Fifth Edition

ADVANCED BREAST CANCER
A TREATMENT GUIDE FOR PATIENTS AND THEIR FAMILIES

WHERE INFORMATION EQUALS HOPE

CONTENTS REVIEWED BY A DISTINGUISHED MEDICAL ADVISORY BOARD

FREE

PATIENT RESOURCE

PRP PATIENT RESOURCE PUBLISHING®
A CHANCE TO LIVE LONGER FOR CERTAIN PATIENTS WITH

Who is HALAVEN (eribulin mesylate) Injection for?
HALAVEN is a prescription medicine used to treat adults with breast cancer that has spread to other parts of the body, and who have already received other types of anticancer medicines after the cancer has spread.

What safety information do I need to know about HALAVEN?
HALAVEN can cause serious side effects, including

- **Low white blood cell count (neutropenia).** This can lead to serious infections that could lead to death. Your health care provider will check your blood cell counts. Call your health care provider right away if you develop fever (temperature above 100.5°F), chills, cough, or burning or pain when you urinate, as any of these can be symptoms of infection.

- **Numbness, tingling, or pain in your hands or feet (peripheral neuropathy).** Peripheral neuropathy is common with HALAVEN and sometimes can be severe. Tell your health care provider if you have new or worsening symptoms of peripheral neuropathy.

- Your health care provider may delay or decrease your dose or stop treatment with HALAVEN if you have side effects.

Before you receive HALAVEN, tell your health care provider about all of your medical conditions, including if you

- have liver or kidney problems
- have heart problems, including a problem called congenital long QT syndrome
- have low potassium or low magnesium in your blood
HALAVEN® is the only chemotherapy proven to help some women live longer when used alone after 2 prior chemotherapies for metastatic breast cancer (mBC)

Although some women lived longer and some women did not live as long, women with mBC who were treated with HALAVEN in a clinical trial lived an average of 13.2 months, compared with women treated with other chemotherapy or hormone therapy, who lived an average of 10.6 months.

Take time to learn about HALAVEN—talk to your doctor today

To learn more about HALAVEN and to hear from patients about their experiences, visit www.halaven.com

Before you receive HALAVEN, also tell your health care provider about all of your medical conditions, including if you

- are pregnant or plan to become pregnant. HALAVEN can harm your unborn baby. Tell your health care provider right away if you become pregnant or think you are pregnant during treatment with HALAVEN. Females who are able to become pregnant should use an effective form of birth control during treatment with HALAVEN and for at least 2 weeks after the final dose of HALAVEN and males should use an effective form of birth control when having sex with female partners who are able to become pregnant during treatment with HALAVEN and for 3½ months (14 weeks) after the final dose of HALAVEN.
- are breastfeeding or plan to breastfeed. It is not known if HALAVEN passes into your breast milk. Do not breastfeed during treatment with HALAVEN and for 2 weeks after the final dose of HALAVEN.

Tell your health care provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

What are the possible side effects of HALAVEN?

HALAVEN can cause changes in your heartbeat (called QT prolongation). This can cause irregular heartbeats. Your health care provider may do heart monitoring (electrocardiogram or ECG) or blood tests during your treatment with HALAVEN to check for heart problems.

The most common side effects of HALAVEN in adults with breast cancer include low white blood cell count (neutropenia), low red blood cell count (anemia), weakness or tiredness, hair loss (alopecia), nausea, and constipation.

Your health care provider will do blood tests before and during treatment while you are taking HALAVEN.

Please see the Patient Information for HALAVEN on the following page.
What is the most important information I should know about HALAVEN?

HALAVEN can cause serious side effects, including:

- Low white blood cell count (neutropenia). This can lead to serious infections that could lead to death. Your healthcare provider will check your blood cell counts before you receive each dose of HALAVEN and during treatment. Call your healthcare provider right away if you develop any of these symptoms of infection:
  - fever (temperature above 100.5°F)
  - chills
  - cough
  - burning or pain when you urinate

- Numbness, tingling, or pain in your hands or feet (peripheral neuropathy). Peripheral neuropathy is common with HALAVEN and sometimes can be severe. Tell your healthcare provider if you have new or worsening symptoms of peripheral neuropathy.

- Your healthcare provider may delay, decrease your dose, or stop treatment with HALAVEN if you have side effects.

See “What are possible side effects of HALAVEN?” for more information about side effects.

What is HALAVEN?

HALAVEN is a prescription medicine used to treat people with:

- Breast cancer
  - that has spread to other parts of the body, and
  - who have already received certain types of anticancer medicines after the cancer has spread

- Liposarcoma
  - that cannot be treated with surgery or has spread to other parts of the body, and
  - who have received treatment with a certain type of anticancer medicine

It is not known if HALAVEN is safe and effective in children under 18 years of age.

Before you receive HALAVEN, tell your healthcare provider about all of your medical conditions, including if you:

- have liver or kidney problems
- have heart problems, including a problem called congenital long QT syndrome
- have low potassium or low magnesium in your blood
- are pregnant or plan to become pregnant. HALAVEN can harm your unborn baby. Tell your healthcare provider right away if you become pregnant or think you are pregnant during treatment with HALAVEN
  - Females who are able to become pregnant should use an effective birth control during treatment with HALAVEN and for at least 2 weeks after the final dose of HALAVEN.
  - Males should use an effective form of birth control when having sex with female partners who are able to become pregnant during treatment with HALAVEN and for 3 1/2 months (14 weeks) after the final dose of HALAVEN.
- are breastfeeding or plan to breastfeed. It is not known if HALAVEN passes into your breast milk. Do not breastfeed during treatment with HALAVEN and for 2 weeks after the final dose of HALAVEN.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How will I receive HALAVEN?

- HALAVEN is given by intravenous (IV) injection in your vein.
- HALAVEN is given in “cycles” of treatment, with each cycle lasting 21 days.
- HALAVEN is usually given on day 1 and day 8 of a treatment cycle.

What are the possible side effects of HALAVEN?

HALAVEN may cause serious side effects, including:

- See “What is the most important information I should know about HALAVEN?”
- HALAVEN can cause changes in your heartbeat (called QT prolongation). This can cause irregular heartbeats. Your healthcare provider may do heart monitoring (electrocardiogram or ECG) or blood tests during your treatment with HALAVEN to check for heart problems.

The most common side effects of HALAVEN in people with breast cancer include:

- low white blood cell count (neutropenia)
- low red blood cell count (anemia)
- weakness or tiredness
- constipation

The most common side effects of HALAVEN in people with liposarcoma include:

- tiredness
- nausea
- hair loss (alopecia)
- constipation
- stomach pain
- fever

Your healthcare provider will do blood tests before and during treatment while you are taking HALAVEN. The most common changes to blood tests in people with liposarcoma include:

- low white blood cell count (neutropenia)
- decreased blood levels of potassium or calcium

Tell your healthcare provider about any side effect that bothers you or that does not go away.

These are not all the possible side effects of HALAVEN. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about HALAVEN

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. You can ask your pharmacist or healthcare provider for information about HALAVEN that is written for health professionals.

What are the ingredients in HALAVEN?

Active Ingredient: eribulin mesylate

Inactive Ingredients: ethanol, water

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Woodcliff Lake, NJ 07677

For more information, go to www.HALAVEN.com or call Eisai Inc. at 1-877-873-4724. If you would like a leaflet with larger printing, please contact Eisai Inc. at 1-877-873-4724.

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What is HALAVEN?

HALAVEN can cause serious side effects, including:

- weakness or tiredness
- low red blood cell count (anemia)
- low white blood cell count (neutropenia)
- nausea
- fever (temperature above 100.5°F)
- who have received treatment with a certain type of anticancer medicine

Peripheral neuropathy is common (peripheral neuropathy).

This can lead to blood tests in people with liposarcoma include:

- low white blood cell count (neutropenia)
- low red blood cell count (anemia)
- fever (temperature above 100.5°F)
- who have received treatment with a certain type of anticancer medicine

Tell your healthcare provider about any side effect that bothers you or

Consider a clinical trial. Medical research is advancing and new medications are being tested.

— Sandra Spivey

Conclusion
Finding out you have advanced breast cancer will change your life. Your diagnosis will lead you down a path filled with challenges you hadn’t planned on, but the promising news is that you are not alone. Surrounding yourself with a skilled medical team you trust and supportive family and friends will enable you to face this diagnosis head on.

