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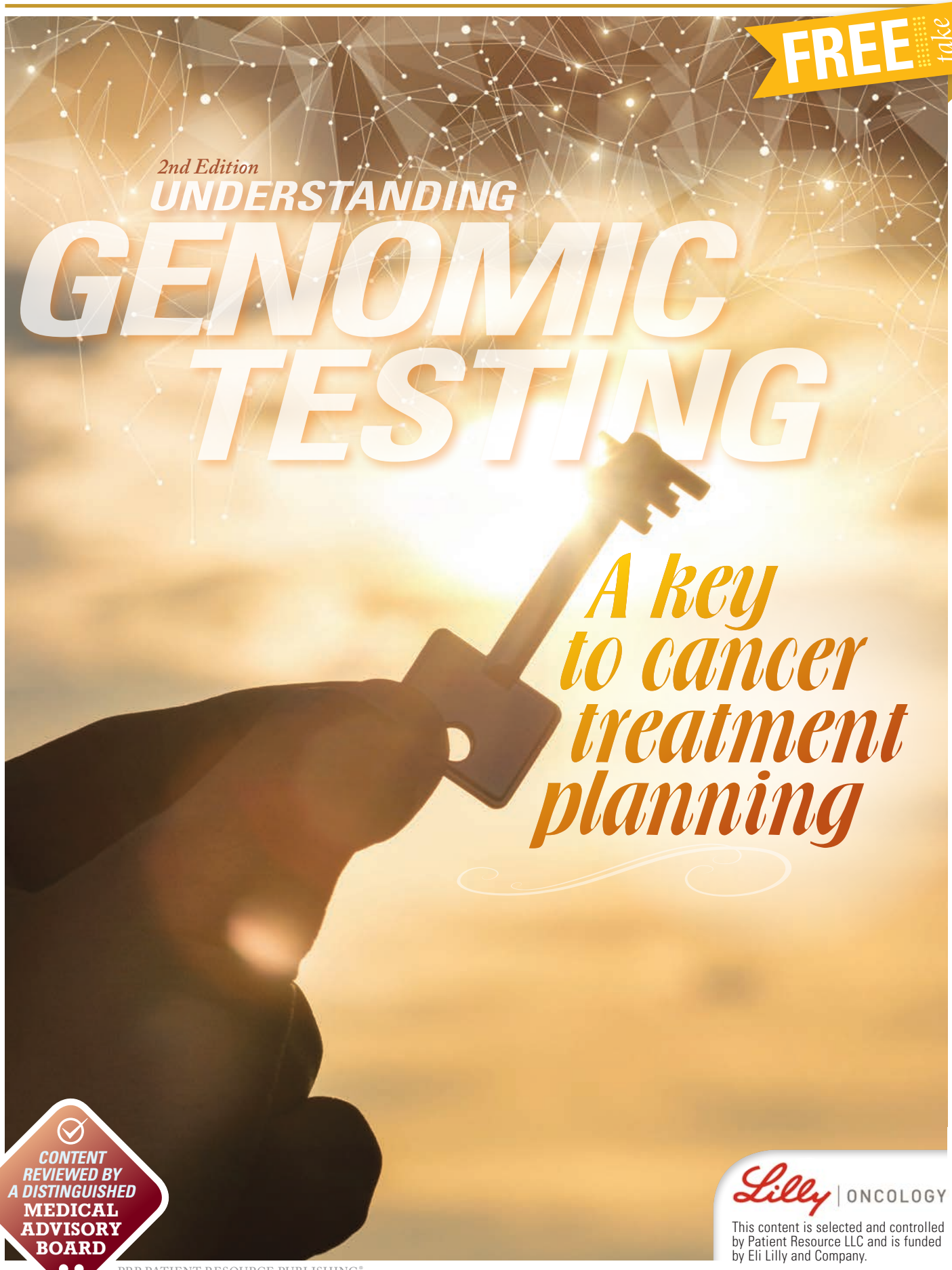
## UNDERSTANDING

# GENOMIC TESTING

## *A key to cancer treatment planning*



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2nd Edition

# UNDERSTANDING GENOMIC TESTING

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Facing cancer is hard enough.
Getting resources and medication shouldn't be.

