effects.
- Most clinical trials are designed to test a new treatment against, or in combination with, a standard treatment to find out whether the new treatment has any added benefit.
- You can stop taking part in a clinical trial at any time for any reason.

Treatment Side Effects

All cancer treatments can cause side effects. It's important that you report any side effects you experience to your health care team so they can help you manage them. Report them right away—don't wait for your next appointment. Doing so will improve your quality of life and allow you to stick with your treatment plan. It's important to remember that not all patients experience all side effects, and patients may experience side effects not listed here.

There are certain side effects that may occur across different treatment approaches. Following are tips and guidance for managing these side effects.

Managing Digestive Tract Symptoms

Nausea and vomiting

- Avoid food with strong odors as well as overly sweet, greasy, fried or highly seasoned food.
- Eat meals that are chilled, which often makes food more easily tolerated.
- Nibble on dry crackers or toast. These bland foods are easy on the stomach.
- Having something in your stomach when you take medication may help ease nausea.

Diarrhea

- Drink plenty of water. Ask your doctor about using drinks such as Gatorade that provide electrolytes. Electrolytes are body salts that must stay in balance for cells to work properly.
- Over-the-counter medicines such as loperamide (Imodium A-D and others) and prescription drugs are available for diarrhea but should be used only if necessary. If the diarrhea is bad enough that you need medicine, contact a member of your health care team.
- Choose foods that contain soluble fiber, like beans, oat cereals and flaxseed, and high-pectin foods such as peaches, apples, oranges, bananas and apricots.
- Avoid foods high in refined sugar and those sweetened with sugar alcohols such as sorbitol and mannitol.

Loss of appetite

- Eating small meals throughout the day is an easy way to take in more protein and calories, which will help maintain your weight. Try to include protein in every meal.
- To keep from feeling full early, avoid liquids with meals or take only small sips (unless you need liquids to help swallow). Drink most of your liquids between meals.
- Keep high-calorie, high-protein snacks on hand such as hard-boiled eggs, peanut butter, cheese, ice cream, granola bars, liquid nutritional supplements, puddings, nuts, canned tuna or trail mix.
- If you are struggling to maintain your appetite, talk to your health care team about whether appetite-building medication could be right for you.

Managing Fatigue

Fatigue (extreme tiredness not helped by sleep) is one of the most common side effects of many cancer treatments. If you are taking a medication, your doctor may lower the dose of the drug, as long as it does not make the treatment less effective. If you are experiencing fatigue, talk to your doctor about whether taking a smaller dose is right for you.

There are a number of other tips for reducing fatigue:

- Take several short naps or breaks during the day.
- Take walks or do some light exercise, if possible.
- Try easier or shorter versions of the activities you enjoy.
- Ask your family or friends to help you with tasks you find difficult or tiring.

There are also prescription medications that may help, such as modafinil. Your health care team can provide guidance on whether medication is the right approach for your individual circumstances.

Managing Pain

There are a number of options for pain relief, including prescription and over-the-counter medications. It's important to talk to a member of your health care team before taking any over-the-counter medication to determine if it is safe and to make sure it will not interfere with your treatment. Many pain medications can lead to constipation, which may make your pain worse. Your doctor can prescribe medications that help to avoid constipation.

Physical therapy, acupuncture and massage may also be of help in managing your pain. Consult with a member of your health care team before beginning any of these activities.

Bone Loss

Chemotherapy can cause bone loss, which increases the risk of osteoporosis (a condition in which bones become weak and brittle). Talk with your health care team about how exercise and changes in your diet may help keep your bones healthy, and about the medications available for bone health:

- Bisphosphonates such as zoledronic acid (Zometa and others) slow the process by which bone wears away and breaks down. These medications belong to a class of drugs called osteoclast inhibitors.
- RANK ligand inhibitors block a factor in bone development known as RANK ligand, which stimulates cells that break bone down. By blocking RANK ligand, these drugs increase bone density and strength. Currently, the only drug approved in this class is denosumab (Xgeva, Prolia). Like bisphosphonates, RANK ligand inhibitors are a type of osteoclast inhibitor.

Hot Flashes

Breast cancer treatments can lead to menopausal symptoms, such as hot flashes and night sweats. If you are experiencing these side effects, speak with your health care team about ways to cope with them. There are several medications that potentially help decrease hot flashes. Talk to your doctor to determine if medication is an option for you.

The following tips may also help:

- Identify the triggers for your hot flashes. For many, hot flashes can be triggered by stress, a hot shower, caffeine or spicy foods.
- Change your lifestyle habits to cope with your specific triggers. That may mean regular exercise, using relaxation techniques and changing your diet.
- Dress in layers so that you can remove clothing if needed.