Advanced breast cancer is also referred to as metastatic and Stage IV breast cancer. Although Stage III cancers are considered locally advanced and treated with curative intent, some of this information may be helpful. In most cases, it is diagnosed during a follow-up appointment after treatment for early-stage disease or during evaluation of symptoms, such as persistent cough, shortness of breath or bone pain. In some people, breast cancer is advanced at the time of initial diagnosis.

Where a cancer starts, or its primary site, often plays a role in where it will metastasize (spread). Most cancer cells that break free from the primary tumor are carried in the blood or lymph until they get trapped in nearby lymph nodes or organs. This is why breast cancer often spreads to lymph nodes in the underarm but rarely to lymph nodes in the groin. When breast cancer metastasizes farther, it typically lands in the liver, lungs, bones or brain.

Breast cancer that spreads to another part of the body is still considered breast cancer. For example, breast cancer that has metastasized to the lung is still breast cancer, not lung cancer, and will be treated with the breast cancer therapy you decide on with your medical team.

A cure is not yet available for advanced breast cancer. Because of this, the goal of treatment is to control the growth of the cancer while providing the highest quality of life possible. In this way, advanced breast cancer is like many other chronic health conditions. Your doctor will work closely with you to select the treatment that will be most effective at controlling the cancer and making you feel your best. Ongoing advances in research are resulting in treatments that let many people with advanced breast cancer live longer, with a good quality of life.

**Molecular testing**

Once advanced breast cancer is diagnosed, staging is next. Doctors also recommend molecular testing to see if specific protein receptors are present in or on the breast cancer cells. These protein receptors are estrogen and progesterone receptors (ER and PR) and human epidermal growth factor receptor-2 (HER2). If ER and/or PR receptors are present in your cancer cells, the hormones estrogen and progesterone are stimulating the growth of the cancer cells. If too much of the HER2 protein (or extra copies of the HER2 gene) are found on the surface of the breast cancer cells, the cells are growing and dividing in an uncontrolled way.

Your cancer will respond to types of treatment differently depending on the presence of ER, PR and HER2, so this information is crucial in helping your doctor recommend the type of treatment that is best for you (see Table 1).

Most people with advanced breast cancer have HER2-negative (HER2-) disease. If your HER2- breast cancer is hormone receptor-positive (ER+ and PR+), the most common treatment is hormone therapy, but chemotherapy and targeted therapy may also be options. If you have ER+, PR+ and HER2+ breast cancer, your doctor may recommend a combination of hormone therapy and an anti-HER2 drug.

Less often, an advanced breast cancer is negative for ER, PR and HER2. This type of cancer is called triple negative breast cancer. Triple negative breast cancer does not respond to the hormone or targeted therapies typically used to treat advanced breast cancer, so chemotherapy is the only treatment option. Often, triple negative breast cancer responds better to chemotherapy than other breast cancers do. Turn this guide over to read the Patient Resource Triple Negative Breast Cancer Guide.

Another less common type of breast cancer is inflammatory breast cancer (IBC). With this very aggressive type of breast cancer, cancer cells block the lymph vessels in the skin. Named because the breast often looks red or inflamed and feels warm, IBC may also cause the breast skin to be thick and look pitted, much like an orange peel looks.

Most IBCs are invasive ductal carcinomas, which means they developed from cells that line the milk ducts of the breast and then spread beyond the ducts. IBC progresses rapidly and is always staged as at least
Stage IIIB (locally advanced) when first diagnosed because the breast cancer cells have metastasized into the skin. If cancer has spread to the lymph nodes, surrounding tissues or other body parts, it is diagnosed as Stage IV. The advanced stage of IBC, along with its tendency to grow and spread quickly (sometimes in a matter of weeks or months), makes it more challenging to treat than most other types of breast cancer.

IBC accounts for about 1 to 5 percent of all breast cancers. Some experts believe it actually may be more common, but diagnosing it can be difficult because of its atypical symptoms. Breast lumps are not common, and it may not show up on a mammogram. Additionally, the swelling and tenderness often lead to a misdiagnosis of mastitis, an infection of the breast tissue that is accompanied by breast pain, swelling, warmth and redness.

More about inflammatory breast cancer:
- Compared with other types of breast cancer, IBC tends to be diagnosed at younger ages. It is also diagnosed at a younger age in African American women (average age, 52 years) than in Caucasian women (average age, 57 years).
- Obesity is a risk factor for IBC.
- Treatment usually includes a combination of chemotherapy drugs, surgery and radiation therapy. Inflammatory breast tumors are frequently hormone receptor-negative, which means that hormone therapy may not be effective.
- Like other types of breast cancer, IBC can occur in men, but it is usually diagnosed at an older age (after 67 years) than in women.

Because IBC is rare, patients are encouraged to take part in a clinical trial for access to the most leading-edge treatments. To learn more about clinical trials and where to find information about available trials, see page 9.

**Ongoing care**

Because advanced breast cancer is treated somewhat like a chronic condition, treatment is continual. This means that treatment is typically given until disease starts to progress or until you cannot tolerate treatment-related side effects. This also means that close, ongoing care is needed to keep track of how the cancer is responding to treatment. If the cancer stops responding or starts to progress, other treatment options are available. You will have routine visits with your doctor and/or medical team, which will likely include regular testing. You can learn more about these tests on page 12.

When you’re faced with an advanced breast cancer diagnosis, knowledge is empowering. This guide is filled with valuable resources that will help you better cope with your disease. You can learn more about the available treatment options, including clinical trials and side effects and how to manage them, along with helpful suggestions and support resources for you, your caregiver and your loved ones. Talk to your health care team for additional resources.

**ADDITIONAL RESOURCES**

- Ixempra Patient Support: www.ixempra.com, 855-991-7277
- Janssen Prescription Assistance: www.janssenprescriptionassistance.com
- Kadryca Access Solutions: www.kadryca.com/financial-assistance-programs, 888-249-4918
- Kisqali Care Patient Support Program: us.kisqali.com, 800-282-7630
- Lilly PatientOne: www.lillypatientone.com, 866-472-8663
- Novartis Oncology Universal Co-Pay Program: www.copay.novartisoncology.com, 877-571-7756
- Novartis Patient Assistance Now: www.patientassistanceon.com, 800-245-5558
- Pfizer RxPathways: www.pfizeroncologytogether.com/patient, 877-744-5675
- Pfizer Oncology Together: www.pfizeroncologytogether.com/patient, 877-744-5675
- Pfizer RxPathways: www.pfizeroncologytogether.com/patient, 877-744-5675
- Verzenio: www.verzenio.com

**ADVANCED BREAST CANCER IN MEN**

Breast cancer in men is rare and, as in women, occurs when malignant cells invade the breast tissue. Although breast cancer can develop in men at any age, the average age at diagnosis is between 65 and 70 years. Although a lump is easier to feel because men have less breast tissue than women, they may ignore breast changes or not report them to their doctor because they don’t realize they are at risk. As a result, breast cancer in men is often at a late stage when diagnosed. That delay in diagnosis can allow the cancer to spread to lymph nodes under the arm or around the collarbone, even before the original tumor in the breast tissue is large enough to be felt.

Most breast cancers in men are hormone receptor-positive, meaning that the growth of cancer cells is stimulated by estrogen and/or progesterone. Typical treatments for hormone receptor-positive cancers include the following:
- Surgery to remove the tumor
- Chemotherapy to kill the cancer cells
- Hormone therapy to stop cancer cell growth
- Radiation therapy to help reduce the risk of recurrence, relieve symptoms and avoid complications from areas of metastases

Because breast cancer in men is less common, fewer clinical trials have taken place than for female breast cancer. Most treatments for men are modeled on treatments for women because the disease tends to respond similarly in both men and women, but researchers are investigating ways to treat the disease in men. Talk with your doctor about each type of treatment, potential side effects and clinical trials so you can make an informed treatment decision.

When a man hears his diagnosis, his shock at learning he has cancer is often compounded by embarrassment at having what is traditionally known as a “woman’s disease.” It is crucial to remember that you’re not alone. Your feelings are valid. Discussing them and comparing notes with other men who have breast cancer can be immensely helpful. Talk openly with your medical team about support groups and other resources.

