PATIENT RESOURCE

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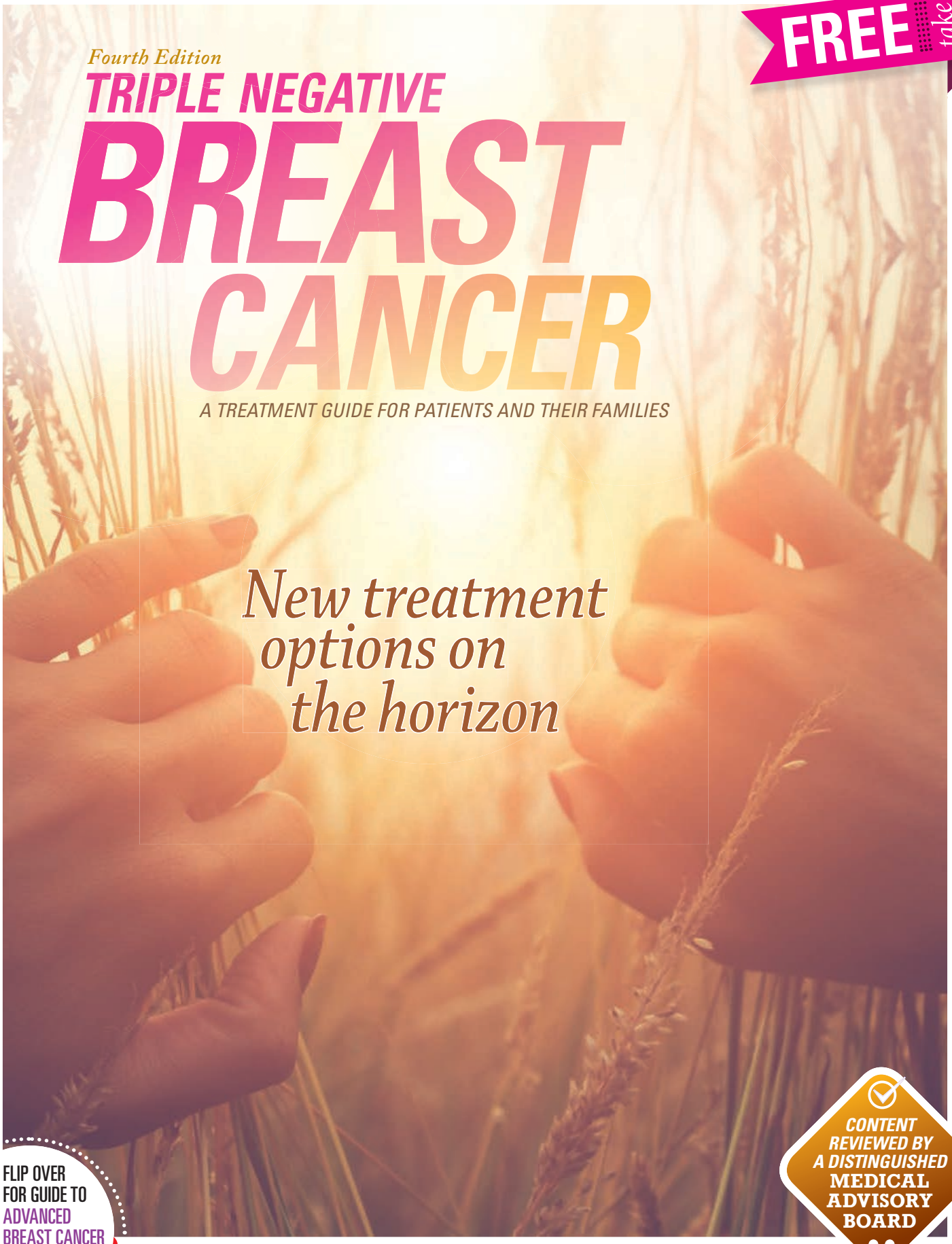
Fourth Edition

TRIPLE NEGATIVE BREAST CANCER

A TREATMENT GUIDE FOR PATIENTS AND THEIR FAMILIES



New treatment options on the horizon

CONTENT REVIEWED BY A DISTINGUISHED MEDICAL ADVISORY BOARD

FLIP OVER FOR GUIDE TO ADVANCED BREAST CANCER

PRP PATIENT RESOURCE PUBLISHING®

Live for the moments that haven't happened yet

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)

- In a clinical study of more than 750 women, HALAVEN was compared with other chemotherapies or hormone therapies commonly used to treat mBC. Although some women lived longer and some women did not live as long, women who were treated with HALAVEN lived, on average, 25% longer (13.2 months vs 10.6 months, respectively) than those who received another chemotherapy or hormone treatment
- In this study, 8 out of 10 women had breast cancer that had spread to other sites including their lungs and/or liver

Ask your doctor how **HALAVEN** may be able to help you live longer

Hear from real women who are living with mBC as they share their experiences at **www.halaven.com**

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

- 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.

For more information about HALAVEN, please visit www.halaven.com.

Eisai

Halaven®
(eribulin mesylate) Injection | 0.5 mg/mL

PATIENT INFORMATION
HALAVEN® (HAL-ih-ven)
(eribulin mesylate)
injection, for intravenous use

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
- hair loss (alopecia)
- nausea
- 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

HALAVEN® is a registered trademark used by Eisai Inc. under license from Eisai R&D Management Co., Ltd.

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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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Eisai

TRIPLE NEGATIVE BREAST CANCER

Fourth Edition

IN THIS GUIDE

> ***"It's important to make sure that we provide comprehensive support and educational services to TNBC patients because the label 'triple negative breast cancer' has been receiving increased media and internet attention; sometimes this attention includes unnecessarily alarming or inaccurate information."***
>
> ~ Dr. Lisa A. Newman

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Strive to understand your diagnosis as you move forward

Many people are familiar with breast cancer, but fewer know about triple negative breast cancer (TNBC), a subtype with distinct characteristics. TNBC tends to be more aggressive (fast growing) and may recur (come back) within a few years after initial diagnosis. Women with this subtype may now have a new treatment option — immunotherapy. The first immunotherapy for any type of breast cancer was approved in 2019 specifically for TNBC, marking a significant advancement and offering new hope.