**Lilly Oncology Support Center™:**
**1-866-472-8663,** Monday–Friday, 8 AM–10 PM ET;
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Lilly

# Lilly Oncology Support Center

## Resources and programs to help support eligible Patients during treatment

Lilly is dedicated to developing cancer treatments, but we're more than just our medicines. That's why we created the **Lilly Oncology Support Center**, a comprehensive Patient Support Program focusing on two important areas for Patients and their loved ones:

- Financial and coverage issues for eligible Patients (whether they're uninsured, underinsured, or insured), including financial assistance, help with benefits verification, Prior Authorization support, Specialty Pharmacy coordination, access, reimbursement, and more.
- Ongoing personalized care (for some products) from a dedicated staff, including emotional support and other services.

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- No income eligibility requirement

*This offer is invalid for Patients whose prescription claims are eligible to be reimbursed, in whole or in part, by any governmental program.

### Insurance Support

- Eligibility Determination
- Benefits Investigation
- Prior Authorization Assistance
- Appeals Information
- Specialty Pharmacy Coordination

*Note: These services are provided through coordination with a Patient's physician's office.*

### Resources

*For Patients:*

- Information about potential sources of assistance, including medication provided at no cost to qualifying Patients

*For Healthcare Professionals:*

- Coding and Billing Information
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- Payer Policy Information
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The **Lilly Oncology Support Center** is committed to helping qualified Patients when they're prescribed a Lilly Oncology product. The aim is to help Patients understand their coverage options, locate the appropriate pharmacy, and identify the lowest possible out-of-pocket cost.

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# Genomic testing helps unlock the mysteries of cancer

***Treating cancer*** is no longer one size fits all. Doctors now know that cancer is as unique as the person who has it because cancer forms when genes begin to change, or mutate, within the structure of normal cells. Therefore, cancer is ultimately a disease of our genes, which are pieces of DNA — the information plan for the growth and control of cells. And one key to understanding and treating cancer is through genomic testing.

Also known as molecular testing or tumor profiling, genomic testing is performed in a laboratory on samples of tumor tissue or blood (see *Testing*, page 8). This type of testing allows doctors to learn about the tumor's genome, which is a complete set of its DNA. By unlocking the DNA code of the tumor, doctors can better understand its unique characteristics. Genomic testing is not performed for every person or cancer type. In the cases where this testing has a clinical benefit, some of the potential uses include the following:

- Diagnosing and staging a cancer
- Determining prognosis (outlook)
- Evaluating whether therapies are available to treat mutations in that specific cancer
- Choosing treatment
- Monitoring treatment effectiveness
- Watching for progression or recurrence
- Predicting how the tumor might behave, such as how fast-growing it is and how likely it is to spread (metastasize)

This approach to treating cancer is more personalized and precise than traditional treatment strategies. Benefits of using genomic testing include delivering a more accurate diagnosis, selecting more precise treatments and sparing people with slow-growing disease from aggressive treatments that could have many side effects.

This guide focuses primarily on explaining what genomic testing is in an easy-to-understand way, and it offers a brief explanation of genetic testing.

### WHAT ARE MUTATIONS?

The foundation of genomic testing is built on finding mutations (changes that occur in the DNA of a cell). It is important to understand that just as every person has a specific mix of genes that are unique to them, cancers are driven by a mixture of specific mutations.

Mutations are generally described as one of two types. They can be acquired during a person's lifetime from environmental factors, such as tobacco use, ultraviolet radiation, viruses and age; or they are hereditary (inherited from a parent).

Acquired mutations are the most common cause of cancer. These mutations may be caused by mistakes during cell division or by exposure to DNA-damaging agents in the environment. They can be harmful, beneficial or have no effect. Certain mutations may lead to cancer or other diseases. A mutation is sometimes called a variant.

Testing for acquired and inherited mutations through genomic and genetic testing is changing how doctors look at and treat cancer. By using new advanced technologies, doctors can now find mutations in the genes that are causing your specific cancer. This approach to treating cancer is also known as precision medicine or precision oncology.