**MALE BREAST ANATOMY**

- Lymph nodes
- Fatty tissue
- Ducts
- Nipple
- Areola
- Rib
- Muscle
- Areola

*As a man who’s been in your shoes, I advise you to find a doctor with experience in treating male breast cancer. This rare disease is best dealt with head-on, aggressively, and in as good a spirit as you can muster.*

Oliver B., advanced breast cancer survivor
Staging is how physicians determine the extent of your cancer. The staging system used for breast cancer is the TNM system, developed by the American Joint Committee on Cancer (AJCC) (see Table 1). It’s based on the size and location of the tumor (T), whether cancer cells are found in nearby lymph nodes (N), and whether the cancer has metastasized, or spread, to other parts of the body (M). The results of the TNM analysis are then used to determine the overall stage of breast cancer for each individual (see Table 2).

The AJCC also recommends testing for the presence of estrogen and progesterone receptors (ER and PR) on the cancer cells and human epidermal growth factor receptor-2 (HER2) on the surface of breast cells. Your cancer will respond to types of treatment differently depending on the presence of ER, PR and HER2. Knowing if ER, PR and HER2 are present in your cancer cells, along with the stage of your cancer, will guide your doctor in recommending the best treatment for you.

A grade, which is based on the microscopic features of tumor cell growth rate and aggressiveness, is assigned by a pathologist. Knowing the grade helps determine how fast a cancer is likely to grow and how likely it is to spread.

### TABLE 1
**AJCC TNM SYSTEM FOR CLASSIFYING BREAST CANCER**

<table>
<thead>
<tr>
<th>Classification</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tumor (T)</strong></td>
<td></td>
</tr>
<tr>
<td>TX</td>
<td>Primary tumor cannot be assessed.</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor.</td>
</tr>
<tr>
<td>Tis (DCIS)</td>
<td>Ductal carcinoma in situ.</td>
</tr>
<tr>
<td>Tis (Paget)</td>
<td>Paget disease of the nipple NOT associated with invasive carcinoma and/or cancer in situ (DCIS) in the underlying breast parenchyma (tissue).</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor ≤ (not more than) 20 mm in greatest dimension.</td>
</tr>
<tr>
<td>T1a</td>
<td>Tumor ≤ (not more than) 1 mm in greatest dimension.</td>
</tr>
<tr>
<td>T1b</td>
<td>Tumor &gt; (more than) 5 mm but ≤ (not more than) 10 mm in greatest dimension.</td>
</tr>
<tr>
<td>T1c</td>
<td>Tumor &gt; (more than) 10 mm but ≤ (not more than) 20 mm in greatest dimension.</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor &gt; (more than) 20 mm but ≤ (not more than) 50 mm in greatest dimension.</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor &gt; (more than) 50 mm in greatest dimension.</td>
</tr>
<tr>
<td>T4</td>
<td>Tumor of any size with direct extension to the chest wall and/or to the skin (ulceration or macroscopic nodules).</td>
</tr>
<tr>
<td>T4a</td>
<td>Extension to the chest wall.</td>
</tr>
<tr>
<td>T4b</td>
<td>Ulceration and/or ipsilateral (on the same side) macroscopic satellite nodules and/or edema (including peau d’orange) of the skin that does not meet the criteria for inflammatory carcinoma.</td>
</tr>
<tr>
<td>T4c</td>
<td>Both T4a and T4b are present.</td>
</tr>
<tr>
<td>T4d</td>
<td>Inflammatory carcinoma.</td>
</tr>
<tr>
<td><strong>Node (N)</strong></td>
<td></td>
</tr>
<tr>
<td>pNX</td>
<td>Regional lymph nodes cannot be assessed.</td>
</tr>
<tr>
<td>pN0</td>
<td>No regional lymph node metastasis identified.</td>
</tr>
<tr>
<td>pN0(+/-)</td>
<td>Some regional lymph nodes contain tumor cells.</td>
</tr>
<tr>
<td>pN0(mol+)</td>
<td>Positive molecular findings by reverse transcriptase polymerase chain reaction (RT-PCR); no ITCS (isolated tumor cells) detected.</td>
</tr>
<tr>
<td>pN1</td>
<td>Micrometastases; or metastases in 1-3 axillary (armpit) lymph nodes; and/or clinically negative internal mammary nodes with micrometastases or macrometastases by sentinel lymph node biopsy.</td>
</tr>
<tr>
<td>pN1mi</td>
<td>Micrometastases (approximately 200 cells, larger than 0.2 mm, but none larger than 2.0 mm).</td>
</tr>
<tr>
<td>pN1a</td>
<td>Metastases in 1-3 axillary (armpit) lymph nodes, at least one metastasis larger than 2.0 mm.</td>
</tr>
<tr>
<td>pN1b</td>
<td>Metastases in ipsilateral (on the same side) internal mammary sentinel nodes, excluding ITCS (isolated tumor cells).</td>
</tr>
<tr>
<td>pN1c</td>
<td>Micrometastases; or metastases in 1-3 axillary (armpit) lymph nodes; and/or clinically negative axillary (armpit) lymph node metastases.</td>
</tr>
<tr>
<td>pN2</td>
<td>Metastases in 4-9 axillary (armpit) lymph nodes; or positive ipsilateral (on the same side) internal mammary lymph nodes by imaging in the absence of axillary (armpit) lymph node metastases.</td>
</tr>
<tr>
<td>pN2a</td>
<td>Metastases in 4-9 axillary (armpit) lymph nodes (at least one tumor deposit larger than 2.0 mm).</td>
</tr>
<tr>
<td>pN2b</td>
<td>Metastases in clinically detected internal mammary lymph nodes with or without microscopic confirmation; with pathologically negative axillary (armpit) lymph nodes.</td>
</tr>
<tr>
<td>pN3</td>
<td>Metastases in 10 or more axillary (armpit) lymph nodes; or in infracavicular (below the clavicle) (Level III) axillary (armpit) lymph nodes; or positive ipsilateral (on the same side) internal mammary lymph nodes by imaging in the presence of one or more positive Level I, II axillary (armpit) lymph nodes; or in more than three axillary (armpit) lymph nodes and micrometastases or macrometastases by sentinel lymph node biopsy clinically negative ipsilateral (on the same side) internal mammary lymph nodes; or in ipsilateral (on the same side) supraclavicular (above the clavicle) lymph nodes.</td>
</tr>
<tr>
<td>pN3a</td>
<td>Metastases in 10 or more axillary (armpit) lymph nodes (at least one tumor deposit larger than 2.0 mm); or metastases to the infracavicular (below the clavicle) (Level III) axillary (armpit) lymph nodes.</td>
</tr>
<tr>
<td>pN3b</td>
<td>Metastases in the presence of pN1a or pN1b detected by clinical and radiographic means.</td>
</tr>
<tr>
<td>pN3c</td>
<td>Metastases in ipsilateral supraclavicular (above the clavicle) lymph nodes.</td>
</tr>
</tbody>
</table>

**Note:** (a) and (b) should be added to the N category to denote confirmation of metastasis by sentinel node biopsy or FNA/core needle biopsy respectively, with or without axillary lymph node dissection.

<table>
<thead>
<tr>
<th><strong>Metastasis (M)</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td>No clinical or radiographic evidence of distant metastases.</td>
</tr>
<tr>
<td>cM0(+/-)</td>
<td>No clinical or radiographic evidence of distant metastases in the presence of tumor cells or deposits no larger than 0.2 mm detected microscopically or by molecular techniques in circulating blood, bone marrow, or other nonregional nodal tissue in a patient without symptoms or signs of metastases.</td>
</tr>
<tr>
<td>cM1</td>
<td>Distant metastases detected by clinical and radiographic means.</td>
</tr>
<tr>
<td>pM1</td>
<td>Any histologically proven metastases in distant organs; or if in nonregional nodes, metastases greater than 0.2 mm.</td>
</tr>
</tbody>
</table>

### TABLE 2
**STAGES OF ADVANCED BREAST CANCER**

<table>
<thead>
<tr>
<th>Stage</th>
<th>TNM classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIA</td>
<td>T0-T3, N0-N2, M0</td>
</tr>
<tr>
<td>IIB</td>
<td>T4, N0-N2, M0</td>
</tr>
<tr>
<td>IIC</td>
<td>Any T, N3, M0</td>
</tr>
<tr>
<td>IV</td>
<td>Any T, Any N, M1</td>
</tr>
</tbody>
</table>


### STAGES OF ADVANCED BREAST CANCER

<table>
<thead>
<tr>
<th>Stage</th>
<th>Tumor may be any size</th>
<th>Possible multiple lymph node metastases</th>
<th>Stage III C</th>
<th>The tumor may be any size but has not spread to distant parts of the body</th>
<th>Stage IV</th>
<th>Likely multiple lymph node metastases</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIIA</td>
<td>Tumor has spread to the chest wall or caused swelling or ulceration of the breast</td>
<td>Multiple lymph node metastases</td>
<td>Stage III C</td>
<td>Multiple lymph node metastases</td>
<td>Stage IV</td>
<td>Multiple lymph node metastases</td>
</tr>
</tbody>
</table>

Metastasis:
- Brain
- Lung
- Liver
- Bone

©PatientResource LLC
Several treatment options are available for advanced breast cancer. The strategies you and your doctor will consider depend on many factors:

- Whether advanced breast cancer is the initial diagnosis or is recurrent disease
- How many metastatic sites are there and where they are located
- How old you are, what your menopausal status is (if applicable) and how healthy you are overall
- How quickly or slowly the disease is progressing
- Whether you have had previous treatment and, if so, what the response was

A key factor in determining the best treatment for you is the results of testing for estrogen (ER), progesterone (PR) and human epidermal growth factor-2 (HER2) receptors in the tumor tissue. When ER and PR testing is positive, it means that these hormones are stimulating the growth of cancer cells. When HER2 testing is positive, that protein is helping cancer cells to grow. Testing for ER, PR and HER2 is recommended in all cases of breast cancer because the results are essential for selecting the most appropriate treatments.