TNBC is more prevalent in young women, African American women and *BRCA1* mutation carriers. Though a TNBC diagnosis can be unsettling because of its nature, one of the most important things you can do is to educate yourself about this disease and how to treat it.

Breast cancer starts from one abnormal cell that grows out of control and forms a mass of abnormal cells called a tumor. Some breast cancers need hormones to grow. The cancer cells in these breast cancers contain large amounts of receptors for the hormones estrogen and/or progesterone. These breast cancers are referred to as *ER*-positive (*ER*+) and/or *PR*-positive (*PR*+).

In addition, a breast cancer cell can have too many receptors for a certain protein called *HER2*-neu, which is a growth factor. This type of a breast cancer is referred to as *HER2*-positive (*HER2*+). The discovery of these differences led to the development of targeted treatments for these specific breast cancers. For example, hormone therapy is used for *ER*+ and/or *PR*+ breast cancers, and anti-*HER2* drugs are used to treat *HER2*+ breast cancers.

TNBC is so named because it lacks *ER*, *PR* and *HER2*, which are the three most commonly tested biomarkers for diagnosing and staging breast cancer. Because TNBC is not driven by estrogen, progesterone or *HER2*, it is not likely to respond to hormone therapy or anti-*HER2* drugs. Although this may feel discouraging, research has led to new treatments recently that were previously unavailable to women with TNBC.

Scientists have discovered that TNBC tumors have differences in their molecular structure. These different TNBC subtypes can affect the likelihood of treatment response.

- Basal-like tumors look similar to the basal (outer) cells around the mammary ducts. The majority of TNBC tumors are basal-like, and they can either be immune-enriched or without immune enrichment. The immune-enriched tumors contain immune cells, which indicate they may respond to immunotherapy. The tumors without immune enrichment show sensitivity to chemotherapy, meaning that chemotherapy may offer more benefit to these patients. TNBC tends to be more aggressive than other breast cancers because approximately 80 percent of TNBCs are basal-like, which metastasizes more easily than other types of breast cancer.
- *BRCA*-mutated TNBC indicates tumors that are driven by this mutation. Research shows the majority of TNBC patients have the *BRCA1* mutation. The *BRCA2* mutation is also found in TNBC, but less frequently. Some targeted therapies are available to treat TNBC with *BRCA* mutations, and research is ongoing to find and develop others.

Since many TNBC cases are associated with *BRCA* mutations (especially *BRCA1*), genetic testing is recommended for all patients diagnosed with TNBC prior to age 60, regardless of their family history. Ask your doctor about genetic testing to find out if you have a *BRCA1* mutation and to potentially help identify treatments and/or clinical trials that will be most appropriate for you.

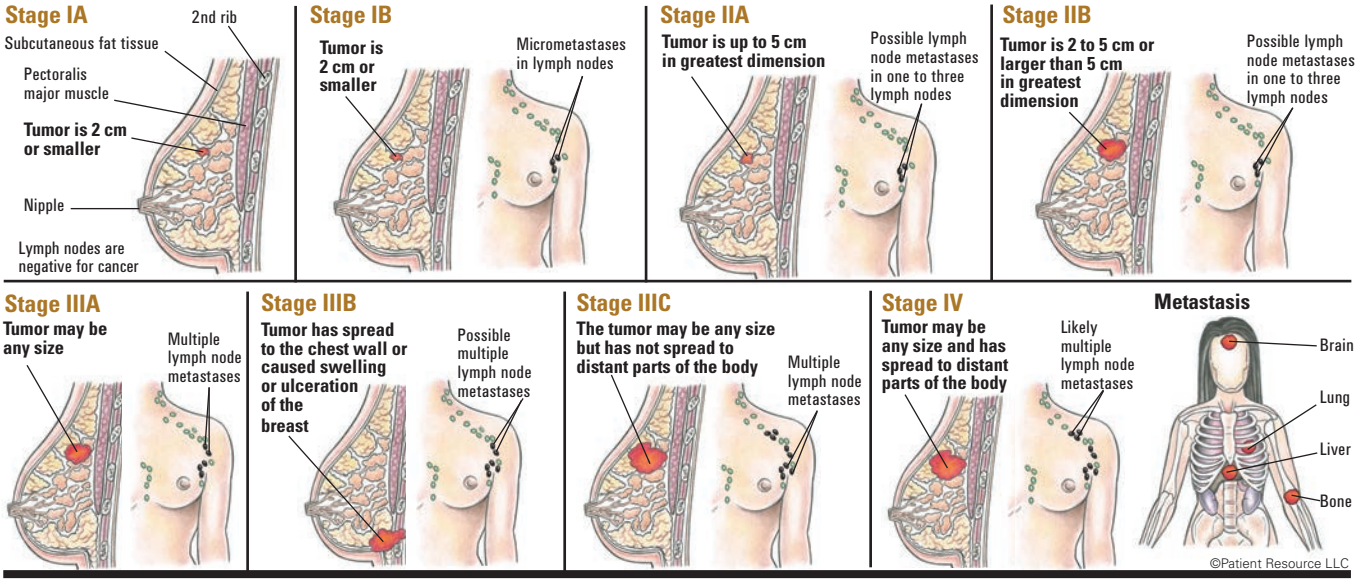
Treatment for TNBC may include chemotherapy, surgery, radiation therapy, targeted therapy or immunotherapy (see *Treatment Options,* page 6).

Your doctor will consider the best treatment options for you to help eliminate cancer cells and to lower the risk of recurrence. In addition, your doctor will recommend close follow-up care after treatment so that if cancer does recur, it can be treated early.

Staging & grading

Staging enables your doctor to develop the best treatment plan for your diagnosis. Along with considering the results of your physical exam, imaging studies and laboratory tests, your doctor will classify and stage the breast cancer according to the tumor, node and metastasis (TNM) system developed by the American Joint Committee on Cancer (AJCC).

STAGES OF BREAST CANCER



In this system, the tumor (T) is categorized according to its size and location; the node (N) category describes whether cancer cells are found in lymph nodes; and the metastasis (M) category indicates whether the cancer has metastasized, or spread, to other parts of the body, such as the bones, brain, liver or lungs (see Table 1). The stage is described by Roman numerals from 0 to IV and the letters A, B or C, if applicable (see Table 2).