### WHAT IS GENOMIC TESTING?

Genomic testing for cancer developed as a result of the Human Genome Project. This project was led by an international team of researchers attempting to sequence and map all of the genes – together known as the genome – of humans.

Sequencing is a process that scientists use to determine the order of the four chemical building blocks – called "bases" – that make up the DNA molecule. DNA refers to the molecules inside cells that carry genetic information that is passed from one generation to the next through offspring. Almost every cell in the body contains a complete copy of the genome, which contains all the information needed for a person to develop and grow.

Genomic testing is typically performed during the diagnostic process 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. They are routinely tested for in certain cancers.

Testing for biomarkers is known as molecular testing. This type of testing is not used for every cancer diagnosis. Your doctor will talk with you if it may be beneficial for your treatment strategy (see Table 1).

It can also be done during treatment or if the cancer returns. When a tumor returns, it may have different mutations than before, which may affect treatment options.

A variety of tests are used to find genomic mutations, and the tests your doctor chooses may depend on the type of cancer you have

TABLE 1

## HOW BIOMARKERS ARE USED

| Purpose | Description |
|---|---|
| **Screening** | Most biomarkers are not useful for screening; only 1 biomarker (prostate-specific antigen) is used for screening |
| **Aid diagnosis** | Biomarkers can help identify the type of cancer when considered along with other clinical factors, such as symptoms and findings on imaging studies |
| **Determine prognosis** | Some biomarkers are factors considered when determining prognosis or predicting the outcome |
| **Guide treatment** | Some biomarkers can provide information about the types of treatment that are more likely to produce a response |
| **Monitor response to treatment** | Biomarkers can monitor the effectiveness of treatment, especially for advanced cancers |
| **Detect recurrence or progression** | One of the primary uses of biomarkers; if the level of a tumor marker is elevated before treatment, is low after treatment and then begins to increase after treatment, it is likely that cancer is recurring or progressing |

and the known mutations associated with it. This testing is usually performed on tumor tissue (biopsy) and sometimes blood (liquid biopsy). Liquid biopsies test a sample of blood to identify circulating cancer cells shed from the tumor or pieces of DNA from the tumor, and check those cells for mutations. Liquid biopsies are increasingly being used because of the ease and convenience of taking a blood sample versus a tissue sample. Tissue and liquid biopsy results are included in the pathology report (see *Your Pathology Report*, page 13).

**SELECTING TREATMENT**

Understanding the types of mutations your tumor has will help you make informed decisions with your doctor about your treatment options. If a mutation is found, your doctor will select a treatment that may target your cancer's specific mutation. But not all mutations have uniquely approved treatments available. If the testing does not identify a biomarker for which a specialized treatment exists, standard of care and clinical trials will be the options to consider. Ongoing trials are investigating treatments for more mutations, which may offer patients the chance to receive leading-edge therapies.

When genomic testing is used to select a specific treatment option, the results help doctors determine whether a person may benefit from certain types of drug therapy (see *Treatment Options*, page 10).

Targeted therapy is a form of systemic therapy that targets genes, proteins or other factors that support the tumor. Genomic testing is used to determine whether any of the known targets in a person's cancer exist that may respond to this treatment.

Immunotherapy uses the power and complexity of the body's natural immune system to find and attack cancer cells. The goal is to target cancer cells exclusively, leaving healthy cells alone. Special testing helps determine whether a patient is a candidate for certain types of immunotherapy.

Chemotherapy travels through the bloodstream and affects cells all over the body. Because healthy cells as well as cancer cells are affected, some genomic tests are used to determine whether a person's cancer will respond well to chemotherapy.

Hormone therapy blocks the stimulating effect of hormones. Genomic testing is used in cancers where hormones may be driving the cancer to determine whether hormone therapy may be helpful. ■

## Understanding Genetic Testing

The words genetic and genomic are often used interchangeably, but they have different goals and outcomes. Genomic testing is used to understand your cancer for diagnosis, staging and treatment purposes, while genetic testing helps determine whether you have inherited a mutation that increases your risk for developing certain types of cancer — even if you have not been diagnosed with cancer.

Genomic testing is performed on a tumor sample or a liquid biopsy, and genetic testing may be done with a saliva or blood sample.

