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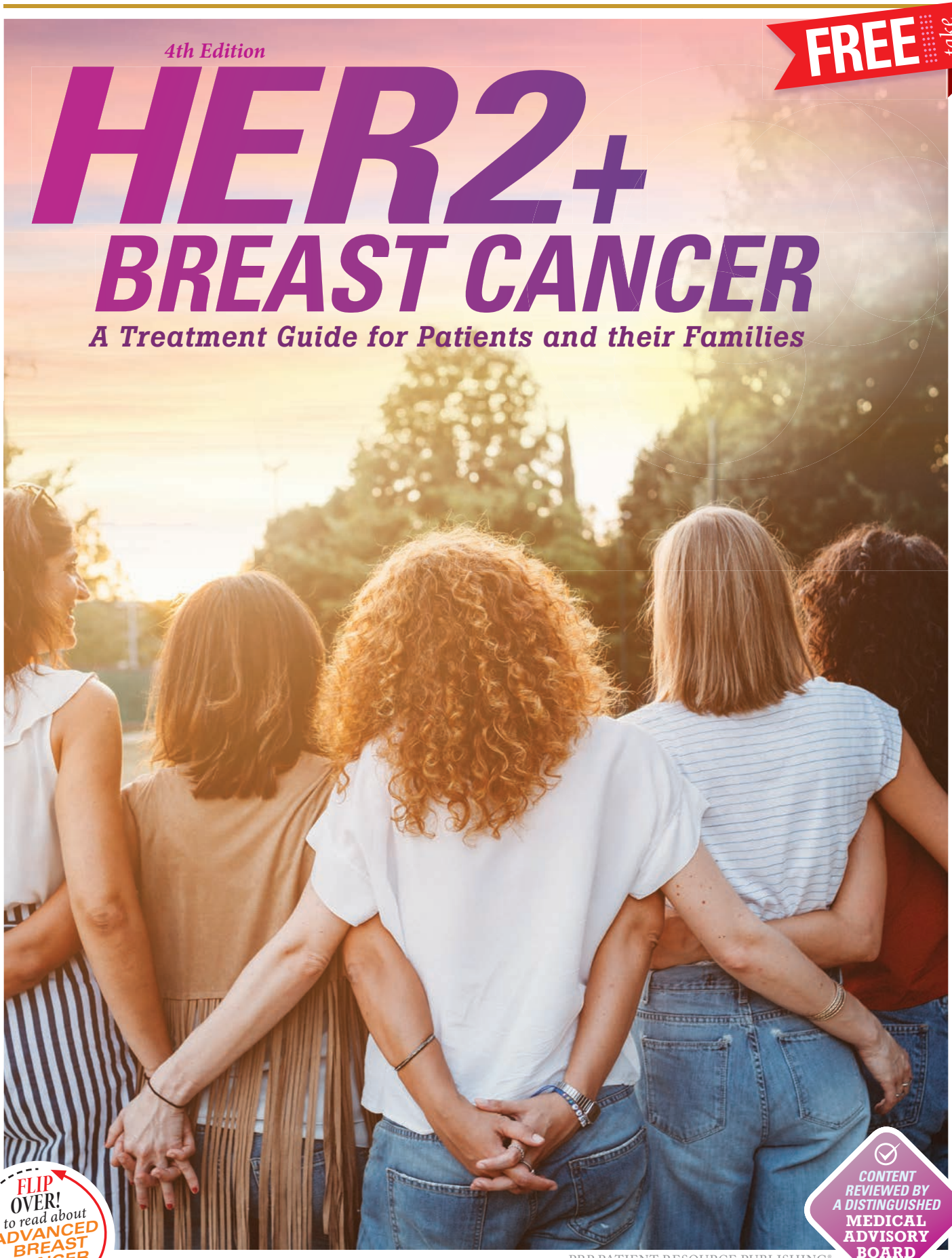
4th Edition

HER2+ BREAST CANCER

A Treatment Guide for Patients and their Families



FLIP OVER! to read about ADVANCED BREAST CANCER

CONTENT REVIEWED BY A DISTINGUISHED MEDICAL ADVISORY BOARD

PRP PATIENT RESOURCE PUBLISHING®

Granted FDA BREAKTHROUGH STATUS and approved for adults with metastatic breast cancer (mBC) who received a prior treatment for HER2+ mBC or have breast cancer that has come back within 6 months of completing treatment for their early-stage breast cancer

Not an actual patient.

ENHERTU REDUCED THE RISK OF PEOPLE'S CANCER PROGRESSING, or of them dying, by 72% compared to Kadcyla*

ENHERTU was compared to Kadcyla® (ado-trastuzumab emtansine) in a clinical trial of 524 people who:

- Had HER2+ breast cancer that had spread to other parts of their body or could not be removed by surgery, and
- Had received a prior treatment for HER2+ metastatic breast cancer that came back during or within 6 months of treatment after surgery

In this trial, 261 people were treated with ENHERTU and 263 were treated with Kadcyla.

Find out more about ENHERTU by speaking to your healthcare provider, and by visiting ENHERTU.com/learnmore

*Median progression-free survival (mPFS) was not reached with ENHERTU at the time it was assessed, and mPFS for people taking Kadcyla was about 7 months. Median progression-free survival is the length of time from the start of treatment that half of the people in the trial had gone without disease progression. When more than half of the people had lived without disease progression, mPFS has not been reached.

What is ENHERTU?

ENHERTU is a prescription medicine used in adults to treat human epidermal growth factor receptor 2 (HER2)-positive:

- Breast cancer that cannot be removed by surgery or that has spread to other parts of the body (metastatic), and who have received a prior anti-HER2 breast cancer treatment:
  - for metastatic disease, or
  - have breast cancer that has come back during or within 6 months of completing treatment for their early-stage breast cancer.

It is not known if ENHERTU is safe and effective in children.

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about ENHERTU?

ENHERTU can cause serious side effects, including:
Lung problems that may be severe, life-threatening or that may lead to death. If you develop lung problems your healthcare provider may treat you with corticosteroid medicines. Tell your healthcare provider right away if you get any of the following signs and symptoms: • Cough • Trouble breathing or shortness of breath • Fever • Other new or worsening breathing symptoms (e.g., chest tightness, wheezing)

Please see additional Important Safety Information and a Brief Summary of full Prescribing Information, including Boxed WARNINGS, on following pages.

ENHERTU®
fam-trastuzumab deruxtecan-nxki
20 mg/mL INJECTION FOR INTRAVENOUS USE

Important Safety Information

What is the most important information I should know about ENHERTU® (fam-trastuzumab deruxtecan-nxki)?