Breast cancer is also classified into subtypes based on molecular or genetic changes. Identifying the subtype is important because treatments and monitoring milestones, such as the length of time without progression and response to therapy, will vary by subtype. As a result, AJCC recommends molecular testing along with staging to identify the most effective therapy. Tumors can be tested for proteins produced either by the cancer cells themselves or other cells in response to cancer as well as for genetic mutations (see *Genetic Testing*, page 10). Results of multi-gene panels, such as MammaPrint, Oncotype DX 21-gene recurrence score, PAM 50 (Prosigna), and the Breast Cancer Index may be considered to guide treatment planning.

The tables included here share information based on the size and spread of disease. Your final stage will be determined after your doctor considers other factors, such as tumor marker expression and tumor grade. The most well-known tumor markers to guide breast cancer treatment are estrogen receptor (*ER*), progesterone receptor (*PR*) and human epidermal growth factor-2 (*HER2*) status. As noted above, TNBC is negative for these three markers. The grade is assigned by a pathologist, a doctor who is specially trained to identify diseases by studying cells and tissues under a microscope. Based on the microscopic features of tumor cell growth rate and aggressiveness, the grade helps determine how fast a cancer is likely to grow and spread. Grades range from 1 to 3, and TNBC is often diagnosed as Grade 3, meaning it tends to grow quickly and may spread quickly. ■

TABLE 1
AJCC TNM SYSTEM FOR CLASSIFYING BREAST CANCER

Classification	Definition
Tumor (T)	
TX	Primary tumor cannot be assessed.
T0	No evidence of primary tumor.
Tis (DCIS)	Ductal carcinoma in situ.
Tis (Paget)	Paget disease of the nipple NOT associated with invasive carcinoma and/or carcinoma in situ (DCIS) in the underlying breast parenchyma (tissue).
T1 **T1mi** **T1a** **T1b** **T1c**	Tumor ≤ (not more than) 20 mm in greatest dimension. Tumor ≤ (not more than) 1 mm in greatest dimension. Tumor > (more than) 1 mm but ≤ (not more than) 5 mm in greatest dimension. Tumor > (more than) 5 mm but ≤ (not more than) 10 mm in greatest dimension. Tumor > (more than) 10 mm but ≤ (not more than) 20 mm in greatest dimension.
T2	Tumor > (more than) 20 mm but ≤ (not more than) 50 mm in greatest dimension.
T3	Tumor > (more than) 50 mm in greatest dimension.
T4 **T4a** **T4b** **T4c** **T4d**	Tumor of any size with direct extension to the chest wall and/or to the skin (ulceration or macroscopic nodules). Extension to the chest wall. 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. Both T4a and T4b are present. Inflammatory carcinoma.
Node (N)	
pNX	Regional lymph nodes cannot be assessed.
pN0 **pN0(i+)** **pN0(mol+)**	No regional lymph node metastasis identified or ITCs (isolated tumor cells) only. ITCs (isolated tumor cells) only (malignant cell clusters no larger than 0.2 mm) in regional lymph node(s). Positive molecular findings by reverse transcriptase polymerase chain reaction (RT-PCR); no ITCs (isolated tumor cells) detected.
pN1 **pN1mi** **pN1a** **pN1b** **pN1c**	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. Micrometastases (approximately 200 cells, larger than 0.2 mm, but none larger than 2.0 mm). Metastases in 1-3 axillary (armpit) lymph nodes, at least one metastasis larger than 2.0 mm. Metastases in ipsilateral (on the same side) internal mammary sentinel nodes, excluding ITCs (isolated tumor cells). pN1a and pN1b combined.
pN2 **pN2a** **pN2b**	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 lymph node metastases. Metastases in 4-9 axillary (armpit) lymph nodes (at least one tumor deposit larger than 2.0 mm). Metastases in clinically detected internal mammary lymph nodes with or without microscopic confirmation; with pathologically negative axillary (armpit) nodes.
pN3 **pN3a** **pN3b** **pN3c**	Metastases in 10 or more axillary (armpit) lymph nodes; *or* in infraclavicular (below the clavicle) (Level III axillary) 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 lymph nodes; *or* in more than three axillary lymph nodes and micrometastases or macrometastases by sentinel lymph node biopsy in clinically negative ipsilateral internal mammary lymph nodes; *or* in ipsilateral supraclavicular (above the clavicle) lymph nodes. Metastases in 10 or more axillary (armpit) lymph nodes (at least one tumor deposit larger than 2.0 mm); *or* metastases to the infraclavicular (below the clavicle) (Level III axillary) lymph nodes. pN1a or pN2a in the presence of cN2b (positive internal mammary nodes by imaging); *or* pN2a in the presence of pN1b. Metastases in ipsilateral (on the same side) supraclavicular (above the clavicle) lymph nodes.
Note: (sn) and (f) suffixes should be added to the N category to denote confirmation of metastasis by sentinel node biopsy or FNA/core needle biopsy respectively, with N0 further resection of nodes.	
Metastasis (M)	
M0	No clinical or radiographic evidence of distant metastases.
cM0(i+)	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.
cM1	Distant metastases detected by clinical and radiographic means.
pM1	Any histologically proven metastases in distant organs; or if in nonregional nodes, metastases greater than 0.2 mm.

TABLE 2
STAGES OF BREAST CANCER

Stage	TNM Classification
0	Tis, N0, M0
IA	T1, N0, M0
IB	T0 or T1, N1mi, M0
IIA	T0 or T1, N1, M0 // T2, N0, M0
IIB	T2, N1, M0 // T3, N0, M0
IIIA	T0-T3, N2, M0 // T3, N1, M0
IIIB	T4, N0-N2, M0
IIIC	Any T, N3, M0
IV	Any T, Any N, M1

Used with permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original and primary source for this information is the AJCC Cancer Staging Manual, Eighth Edition (2017) published by Springer Science+Business Media.

ADDITIONAL RESOURCES

- **Dr. Susan Love Research Foundation:**
  www.drsusanloveresearch.org
  Triple Negative Breast Cancer
- **Susan G. Komen:**
  ww5.komen.org
- **Triple Negative Breast Cancer Foundation:**
  www.tnbcfoundation.org
  Helpline: 877-850-8622

Leading-edge strategies provide more choices, more hope

New therapies are emerging that are providing a renewed sense of hope to many who have this aggressive disease. Research is ongoing, and the medical community is actively pursuing new forms of treatment for this subset of breast cancer. As a result, you may be a candidate for a clinical trial, which may offer you the chance to have treatments not available to everyone.

