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BREAST CANCER RESOURCE GUIDE

Focus on making the best plan for you

CYNTHIA NEWSOME

AWARD-WINNING JOURNALIST SHARES HER BREAST CANCER JOURNEY

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New treatment advances are due to specialized testing

Diagnosing and treating breast cancer has changed dramatically in recent years due to the increasing use of genomic and genetic testing. These tests help a doctor pick the treatment course best suited for a specific type of breast cancer. This emphasis on specialized testing is helping to drive treatment choices, providing more personalized therapy options.

Doctors now understand that not all breast cancers are alike. In fact, breast cancer is a complex disease characterized by mutations in genes and proteins that cause cells to grow out of control. Diagnosing any breast cancer involves blood tests, imaging tests and a biopsy, but the definitive factor to determining a breast cancer diagnosis begins with genomic testing of the biopsy sample after surgery.

UNDERSTANDING GENOMIC TESTING

Genomic testing may reveal mutations and biomarkers that could indicate the cancer's subtype and behavior, how aggressive it might be and how likely it is to metastasize (spread). Biomarkers are substances such as genes or molecules that can be measured in the blood, plasma, urine, cerebrospinal fluid or other body fluids or tissues. They are produced by cancer cells or other cells of the body in response to cancer.

The three biomarkers routinely tested for during the breast cancer diagnostic process are estrogen receptor (*ER*), progesterone receptor (*PR*) and human epidermal growth factor receptor-2 (*HER2*). Knowing the status of these three biomarkers helps your doctor know whether you will benefit from chemotherapy and/or hormone therapy (also called endocrine therapy). If the cancer is driven by estrogen or progesterone, hormone therapy may be used to lower the risk of a recurrence. If a *HER2* mutation is driving the cancer, drugs that target *HER2* may be recommended.

The genomic tests can also be performed during treatment or if the cancer returns to identify different mutations than before that may affect treatment options. The development of a new tumor in the breast will also require testing because it may have different mutations than the first tumor.

Other genomic tests may be performed to evaluate and predict a possible recurrence. Tests provide a score that may be useful in determining whether hormone therapy or chemotherapy is recommended to prevent a recurrence. These tests are multi-gene panels,

which are used to determine whether adjuvant or extended adjuvant chemotherapy should be used.

TYPES OF TESTS

A variety of tests may be used for genomic testing (see Table 1). Some of the tests are known by specific names and are used to find different types of information about your breast cancer.

Your doctor will decide which test provides the kind of information that will aid in treatment. Following are some of the types used for genomic testing.

- Immunohistochemistry (IHC) tests for certain antigens (markers) and may also be used to determine the difference between cancer subtypes. In breast cancer, it is used to measure 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 fluorescence in situ hybridization (FISH) test, may be used. Results may also be sent 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.
- FISH testing uses fluorescent dye that attaches to certain pieces of DNA in a tissue sample. It looks at genes or chromosomes in cells and tissues and identifies where a specific gene is located on a chromosome, how many copies of the gene are present and any chromosome abnormalities. For breast cancer, 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.
- Microarray testing generates a genetic profile for a given tissue sample that reflects the activity of thousands of genes and helps to identify subtypes.
- Polymerase chain reaction (PCR) looks for certain changes in a gene or chromosome.
- Reverse transcription PCR (RT-PCR) is used to look for activation of certain genes that may help diagnose cancer.

THE ROLE OF GENETIC TESTING

Though genomic testing is used to determine the status of *ER*, *PR* and *HER2*, genetic testing may also be performed to identify the BReast CAncer 1 (*BRCA1*) and BReast CAncer 2 (*BRCA2*) genes, 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 does not mean you will automatically develop cancer; it only means the risk is increased.

The following risk factors may indicate that you have inherited an abnormal gene:

- Family history of cancer
- Cancer at an early age
- Multiple cancers in one relative
- History of rare cancers
- Certain ancestry, such as Ashkenazi Jewish heritage

These tests are generally ordered by a doctor or other health care provider if there is a concern that 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. Typically, the blood or saliva sample is collected and sent to a laboratory for testing.

Though some genetic tests are available to purchase without a doctor's involvement, they are not recommended for a person who may have cancer. The sensitivity of these tests is unknown compared to those used by doctors and designated laboratories, and the tests may not screen for all the possible genes and mutations for a particular cancer. The laboratories doctors use are regulated by the Clinical Laboratory Improvements Amendments program to meet standards for accuracy and reliability.