ENHERTU can cause serious side effects, including:

Lung problems that may be severe, life-threatening or that may lead to death. If you develop lung problems your healthcare provider may treat you with corticosteroid medicines. Tell your healthcare provider right away if you get any of the following signs and symptoms:

- Cough
- Trouble breathing or shortness of breath
- Fever
- Other new or worsening breathing symptoms (e.g., chest tightness, wheezing)

Low white blood cell count (neutropenia). Low white blood cell counts are common with ENHERTU and can sometimes be severe. Your healthcare provider will check your white blood cell counts before starting ENHERTU and before starting each dose. Tell your healthcare provider right away if you develop any signs or symptoms of an infection or have fever or chills during treatment with ENHERTU.

Heart problems that may affect your heart's ability to pump blood. Your healthcare provider will check your heart function before starting treatment with ENHERTU. Tell your healthcare provider right away if you get any of the following signs and symptoms:

- New or worsening shortness of breath
- Coughing
- Feeling tired
- Swelling of your ankles or legs
- Irregular heartbeat
- Sudden weight gain
- Dizziness or feeling light-headed
- Loss of consciousness

Your healthcare provider will check you for these side effects during your treatment with ENHERTU. Your healthcare provider may reduce your dose, delay treatment or completely stop treatment with ENHERTU if you have severe side effects.

Harm to your unborn baby. Tell your healthcare provider right away if you become pregnant or think you might be pregnant during treatment with ENHERTU.

- If you are able to become pregnant, your healthcare provider should do a pregnancy test before you start treatment with ENHERTU.
- **Females** who are able to become pregnant should use effective birth control (contraception) during treatment with ENHERTU and for at least 7 months after the last dose.
- **Males** who have female partners that are able to become pregnant should use effective birth control (contraception) during treatment with ENHERTU and for at least 4 months after the last dose.

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

- Have lung or breathing problems.
- Have signs or symptoms of an infection.
- Have or have had any heart problems.
- Are breastfeeding or plan to breastfeed. It is not known if ENHERTU passes into your breast milk. Do not breastfeed during treatment with ENHERTU and for 7 months after the last dose.

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 ENHERTU?

- You will receive ENHERTU into your vein through an intravenous (IV) line by your healthcare provider.
- ENHERTU is given 1 time every three weeks (21-day treatment cycle).
- Your healthcare provider will decide how many treatments you need.
- Your healthcare provider will give medicines before your infusion to help prevent nausea and vomiting.
- Your healthcare provider may slow down or temporarily stop your infusion of ENHERTU if you have an infusion-related reaction, or permanently stop ENHERTU if you have severe infusion reactions.
- If you miss a planned dose of ENHERTU, call your healthcare provider right away to schedule an appointment. Do not wait until the next planned treatment cycle.

What are the possible side effects of ENHERTU?

ENHERTU can cause serious side effects. See "What is the most important information I should know about ENHERTU?"

The most common side effects of ENHERTU, when used in people with breast cancer, include:

- Nausea
- Low white blood cell counts
- Low red blood cell counts
- Increased liver function tests
- Feeling tired
- Vomiting
- Low platelet counts
- Hair loss
- Constipation
- Low levels of blood potassium
- Decreased appetite
- Diarrhea
- Pain in muscles and bones
- Infections of the respiratory tract
- Headache
- Stomach-area (abdominal) pain

ENHERTU may cause fertility problems in males, which may affect the ability to father children. Talk to your healthcare provider if you have concerns about fertility.

These are not all of the possible side effects of ENHERTU. Call your doctor for medical advice about side effects. You may report side effects to Daiichi Sankyo at 1-877-437-7763 or to FDA at 1-800-FDA-1088.

What is ENHERTU?

ENHERTU is a prescription medicine used in adults to treat human epidermal growth factor receptor 2 (HER2)-positive:

- Breast cancer that cannot be removed by surgery or that has spread to other parts of the body (metastatic), and who have received a prior anti-HER2 breast cancer treatment:
  - for metastatic disease, or
  - have breast cancer that has come back during or within 6 months of completing treatment for their early-stage breast cancer.

It is not known if ENHERTU is safe and effective in children.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Please see a Brief Summary of full Prescribing Information, including Boxed WARNINGS, on following pages.

Daiichi-Sankyo | AstraZeneca

Medication Guide
ENHERTU® (en-HER-too)
(fam-trastuzumab deruxtecan-nxki) for injection

What is the most important information I should know about ENHERTU?

ENHERTU can cause serious side effects, including:

- **Lung problems that may be severe, life-threatening or that may lead to death.** If you develop lung problems your healthcare provider may treat you with corticosteroid medicines. Tell your healthcare provider right away if you get any of the following signs and symptoms:
  - cough
  - trouble breathing or shortness of breath
  - fever
  - other new or worsening breathing symptoms (e.g., chest tightness, wheezing)
- **Low white blood cell count (neutropenia).** Low white blood cell counts are common with ENHERTU and can sometimes be severe. Your healthcare provider will check your white blood cell counts before starting ENHERTU and before starting each dose. Tell your healthcare provider right away if you develop any signs or symptoms of an infection or have fever or chills during treatment with ENHERTU.
- **Heart problems that may affect your heart's ability to pump blood.** Your healthcare provider will check your heart function before starting treatment with ENHERTU. Tell your healthcare provider right away if you get any of the following signs and symptoms:
  - new or worsening shortness of breath
  - coughing
  - feeling tired
  - swelling of your ankles or legs
  - irregular heartbeat
  - sudden weight gain
  - dizziness or feeling light-headed
  - loss of consciousness

Your healthcare provider will check you for these side effects during your treatment with ENHERTU. Your healthcare provider may reduce your dose, delay treatment or completely stop treatment with ENHERTU if you have severe side effects.

- **Harm to your unborn baby.** Tell your healthcare provider right away if you become pregnant or think you might be pregnant during treatment with ENHERTU.
  - If you are able to become pregnant, your healthcare provider should do a pregnancy test before you start treatment with ENHERTU.
  - **Females** who are able to become pregnant should use effective birth control (contraception) during treatment with ENHERTU and for at least 7 months after the last dose.
  - **Males** who have female partners that are able to become pregnant should use effective birth control (contraception) during treatment with ENHERTU and for at least 4 months after the last dose.

See **"What are the possible side effects of ENHERTU?"** for more information about side effects.

What is ENHERTU?

ENHERTU is a prescription medicine used in adults to treat human epidermal growth factor receptor 2 (HER2)-positive:

- breast cancer that cannot be removed by surgery or that has spread to other parts of the body (metastatic), and who have received a prior anti-HER2 breast cancer treatment:
  - for metastatic disease, **or**
  - have breast cancer that has come back during or within 6 months of completing treatment for their early-stage breast cancer.
- stomach cancer called gastric or gastroesophageal junction (GEJ) adenocarcinoma that has spread to areas near your stomach (locally advanced) or that has spread to other parts of your body (metastatic), and who have received a prior trastuzumab-based regimen.

It is not known if ENHERTU is safe and effective in children.

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

- have lung or breathing problems.
- have signs or symptoms of an infection.
- have or have had any heart problems.
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- If you miss a planned dose of ENHERTU, call your healthcare provider right away to schedule an appointment. Do not wait until the next planned treatment cycle.