Your diagnosis will be factored into your unique treatment plan. Your doctor will consider your age, general health, menopausal status and size and stage of the tumor, as well as biomarkers and genetic testing results. Your plan may include some of the following.

Surgery is often the first option used to treat TNBC and includes either a lumpectomy or a mastectomy. Surgery for TNBC often follows chemotherapy (which is called neoadjuvant chemotherapy). As you consider your surgical options, be aware of the common misperception that surgery eliminates the chance of recurrence.

A ***lumpectomy,*** also referred to as breast-conserving or breast-sparing surgery, removes only the tumor (lump) and a small margin of normal-appearing tissue around the lump (see Figure 1). A lumpectomy can be done for most small tumors. It is usually followed by radiation therapy designed to kill microscopic cancer cells hiding in other parts of the breast. For patients with TNBC, chemotherapy is either given before surgery or given after surgery but before radiation.

A ***mastectomy*** involves removing the entire breast and may be preferred for larger tumors, especially when they occur in a smaller breast (see Figure 2). Several types of mastectomy exist, including total mastectomy and modified radical mastectomy. Total mastectomy surgically removes the entire breast without removing muscle. A modified radical mastectomy is a total mastectomy that is performed along with removing a block of underarm/axillary lymph node tissue (axillary dissection). Your doctor may recommend a mastectomy if you have a large tumor, multiple tumors in the breast or cancer that has spread to the skin, or if you were previously treated with lumpectomy and radiation therapy for a cancer in that same breast.

Patients with hereditary breast cancer, such as those with *BRCA* mutations (see *Genetic Testing,* page 10), may opt to undergo bilateral mastectomy even if they only have a single small tumor as a strategy for reducing their chances of developing a future second breast cancer. Since outcome from breast cancer tends to be determined by the aggressiveness and metastatic risk of a woman's first breast cancer (rather than whether she chooses mastectomy versus lumpectomy), patients with *BRCA* mutations may still be candidates for breast-conserving surgery.

Most TNBC, as well as non-TNBC, patients will need to undergo surgery to remove some of the lymph nodes (glands) in the underarm (axillary) region. Information regarding whether or not the breast cancer has spread into these lymph nodes is important prognostically and can influence other aspects of treatment, such as your chemotherapy and radiation plan.

Some patients will be candidates for a relatively small axillary procedure called a ***sentinel lymph node biopsy***, which involves removing only the few most important axillary nodes. Other patients require a more extensive operation to control their disease called an ***axillary lymph node dissection*** (see Figure 1). The axillary surgery plan that is most appropriate for your cancer will be based upon the extent of your disease and your other treatments, including radiation therapy and chemotherapy.

Additional surgical procedures may be an option for people who have *BRCA* mutations and/or hereditary breast cancer. These women have a higher-than-average risk for developing new cancers in the contralateral (opposite) breast, or in either breast if they have had a lumpectomy.

Prophylactic mastectomy reduces the risk of a new breast cancer but it does not completely eliminate the risk because microscopic amounts of breast tissue can remain hidden in the skin flaps or in the underarm fatty tissue after a mastectomy. Talk to your doctor about these potential options before deciding if prophylactic surgery is right for you.

Radiation therapy uses high-energy X-rays to kill cancer cells or keep them from growing. The most common type of radiation is external-beam radiation therapy (EBRT).

Radiation therapy is almost always delivered after lumpectomy to destroy any cancer cells that may be hidden in normal-appearing breast tissue. Post-mastectomy radiation therapy is sometimes necessary, particularly for people who face a high risk of the cancer growing back on the chest wall area (mastectomy skin flaps, underarm/axillary region). Post-mastectomy radiation therapy can lower this risk.

Chemotherapy uses powerful drugs to kill rapidly multiplying cells throughout the body. Neoadjuvant (preoperative) chemotherapy is used frequently with TNBC to shrink a large, bulky tumor so it can be removed surgically or to reduce the tumor's size so a patient can undergo a lumpectomy rather than a mastectomy. Neoadjuvant chemotherapy also helps the doctor determine how well the chemotherapy drugs work against the tumor.

FIGURE 1
LUMPECTOMY & AXILLARY LYMPH NODE DISSECTION

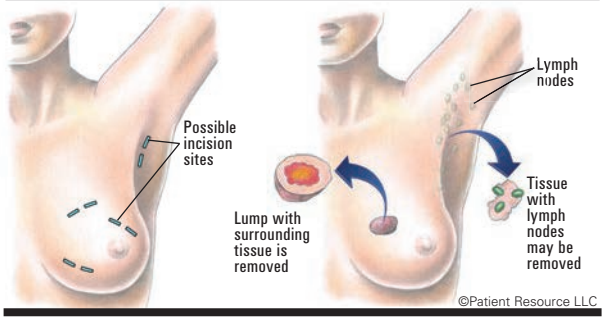
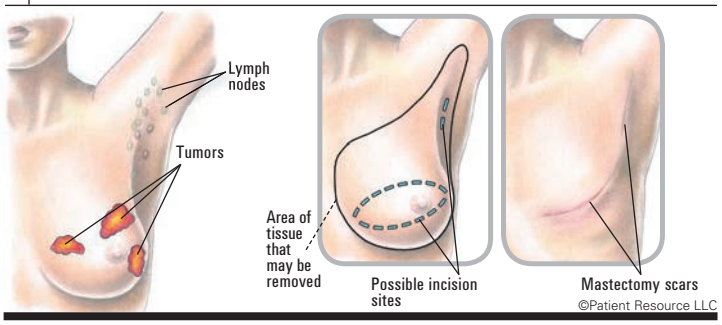


FIGURE 2
MASTECTOMY



COMMONLY USED MEDICATIONS

CHEMOTHERAPY
- capecitabine (Xeloda)
- cyclophosphamide
- docetaxel (Taxotere)
- doxorubicin (Adriamycin)
- epirubicin (Ellence)
- fluorouracil – also known as 5-FU
- paclitaxel (Taxol)

Combinations
- AC: doxorubicin (Adriamycin), cyclophosphamide
- ACT/AC-D: doxorubicin (Adriamycin), cyclophosphamide, docetaxel (Taxotere)
- FAC/CAF: fluorouracil (5-FU), doxorubicin (Adriamycin), cyclophosphamide
- FEC/CEF/EC: fluorouracil (5-FU), epirubicin (Ellence), cyclophosphamide
- TAC: docetaxel (Taxotere), doxorubicin (Adriamycin), cyclophosphamide
- TC: docetaxel (Taxotere), cyclophosphamide

IMMUNOTHERAPY
- atezolizumab (Tecentriq)

TARGETED THERAPY

PARP inhibitors
- olaparib (Lynparza)
- talazoparib (Talzenna)

As of 10/8/19

Adjuvant chemotherapy is given post-operatively to destroy cancer cells that may remain, some of which may be too small to detect with laboratory testing or imaging studies. This can be lifesaving and decrease the risk of recurrence in higher-risk patients and most patients with TNBC.