Your treatment plan may include a combination of systemic therapies, such as hormone therapy, chemotherapy and targeted therapy. Radiation therapy or surgery may be recommended for specific situations, but these options are primarily to relieve symptoms, not to treat the disease. You may be a candidate for a clinical trial, which can give you access to the most innovative treatments, such as immunotherapy, that are still in development (see Clinical Trials, page 9).

Once you feel educated about your options, consider seeking a second opinion from another doctor who has experience treating advanced breast cancer. The best doctors may have different opinions about the best treatment plan, and hearing more than one expert opinion can help you make a more informed decision.

Types of treatment

Hormone therapy

Hormone therapy, also known as endocrine therapy, is the primary choice for tumors that are ER-positive or PR-positive. Hormone therapy shrinks tumors by either lowering the amount of estrogen in your body or blocking estrogen to slow or stop the growth of cancer cells.

Many types of hormone therapy drugs are available (see Table 1, page 8). Your doctor will work with you to determine which drug or combination of drugs may be your best option. Most people with advanced breast cancer continue taking hormone therapy for as long as the cancer is not growing and the drug is being well-tolerated. If the tumor grows during hormone therapy, other options may be available. Chemotherapy may be added either at the start of treatment or if disease progresses.

CHEMOTHERAPY OPTIONS

<table>
<thead>
<tr>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>capecitabine (Xeloda)</td>
</tr>
<tr>
<td>carboplatin (Paraplatin)</td>
</tr>
<tr>
<td>cisplatin</td>
</tr>
<tr>
<td>cyclophosphamide</td>
</tr>
<tr>
<td>docetaxel (Taxotere)</td>
</tr>
<tr>
<td>doxorubicin (Adriamycin)</td>
</tr>
<tr>
<td>epirubicin (Ellence)</td>
</tr>
<tr>
<td>eribulin (Halaven)</td>
</tr>
<tr>
<td>fluorouracil – also known as 5-FU</td>
</tr>
<tr>
<td>gemcitabine (Gemzar)</td>
</tr>
<tr>
<td>ixabepilone (Ixempra)</td>
</tr>
<tr>
<td>liposomal doxorubicin (Doxil)</td>
</tr>
<tr>
<td>paclitaxel (Taxol)</td>
</tr>
<tr>
<td>protein-bound paclitaxel (Abraxane)</td>
</tr>
<tr>
<td>vinorelbine (Navelbine)</td>
</tr>
</tbody>
</table>

Chemotherapy

Chemotherapy is a treatment option if your cancer cells are triple negative (negative for ER, PR and HER2) or if hormone therapy is unsuccessful. Chemotherapy is also usually given with anti-HER2 agents for HER2-positive breast cancer. Chemotherapy is typically given as a single drug or may be given as a combination of two drugs if the tumor is growing rapidly, if the tumor is large or there are many metastatic sites, or if you have many cancer-related symptoms. Your doctor will discuss the potential side effects of different chemotherapy drugs with you so you can weigh the advantages and disadvantages. Treatment is usually continued if the cancer does not grow, or for as long as the side effects are tolerable. However, if the tumor grows or side effects are too severe, another chemotherapy option may be considered.

Targeted therapy

The goal of targeted therapy is to slow the progression of disease by pinpointing and blocking the genes, proteins or other substances that help cancer cells develop and grow (see Table 2, page 8). Targeted therapy is typically used for HER2-positive breast cancer, and the anti-HER2 agent is usually combined with chemotherapy. Other targeted agents are sometimes used in combination with hormone therapy for ER-positive or PR-positive breast cancer. There are currently no approved targeted therapy drugs for triple negative breast cancer.

A class of drugs currently being explored is poly (ADP-ribose) polymerase (PARP) inhibitors. PARP is an enzyme that cancer cells use to repair DNA damage. PARP inhibitors are designed to disable those enzymes along with enzymes damaged by chemotherapy. PARP inhibitors also promote cancer cell death and make cancer cells more sensitive to other chemotherapy agents, which increases the effect of chemotherapy drugs. Treatment with PARP inhibitors is available only in clinical trials.

Radiation therapy

Radiation therapy is commonly used for brain metastases. When there is only one small tumor in the brain, treatment is focused on the area of the tumor. This treatment is known as stereotactic radiation, or Gamma Knife surgery. When there are multiple metastatic tumors, whole-brain radiation is given. Radiation therapy can also be used to treat other metastatic sites, such as the bone, if you have symptoms that don’t respond to medical therapy.

Resistance to treatment

Resistance occurs when breast cancers that were responding to treatment begin to grow again. Resistance may be caused by several factors. Sometimes it occurs after a particular type of drug therapy or long-term use of a drug, and sometimes a tumor may be naturally resistant to systemic therapy. The promising news is that if disease progresses during treatment, a different drug may be an option.

Overcoming drug resistance is a focus in breast cancer research. Scientists are studying different drug combinations, developing new drugs and evaluating the order in which drugs are given (sequential treatment) to see the effect on drug resistance.
TREATMENT STRATEGIES

Palliative treatment
Palliative care is treatment focused on symptoms and side effects, such as pain, fatigue, nausea and neuropathy. Ask your doctor about palliative care early on to help manage symptoms, as this has been shown not only improve the quality of life but also lengthen life. See page 10 to learn more about managing pain and treatment-related side effects.

Palliative care is often mistaken for hospice care. Palliative care accompanies your regular treatment and provides physical and emotional relief. The doctors, nurses, social workers, psychiatrists, dietitians and chaplains who make up your treatment team will work with you to improve your quality of life throughout every part of your treatment.

Immunotherapy
Checkpoint inhibitors are a type of immunotherapy that are being evaluated in clinical trials for advanced breast cancer. Immunotherapy uses the body's own immune system to fight cancer cells. Immunotherapy has been successful in treating other cancers, such as melanoma and lung cancer, which has encouraged researchers to evaluate its effectiveness in breast cancer. The immunotherapy drugs most often investigated are known as checkpoint inhibitors. Checkpoints are molecules on certain immune cells that, when activated, start an immune response. Cancer cells can sometimes find ways to use these checkpoints to avoid being attacked by the immune system. Checkpoint inhibitors target checkpoints to ensure that immune cells fight cancer cells. An important advantage of immunotherapy compared with traditional treatments is its "memory" — giving it the ability to remain effective for a long period of time after the end of treatment.

Choosing the right path for yourself
Undergoing continual treatment can take a toll on you. You may reach a point where you feel you need a break, or you might be enjoying a good quality of life and choose to forgo treatment for a while. Talk with your doctor to ensure you understand the pros and cons of interrupting your treatment plan, even for a short time.

You will receive input from your doctors, nurses, family members and friends, but remember — the decision is yours to make. Consider talking with your doctor about your feelings. If you make that difficult decision, you are strongly encouraged to consider hospice care, where your care is focused on managing symptoms and supporting you and your family instead of using cancer therapies. Hospice care can take place at home or in a hospice center and offers physical, emotional and spiritual support for you and your loved ones.