What are the possible side effects of ENHERTU?

ENHERTU can cause serious side effects. See "What is the most important information I should know about ENHERTU?"

The most common side effects of ENHERTU, when used in people with breast cancer, include:

- nausea
- low white blood cell counts
- low red blood cell counts
- increased liver function tests
- feeling tired
- vomiting
- low platelet counts
- hair loss
- constipation
- low levels of blood potassium
- decreased appetite
- diarrhea
- pain in muscles and bones
- infections of the respiratory tract
- headache
- stomach-area (abdominal) pain

The most common side effects of ENHERTU, when used in people with stomach cancer, include:

- low red blood cell counts
- low white blood cell counts
- low platelet counts
- nausea
- decreased appetite
- increased liver function tests
- feeling tired
- diarrhea
- low levels of blood potassium
- vomiting
- constipation
- fever
- hair loss

ENHERTU may cause fertility problems in males, which may affect the ability to father children. Talk to your healthcare provider if you have concerns about fertility.

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

General information about the safe and effective use of ENHERTU.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. You can ask your pharmacist or healthcare provider for information about ENHERTU that is written for healthcare professionals.

What are the ingredients in ENHERTU?

Active Ingredient: fam-trastuzumab deruxtecan-nxki.
Inactive Ingredients: L-histidine, L-histidine hydrochloride monohydrate, polysorbate 80, and sucrose.

Manufactured by: Daiichi Sankyo, Inc., Basking Ridge, NJ 07920 U.S. License No. 2128
Marketed by: Daiichi Sankyo, Inc., Basking Ridge, NJ 07920 and AstraZeneca Pharmaceuticals LP, Wilmington, DE 19850
 USMG-ENH-C8-0522-r003
For more information, call 1-877-437-7763 or go to https://www.ENHERTU.com

This Medication Guide has been approved by the U.S. Food and Drug Administration.
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4th Edition

HER2+ BREAST CANCER

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IN THIS GUIDE

For Breast Cancer Financial and Support Resources, flip this guide over and turn to pages 12 & 13.

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Understanding a *HER2+* breast cancer diagnosis

Being diagnosed with breast cancer is always overwhelming. Take a deep breath and learn all you can about *HER2+* breast cancer to be better prepared for making treatment decisions with your medical team. They will guide you to understand this aggressive type of cancer that may develop a resistance to treatment at some point.

Breast cancer is a complex disease characterized by mutations in genes and proteins that cause cells to grow out of control. *HER2+* breast cancer exhibits a specific marker that requires a more targeted approach. Understanding the components of that approach and the details of your breast cancer diagnosis is important for making key decisions with your doctor.

Your doctor will consider the details of your breast cancer diagnosis, which includes the type (noninvasive or invasive) and the status of three main biomarkers: estrogen receptor (*ER*), progesterone receptor (*PR*) and human epidermal growth factor receptor-2 (*HER2*).

The BReast CAncer 1 (*BRCA1*) and BReast CAncer 2 (*BRCA2*) genes are the most common hereditary susceptibility genes, and your doctor may test for others. Individuals that have inherited abnormalities in the *BRCA1* or *BRCA2* genes have an increased likelihood of developing breast cancer and/or ovarian cancer. Determining whether you have hereditary breast cancer is also important. Newly-diagnosed breast cancer patients found to have a *BRCA* mutation face an increased risk of another new breast cancer. As a result, the presence of inherited mutations in the *BRCA1* and *BRCA2* genes or other cancer-susceptibility genes may influence decisions regarding drugs for cancer prevention or prophylactic surgery to remove the breasts and/or ovaries, or lead to different systemic treatments.

MORE ABOUT *HER2*

Normal breast cells have two copies of the *HER2* gene. Sometimes, breast cells grow and reproduce in an uncontrolled way, producing too many *HER2* genes. *HER2* is also a protein receptor found on the surface of breast cells.

Approximately 20 percent of all breast cancers make extra copies of *HER2*, which encodes a growth-promoting protein. Breast cancers with too much of this protein tend to grow and spread more aggressively.

A diagnosis of *HER2+* breast cancer means your breast cancer cells have too many *HER2* genes or receptors or both. When breast cells have too many *HER2* genes, it is referred to as *HER2* amplification. When breast cells have too many *HER2* receptors, it is known as *HER2* overexpression.

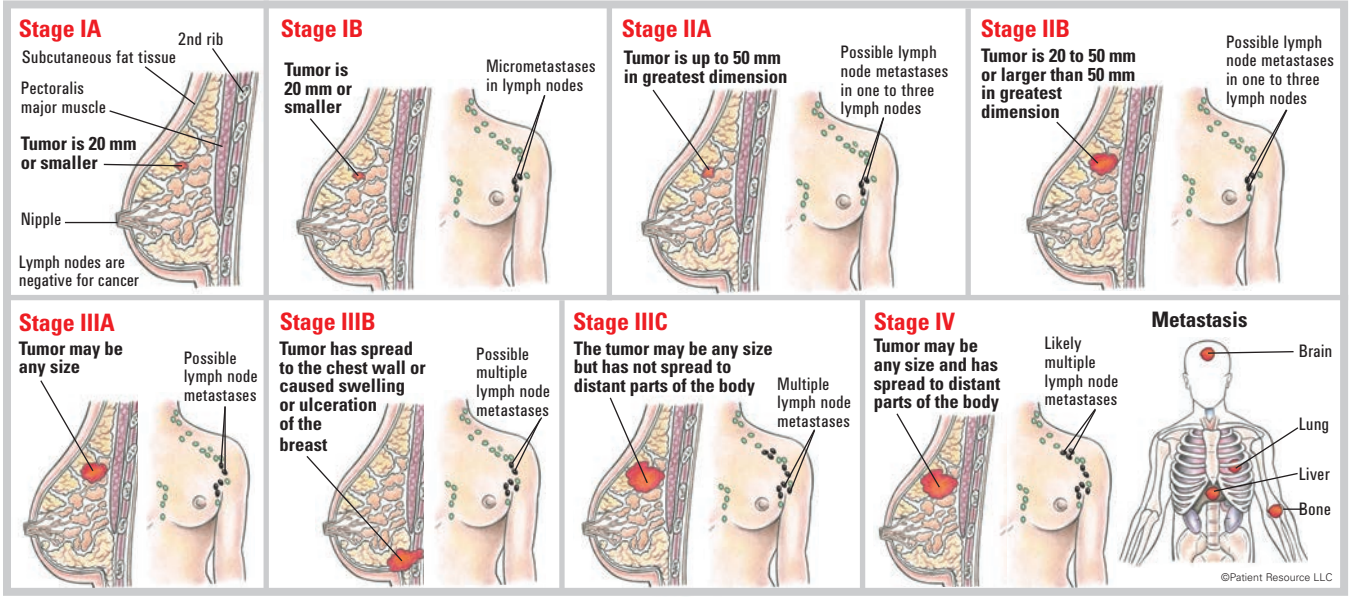
STAGING

Following your diagnosis, your doctor needs to determine the extent of the disease – a process called staging – to select the best treatment option for you. Staging determines the extent of your cancer, where it is located and whether it has metastasized (spread) to nearby organs, tissues or lymph nodes, or to other parts of your body.