- Keep ice water handy to help you cool off.
- Avoid synthetic materials, especially at nighttime. Wear pajamas and use sheets made of cotton.
- Take a cool shower before going to bed.

Vaginal Dryness

Treatments for breast cancer can lead to vaginal dryness and a lowered sex drive. Use of a personal lubricant (such as Astroglide) and/or a moisturizer (such as Replens) can often help. If vaginal dryness persists, talk to your doctor about whether a prescription medicine is right for you. You may wish to ask for a referral to a health care professional who specializes in these issues.

Treatment-Specific Side Effects

Chemotherapy

The side effects specific to chemotherapy depend on the type and dose of drugs given and the length of time they are used. They can include the following:

- **Hair loss.** Depending on the treatment, hair loss may start anywhere from one to three weeks after the first chemotherapy session. If you choose to wear a wig, consider buying one before you lose much hair so you feel more prepared and you can match your own hair color. You can have your wig professionally fitted and styled by a full-service wig salon. Look for a salon in your community that specializes in hair loss resulting from chemotherapy. Hair usually starts to grow back after the end of treatment. It may have a different texture or color, but these changes are usually temporary. Specially-designed scalp-cooling caps worn during chemotherapy infusions can reduce hair loss from some chemotherapies for some patients.

- **Nerve damage.** Some people being treated with chemotherapy experience nerve damage with symptoms that may include difficulty picking up objects or buttoning clothing, problems maintaining balance, difficulty walking and hearing loss. Peripheral neuropathy is a form of nerve damage that may cause numbness or tingling in the hands and feet. Often, nerve damage due to cancer treatments is temporary. If you are coping with this side effect, take extra care when handling hot, sharp or dangerous objects. You should also use handrails on stairs and in the tub or shower.
- **Low white blood cell counts.** Chemotherapy may lead to low white blood cell counts, a condition called neutropenia. White blood cells play a key role in fighting infection. Your doctor can prescribe medication designed to help increase white blood cell counts. If you develop a fever (a sign of infection), let your health care team know immediately so that you can get proper treatment.
- **Mouth sores (mucositis)** are also a side effect of chemotherapy. Your doctor may recommend treatments such as:
 - ✓ **Coating agents.** These medications coat the entire lining of your mouth, forming a film to protect the sores and minimize pain.
 - ✓ **Topical painkillers.** These are medications that can be applied directly to your mouth sores.
 - ✓ **Over-the-counter treatments.** These include rinsing with baking soda or salt water or using “magic mouthwash,” a term given to a solution to treat mouth sores. Magic mouthwash usually contains at least three of these ingredients: an antibiotic, an antihistamine or local anesthetic, an antifungal, a corticosteroid and/or an antacid.

Chemotherapy can also cause changes in the way food and liquids taste, including an unpleasant metallic taste in the mouth. Many people find that switching to plastic utensils helps. It may also help to avoid eating or drinking anything that comes in a can and to use enamel-coated pots and pans for food preparation.

Immunotherapy

Immunotherapy travels through the bloodstream, helping to prompt what is called an “immune response.” Because immunotherapy can attack healthy cells as well as cancer cells, certain side effects may be experienced.

Common side effects of immunotherapy used in the treatment of TNBC include rash, diarrhea, fatigue, shortness of breath, thyroid dysfunction and joint pain.



Communicating With Your Health Care Team

As you manage your metastatic TNBC, it's important to remember that you are a consumer of health care. The best way to make decisions about health care is to educate yourself about your diagnosis and get to know the members of your health care team, including doctors, nurses, nurse practitioners, physician assistants, dietitians, social workers and patient navigators.

Here are some tips for improving communication with your health care team:

Start a health care journal. Having a health care journal or notebook (either on paper or in a digital format) will allow you to keep all of your health information in one place. You may want to write down the names and contact information of the members of your health care team, as well as any questions for your doctor.

Prepare a list of questions. Before your next medical appointment, write down your questions and concerns. Because your doctor may have limited time, ask your most important questions first and be as specific as possible.

Bring someone with you to your appointments or have them be present during telehealth sessions. Even if you have a journal and a prepared list of questions or concerns, it's always helpful to have support when you go to your appointments. The person you bring may also think of questions to ask your doctor or remember details about your symptoms or treatment that you may have forgotten.

Write down your doctor's answers. Taking notes will help you remember your doctor's responses, advice and instructions. You can also ask the person who accompanies you to take notes for you, either in your journal or on a tablet or smartphone.

Record your visit if your doctor allows it. Recording the conversation with your doctor gives you a chance to hear specific information again or share it with family members or friends.

Incorporate other health care professionals into your team.