Targeted therapy uses drugs or other substances to attack specific types of cells that play important roles in the growth and survival of cancer cells.

It is used to treat breast cancer in patients with *BRCA* mutations. A poly (ADP ribose) polymerase (PARP) inhibitor targets *HER2*-negative cancers associated with a *BRCA1* or *BRCA2* mutation. PARPs are a family of enzymes that are involved with a DNA repair gene, which is often present in TNBC.

Immunotherapy uses the body's own immune system to recognize and attack cancer cells that have been hiding and targets them for destruction. Immune checkpoint inhibitors target the protein PD-L1 (programmed death-ligand 1) found on cells and boost the immune system's cancer-fighting response.

In some cases, patients may qualify for tumor-agnostic treatment. This is a new class of drug therapy that is approved to treat solid tumors anywhere in the body that meet specific criteria:
- It is only available for people with tumors that are metastatic or unresectable (cannot be removed with surgery).
- The tumor must contain a greater than normal amount of molecular alterations.
- The cells must contain a mutation that prevents them from fixing errors that occur during duplication.

Breast reconstruction may be an option to consider after having a lumpectomy or mastectomy. Breast reconstructive surgery, which should be performed by an experienced plastic surgeon, is typically started or even completed at the same time as a mastectomy but can happen later (within months or even years after the mastectomy, depending on individual circumstances). It may be done during or after a lumpectomy when the surgery will cause the affected breast to appear significantly different from the other.

Different breast reconstruction techniques are available. They may involve the use of a breast implant or a flap of tissue (usually containing skin, fat, possibly muscle and blood vessels) from elsewhere in your body, or a combination of the two (see *Reconstructive Techniques*). The use of a tissue flap depends on the size of your breasts, your body type and preferences regarding appearance.

Reconstruction requires a long healing period, which could delay the start of chemotherapy or interfere with potential radiation therapy. If you're considering reconstructive surgery (even if it will be done later), discuss this with your cancer surgeon and a plastic surgeon before the mastectomy so they can properly plan your treatment.

Non-surgical options to restore the breast appearance also exist. If you prefer not to have additional surgery but want the appearance of breasts or while you are waiting to have reconstructive surgery later, you may consider a breast prosthesis. Or, you may choose none of these options, also referred to as "going flat."

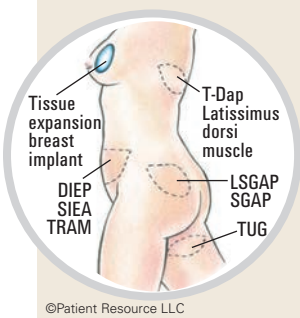
Talk with your doctor about the options that are available to you. ■

If breast cancer returns

Cancer recurrence is when the breast cancer comes back in the chest wall or in the same or opposite breast or in a distant site after initial treatment. Recurrent breast cancer may occur months or years after initial treatment. The cancer may come back in the same place as the original cancer (local recurrence), or it may spread to other areas of your body. If it recurs in the lymph nodes on the same side as the original breast cancer, it is called a regional recurrence. Local and regional recurrences usually occur on the same side of the body as the original breast cancer; the development of cancer in the contralateral (opposite) breast typically represents a completely new breast cancer. When breast cancer recurs in a different organ of the body (such as the liver, lungs or bones), this is called distant, or metastatic, recurrence. All metastatic recurrences are considered advanced disease.

Because TNBC is typically an aggressive disease, it is important to maintain your follow-up care to monitor for recurrence and track ongoing treatment, if applicable. Your doctor will schedule regular exams at which you will be tested for signs of recurrence. Tell your doctor if you notice any health changes at these exams or in between appointments.

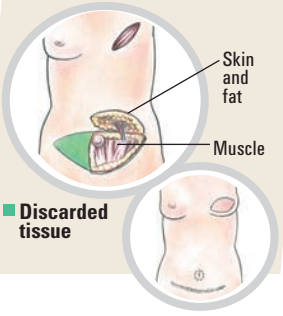
RECONSTRUCTIVE TECHNIQUES



There are two surgical methods for flap surgery. A pedicled flap is one in which the muscle is the carrier of the blood supply. A free flap contains one or two blood vessels that are attached to blood vessels in the breast area. Types of flap surgeries are listed below.

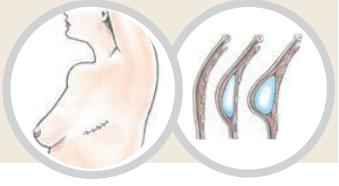
[DIEP] deep inferior epigastric perforator flap
[SIEA] superficial inferior epigastric artery flap
[TRAM] transverse rectus abdominis muscle flap
[LSGAP] lateral septocutaneous perforating branches of the superior gluteal artery perforator flap
[SGAP] superior gluteal artery perforator flap
[TUG] transverse upper gracilis flap

DIEP FLAP RECONSTRUCTION



EXPANDER IMPLANT

Implants may be used for breast reconstruction. With this option, a tissue expander is inserted at the time of the breast cancer surgery. The expander slowly expands the skin and subcutaneous tissue. A permanent implant is inserted in a second operation.



Discover the potential advantages of clinical trials

As you and your doctor work together on your treatment plan, it's important to talk about all the available options. Your doctor may discuss clinical trials as a potential option, so it's important for you to understand what that may mean.