All types of breast cancer, including *HER2+* breast cancer, are classified according to the tumor, node, metastasis (TNM) system developed by the American Joint Committee on Cancer (AJCC). Once classified, they are given a stage (see Tables 1 and 2).

The T classification categories are the same for both clinical and pathologic staging and provide information on the size and ex-

ILLUSTRATED STAGES OF BREAST CANCER



tent of the tumor within the breast. Clinical T (described as cT) refers to the tumor size estimate based on physical/clinical examination and breast imaging; pathologic T (described as pT) refers to the size of the tumor when it has been removed and measured in the pathology laboratory.

Clinical staging for the N category (cN) describes the location and bulkiness of lymph nodes (usually in the axilla, under the arm) that seem to be malignant (from spread of the breast cancer) upon physical examination. Location and extent of any cancerous lymph nodes provide clues regarding the likelihood that the breast cancer might have spread to other organs. The pathologic N category (pN) is determined postoperatively and describes how many lymph nodes are involved.

The M category indicates whether the cancer has metastasized, or spread, to another part of the body beyond the breast and nearby lymph nodes.

Additionally, many other important factors are considered (and documented on your pathology report) before you receive your final stage: tumor grade; biomarkers, including your *HER2*, *ER* and *PR* status; molecular and genetic changes in cancer tissue; and results from multi-gene panels such as MammaPrint, Oncotype DX, PAM 50 (Prosigna), EndoPredict and Breast Cancer Index.

As you talk with your doctor about the recommended treatment plan, consider seeking a second opinion from a doctor or cancer center with extensive experience treating *HER2*+ breast cancer.

GUIDING TREATMENT DECISIONS

With *HER2*+ breast cancer, it is common to use anti-*HER2* targeted therapy to slow or stop the growth of the cancer (see *Treatment Planning*, page 8). Anti-*HER2* drugs are approved for all stages of *HER2*+ breast cancer, and they are often used along with other treatments.

It is common to begin one targeted therapy and then be switched to a different one. Because *HER2*+ breast cancer is characterized by multiple mutations, the cancer may become resistant to treatment. This means the cancer stops responding to therapy and begins to grow again, requiring a change of treatment. In *HER2*+ breast cancer, this has been reported with some types of chemotherapy and targeted therapy. Research is ongoing to determine what causes resistance so that it can be prevented. ■

TABLE 1

STAGES OF BREAST CANCER

Stage	T	N	M
0	Tis	N0	M0
IA	T1	N0	M0
IB	T0 or T1	N1mi	M0
IIA	T0 or T1 T2	N1 N0	M0 M0
IIB	T2 T3	N1 N0	M0 M0
IIIA	T0-T3 T3	N2 N1	M0 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.

TABLE 2

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 cM0(i+)	No clinical or radiographic evidence of distant metastases. 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.

Testing provides pathway to personalized treatment plan

Diagnosing any breast cancer involves blood tests, imaging tests and a biopsy, but the definitive factor to determining a *HER2+* breast cancer diagnosis begins with genomic testing. This type of molecular testing uses a microscope to examine the DNA of a tumor and look for extra *HER2* genes or *HER2* receptors on the cancer cell — the two main characteristics of *HER2* status. Once the results of all the testing are reviewed, your doctor will suggest a treatment plan specifically for you.

All breast cells contain two copies of the human epidermal growth factor receptor-2 (*HER2*) gene. The normal gene makes *HER2* proteins, which are receptors on the surface of a cell. Together, the genes and protein receptors help manage how a breast cell grows, divides and repairs itself.

Some breast cancers have more than the normal two copies of the *HER2* gene, leading to an overexpression of *HER2* receptors as well as an increased number of copies of genes.

HER2 testing is typically performed with invasive breast cancer. It is not routinely tested with ductal carcinoma in situ. Testing may be repeated if the breast cancer spreads or recurs after treatment.

WHAT IS GENOMIC TESTING?

By examining a cancer's genes, genomic testing may reveal mutations that could indicate the cancer's behavior, how aggressive it might be and how likely it is to metastasize (spread).

Genomic testing is typically performed on the initial biopsy material and may be repeated if the cancer recurs. It may also be used to detect biomarkers, which are substances such as genes or molecules that can be measured in the blood, plasma, urine, cerebrospinal fluid or other body fluids or tissues. Biomarkers are produced by cancer cells or other cells of the body in response to cancer.

Estrogen receptor (*ER*), progesterone receptor (*PR*) and *HER2* are considered the three main biomarkers in breast cancer. Doctors will test the tumor for these three biomarkers at the time of initial diagnosis and usually if it recurs. If the cancer is *ER+* or *PR+*, it is driven by hormones. As a result, hormone (endocrine) therapy designed to block the hormones that feed the cancer may be used. For *HER2+* breast cancer, anti-*HER2* drug therapy is often used along with other therapies (see *Treatment Planning*, page 8).

Other biomarkers in breast cancer that may be tested include cancer antigen 15-3 (CA 15-3), cancer antigen 27.29 (CA 27.29) and/or carcinoembryonic antigen (CEA). In some cases, testing may be done for circulating tumor cells, which may indicate spread.

Other mutations that have been found in *HER2+* cancers that may also be tested include *BRAF*, *EGFR*, *KIT* and *PIK3CA*. These mutations may indicate a cancer that is likely to become resistant to some forms of therapy. Research is ongoing to find more mutations that may influence how *HER2+* breast cancer is treated.

The *HER2* biomarker may be detected by two possible tests that are performed on biopsied tumor tissue.

- Immunohistochemistry (IHC) testing measures the amount of *HER2* proteins on the surface of breast cancer cells. Based on the number of proteins, a score is given to determine whether the cancer is *HER2+*. It uses a scale of 0 to 3+ with 0 meaning the cancer is *HER2-*, and 3+ meaning the cancer is *HER2+*. If the score is 2, another test such as the FISH test may be used or you may send your results to another cancer center for a second opinion. The IHC test is typically performed first because the results can be returned quicker, and a 0 or 3+ usually requires no further testing.
- Fluorescence in situ hybridization (FISH) testing uses fluorescent dye that attaches to certain pieces of DNA in a tissue sample. This test evaluates *HER2* gene amplification. It is performed if the results of the IHC testing were inconclusive or in doubt. The results take longer to return than for IHC testing, but this test is considered more definitive.

Genomic testing of the tumor may also be performed to determine a person's risk for a recurrence. Tests provide a score that may be useful in determining whether hormonal therapy or chemotherapy is recommended to prevent a recurrence.