Getting genetic testing is a decision that can affect your entire family. Knowing and

TABLE 1

SOME TYPES OF GENOMIC TESTING USED FOR BREAST CANCER

Genomic Test	Type of Test	Reason for Test	Indications
21-Gene Recurrence Score (Oncotype DX)	Quantitative polymerase chain reaction	Determine the use of adjuvant chemotherapy in *ER*+, *HER2*- breast cancer with or without lymph node involvement	Only patients with high-risk recurrence scores may benefit from chemotherapy
70-Gene Breast Cancer Recurrence Assay (MammaPrint)	Algorithm on whole-genome expression array	Determine prognosis for Stage I and II *HER2*- invasive breast cancer regardless of *ER* or *HER2* status that has spread to 3 or fewer lymph nodes	Prognostic tool for early-stage breast cancer; high risk score indicates a benefit from chemotherapy
Breast Cancer Index	Anti-apoptotic homeobox B13-to-interleukin 17B receptor expression ratio (H:I ratio), representing a 2-gene ratio, and the Molecular Grade Index, representing five proliferation genes	Determines probability of benefiting from extended adjuvant endocrine therapy in post-menopausal patients with *ER*+, lymph node negative disease	A high H:I ratio in *ER*+ and positive lymph node involvement breast cancer indicates benefit from extended adjuvant endocrine therapy
EndoPredict	Reverse transcriptase polymerase chain reaction (RT-PCR)	Used to calculate a comprehensive risk score. Identifies patients with *ER*+, *HER2*- tumors with 3 or fewer lymph nodes affected and who have a low risk for late recurrence without adjuvant chemotherapy	Guides treatment decisions on whether to use chemotherapy and anti-hormonal therapy
Ki-67 Assay, including ICH4, PEPI	Immunohistochemical staining	An estimate of the rate of growth (proliferation) that is helpful in selecting the type of chemotherapy given	High Ki-67 expression indicates higher tumor growth rate
PAM50	Microarray and quantitative reverse transcriptase	Measures expression levels of 50 genes, defines subtype, provides a risk category and creates a risk of recurrence score	Adds prognostic value to the characteristics of the tumor

sharing the information could help them be screened and monitored closely if they have a gene mutation associated with cancer. Prevention and detection offer the best chance of a successful treatment outcome.

The results may be complicated and difficult to interpret. A genetic counselor can guide you through the testing process so you understand what the results mean for you, your family members and their future health. Family members may be offered genetic testing if a mutation is found.

Special training enables a genetic counselor to provide guidance to you and your family members before and after you have genetic testing. The genetic counselor will discuss your medical history and cancer screening history, your family's cancer history, the possibility of an inherited cancer risk, the benefits and limitations of genetic testing, and current laws regarding the privacy of genetic information. The counselor can also help find out whether your health insurance will pay for the cost of the test.

Ask your nurse navigator for a referral to a genetic counselor. ■

The Importance of Getting a Second Opinion

Gathering as much information as you can before starting treatment may help you feel more confident in making the decisions ahead. This may include getting a second or third opinion to confirm the diagnosis and potential treatment options. Another doctor's opinion may change the diagnosis or reveal a treatment your first doctor was not aware of. And, this is the perfect time to seek out a doctor that specializes in your type of breast cancer who may have access to leading-edge therapies.

Doctors bring different training and experience to treatment planning. Some doctors may favor one treatment approach, while others might suggest a different combination of treatments.

A second opinion is also a way to make sure your pathology diagnosis and staging are accurate, and that you are aware of clinical trials that you might want to consider. You need to hear all the facts about your treatment options. There is often collective wisdom gained from the experience and opinions of different oncology specialists who are experts in your type of cancer.

The process involves asking another cancer specialist or group of specialists to review your medical records and confirm your doctor's diagnosis and treatment plan. Finding these experts is not always easy, and you may worry that you will offend or hurt your doctor's feelings if you seek the advice of another expert. Many people feel uncomfortable and even disloyal seeking another opinion, but you should not. Most doctors welcome a second opinion and will recommend another physician or hospital. Above all, the goal is for you to have the best care available.

Before meeting with another medical professional for a second opinion, make sure medical records related to your cancer are available. This may include laboratory, biopsy or imaging test results as well as any other tests or procedures. It may be helpful to call the doctor's office to find out whether any information needs to be sent ahead of the appointment.

Many factors influence your treatment strategy

People who have breast cancer are frequently asked about the stage of their disease. Generally, a lower stage, such as Stage I, is often curable, whereas a higher stage cancer, such as Stage IV, indicates a more serious prognosis. Your doctor uses the staging process to determine 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. That information helps your doctor determine the treatment approach that is likely to be most effective for you.

The results of a biopsy, imaging scans, immunohistochemistry and genomic testing are used to classify and stage all types of breast cancer according to the American Joint Committee on Cancer (AJCC). The system includes the tumor (T) size, cancer cells found in nearby lymph nodes (N), and cancer that has metastasized (M), or spread, to other parts of the body (see Table 1).