Clinical trials investigate whether a new type of treatment, such as a drug, surgery or radiation therapy or a combination of them, is better than the current standard of care. You may not be aware that all of the cancer treatments approved today are the result of these research studies. Clinical trials offer several possible benefits:

- Access to leading-edge therapies that aren't yet widely available.
- An alternative strategy if your cancer becomes resistant to your current treatment.
- A higher level of care because you will be closely monitored by your regular oncologist and the clinical trial medical team. This extra attention may help identify and then treat side effects or other problems early.
- The role of being an active partner in your care.

As your own best advocate, it's important to know that it is always your decision to participate in a clinical trial, even if you've already started it.

If the trial doesn't meet your expectations at any time or for any reason, you may leave it and return to standard-of-care treatment.

Now that you have the basic information, where do you go from here? Asking your doctor if you should consider a clinical trial is a great start. You can also search for a trial online. Enlist the help of family members and friends to help you search, and go to your doctor with suggestions.

Because finding trials that may work for you can be complicated, below is a mock search site to help you navigate the process. Before you begin, have your exact diagnosis, pathology report and details of previous treatments handy because eligibility requirements will differ for each trial. ■

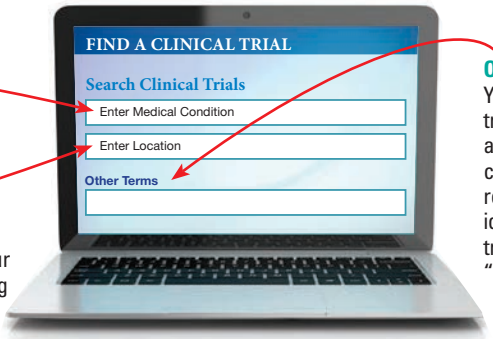
SEARCHING FOR A CLINICAL TRIAL

Be an active participant in your own care by looking online at available trials. These step-by-step instructions will help guide you. Once you feel comfortable with the search process, use the list of clinical trial resources on this page to look for a trial that may apply to you.

[STEP 1] FILL IN YOUR INFORMATION

Your Diagnosis
Enter "triple negative breast cancer." To create more options, you can also search for "TNBC" and compare results.

Desired Location
If you prefer a clinical trial close to home, use your address. Enter additional locations if you're willing and able to travel for treatment.



Other Terms
You can refine your search by adding a treatment type such as immunotherapy, a specific drug or a National Clinical Trial (NCT) identifier. During your research, you may notice that an NCT identifier is assigned to each clinical trial. Identifiers begin with the letters "NCT" followed by eight numbers.

[STEP 2] READ YOUR SEARCH RESULTS

Recruitment Status
This indicates whether the trial is actively seeking patients, not yet recruiting or otherwise inactive. The status will change, so check for updates.

Summary of Study
Here you'll find details about the purpose of the clinical trial and the treatment being studied. This section is usually written for health care providers, so it may be difficult to understand. In that case, print out the information to discuss with your doctor.

Eligibility Criteria
This outlines the requirements you must meet to be eligible for the trial, such as the stage of disease, sites of metastasis, overall health requirements and previous treatments.

Contacts and Locations
This may contain contact information for the clinical trial investigators, staff or sponsors who may be able to provide more details about the study. Trial locations may be included.

Sponsor
This is the organization responsible for the clinical trial. It may be a pharmaceutical or a biotechnology company, a university or the National Cancer Institute.

CLINICAL TRIAL RESOURCES

ACCESS: cantria.com/access / **ACT (About Clinical Trials):** www.learnaboutclinicaltrials.org / **AccrualNet:** accrualnet.cancer.gov
BreastCancerTrials.org: breastcancertrials.org / **Center for Information & Study on Clinical Research Participation:** www.searchclinicaltrials.org
CenterWatch: www.centerwatch.com / **ClinicalTrials.gov:** www.clinicaltrials.gov
Facing Our Risk of Cancer Empowered: www.facingourrisk.org/research-clinical-trials / **Lazarex Cancer Foundation:** www.lazarex.org
LIVESTRONG Foundation: www.livestrong.org / **Metastatic Breast Cancer Trial Search:** www.breastcancer.org/treatment/clinical_trials/metastatic-trials-tool
National Cancer Institute: www.cancer.gov/clinicaltrials / **National Cancer Institute (NCI) Contact Center (cancer information service):** 800-422-6237
National Institutes of Health (NIH): 800-411-1222 / **SHARE Cancer Support:** www.sharecancersupport.org/breast-cancer/clinical-trial-matching-service
TNBC Foundation Clinical Trials Matching Service: www.tnbcfoundation.org/research/clinical-trials

Heart disease – not breast cancer – ran in Sally Deghand's family. Thus, her diagnosis at age 57 of Stage III triple negative breast cancer was quite a surprise. However, she met the challenges of treatment head on and is now cancer-free and happy to share practical advice with others who find themselves in a similar situation.

Sally and her daughter, Jami

Assemble YOUR BEST ARMY

I spent a lot of time caring for my elderly parents while working full time. After my dad passed away, my mom was diagnosed with Alzheimer's disease. It was a hectic time, so my annual mammogram was three months late. After getting abnormal results, my doctor scheduled a sonogram and then a needle biopsy. Shortly after, I was driving my dog to the vet when a nurse called. She realized I was driving and hesitated. I knew the results weren't good. I got right to the point and said, "So, I have cancer. What do we do now?"

The diagnosis was triple negative invasive ductal carcinoma and would require multiple treatments. As I had them, I learned a few things that I offer as advice to anyone facing a cancer diagnosis:

1. Assemble your best army ASAP, and include a specialist in your type of cancer.
2. Don't be afraid to ask for a second or third opinion, and make sure you understand all explanations.
3. Drive as far as you need to for treatment because it could boil down to survival versus convenience.

Very soon after diagnosis, I had a mastectomy to remove my left breast. Initial biopsy results indicated the cancer was contained in the two tumors in my left breast, with no lymph node involvement. Later on, after reading the full pathology report, my doctor discovered one of the two tumors encapsulated five or six lymph nodes. A panel of doctors was undecided as to whether an axillary lymph node dissection was needed.

I had eight weeks of a strong chemotherapy nicknamed "The Red Devil" after my first surgery, followed by 12 weeks of another type of chemo. I'd had a port installed but it continually clogged, so it was removed during my second round. From then on, all chemo was administered intravenously. I was given another chemo simultaneously. I took it for 12 months. I had an EKG every three months to see if my heart muscle was being affected, a side effect they neglected to mention.