UNDERSTANDING GENETIC TESTING

Though genomic testing is used to determine the *HER2* status, genetic testing may also be performed because the BReast CAncer 1 (*BRCA1*) and BReast CAncer 2 (*BRCA2*) genes are the most commonly inherited mutated genes known to cause breast cancer.

Identifying inherited mutations allows people at an increased risk to be monitored more closely for the development of cancer. A family history of a certain cancer may prompt you to be tested to see whether you carry a mutated gene. The test to see whether you have an inherited mutation is usually performed on saliva or blood. Having an inherited mutation doesn't mean you will automatically develop cancer; it only means the risk is increased.

These tests are generally ordered by a doctor or other health care provider if there is concern you may have an inherited risk of cancer. Doctors may test for one gene or a small number of genes, which is called single/limited gene panel testing, or many genes, which is called multi-gene panel testing. Typically, the blood or saliva sample is collected and sent to a laboratory for testing.

Keep in mind that getting genetic testing is a decision that affects your entire family. Knowing and sharing the information could help them be screened and monitored closely if they have a gene mutation associated with cancer. Preventing or detecting a cancer early offers the best chance of a successful treatment outcome. ■

What is a Mutation? ▸ **Doctors now understand that cancer arises from changes that occur in a person's genes. Known as mutations, they can cause cells to grow out of control and become cancer cells. Mutations can be acquired during a person's lifetime from environmental factors or inherited from a parent at conception. Understanding the role of mutations in cancer has allowed doctors to develop better prevention strategies and treatments that target these specific characteristics.**

When Connie Stafford received a Stage II triple positive breast cancer diagnosis at 60, she was grateful for the love and support provided by her friends and family. Notorious for taking copious amounts of notes, she dedicated herself to being informed and asked lots of questions. Today, she is cancer-free and loving life.

A lot of research and support helped this survivor never give up

From the start, I focused on my desire to learn, the encouragement of family and friends, an amazing medical team and faith in God to get me through cancer. As soon as I found out I had Stage II *ER+*, *PR+*, *HER2+* breast cancer, I called my family from the doctor's office. They, in turn, contacted more family and friends. By the time I arrived home, 20 to 30 people were waiting for me. They laid their hands on me and prayed over me. I knew then I was never going to be alone.

My family made sure that I never went to an appointment or treatment without someone with me. It was helpful to have someone to help me remember what the doctors said.

I carried a notebook with me to every appointment, took a lot of notes and always had a list of questions ready for the doctors. During a visit for a second opinion, the doctor asked me if I would put down the notebook so he could do a physical exam. I agreed, but picked it right back up once he was finished.

As a goal-oriented person, I made sure I understood everything the doctors said. I researched my type of breast cancer and spoke with many specialists to gather the most information to help me make the best decisions for me. I told them to tell me everything!

After doing my research and talking with my oncologist, breast surgeon, plastic surgeon and radiologist, the consensus was that I should have chemotherapy as well as drug therapy specifically for *HER2+* patients, followed by surgery to remove the tumor and reduce the size of my breast, which in turn, would reduce the area that needed radiation therapy. About a month after I was diagnosed, I had a port put in and started the drug therapies. At the time, I was an early childhood resource teacher, and I was determined to finish my 29-year career. I scheduled chemotherapy on Thursdays, stayed home Fridays and returned to work Mondays. Every three weeks I would additionally receive the *HER2+* drug therapy along with the chemotherapy. Luckily, my employer was flexible with me.

Once chemotherapy made my hair fall out, my nephew shaved it all off for me. I took advantage of the hospital's free wig program but soon realized I hated wearing wigs. Once my chemotherapy was finished, I removed the wig, put on makeup, eyelashes and some jewelry and walked back into work bald. I was worried my students and other teachers would think I was a man without my hair, but they didn't and I was very relieved. Over time, my hair grew back.

Follow-up scans four months later showed the tumor was gone. The surgeon moved forward with removing any tissue the tumor may have touched and performed the breast reduction surgery. I then began radiation therapy.

Before my diagnosis, I was a very healthy person. I enjoyed line dancing every Tuesday night, walked regularly and watched my weight. Being healthy got me through treatment. However, the steroids I took along with the chemotherapy made me ravenously hungry. At first, I ate what I wanted, but once I started gaining weight, I backed off. Then when I felt hungry, I'd stir fry a bunch of vegetables instead of reaching for a milkshake. I only gained 15 pounds and lost most of it after treatment ended.

Learning I had cancer devastated me. At first, I was shattered and angry. I had been so careful about leading a healthy lifestyle that I felt a bit betrayed by my body for getting cancer. That's where leaning on my family, my church and my faith in God helped. When I felt down, I took advantage of the many supportive services my cancer center offered, including a free massage every month, lectures, educational materials, where to find free wigs, and so much more. If you don't know if your cancer center offers these services, be sure to ask. They were incredibly helpful.

After my surgery, I remained on the *HER2+* medication for a year until my treatment was finished and I was considered cancer-free. Then for five years, I took a different medication to prevent a recurrence.

My doctor also recommended I get genetic testing. Although cancer did not run in my family, I decided to have it done. No mutations were found. Certain factors indicated an increased risk but nothing definitive. Ten years later, they repeated the testing because technology had improved and they wanted to see if they could learn anything new. But nothing new was found.

If you are facing a breast cancer diagnosis, I recommend getting different opinions, not just one. Believe in prayer, and trust in God. Push yourself. You may not be able to do as much if you're on chemotherapy because it can slow you down, but don't give up on yourself or your treatment. Stay as positive as you can, and never quit. ■

Ongoing progress means more treatment options

Advances in research and approved therapies designed to target *HER2*+ breast cancer provide doctors with more tools to design a treatment plan that is uniquely personalized for you and your diagnosis. Targeted agents and chemotherapy are often effective treatment in combination with surgery and radiation therapy.

You will work closely with your medical team to define your goals of treatment. Your doctor will consider key information, including your age and general health, menopausal status (for women), size of the tumor, its biomarker status (*HER2*, *ER*, *PR*), stage and, if applicable, genetic mutations such as *BRCA1* (BReast CAncer 1) and *BRCA2* (BReast CAncer 2). You will contribute information about things that are important to you, such as being able to continue working, ensuring you are able to attend and participate in key life events, and your expectations for your quality of life in general.

CANCER TREATMENT BASICS

Right from the beginning, you should be aware that cancer treatment may be fluid. The treatment plan you start with will likely change based on many factors. Your doctor may adjust your treatment if your cancer becomes resistant (when breast cancers stop responding to therapy and begin to grow again) or if it recurs (returns), or to make side effects more tolerable.

It is common to have more than one type of treatment. Local treatments, including surgery and radiation therapy, target specific areas of the body. Systemic treatments, including drug therapies, travel throughout your body. Drug therapies can be given by injection, orally or intravenously (IV) through a vein in your arm or through a port. Many people have a port placed so they can receive the medicine without repeatedly being stuck with a needle or damaging their veins. A port is surgically inserted under the skin in the upper chest area or arm to gain easy access to veins (see Figure 3).