Table 1: COMMON HORMONE THERAPY OPTIONS

<table>
<thead>
<tr>
<th>Drug</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>fluoxymesterone</td>
<td>Androgen (male hormone)</td>
</tr>
<tr>
<td>goserelin (Zoladex), leuprolide (Lupron)</td>
<td>Luteinizing hormone receptor hormone (LHRH)</td>
</tr>
<tr>
<td>megestrol acetate (Megace)</td>
<td>Progestin</td>
</tr>
<tr>
<td>tamoxifen</td>
<td>Selective estrogen receptor modulator (SERM)</td>
</tr>
</tbody>
</table>

Table 2: COMMON TARGETED THERAPY OPTIONS

<table>
<thead>
<tr>
<th>Targeted therapy agent</th>
<th>Type of breast cancer</th>
<th>Approved/recommended treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>abemaciclib (Verzenio)</td>
<td>ER+/PR+, HER2+, metastatic</td>
<td>In combination with fulvestrant for patients with disease progression following hormone therapy and chemotherapy in the metastatic setting</td>
</tr>
<tr>
<td>ado-trastuzumab emtansine (Kadcyla T-DM1)</td>
<td>HER2+, metastatic</td>
<td>For individuals previously treated with trastuzumab and a taxane, separately or in combination</td>
</tr>
<tr>
<td>everolimus (Afinitor)</td>
<td>ER+/PR+, HER2+, metastatic</td>
<td>In combination with exemestane for postmenopausal women who have been treated with letrozole or anastrozole</td>
</tr>
<tr>
<td>lapatinib (Tykerb)</td>
<td>HER2+, metastatic</td>
<td>In combination with capcitabine (Xeloda) or trastuzumab (Herceptin), typically after treatment with trastuzumab-based therapy and ado-trastuzumab emtansine</td>
</tr>
<tr>
<td>palbociclib (Ibrance)</td>
<td>ER+, HER2+, metastatic</td>
<td>In combination with letrozole for postmenopausal women as a first hormone-based therapy</td>
</tr>
<tr>
<td>pertuzumab (Perjeta)</td>
<td>HER2+, metastatic, or as neoadjuvant therapy</td>
<td>In combination with trastuzumab and docetaxel in individuals who have not been treated with anti-HER2 therapy or chemotherapy</td>
</tr>
<tr>
<td>ribociclib (Kisqali)</td>
<td>ER+/PR+, HER2+, metastatic</td>
<td>In combination with an aromatase inhibitor as first-line endocrine-based therapy for post-menopausal women</td>
</tr>
<tr>
<td>trastuzumab (Herceptin)</td>
<td>HER2+, metastatic</td>
<td>In combination with paclitaxel as first-line treatment, with other chemotherapy drugs, or with lapatinib for later lines of therapy, as a single agent in patients who have received one or more chemotherapy regimens</td>
</tr>
</tbody>
</table>

If you reach a time when you choose to stop treatment altogether, talk with your doctor about your feelings. If you make that difficult decision, you are strongly encouraged to consider hospice care, where your care is focused on managing symptoms and supporting you and your family instead of using cancer therapies. Hospice care can take place at home or in a hospice center and offers physical, emotional and spiritual support for you and your loved ones.

Additional resources
- Advanced Breast Cancer Community: www.advancedbreastcancercommunity.org
- American Cancer Society: www.cancer.org
- Breastcancer.org: www.breastcancer.org
- Metastatic Breast Cancer Network: www.mbcn.org
- National Breast Cancer Foundation: www.nationalbreastcancer.org
- Susan G. Komen: www.komen.org

Factors that Affect Treatment and Prognosis

- Premenopausal
  - tamoxifen
  - anastrozole (Arimidex), exemestane (Aromasin), letrozole (Femara)
  - ethinyl estradiol
  - fluoxymesterone
  - fulvestrant (Faslodex)
  - megestrol acetate (Megace)
  - tamoxifen, toremifene (Fareston)

- Postmenopausal
  - anastrozole (Arimidex), exemestane (Aromasin), letrozole (Femara)
  - ethinyl estradiol
  - fluoxymesterone
  - fulvestrant (Faslodex)
  - megestrol acetate (Megace)
  - tamoxifen, toremifene (Fareston)
- Selective estrogen receptor modulator (SERM)
- Androgen (male hormone)
- Estrogen
- Androgen (male hormone)
- Selective estrogen receptor downregulator
- Progestin
- Selective estrogen receptor modulator (SERM)
- Aromatase inhibitor

Standard Treatments for Metastatic Breast Cancer
- Standard treatment for metastatic breast cancer
- Hormone therapy
- Immunotherapy
- Targeted therapy

Factors that Affect Treatment and Prognosis

- Premenopausal
  - tamoxifen
  - anastrozole (Arimidex), exemestane (Aromasin), letrozole (Femara)
  - ethinyl estradiol
  - fluoxymesterone
  - fulvestrant (Faslodex)
  - megestrol acetate (Megace)
  - tamoxifen, toremifene (Fareston)
- Selective estrogen receptor modulator (SERM)
- Aromatase inhibitor

- Postmenopausal
  - anastrozole (Arimidex), exemestane (Aromasin), letrozole (Femara)
  - ethinyl estradiol
  - fluoxymesterone
  - fulvestrant (Faslodex)
  - megestrol acetate (Megace)
  - tamoxifen, toremifene (Fareston)
- Selective estrogen receptor modulator (SERM)
- Androgen (male hormone)
- Estrogen
- Androgen (male hormone)
- Selective estrogen receptor downregulator
- Progestin
- Selective estrogen receptor modulator (SERM)
- Aromatase inhibitor
Clinical trials offer many potential benefits, such as the opportunity for individuals with cancer to access cutting-edge treatments that are not yet widely available. In fact, many of the advances in cancer treatment are helping to save lives today because of the research conducted through trials. Depending on your diagnosis and other factors, such as if your cancer is not responding to treatment as well as expected, a clinical trial may be a valuable option, so it’s important to understand what it is and what it may mean for you.

Clinical trials are research studies that do the following:
- Evaluate the safety and effectiveness of a medical strategy, treatment or device.
- Develop a “standard of care” by helping identify which treatments work best for certain illnesses or groups of people.
- Offer opportunities for people with cancer to help others by being involved in clinical research.

Clinical trials are sponsored (funded) by government agencies (such as the National Cancer Institute), independent groups of doctors and health care institutions, or the pharmaceutical or biotechnology industry. Once a treatment or device has been evaluated in clinical trials, the results are sent to the U.S. Food and Drug Administration (FDA). No treatment or device is made available for public use in the United States until the FDA reviews the results and grants its approval.

Types of clinical trials

There are three types of clinical trials: treatment trials; quality-of-life trials; and prevention, screening and diagnostic trials. The most common trials for individuals with advanced breast cancer are treatment and quality-of-life trials. In a treatment trial, researchers evaluate whether a new type of treatment (drug, surgery, radiation therapy) or a combination of treatments is better than the treatment options that are currently available. In a quality-of-life trial, researchers study to improve the quality of life, or the overall well-being of people during or after treatment.

What to expect

When you volunteer to participate in a clinical trial, you will receive specific instructions and an Informed Consent form. You are encouraged to ask questions about anything you don’t understand before signing and returning the form. This is the ideal time to talk with your medical team about the many falsehoods that persist about clinical trials. For example, many people fear that they will receive a placebo instead of treatment, but all participants are guaranteed to receive, at minimum, the current standard of care during the trial.

Trials are carefully planned and performed in a consistent manner so that all patients are treated exactly the same, from the dose and schedule of the medication to the frequency of follow-up appointments. Institutional review boards or ethics committees carefully set up safeguards to make sure that all participants in the clinical trial remain safe throughout the process. Whether you’re at a small hospital or a large facility, your medical team will follow all of the same protocols and safety measures for your treatment plan. In addition to continuing to see your regular oncologist, you will also have a dedicated trial team closely monitoring you throughout the clinical trial. Even after the treatment ends, you will continue to be in close contact with the trial’s medical team.

Almost every type of cancer treatment has side effects, and the treatments used in clinical trials are no different. If you consider volunteering for a clinical trial, talk with your medical team about what you can expect so you are not surprised by any effects.

Participation is always voluntary, even after the study begins. If your expectations aren’t met or if you experience too many side effects, you can leave the trial at any time and return to standard of care treatment.

Cost is a common consideration with clinical trials. Routine patient care costs typically include those related to doctor visits and hospital stays. Some testing procedures that are part of standard care may be covered by your insurance. Research costs, which are directly related to the clinical trial and include drugs and procedures, are typically covered by the trial sponsor. Before dismissing the idea of participating because of the cost, search for resources and explore your insurance plan benefits. You may find that you can participate without a great deal of additional expense.