Your medical oncologist is an essential member of your health care team, but there are other health care professionals who can help you manage your diagnosis and treatment:

- Your primary care physician should be kept updated about your cancer treatment and any test results.
- Your local pharmacist is a great source of knowledge about the medications you are taking. Have all of your prescriptions filled at the same pharmacy to avoid the possibility of harmful drug interactions.
- Make sure your oncologist knows of any other medical conditions you have or any pain you are experiencing so that they can consult with your primary care physician or specialist as needed.

Remember, there is no such thing as over-communication.

CancerCare's Free Support Services and Programs

It can be very difficult to receive a diagnosis of metastatic TNBC, and adjusting to the necessary changes in your life can be challenging.

CancerCare® can help. We are a national nonprofit organization providing free, professional services to anyone affected by cancer. Our licensed oncology social workers can provide support and education, help navigate the complicated health care system and provide information on support groups and other resources.

To learn more about how CancerCare helps, call us at 800-813-HOPE (4673) or visit www.cancercare.org.

You will likely also build your own personal support network, composed of family and friends. In doing so, it's best to take some time to think about the people in your life and how they are best suited to help. Match the task to their strengths—ask a family member who loves to shop to pick up something for you at the store; ask a friend who's a good listener to come over for a chat.



Frequently Asked Questions

Q: Are there any recent clinical trial results for the treatment of metastatic TNBC?

A: TNBC continues to be studied in clinical trials. Recent results include:

- **KEYNOTE-355.** The final analysis of the phase III KEYNOTE-355 trial showed a statistically significant improvement in overall survival when pembrolizumab was added to chemotherapy as a first-line treatment of metastatic TNBC that is strongly positive for the protein PD-L1. These findings provide support for the combination of pembrolizumab and chemotherapy as a standard of care for the treatment of PD-L1-positive TNBC.
- **TROPION-PanTumor01.** Updated data from the phase I TROPION-PanTumor01 trial showed the investigational drug datopotamab deruxtecan had encouraging durable tumor response and disease control in the treatment of metastatic triple-negative breast cancer that had progressed after standard therapy. Datopotamab deruxtecan is an antibody drug conjugate (ADC), a type of targeted therapy.
- **ASCENT.** In April 2021, sacituzumab govitecan-hziy (Trodelyv) was approved by the FDA for the treatment of metastatic triple-negative breast cancer that has been treated with at least two prior therapies. Additional data from the phase III ASCENT trial reinforce the benefits of sacituzumab govitecan-hziy when given in these circumstances.

Q: I have been diagnosed with TNBC and am being treated with chemotherapy. What can I do to preserve my fertility?

A: Chemotherapy may induce a temporary or permanent menopause among younger patients. For many of these individuals, preserving their fertility (the ability to have a child) plays a large part in their treatment decisions and should be discussed with their oncologist before starting chemotherapy.

There are steps that can be taken if you are concerned about your ability to have children after treatment:

- Discuss treatment plans with members of your health care team. The discussion should include the coverage provided by your health insurance plan.
- Consider consulting with a specialist in reproductive medicine, who can help weigh the benefits and risks of a specific treatment.
- Ask about newer options for preserving fertility, such as oocyte cryopreservation, also known as egg freezing. In this process, the patient's eggs are removed, frozen and stored for later use. Another option includes freezing fertilized eggs. You can discuss which option is best for you with your fertility specialist.



Q: What is a treatment summary and why is it important?

A: Keeping your own records up-to-date in the form of a treatment summary can be helpful, as it allows you and your family members to have instant access to the specifics of your TNBC diagnosis and treatment. A treatment summary should include:

- Your name and date of birth
- Date of diagnosis
- Prescribed therapy/therapies, including dates started and stopped and dosages when appropriate
- Dates and types of baseline and post-diagnosis testing and the results of these tests
- Other medications and supplements you are taking
- Names, affiliations and contact information of all members of your health care team

Ask the members of your health care team what they suggest be included. Take your personal record with you when you visit any doctor, not just your oncologist.



Resources

CancerCare®
800-813-HOPE (800-813-4673)
www.cancercares.org

American Cancer Society
800-227-2345
www.cancer.org

Cancer.Net
Patient information from
the American Society of
Clinical Oncology
888-651-3038
www.cancer.net

National Cancer Institute
800-422-6237
www.cancer.gov

Cancer Support Community
888-793-9355
www.cancersupportcommunity.org

**National Coalition for
Cancer Survivorship**
877-622-7937
www.canceradvocacy.org

Breastcancer.org
610-642-6550
www.breastcancer.org

Living Beyond Breast Cancer
855-807-6386
www.lbbsc.org

Susan G. Komen
877-465-6636
www.komen.org

**Triple Negative
Breast Cancer Foundation**
877-880-8622
www.tnbcfoundation.org

Medicine Assistance Tool
www.medicineassistancetool.org

CLINICAL TRIALS WEBSITES

ClinicalTrials.gov
www.clinicaltrials.gov

EmergingMed
www.emergingmed.com

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