Treatments are often referred to by when they're given. Because surgery is the most common option for many types of breast cancer, treatment given before surgery is called neoadjuvant therapy. Treatment given after surgery is called adjuvant therapy. Whether delivered before or after surgery, an important goal of systemic therapy is to destroy breast cancer cells that may be hiding in other organs of the body, such as the liver, lungs, bones or brain. These hidden cancer cells, called micrometastatic disease, are usually too small to detect with laboratory testing or imaging studies. Delivering carefully selected systemic therapy to appropriate patients can often completely eliminate micrometastatic disease and is, therefore, extremely important as a partner with surgery for breast cancer in helping a patient become disease-free.

Before surgery, your doctor may choose to treat your breast cancer with targeted therapy, chemotherapy or radiation therapy to shrink a tumor so it can be more easily or safely removed with surgery. It may offer you more surgical options, including breast-sparing treatment (lumpectomy and breast irradiation therapy). It may also offer valuable information about how your tumor responds to certain drugs and even help inform the need for additional treatment postoperatively. After surgery, these and other treatments may be used to destroy remaining cancer cells.

You may be a candidate for extended adjuvant therapy, which is designed to further reduce the risk of the cancer returning.

TYPES OF TREATMENT

Surgery is often the first treatment used for early-stage *HER2*+ breast cancers. For metastatic cancer that has spread beyond axillary lymph nodes, surgery typically is used only to prevent or treat symptoms or complications.

A *lumpectomy* removes the tumor along with a small margin of normal-appearing tissue around it (see Figure 1). It is used for early-stage breast cancers detected as small tumors, including Stages 0, I and II, and it is considered to be breast-conserving or breast-sparing.

Lumpectomy is usually followed by adjuvant breast radiation treatments designed to kill microscopic cancer cells hiding in other parts of the breast. If your tumor is relatively small and you wish to spare as much of your breast as possible, this surgical plan may be an option. Some patients are considered to be poor candidates for a breast-conserving lumpectomy because of abnormalities seen on their breast imaging (mammogram or ultrasound) or because of the inability to receive radiation treatment. It is also important that you discuss the likely cosmetic outcome of breast-conserving surgery with your doctor because surgery and radiation can cause some alteration to the shape of the breast.

Removal of the entire breast is known as a *mastectomy*. It may be the preferred opera-

FIGURE 1
LUMPECTOMY AND AXILLARY SURGERY

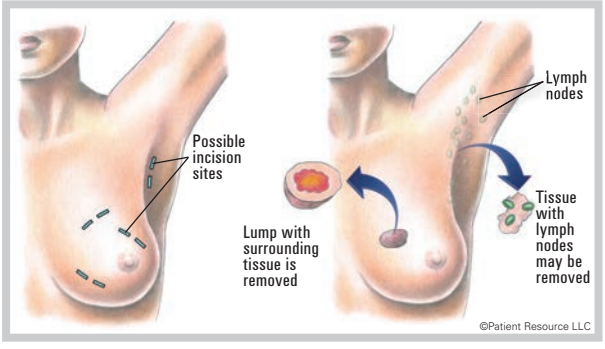
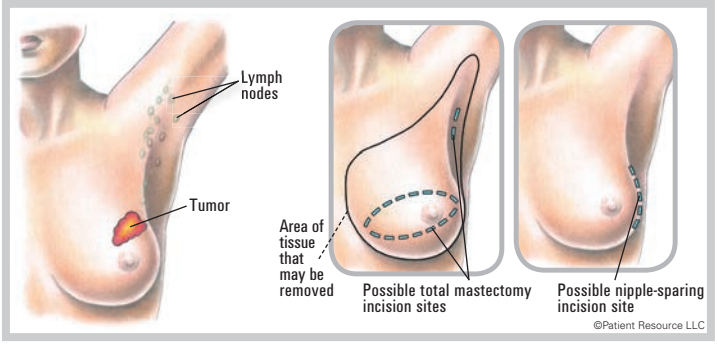


FIGURE 2
MASTECTOMY



tion for patients with 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 is the surgical removal of the entire breast without removing muscle. A modified radical mastectomy means that the total mastectomy is being performed along with removal of a block of underarm/axillary lymph node tissue (axillary dissection). Skin-sparing and nipple-sparing mastectomies that improve the cosmetic outcome of reconstruction can be performed.

At the end of the mastectomy procedure, it is common for the surgeon to place drains into the area to collect fluid from the breast region. The incision will then be closed, and the area will be covered by a bandage. Your health care team will give you information for incision and drain care, if applicable.

After the incisions have healed, outpatient radiation treatment to the breast may be necessary usually for treatment of larger tumors or those with multiple metastases to lymph nodes.

Chronic nerve pain, known as post-mastectomy pain syndrome (PMPS), may occur. The most common areas to feel this pain are in the chest, armpit and/or arm. Symptoms include tightness, burning, tingling or itching. The surgical site may also have numbness or may be extra sensitive. Tell your doctor immediately to ensure your PMPS is managed as effectively as possible. PMPS usually will not go away without treatment.

After a mastectomy, you may have phantom pain. Your brain may treat your mastectomy site as if the breast were still present, and you may feel nipple or breast pain. Over time, the brain adjusts to the absence of the breast.

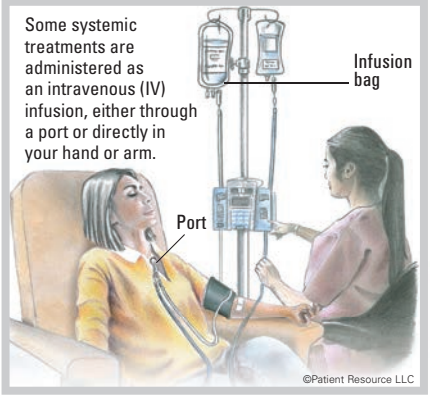
Lymph node surgery is usually necessary to either stage the cancer or to control cancer that is known to have spread to the nodes. The underarm (axilla) is the most important location for management of lymph nodes in breast cancer patients as it is the most common site for breast cancer to spread.

Most women will undergo an initial staging procedure of their lymph nodes at the same time as their breast surgery. This staging procedure is called a sentinel lymph node biopsy. The sentinel node is the first node to which a cancer spreads. If the sentinel nodes contain a tumor, sometimes a more extensive operation to remove additional lymph node-bearing tissue from the underarm may be necessary, and this is called an axillary lymph node dissection (see Figure 1). As you discuss this part of your treatment plan, ask your doctor about strategies for this surgery that may reduce the risk of lymphedema, a common side effect of surgery.