Your doctor or member of your medical team can give you more information about clinical trials in your area, but they may not be aware of all the trials available in other locations. A wide variety of online tools, including the resources below, are available to help you search for trials that may apply to you.
Almost every cancer treatment can cause side effects because when cancer cells are destroyed, healthy cells are also destroyed. Not everyone has the same side effects, even if they have the same type of treatment for the same type of cancer. Many side effects can be managed by you and your medical team. Following are treatment types and some side effects that may occur specifically from them.

Chemotherapy

Chemotherapy acts to damage cells that divide quickly because cancer cells divide quickly. Unfortunately, it also affects normal cells that divide quickly, such as hair and nail cells and the cells lining the inside of the gastrointestinal tract. Side effects can include hair loss, nail changes, mouth sores, diarrhea, constipation, nausea and vomiting, changes in appetite and low blood cell counts.

Hormone therapy

Hormone therapy may cause fatigue, muscle and joint pains, vaginal dryness or discharge, hot flashes and mood swings. Blood clots are a less common but more serious side effect of some hormone therapy drugs. If a blood clot develops, it is usually in a leg, but a clot there can sometimes break off and travel to the lungs, where it can pose more harm. If pain, redness or swelling develops in your calf or if you have shortness of breath or chest pain, call your doctor right away. These symptoms could be signs of a clot.

Targeted therapy

Targeted therapies tend to damage only the cells they target, which may result in fewer side effects. Although most effects of targeted therapy are mild, some carry a risk of congestive heart failure, which usually goes away after the drug is no longer taken.

Radiation therapy

Radiation usually damages the areas that are being targeted. Side effects may include fatigue, loss of appetite, skin changes and low blood cell counts. Whole-brain radiation therapy is associated with potential side effects such as memory loss, extreme fatigue, temporary baldness, skin rash and hearing loss.

Steroid therapy

Corticosteroids, drugs given to help decrease swelling around the brain when there is brain metastasis, may be associated with a range of side effects. Some common side effects include weight gain, acid indigestion, muscle weakness, difficulty sleeping, mood swings, elevated blood sugar, acne and swelling of the face.

Medical supportive therapies

Bone-modifying drugs, which help prevent bone problems, are associated with fatigue and nausea. These drugs may also cause damage to the jawbone. Take special care of your mouth, gums and teeth; visit your dentist regularly; and avoid invasive dental work.

Be sure to tell your medical team when symptoms persist despite treatment or if you experience any new ones. They will work with you to manage your symptoms, provide you with greater control over your daily activities and improve your quality of life.

DEFINING CANCER-RELATED PAIN

Cancer-related pain is directly tied to the cancer itself and the location of the tumor(s). As a tumor grows, it can press on internal organs, tissues and joints, creating pressure that ultimately leads to pain in that specific area. Pain can also be caused by cancer that has spread to bone. This pain is typically felt in the back, pelvis and hips, as these bones are the most common sites of cancer metastasis (spread). Cancer-related pain may be felt in parts of the body other than where the primary tumor is located, especially in advanced disease. Cancer treatment may also cause pain. After surgery, pain is usually felt in the area of the surgery and will gradually go away as your body heals and recovers. The pain or discomfort caused by chemotherapy and radiation therapy can be mild to severe, but often (although not always) ends when treatment does. Sometimes, a hormone imbalance or treatment-related nerve damage may contribute to chronic pain.

TYPES OF PAIN

- **Acute pain** is pain that occurs suddenly; it is sometimes related to a diagnostic procedure or treatment. This type of pain is time-limited; in other words, the pain usually resolves once the body heals and recovers.
- **Chronic pain**, also called persistent pain, lasts for at least one month – usually longer – after treatment. This type of pain may be related to the direct effects of a tumor or cancer treatment but, in a small number of people, pain may be unrelated to either the cancer or the treatment.
- **Breakthrough pain** includes severe flares of pain that “break through” during treatment with pain medication. It can range from mild to severe and can last minutes to hours.

DESCRIPTIONS OF PAIN

Your doctor will ask you to describe your pain. Think about your pain and describe it carefully, as your doctor will be better able to determine the cause of your pain. For example, if pain feels like burning or “shock-like,” it is most likely related to damaged nerves. Your doctor will also ask about the severity of your pain. A scale of 0 to 10 (with 10 being the worst) is the most common way to rate how bad pain is. Also give your doctor details about your pain. What makes it worse? Does anything make it better? How does it affect your daily life?

CAUSES OF CANCER-RELATED PAIN

Following are common side effects of cancer and cancer treatments that can cause pain.

- **Loss of motion** may occur after surgery. For example, many people have pain related to loss of motion in the arm after a mastectomy.
- **Lymphedema** occurs when excess fluid builds up and causes abnormal swelling, typically in an arm or a leg. Swelling ranges from mild to extreme and is most likely to occur after surgery involving removal of lymph nodes from the underarm, groin, pelvis or neck. Typically, the more lymph nodes removed, the greater the risk for lymphedema.
- **Peripheral neuropathy** is a condition caused by damage to the peripheral nerves, the nerves outside the brain and spinal cord. Some chemotherapy drugs cause peripheral neuropathy, which is experienced as numbness and tingling in the hands and feet, a decreased sensation of hot and cold, muscle weakness, cramping and balance problems.
- **Osteoporosis** occurs when healthy bone isn’t rebuilt at the same rate as it is being destroyed by cancer cells or certain treatments. As a result, bone becomes weak, brittle and painful. This condition can happen naturally with age but is intensified by cancer.
- **Bone metastasis** is the spread of cancer into bones. Pain is caused by damage to bone cells as cancer cells invade.

TALKING ABOUT PAIN

Regardless of the cause or type of cancer-related pain, options for managing it are available so that you can have less pain and a better quality of life. Be sure to talk to your doctor about your options.
COMMON SIDE EFFECTS

Alopecia (hair loss) is often caused by chemotherapy and radiation therapy. Hair loss associated with chemotherapy can occur all over the body, affecting not only the head but also the eyebrows, face, chest, pubic area, etc. Hair loss associated with radiation therapy occurs only in the area receiving radiation.

MANAGEMENT STRATEGIES
- Use a soft-bristled hairbrush or wide-toothed comb. • Ask your doctor about a cooling cap. • Sleep on a satin or silk pillowcase. • Avoid using hair dye and heating devices (dryers, curling irons, etc.). • Ask your doctor for a prescription for a wig which may make it eligible for insurance coverage. • Use a gentle, pH-balanced shampoo.

Cognitive dysfunction (“Chemo brain”) is the feeling of not being able to think clearly or having trouble remembering details, but it doesn’t just happen with chemotherapy. It can occur in people receiving many types of treatments during or after treatment.

MANAGEMENT STRATEGIES
- Use a daily planner or calendar to keep track of “to-do” lists and events. • Solve crossword puzzles or number games to strengthen your mental ability. • Focus on one thing at a time. It’s okay not to multitask. • Organize your home and work spaces, and keep important items, such as keys, in a specific place.

Diarrhea can be caused by many types of treatment, and it can feel like a life-interrupting event. Eliminating it or learning how to manage it can greatly improve your quality of life. Left untreated, it can lead to serious problems, such as dehydration, loss of important nutrients, weight loss and fatigue.

MANAGEMENT STRATEGIES
- Drink plenty of fluids (water and other clear liquids, such as broth). • Eat several small meals throughout the day rather than three big meals. • Ask your doctor about anti-diarrhea medications. • Avoid alcohol, caffeine and fatty foods. • Eat bland foods. If you experience any of the following serious effects, contact your doctor immediately:
  - Six or more loose bowel movements per day for more than two days in a row
  - Blood in the stool, around the anal area, on the toilet paper or in the toilet bowel
  - Inability to urinate for at least 12 hours
  - Fever
  - Loss of five pounds or more after the diarrhea starts
  - Swollen or painful abdomen
  - Dizziness or light headedness upon standing up

Fatigue related to cancer and its treatments is different from the fatigue that healthy people feel. It usually lasts longer, is more severe and is unrelied by sleep.

MANAGEMENT STRATEGIES
- Take frequent naps that are not more than 45 minutes each. Get eight hours of sleep each night. • Do some form of regular physical activity, such as walking, yoga or bike riding. • Set a routine for sleeping and waking. • Prioritize. Rest up for what you really want to do.