The T classification categories are the same for both clinical and pathologic staging and provide information on the size and extent 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 classification for the N category (cN) describes the location and bulkiness of lymph nodes (usually in the axilla, under the arm) that appear 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 to another part of the body beyond the breast and nearby lymph nodes.

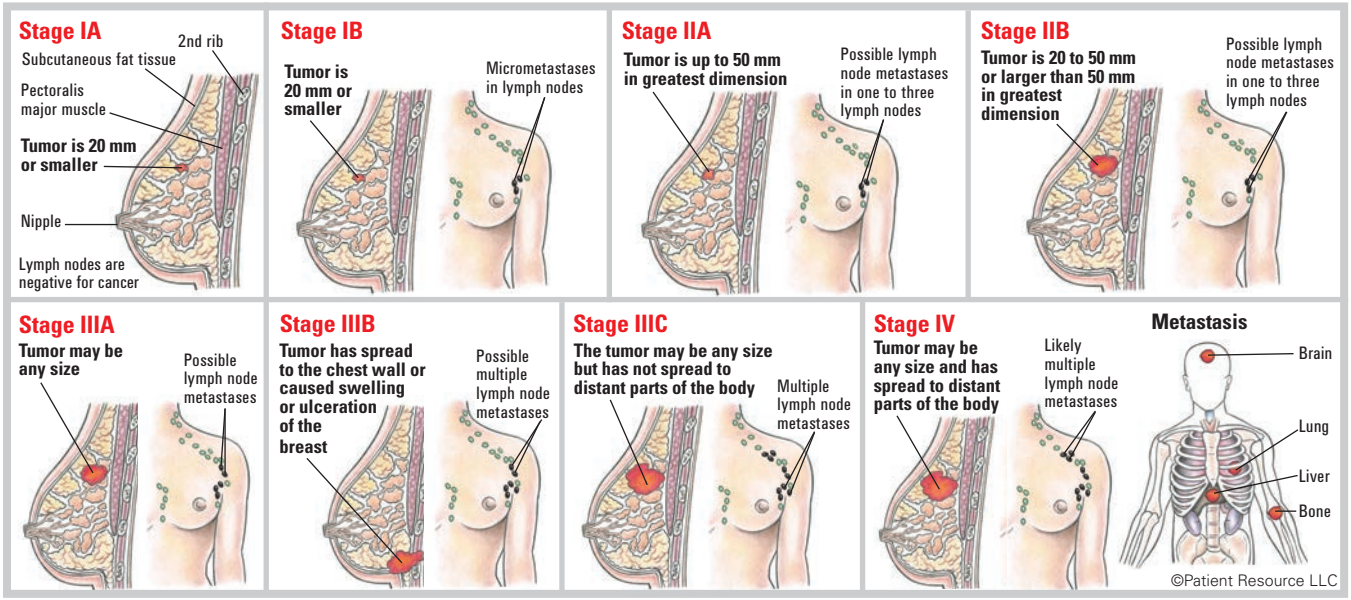
After breast cancer is classified, it is staged (see Table 2).

Stage 0 refers to ductal carcinoma in situ (DCIS) breast cancer, and Stage IV represents breast cancer that has spread beyond the breast and lymph nodes into distant organs, such as the bones, brain, liver or lungs. Regardless of where the cancer spreads, it is still considered breast cancer and is treated as such.

This information and many other important factors are considered and documented on your pathology report before you receive your final stage.

A pathology report (sometimes called a surgical pathology report) is a medical report that describes the characteristics of a tissue specimen that is taken from a patient. The pathology report is written by a pathologist, a doctor who has special training in identifying diseases by studying cells and tissues under a microscope. The pathology report provides the definitive cancer diagnosis. Tumor grade, biomarkers, and molecular

ILLUSTRATED STAGES OF BREAST CANCER



and genetic changes in cancer tissue identified in multigene panels are also considered and included on the pathology report and may be considered for staging.

Immunohistochemistry, a type of test used to help diagnose cancer, may be performed on the initial biopsy material and will include the tumor's estrogen receptor (*ER*), progesterone receptor (*PR*) and human epidermal growth factor receptor-2 (*HER2*) status to determine the presence (*ER+/PR+/HER2+*) or absence (*ER-/PR-/HER2-*) of these hormone receptors.

The hormone-related biomarkers *ER* and *PR* send signals to special receptor proteins inside normal breast cells and some breast cancer cells (those that carry the *ER* and/or *PR* biomarkers) to "turn on" the growth of 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. Breast cancer that does not express either of the hormone receptors or the *HER2* receptor is referred to as triple negative breast cancer (TNBC), which is an aggressive form of breast cancer.