I had a fear of developing lymphedema, so I really didn't want the axillary lymph node dissection. After seeking a second opinion, my new oncologist felt I should, so I did. The doctor removed some lymph nodes but didn't find more cancer. My body didn't react well to the second surgery. I needed many drain tubes to finally stop the drainage after several months.

After the drainage issue was resolved, I was tattooed then began six weeks of radiation therapy. My radiation oncologist didn't follow my medical oncologist's instructions to radiate above my clavicle, and after six weeks of radiation treatments, I had to stop a week early due to very painful third-degree burns on the left side of my chest. My medical oncologist was very upset. I was referred to a specialist in radiation oncology to complete five to six more weeks of radiation on the area that hadn't been treated.

I left work at 1 p.m. every day to drive more than an hour for each radiation treatment. It was worth it because my new radiation oncologist is an angel on Earth. I later found out he is world-renowned for his breast cancer treatment research. Not only did he treat me like I was his only patient, he thoroughly reviewed my case, explained everything and did not make excuses for the mistakes made by others. Under his care, I had five more weeks of radiation therapy, and my skin never even turned pink. I hope I never need cancer treatment again, but if I do, he will be involved from the very beginning.

Overall, my treatment lasted about 16 months. The day I started losing my hair stands out as my worst day. Most of it fell out in the shower. As I was leaving for work, I realized I didn't have my garage door opener. I ran to jump over the garage door's electric eye. As the door closed, I hit my head on the bottom of it, fell, skinned my knee, tore my jeans and lost a shoe. I was lying there in the rain with my dog on top of me. We looked at each other, then she followed my gaze to my shoe. She grabbed it and took off, and I had to chase her to retrieve it. After finally pulling out of the driveway, I cried for three miles before making myself stop so I could put on makeup at stoplights.

The best day was receiving the results of the genetic testing I requested. It was a huge relief to learn I did not have the cancer gene to pass on to my daughters or granddaughters.

Today, I'm cancer-free. I continue to get annual checkups, and I enjoy spending time with my animals and my family. ■

The role of DNA mutations in hereditary cancer

Genetic testing is a tool that doctors can use to determine a person's risk for certain types of cancer and/or as a guide for making treatment decisions in patients that have already been diagnosed with cancer. It is performed to look for mutations in genes. A genetic mutation is a permanent alteration in the DNA sequence of a gene within a cell. When some genes mutate, they may produce many abnormal genes or proteins that can negatively affect the cells, permitting uncontrolled, interrupted growth, which may lead to cancer.

All cancers are caused by mutations, which are classified as either acquired or hereditary.

- Acquired mutations are genetic damage that accumulates during a person's lifetime from a variety of factors, such as radiation, environmental exposure, smoking and diet. These are the most common mutations leading to cancer, and they can be detected by performing genetic testing on tumor tissue.
- Hereditary mutations are passed from parent to child at conception. Also known as germline mutations, these are less common than acquired mutations. Genetic testing may be used to detect these mutations to determine future cancer risk, especially if there is a history of certain cancers in the family. However, inheriting a germline mutation doesn't mean a person will automatically develop cancer; it only means the risk is increased. These inherited/germline mutations are typically detected by genetic testing performed on a sample of blood or saliva.

The most common hereditary mutations associated with breast cancer risk are detected in the breast cancer 1 and 2 genes (*BRCA1* and *BRCA2*). Mutations in the *BRCA1* and *BRCA2* genes can increase the risk of developing breast and ovarian cancers. Proteins produced by these genes normally repair damaged DNA. When these genes are mutated, the damaged DNA is not repaired, which may lead to additional cellular alterations that may lead to cancer. Most cases of breast and ovarian cancer, however, are not caused by these hereditary/germline genetic mutations.

Researchers have discovered that triple negative breast cancer (TNBC) occurs in three-quarters of women who have *BRCA1* mutations and in about one-tenth of women with *BRCA2* mutations. Knowing you have a specific genetic mutation may help your doctor choose the best treatment option for you, and this information may be useful to family members who can then decide to undergo genetic testing themselves. New treatment options are available for TNBC that expresses a *BRCA* mutation (see *Treatment Options,* page 6).

Who should get genetic testing?

Genetic testing may be performed before or after being diagnosed with cancer. If you have a family history of breast or gynecologic cancers or other factors, your doctor may recommend genetic testing to determine if you have hereditary mutations. Knowing this type of information can empower you to make important decisions about your health.

Breast oncology experts encourage all breast cancer patients to receive genetic testing because they may have the following characteristics associated with an increased likelihood of carrying a *BRCA1* or *BRCA2* mutation:

- A family history of cancer in two or more relatives. It is important to remember that *BRCA1* and *BRCA2* mutations can be passed on from your mother or your father, so you should try to learn about your maternal as well as paternal family history.
- Breast and ovarian cancer on the same side of the family.
- A family member who was diagnosed with cancer at an early age.
- A known genetic mutation linked to breast cancer in your family.
- Family members who were diagnosed with ovarian cancer, sarcoma or certain other rare cancers.
- A woman diagnosed with breast cancer under the age of 50 even if there is no family history of cancer.
- A male family member with breast cancer.
- Selected ancestral backgrounds are associated with *BRCA* mutations as well, such as Ashkenazi Jewish heritage. Several studies are also demonstrating an increased risk of *BRCA* mutations in African American patients, but additional research in this area is warranted.
- Having bilateral breast cancer.
- Having TNBC (regardless of family history), especially if diagnosed younger than the age of 60.

In most cases, genetic tests are ordered by a doctor or other health care provider. Doctors send these tests to laboratories that are regulated under the Clinical Laboratory Improvement Amendments (CLIA) program to meet standards for accuracy and reliability.

Although some direct-to-consumer genetic tests are available, they are not recommended for a person who has cancer. The sensitivity and accuracy of these tests are unknown compared to those used by doctors and designated laboratories; they typically provide raw data without offering assistance interpreting the results or providing genetic counseling; and the tests may not screen for all the possible genes and mutations for a particular cancer.