Lymphedema is an excess of fluid in body tissues that causes abnormal swelling of a limb. It is most likely to occur in people who have surgery that involves removal of lymph nodes from the underarm, groin, pelvis or neck. The more lymph nodes removed, the greater the risk for lymphedema.

MANAGEMENT STRATEGIES
- Use a compression garment or tight bandages to apply pressure to the area. • Elevate the swollen limb to encourage drainage of the lymphatic system. • Talk to your doctor about manual lymphatic drainage and complete decongestive therapy.

Nausea and vomiting can cause severe dehydration and interrupt your treatment plan. Nausea is feeling sick to your stomach and may be accompanied by vomiting (throwing up). Severe cases of vomiting can lead to dehydration. You can also develop environmental nausea, which means that being in a specific physical environment, such as the chemotherapy infusion room, can trigger these side effects. Certain smells, such as the smell of rubbing alcohol used to clean your skin before an injection, can also bring on nausea and vomiting. Talk to your doctor about lowering your medication doses or adding antiemetics (anti-nausea drugs).

MANAGEMENT STRATEGIES
- Eat five to six small meals a day instead of three large meals, and eat a light meal a few hours before certain treatments. • Drink plenty of fluids throughout the day. • Avoid foods or smells that trigger nausea. • Sip ginger ale or chamomile tea, or suck on peppermint candies. • Avoid alcohol, spicy foods and caffeine.

If you experience any of the following serious effects, contact your doctor immediately:
  - More than three episodes of vomiting per hour for at least three hours
  - Blood in vomit
  - Vomit resembling coffee grounds
  - Inability to drink more than eight cups of fluid or ice chips in 24 hours or eat solid food for more than two days
  - Weakness or dizziness
  - Cannot keep your medications down

Neuropathy is pain or discomfort caused by damage to the peripheral nervous system, which includes the nerves that control movement and feeling in the arms and legs. Symptoms are numbness, pain, burning, tingling or loss of feeling in the hands or feet. For patients who are already diabetic, this side effect can become worse.

MANAGEMENT STRATEGIES
- Avoid tight clothes. • Keep your hands and feet warm. • Avoid standing or walking for long amounts of time. • Wear comfortable shoes. • Talk with your oncologist about prescription medicines designed specifically to relieve neuropathic pain.

Neutropenia (low white blood cell count) is a low number of neutrophils, a type of white blood cell. Neutrophils play an important role in preventing infection throughout the body, so having an abnormally low number of neutrophils increases the risk of infection. Neutropenia also makes it more difficult for an infection to resolve if bacteria do enter the body. The lower the neutrophil count, the greater the risk for infection.

MANAGEMENT STRATEGIES
- Talk to your doctor about drugs that may help you produce more white blood cells. • Wash your hands often, and use hand sanitizer regularly. • Wear gloves when doing chores. • Avoid sick people and crowded places.

If you experience any of the following serious effects, contact your doctor immediately:
  - Fever (oral temperature over 100.5°F), OR chills OR sweating
  - Flu-like symptoms (body aches, chills, general fatigue) with or without fever
  - Coughing, shortness of breath or painful breathing
  - Abdominal pain
  - Sore throat or mouth sores
  - Redness, pain or swelling on skin
  - Pus or drainage from any open cut or sore
  - Pain or burning with urination
  - Pain or sores around the anus
  - Vaginal discharge/itching
With advanced breast cancer, keeping track of how the disease responds to treatment is an important part of the overall care plan. Routine testing will be done to see if your treatment is slowing or stopping the growth of your cancer. If it’s not, you and your medical team will discuss alternative treatment options.

Pay attention to any new or changing symptoms you have and tell your doctor or medical team about them during your routine visits. At these visits, your doctor will perform a physical examination to see if there are any clinical signs of response. For example, a lymph node that has gotten smaller may mean the cancer is responding to treatment.

In addition, several different tests can be done to determine how well treatment is working. No single test provides the complete picture of how your cancer is responding to treatment. Your medical team will work with you to determine the kind of testing that is best for you and how often it should be done. The tests to monitor your cancer include imaging studies and tumor marker testing. To have a baseline for comparison with later studies, your doctor will perform one or more of these studies before treatment begins.

**Imaging studies**

Imaging studies are typically done about eight to 12 weeks after treatment starts. These studies enable your doctor to measure the size of a tumor or metastatic site. A tumor or metastasis that is smaller than it was before treatment is one sign that your cancer is responding to treatment. Imaging studies include bone scan, X-rays, computed tomography (CT), magnetic resonance imaging (MRI) and positron-emission tomography (PET) (see Table 1).

**Tumor markers**

Testing on a sample of your blood (taken from a vein in your arm) for tumor markers can help your doctor determine how your tumor is responding to treatment. Tumor markers are specific proteins, called cancer antigens, that cancer cells give off into the bloodstream.

The amount of cancer antigens in a blood sample may provide information about how many cancer cells are in your body. Three cancer antigens are associated with advanced breast cancer: cancer antigen (CA) 15-3, CA 27.29 and carcinoembryonic antigen (CEA). Decreasing or increasing levels of these cancer antigens over time may reflect tumor shrinkage or growth, respectively. Tumor marker testing is usually done before treatment starts and periodically thereafter.

Another tumor marker is circulating tumor cells (CTCs). CTCs are cells that break away from a tumor and enter the bloodstream. A special test can measure the number of CTCs in a blood sample. Studies have shown that CTC testing can help determine the prognosis (predicted outcome) as well as monitor the response to treatment. CTC testing is usually done about three to four months after treatment starts.

Tumor marker testing alone cannot provide complete information about how a tumor is responding to treatment; however, the combination of tumor marker testing and imaging studies provides a clearer picture of how well treatment is working.

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**Additional resources**

- American Society of Clinical Oncology: www.cancer.net
- Biomarkers to Guide Treatment for Metastatic Breast Cancer
- Breastcancer.org: www.breastcancer.org
- Breast Cancer Tests: Screening, Diagnosis and Monitoring
- Blood Marker Tests
- Susan G. Komen: www.komen.org
- Treatments for Metastatic Breast Cancer

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**Table 1: Imaging Studies to Monitor Cancer**

<table>
<thead>
<tr>
<th>Test</th>
<th>Why it’s done</th>
<th>How it’s done</th>
<th>How it feels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone scan</td>
<td>Determine the presence or extent of metastasis to the bones</td>
<td>A small amount of a radioactive substance is injected into a vein in your arm. You then lie on a table, and a special camera shows where radioactive material has collected, which indicates cancer.</td>
<td>Painless</td>
</tr>
<tr>
<td>X-ray</td>
<td>Check or monitor metastatic lesions in various organs</td>
<td>You lie on a table while the X-ray machine is positioned over a specific part of your body.</td>
<td>Painless</td>
</tr>
<tr>
<td>CT</td>
<td>Monitor metastatic lesions in other organs such as lungs, bones or liver</td>
<td>You lie on a table that moves slowly through the CT scanner. Sometimes, a dye (called a contrast) is injected into a vein in your arm before the scan to enhance the quality of the images.</td>
<td>Painless</td>
</tr>
<tr>
<td>MRI</td>
<td>Valuable for viewing the brain, spine and spinal cord</td>
<td>You lie on a table within a long, narrow tube while radio waves and strong magnets linked to a computer produce images.</td>
<td>Painless, but may cause anxiety if you have claustrophobia (fear of closed-in space). Your doctor can prescribe medication to help you relax.</td>
</tr>
<tr>
<td>PET</td>
<td>May be beneficial if the results of other imaging studies are inconclusive</td>
<td>A small amount of radioactive material (tracer) is injected into a vein. You lie on a table and a special camera shows where the tracer collects, which indicates the cancer has spread.</td>
<td>May feel a sting as the tracer is injected, but otherwise painless.</td>
</tr>
</tbody>
</table>

**Managing the risks of a second cancer**

- It is important to be aware that a second cancer, one that is new or unrelated to your advanced breast cancer diagnosis, could develop. People with breast cancer are at risk of developing many types of other cancers, including ovarian, uterine, cervical, colon and skin cancers. In addition to asking your doctor about what to watch for, there are a few things you can do to minimize your risk:
  - Make and keep appointments for preventive screenings.
  - Do monthly skin self-exams, and let your doctor know about new moles or other problems.
  - Follow a healthy diet.
  - Achieve and maintain a healthy weight.
  - Exercise regularly.
  - Avoid tobacco.
  - Limit alcohol intake.
  - Communicate openly and honestly with your doctor.
After thinking she may have beaten Stage IIA triple negative breast cancer, Sandra Spivey didn’t expect to be diagnosed with Stage IV breast cancer. Despite the fact that the cancer has spread to her bones, she continues to try new and different treatments, including a clinical trial. As a 20-year survivor, she shares her experiences with others diagnosed with breast cancer. She has become a breast cancer advocate and serves on scientific review panels to provide a patient’s perspective to aid in research.