Determining whether you have hereditary breast cancer is also important. 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 who have inherited abnormalities in the *BRCA1* or *BRCA2* genes have an increased likelihood of developing breast cancer and/or ovarian cancer.

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 cancer prevention (prophylactic) surgery (removal of the breasts and/or ovaries). The discovery of these mutations may also lead to different systemic treatments.

If breast cancer recurs, your doctor will perform diagnostic tests to determine whether the stage and classification have changed, which in turn may lead to different treatment recommendations. ■

TABLE 2

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 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 **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.

For more than 25 years, former KSHB-41 anchor and award-winning journalist Cynthia Newsome has shared stories that shape Kansas City. Dedicated to reporting that informs and helps others, she decided early on to be an open book about her two triple negative breast cancer (TNBC) diagnoses.

Don't let metastatic breast cancer rob you of your purpose

When I learned that the triple negative breast cancer (TNBC) I'd had several years before had not only returned but metastasized, I instantly went into patient mode. For 20 years, I'd kept up with my annual mammograms and breast self-exams, so when I felt a lump, I immediately got moving, hoping to get on top of it early. I drew on the knowledge I gained from interviewing metastatic breast cancer survivors. That valuable information, combined with my own experience, helped me feel more prepared.

I chose to be treated at a nearby university cancer center, and my oncologist was assigned to me by chance. Coincidentally, I'd interviewed her before I was ever diagnosed with breast cancer. I was thrilled to have her as my doctor because she is both a TNBC researcher and a clinician. Not only is she well-versed in every area of TNBC, she sees patients on a regular basis.

I was very comfortable with her, and that is something I'd encourage other people to look for when selecting a doctor. Some people like to follow their doctor's advice completely. Others, like me, want to collaborate. So, it's important to me to have a doctor who listens, offers advice, allows me to share my feelings and considers my opinions. I am happy to work alongside someone who understands my priorities.

She examined my original breast cancer tissue from my 2011 tumor and then compared it to the 2019 tumor that became metastatic. Once she understood more about my breast cancer, she was able to offer treatment options. My husband Ed and I talked through each treatment option with her…what the drugs did, the proposed treatment plan, and what would happen next. Even though metastatic disease is lifelong, I was anxious to get started to try to stop the cancer from growing and continuing to spread throughout my body.

I started on therapy that combined chemotherapy with immunotherapy. Then my doctor suggested a clinical trial. I hadn't participated in one before, but she explained the treatment in the trial might be more responsive to the molecular structure of my tumors. My husband and I felt it would be the right thing for me and loved the idea that participating could benefit others in the future.

At first, the trial medication left me feeling dizzy, like I was drugged. My doctor was able to reduce the dosage to make it more tolerable. Sometimes I still get very tired, but I'm able to work all day. I haven't had to manage many other side effects. I do have neuropathy, but overall, I'm doing great.

I'm surrounded by supportive people, starting with my husband. He said from the beginning, "You have the cancer in your body, but I have it, too." That is how close he feels to it. He keeps an eye on my physical and mental health, my energy level, my clarity. He always supports me, and he makes sure we have fun.

He also makes sure to take care of himself. He works and is very involved in our church. Like everyone else during COVID-19, we couldn't get together with family much, and Ed and I missed that. Now that we can gather with family, it really makes us happy.

My colleagues at KSHB-41 are also very encouraging. In my new role as the Community Relationships Director, our station General Manager is understanding and supportive when I need to take off for treatment or to recuperate. She knows I'll get the job done, and she gives high priority to family and health.

Adult volunteers at Awesome Ambitions, a college and career readiness program I founded in 1997 for 8th through 12th grade girls in the greater Kansas City area, help shoulder the burden when I need time away.

I also rely on my faith, pastor and church community.

After my first diagnosis, Ed and I decided to share our story. I have interviewed people all my life and I see how their stories help others. It's nice to hear from people who are praying for me or sending positive thoughts my way. Sometimes they share their stories with me, too. ■

Advice from Cynthia

- **Reality is reality.** I have metastatic breast cancer, but I know I'm still here for a reason. God has a purpose for me. I believe that purpose is to make a positive difference in other people's lives. Do what you can to fulfill your purpose.
- **Metastatic breast cancer can eventually outsmart the medications.** Don't be surprised if you have to change your medicine. I wanted all the information I could find about my options so I would be equipped to make the necessary decisions. Everyone has a different reaction and response to their diagnosis, so it's important to listen to your doctor, and listen to your body; don't expect someone else's experience to be the same for you.
- **Know how to encourage yourself.** Find the positive people and meaningful, fun activities that make you happy. Surround yourself with a positive support system.
- **Never give up hope.**