Although *BRCA1* and *BRCA2* are the most well-known genetic mutations in breast cancer, other mutations play a role in developing breast cancer or TNBC specifically. Mutations associated with a high risk of TNBC currently include the genes *BARD1, BRCA1, BRCA2, PALB2* and *RAD51D*. The genes *BRIP1, RAD51C* and *TP53* are associated with a moderate risk of TNBC. Most doctors will order a genetic testing panel looking for multiple mutations in addition to *BRCA*.

The importance of genetic counseling

If you are interested in genetic testing, it is highly recommended that you talk to your doctor or to a genetic counselor who is trained to interpret the results and assist you in lowering your risk for developing cancer. Understanding and interpreting the results of genetic testing can be challenging. Many different types of mutations can be identified in these genes, and some mutations will be associated with a higher risk of cancer than others. Conversely, some cases of hereditary cancer may be associated with genetic mutations that have not yet been identified, and the standard genetic testing will be negative. Consulting with a genetic counselor before testing will help you understand the role of testing in your care as well as your risks for cancer.

After testing, your counselor can use the results to determine and plan future health care, such as a schedule for screenings for you and family members, if appropriate. If a mutation is identified, your genetic counselor may discuss options to reduce your risk, including earlier or more frequent screenings, lifestyle changes or preventive treatments. Family members may be offered testing if a mutation is found. ■

Chart a course to live your best possible life during treatment

Many parts of your diagnosis and treatment are out of your hands, but don't let that overwhelm you. Instead, identify what you can control, and reclaim your life with confidence. Ask your nurse navigator to recommend supportive care resources to help manage the emotional, social and physical challenges related to triple negative breast cancer (TNBC) and its treatment. In the meantime, these suggestions may help.

Watch for serious side effects. Severe side effects are not common but can occur. For people on immunotherapy, immune-related adverse events (irAEs) can develop rapidly and become serious, even potentially life-threatening, without swift medical attention. If immunotherapy is in your treatment plan, ask your doctor about symptoms to watch for, and act immediately if you experience them. Be alert for them up to two years after finishing treatment. See Table 1 for more common treatment-related side effects.

Lead a healthy lifestyle. Following a nutritious diet helps you tolerate treatment better and reduces the risk of cancer recurrence and secondary cancers. Know that your appetite and weight can fluctuate during treatment. A poor appetite may lead to weight loss, whereas fatigue and lack of exercise, combined with steroid treatment, may cause weight gain. Hormone therapy can increase your chance of weight gain and make it difficult to lose weight. Exercising can help you feel better overall. Do some type of physical activity daily, even walking for just 10 minutes. Use sunscreen if your activities are outdoors.

Find a positive emotional outlet. Your feelings may range from stress and fear to anger and depression. Many survivors find it comforting to talk with others who've gone through something similar. Opening up to a TNBC support group or therapist may help you work through some emotions. Journaling, meditating and guided imagery may increase your overall sense of well-being.

Explore fertility preservation options. If having a biological child is in your plans, consult with your medical team and a fertility expert before committing to any treatment options, if possible. Some treatments may affect your ability to have children.

TABLE 1
COMMON TREATMENT-RELATED SIDE EFFECTS*

Side Effects	Ways to Manage
Anemia (low red blood cell count)	Get plenty of rest; participate in regular physical activity
Chemo brain (cognitive dysfunction)	Take notes; keep lists; use a daily planner; don't multitask
Constipation	Drink more liquids; increase physical activity; contact your doctor before trying over-the-counter medications or adjusting your diet
Diarrhea	Drink plenty of fluids; eat several small meals; avoid greasy foods; know where clean restrooms are to prevent accidents
Emotional distress	Speak to a counselor or mental health professional; join a local or online cancer support group; seek help immediately for thoughts of suicide
Fatigue	Balance activity and rest; take short naps; sleep regularly, participate in regular activity; ask for help
Hair loss (alopecia)	Wear a wig, scarf or hat; use a wide-toothed comb; sleep on a satin pillowcase; ask your doctor for a prescription for a wig or a cooling cap
Lymphedema	Wear a compression garment; elevate the swollen limb
Mouth sores	Brush teeth often with a toothbrush with soft bristles; eat soft foods; drink plenty of fluids
Nausea, vomiting	Take antiemetics as prescribed; eat several small meals; drink plenty of fluids; avoid unpleasant odors
Neuropathy	Avoid tight clothes or shoes; keep hands and feet warm; avoid standing for long periods of time
Neutropenia (low white blood cell count)	Wash hands frequently; avoid crowds and children; wash fruits and vegetables carefully; contact your doctor for a fever higher than 100.5°F
Skin reactions	Use mild soap; use thick cream (with no alcohol, perfume or dye) to moisturize skin

*For more side effect information, flip this guide over and see page 12.

Talk to your children about cancer. Telling your kids you have cancer may be difficult, but remind them it won't affect how much you love them. The basic information they need is the name of the cancer, the body part it affects, how it will be treated and how their lives will be affected. Use age-appropriate language. Younger children may only understand that you're sick and need medicine to get better, whereas older children will likely want to know more.

Maintain the household routine. Your family needs to feel some sense of predictability. That means school activities, social events and family dinners must go on, if possible. Ask everyone to do their part to keep the household running. Be careful not to put too much responsibility on older kids. Although they may be very capable of picking up the slack, they still need time to be kids.

Manage your career. Working helps you feel normal, and maintaining normalcy is key right now. Ask your medical team to arrange your treatment plan around your work schedule. For example, if side effects predictably occur 24 hours after treatment, get your treatment on a Friday afternoon so the side effects happen on Saturday when you're home and have family support. Ask your human resources (HR) department at work about accommodations that can be made for you through the Americans with Disabilities Act (ADA) and the Family Medical Leave Act (FMLA). This could be especially helpful if you need to take off for appointments or rest after treatments.

Become comfortable with your body image. Depending on your treatment, your physical appearance may change dramatically, which can affect your self-esteem. Although your physical health is the priority, it's easy to feel down when you're unhappy with your appearance. Ask your nurse navigator about programs geared toward boosting your self-image.

Pay attention to your social self. Changes in how you feel about your sexuality may affect dating and intimacy. Physical changes may make you feel less desirable or insecure about being with a partner. Certain treatments may bring on premature menopause, which can result in additional side effects. Communication is crucial, so talk with your partner or a therapist about these issues. ■