In some cases where radiation therapy and systemic therapy are given after a lumpectomy, no further axillary surgery is recommended even when there are metastases in the sentinel node. Some patients will have cancerous axillary lymph nodes detected by a needle biopsy performed prior to their breast surgical procedure. If a needle biopsy reveals a metastatic lymph node, then neoadjuvant chemotherapy may be recommended. And if the neoadjuvant chemotherapy is successful in clearing/killing the axillary lymph node disease, the axillary lymph node dissection may be avoided.

FIGURE 3

SYSTEMIC THERAPY



Drug therapy may include one or more of the following.

Targeted therapy is systemic therapy that uses drugs or other substances to identify and attack cancer cells. Targeted therapy drugs that specifically treat *HER2*+ breast cancer are called anti-*HER2* drugs or *HER2* inhibitors. These target and attach to specific parts on the cancer cell to interfere with or stop its growth. Some are oral medications given in pill form, and others are given intravenously (IV) into a vein. Some may be given alone or in combination with other drug therapies. Your doctor may prescribe more than one type of anti-*HER2* drug. It may be used as neoadjuvant therapy, adjuvant therapy or extended adjuvant therapy.

Chemotherapy drugs stop the growth of cancer cells by killing them or preventing them from dividing and growing. For early-stage *HER2*+ breast cancer, chemotherapy and *HER2* targeted therapy may be given as a combination of two or three drugs or one after the other. For metastatic *HER2*+ breast cancer, chemotherapy is often combined with other anti-*HER2* drugs.

Chemotherapy may be given as neoadjuvant therapy or adjuvant therapy. When given before surgery, it may be used to shrink a tumor so it can be surgically removed or to reduce the tumor's size to allow for a lumpectomy rather than a mastectomy. It may also permit you to avoid having an axillary dissection if nodal disease is eradicated. Neoadjuvant chemotherapy also has an advantage of helping your doctor determine how well the chemotherapy drugs work against the tumor. Adjuvant chemotherapy is given to destroy cancer cells that may remain after surgery, some of which may be too small to be detected with laboratory testing or imaging studies.

Hormone therapy, also called endocrine therapy, may be prescribed if your disease is estrogen receptor positive (*ER*+) or progesterone receptor positive (*PR*+). Hormone therapy is designed to lower the amount of estrogen in your body or block the hormone receptors on the cancer cells. Many types of hormone therapy drugs are available.

Radiation therapy uses high-energy radiation to destroy cancer cells and shrink tumors. It may be necessary along with surgery. Some people with localized disease or bone pain that does not lessen with chemotherapy may receive it to specific affected parts of the body.

Radiation therapy is usually recommended after a lumpectomy to destroy any cancer cells that may remain hidden in normal-appearing breast tissue. Research shows that women with a small tumor who have radiation therapy after a lumpectomy live as long as those who have a mastectomy. Radiation therapy is sometimes necessary after a mastectomy and is typically recommended for individuals at high risk for cancer recurrence on the chest wall, such as women with cancer in multiple axillary lymph nodes or a large cancer.

The most common type of radiation therapy, external-beam radiation therapy (EBRT), is delivered from an external machine. Brachytherapy may also be used either alone or in combination with EBRT for lumpectomy patients. Brachytherapy involves placing radioactive seeds through a catheter into the breast to deliver radiation directly to the area where the tumor was removed.

Clinical trials are research studies that may offer access to treatments not yet widely available. Research is ongoing to test drug combinations, new drugs and the sequence

Continued on page 10

of prescribing drugs to address drug resistance. Ask your doctor if you should consider a clinical trial.

MONITORING FOR RECURRENCE

Even after successful treatment, breast cancer can recur in one or more ways. Local recurrence is a regrowth of the cancer at the site of a lumpectomy or mastectomy. Regional recurrence is regrowth of cancer in the lymph nodes in the armpit or above the collarbone (clavicle). Distant recurrence is metastasis (spread) of the breast cancer to other organs. You may have symptoms or your doctor will see signs on a CT or PET scan. A cancer that appears in the other breast is most often a new cancer, not a recurrence.

After treatment, your doctor will monitor for signs of cancer with regular exams and blood tests. You will likely have mammograms of both breasts after a lumpectomy. At or between exams, tell your doctor if you notice new symptoms in your breasts or other health changes.

Maintenance medication or extended adjuvant therapy may be used to help prevent recurrence. These drugs are typically taken for many months or years without stopping. Medication adherence is critical. If you miss one or more doses, tell your health care team.

RECONSTRUCTION CONSIDERATIONS

When it is time to make decisions about reconstruction after mastectomy, remember that it is an extremely personal decision that only you can make, and it is one that you should not rush. Before you make any decisions, learn about your options and think about what will make you most comfortable. Meet with a team experienced in breast reconstruction. Sometimes the initial stage of a reconstruction can be done at the time of mastectomy.

Many advocacy groups offer peer counseling so you can ask questions of women who have had reconstruction procedures. Ask your nurse/patient navigator for referrals. In addition, consider the following:

- Do your breasts play a crucial role in your personal sense of femininity and sexuality? If so, you may be eager to replace them to feel more like your pre-cancer self. That may involve reconstructive surgery, which includes flap reconstruction and implant-based reconstruction (see www.PatientResource.com/HER2_Breast_Cancer_Reconstruction.aspx). If you are having a mastectomy or lumpectomy, your doctor will likely discuss breast reconstruction, which involves additional surgeries to restore or reshape one or both breasts. Reconstructive surgery is often performed, or at least started, during a mastectomy or can be delayed for a few months or even years. Mastectomy patients undergoing immediate reconstruction may be eligible for enhanced cosmetic approaches, such as skin-sparing or nipple-sparing mastectomy. Reconstruction may be done during or after a lumpectomy if the surgery will cause the affected breast to look significantly different from the other after the tumor is removed. Your plastic surgeon will work with you to set expectations for your new or reconstructed breast(s). It is important to realize that your breast(s) will not look or feel exactly as they did before or have the same sensation.
- Non-surgical options, such as a breast prosthesis, are also available. Made from artificial materials, the prosthesis is designed to provide a natural, symmetrical appearance when you're dressed. You must wait until you're healed from surgery to be fitted for a prosthesis. One type is worn inside the hidden pocket of a mastectomy bra. Another type attaches to your body with a special adhesive, though this approach may not be recommended after chest wall radiation therapy. Mastectomy bras are available in many styles and colors. Many health insurance providers will cover the costs of a prosthesis and mastectomy bras if you provide a prescription from your oncologist or oncologic surgeon. Call your insurance provider to verify which mastectomy-related products are covered, the documentation required for reimbursement and how often you can purchase replacements.
- Not having reconstruction is an option you may not be aware of. This is often referred to as "going flat," which means not having a breast prosthesis, enhancement or additional surgery. ■

COMMON DRUG THERAPIES FOR *HER2+* BREAST CANCER

These therapies may be used alone or in combination. For some combination therapies your doctor might suggest, go to https://www.patientresource.com/HER2_Breast_Cancer_Treatment.aspx