NEVER GIVE UP

In 1995, an inverted nipple led to my Stage IIA triple negative breast cancer diagnosis. My mother had been diagnosed with breast cancer 15 years earlier and she had come through fine, so I expected the same result. I had surgery, radiation therapy and reconstruction, and I was fine. Three years later, I was sitting at work when I used my left leg to push off toward a cabinet, and I heard a popping sound. I thought I may have dislocated my leg, but it never improved and hurt all the time. My oncologist did new scans and found that the breast cancer had returned and was in my hip. I was diagnosed with Stage IV breast cancer.

I participated in a clinical trial that was testing stem cell transplantation as an option for Stage IV breast cancer. I spent three weeks in the hospital to collect my stem cells, take high-dose chemotherapy and receive my stem cells back. It was a difficult procedure, and I took three to four months to recover. The trial was published and showed that stem cell transplantation was not better than chemotherapy and, therefore, was not considered to be a standard treatment for metastatic breast cancer.

My next treatment included chemotherapy and, in between chemo regimens, I took all of the available hormone treatments twice. The doctors would change my treatments because after about three to four years, the cancer cells would change and forget what they were resistant to. Cancer is smart and the treatments have to outsmart it. Cancer is not one type of cell, it’s multiple cells. I think of a tumor as a bowl of fruit salad. You take one treatment that gets rid of all of the grapes in the salad. Then you try another treatment that targets the melons. No one treatment kills the whole thing. It’s a process.

Overall, I’ve had more than 200 bags of chemotherapy in my body since 1998. When I was first diagnosed, I cried in my bedroom or in the shower where my 13-year-old daughter couldn’t see me. The shower is one of the best places to cry. I tell others that it’s OK to cry. It releases tension. You’ve got to take care of yourself first.

Throughout all of my treatments, I took “mini chemotherapy vacations” where my doctor allowed me to temporarily stop treatment so that I could travel for my job and for pleasure. I called these my cancer-free days, and I would pretend that I didn’t have cancer. I think taking breaks – both mentally and physically – from the treatments to do the things I wanted helped me to keep going long term with my treatments.

Later, I had a flare-up in my sternum, but it felt like I was having a heart attack. I went on another chemotherapy regimen to knock it back. When I had too much bone pain, the doctor suggested radiation therapy to ease my pain. After three treatments, I felt dramatically better. But since the radiation weakened my bones, I am not able to do that treatment again.

While going through treatment, I became very interested in the science of breast cancer because I didn’t want other women to have to go through what I did. I became involved with my local Y-Me chapter to help other women diagnosed with breast cancer. I also began attending National Breast Cancer Coalition conferences and graduated from Project LEAD, which trains advocates to participate in peer review panels and review grant applications for research funding side-by-side with scientists. I became a helpline match counselor for Living Beyond Breast Cancer, After Breast Cancer Diagnosis and SHARE.

The number one thing I tell other Stage IV breast cancer patients is to not go out and run up their credit cards. You may live and then you’ll be stuck having to pay all of the money back. That usually gets a hearty laugh! I also encourage people not to be afraid to seek help if they develop depression. In January 2017, I was feeling even worse after my chemo treatments. I felt there was no point in going on, so I sought help. Depression is nothing to be ashamed of. Get help. Don’t let it take you over.

Some people are dealing with a Stage IV diagnosis as if it were a chronic disease, even though there is no cure. Don’t let a Stage IV diagnosis deter you from seeking treatment. I believe there will be new treatments available when I need them. Consider a clinical trial. Medical research is advancing, and new medications are being tested. So, don’t give up. You will never “lose your battle” to this disease. Cancer is the loser, not you.
The role of a caregiver

Caring for a loved one with advanced breast cancer presents different challenges from caring for someone with a curable disease. Advanced breast cancer becomes a permanent part of a person’s life, and your commitment, support and kindness can make this lifelong burden easier to bear.

■ Attend medical visits. It may be difficult to understand or remember all the information from the doctor. Two heads are better than one. Bring a list of questions to each medical visit, take notes and offer reminders later for follow-up items.

■ Educate yourself. Learn everything you can about advanced breast cancer. When you attend medical visits with your loved one, don’t be afraid to show you’ve done your research by asking questions. Make sure you understand the current status of the cancer and the treatment plan. The more informed you are, the better advocate you will be.

■ Get on the same page. People with breast cancer often refer to themselves as “survivors,” but people with advanced disease tend to feel very strongly about how they identify themselves, opting for alternatives such as “lifers,” “thrivers” or “metsters.” Talk with your loved one about which term you should use.

■ Be a traffic cop. Many people may want to visit. When you’re both up for it, act as the good host. But don’t be afraid to graciously turn away visitors when one or both of you needs to rest or just enjoy quiet time.

■ Be her biggest supporter. Your loved one might prefer a hug, or she might be comforted seeing you take the lead with the kids. You are in this together, so make sure you’re helping her in the most constructive way possible.

■ Open up. Not a fan of talking about your relationship? Since your partner’s diagnosis, communication is much more than just talking about your relationship. It includes talking about her feelings, your feelings and anything else that is on your minds — cancer-related or not. Knowing you’re not bottling up your feelings will be a stress reliever for her, too.

■ Choose to be positive. You will definitely have ups and downs during the course of your loved one’s disease and, at times, you may think it’s too overwhelming. Although you can’t always avoid setbacks, you can choose to adopt a positive and realistic attitude. Your genuine optimism may show your loved one a different, stronger side of you.

■ Vent your frustrations with a friend. Men often feel they need to “fix” everything, which means that your loved one’s advanced breast cancer diagnosis will really challenge you. You may feel angry, cheated and scared that you can’t fix this disease. You’re not the only one! Instead of letting those emotions get the best of you, let them out. Call a friend you’re comfortable with and get it out of your system. Or, ask a member of your loved one’s health care team for the name of a therapist or support group.

■ Take the sexuality out of the diagnosis. Your partner may be overwhelmed by fear that her body will look and react differently after treatment, but she may fear your reaction to these changes even more. Listen to her concerns. Assure her that her breasts, like her lungs or bones, are simply body parts affected by this disease. If this becomes an area of ongoing concern for either of you, don’t hesitate to ask your treatment team for guidance.

■ Be her biggest supporter. Your loved one will feel a range of emotions, but, no matter what, try to maintain a “glass half full” outlook. She’ll learn to count on you for your positivity and upbeat attitude, and that could be contagious.

STRATEGIES FOR THE MALE CAREGIVER

Special advice for men caring for their female partners

If you are a man caring for your partner with advanced breast cancer, you face a unique situation. To provide the best care you can, you may need to step outside some of the stereotypes that have defined your relationship up to this point.

■ Ask her how you can best help. Your loved one might prefer a hug, or she might be comforted seeing you take the lead with the kids. You are in this together, so make sure you’re helping her in the most constructive way possible.

■ Make lists. Keep a list of questions about side effects, treatments, nutrition, exercise, etc., for the treatment team.

■ Be a thoughtful listener. Sometimes your loved one will want to talk about cancer. Don’t dismiss his or her feelings saying such things as “Don’t worry about it,” or “It’s going to be fine.” Just listening is often a source of comfort.

■ Suggest support groups. Offer your loved one other outlets for support. No matter how close you are to your loved one, you are not experiencing the same things. Connecting with others who are dealing with the same fears, feelings and experiences can be a valuable experience for your loved one.

■ Take care of yourself. Caregiving is a mentally and physically exhausting responsibility, and you won’t be any good to your loved one if you aren’t good to yourself. Eat right, exercise and get enough sleep. Don’t ignore your favorite hobby, and don’t feel guilty when you enjoy yourself. Everyone deserves a diversion.

ADDITIONAL RESOURCES

- American Cancer Society: www.cancer.org
- American Society of Clinical Oncology: www.cancer.net
- CancerCare: www.cancercare.org
- Caregiver Action Network: www.caregiveraction.org
- Family Caregiver Alliance: www.caregiver.org
- PearPoint Cancer Support: my.pearpoint.org