CHEMOTHERAPY

- capecitabine (Xeloda)
- carboplatin (Paraplatin)
- cisplatin
- cyclophosphamide
- docetaxel (Taxotere)
- doxorubicin (Adriamycin)
- epirubicin (Ellence)
- eribulin (Halaven)
- fluorouracil (5-FU)
- gemcitabine (Gemzar)
- ixabepilone (Ixempra)
- liposomal doxorubicin (Doxil)
- paclitaxel (Taxol)
- protein-bound paclitaxel (Abraxane)
- vinorelbine (Navelbine)

TARGETED THERAPY

- ado-trastuzumab emtansine (Kadcyla)
- fam-trastuzumab deruxtecan-nxki (Enhertu)
- lapatinib (Tykerb)
- margetuximab-cmkb (Margenza)
- neratinib (Nerlynx)
- pertuzumab (Perjeta)
- pertuzumab, trastuzumab and hyaluronidase-zzxf (Phesgo)
- trastuzumab (Herceptin)
- trastuzumab and hyaluronidase-oysk (Herceptin Hylecta)
- tucatinib (Tukysa)

HORMONE THERAPY

- anastrozole (Arimidex)
- ethinyl estradiol
- exemestane (Aromasin)
- fluoxymesterone
- fulvestrant (Faslodex)
- goserelin acetate (Zoladex)
- letrozole (Femara)
- leuprolide acetate (Eligard, Lupron, Lupron Depot)
- megestrol acetate (Megace)
- tamoxifen
- toremifene (Fareston)

As of 6/29/22

Understanding the importance of medication adherence

Taking the right drug in the right dose at the right time – every time – for as long as prescribed is referred to as medication adherence. Adherence is extremely important to get the most benefit from a drug. Whether you are taking oral therapy (pills) or getting IV treatments, you are responsible for taking your treatment as prescribed.

Make sure you fully understand your medication instructions. Track each dose, including missed doses or appointments, and detail any side effects. Many types of medication reminders and organizers are available.

You may be tempted to skip a dose or an appointment to avoid uncomfortable side effects or save money, but even small changes to your regimen can disrupt your treatment and affect its outcome. Most cancer medications are designed to maintain a specific level of drugs in your system for a certain time based on your cancer type and stage, your overall health, previous therapies and other factors. Talk with your doctor about options for managing any symptoms or side effects. To learn about financial assistance that may be available, flip this guide over and turn to page 12.

Proactively managing side effects

Though a fear of side effects is very normal for people when they are planning cancer treatment, many advances have been made to prevent and relieve them. The most important thing is to communicate honestly with your health care team about how you feel, both physically and emotionally. The sooner they are aware of any changes, the quicker they can help.

Your health care team members will use supportive care services to help address the physical, emotional, practical, spiritual, financial and family-related challenges you may experience. Ask your nurse navigator about the supportive care services offered at your cancer facility and in your area.

COMMON SIDE EFFECTS

As you and your doctor review your treatment options, discuss the potential physical and emotional side effects of each type and what to do should they occur, including any that require immediate attention (see Table 1).

Your doctor may be able to adjust your medications to make them more tolerable, so keep the lines of communication open. And remember, every person's reaction to treatment is unique, even when the diagnosis and the treatment are similar.

YOUR EMOTIONAL WELL-BEING

Find a support group for breast cancer survivors online or in your area. Opening up to people who have had a similar experience can offer comfort and support that are invaluable. Talking with a licensed counselor may also help you work through these and other difficult emotions.

Anxiety can begin as soon as you receive your diagnosis. Moderate to severe anxiety is often treated with medication, therapy or a combination of both. Explore relaxation techniques, such as meditation, muscle relaxation, yoga or guided imagery.

Depression is not "just part of having cancer." If these feelings last more than a few days or if you have thoughts of death or of attempting suicide, seek medical attention immediately.

Fear is common, and every ache and pain may trigger a concern. Do your best to stay focused on the present.

Scanxiety is the anxiety that can happen when you are awaiting results from imaging scans, laboratory tests or exams. These feelings are normal to have because every set of results could be life-changing. Talk with your doctor or nurse so you know when to expect results. Staying busy gives you less time to worry.

Sexuality issues, such as lack of interest or feeling less desirable, may occur. Sexual health is an important part of life. Share your concerns with your doctor. If you have a partner, be open with your feelings and about finding new ways to be intimate. ■

Post-surgical drain care

▶ **After surgery,** fluid buildup can cause pain and slow the healing process. To help, your surgeon is likely to insert one or more drains after breast or lymph node(s) surgery or after reconstruction. Designed to help remove fluid buildup, these drains will remain in place for days to weeks depending on how quickly the excess fluid drains.

While you are in the hospital, a nurse will empty the drains and track the amount of drainage. You and a caregiver will be shown how to care for the drains at home as well as how to monitor for signs of infection.

Consider wearing loose-fitting tops or a drain management garment, which is a special cotton camisole designed for drains. You may have to adjust how you bathe while the drains are in place.

TABLE 1

SOME COMMON SIDE EFFECTS

Side Effect	Symptoms
Anemia	Low energy, weakness, dizziness, light-headedness, shortness of breath, rapid heartbeat
Blood clots	Leg discomfort
Bone loss and pain	Weakened bone caused by the cancer or treatment
Cardiotoxicity	Shortness of breath, chest pain, heart palpitations, fluid retention in legs
Chemo brain	Brain fog, confusion and/or memory problems
Constipation	Difficulty passing stools or less frequent bowel movements
Decreased appetite	Eating less than usual, feeling full after minimal eating, not feeling hungry
Diarrhea	Frequent loose or watery bowel movements
Fatigue	Tiredness that is increased and harder to relieve than typical fatigue
Fever	Raised body temperature that could signal an infection
Hair loss (alopecia)	Hair loss on the head, face and body
Hand-foot syndrome	Pain, swelling, tightness and redness on the palms of the hands or the soles of the feet
Headache	Pain or discomfort in the head
Hepatotoxicity	Jaundice (yellowing of skin and whites of eyes), itching, abdominal pain in upper right abdomen
Lymphedema	Swelling where lymph nodes have been removed or damaged
Mouth sores	Small cuts or ulcers that can affect the gums, tongue, roof of the mouth or lips
Nausea and vomiting	The feeling of needing to throw up and/or throwing up
Neuropathy	Numbness, pain, burning sensations and tingling, usually in the hands or feet
Neutropenia	Low white blood cell count that increases the risk of infection
Pain	Pain and aches in the muscles, bones, tendons, ligaments or nerves
Respiratory problems	Shortness of breath (dyspnea) with or without cough, upper respiratory infections
Skin reactions	Rash, redness and irritation, or dry, flaky or peeling skin that may itch
Sleep problems	Insomnia (the inability to fall asleep or stay asleep), disruption of the wake-sleep cycle and excessive sleepiness
Thrombocytopenia	Low number of platelets in the blood, which can lead to bruising and bleeding
Weight changes	Gaining or losing weight unintentionally

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