Several types of cancer, including breast, ovarian, thyroid, prostate, pancreatic, kidney and stomach cancers, as well as melanoma and sarcoma, are known to run in families. If you have a family history of a particular type of cancer, you may consider genetic testing to find out whether you carry the corresponding gene. However, it is important to understand that if you have inherited a mutated gene, it doesn't mean you will automatically develop cancer; it only means the risk is increased and you can explore ways to lower it, such as surgery, medication, frequent screenings or lifestyle changes.

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
- Rare cancers
- Certain ancestry, such as Ashkenazi Jewish heritage

Though some genetic tests are available to purchase without your 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.

Choosing to have 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.

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 guide 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.

Once you understand your results, you can choose to share them with your children, siblings, nieces, nephews, etc. However, be prepared that they may not want to know or do anything about the information. Learning these results can bring up a range of emotions, including acceptance, relief, hope, confusion, denial, anger and guilt. Each relative must make the decision about what to do with the information.

Depending on the resources available at each cancer institution, it is important to know that a cancer genetic counselor may not be available. If one is not available at your cancer center, ask your nurse navigator to refer one that may be nearby. ■

# How understanding cell basics demystifies genomic testing

***The science and application of genomic testing*** in cancer begins at the cellular level. This requires understanding some of the basics about how normal cells function, what mutations are, how mutations lead to cancer and the components of a person's genome, which includes all of the information needed for a person to develop and grow.

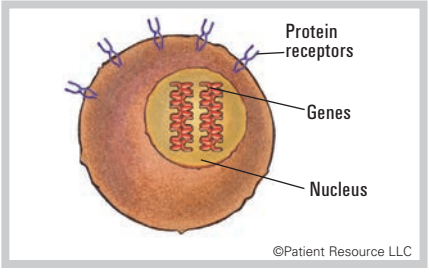
## COMPONENTS OF A CELL

All living organisms and tissues of the body are made of cells, which are the smallest structure of the body capable of performing all of the processes that define life. Almost every cell in the human body contains a complete copy of the genome, which is a complete set of chromosomes containing the DNA code. These are the biological instructions for the types of cells in your body that make each person unique. DNA is passed from adults to their children.

A cell has three main parts:

- The cell membrane surrounds the cell and controls the substances that go into and out of the cell.
- The nucleus is a structure inside the cell that contains most of the cell's DNA.
- The cytoplasm is the fluid inside the cell. The cytoplasm is where most chemical reactions take place and where most proteins are made.

FIGURE 1
### NORMAL HEALTHY CELL




A cell's nucleus contains 46 chromosomes — 23 from your mother and 23 from your father. Each chromosome is made up of DNA, which consists of two twisting, paired strands (base pairs) that create a double helix. Base pairs are bonded to one another forming a "rung of the DNA ladder."

Genes are sections of DNA on a chromosome that contain the instructions for making a specific protein that the body needs to function properly. Proteins are the basis of body structures, such as skin and hair, and of other substances such as enzymes, cytokines and antibodies. Each gene must have the correct instructions to make its protein.

## HOW HEALTHY CELLS WORK

Healthy cells are created to perform specific functions in the body (see Figure 1). They exist for a period of time, reproducing themselves in an orderly fashion and dying off in a normal time frame when they become worn out or damaged.

Typically, cells divide after receiving specific signals from growth factors that circulate in the bloodstream or from a cell with which they are in direct contact. Once they receive the message to divide, the cells go through the cell cycle, a series of steps during which the chromosomes and other cell material double to make two copies. Checkpoints along each step of the process make sure that everything goes the way it should.

Many processes are involved in cell reproduction, and all these processes have to take place correctly for cells to divide properly. If anything goes wrong during this complicated process, cells may become cancerous.

## HOW CANCER DEVELOPS

Cancer begins when genes start to change, or mutate, within the structure of normal cells. These cells – now called cancer cells – tend to grow out of control by ignoring signals to stop dividing. They do not die when they should, accumulating until they form a mass known as a tumor, which can be benign (noncancerous) or malignant (cancerous). Cancer can develop in almost any part of the body.

Unable to recognize their own natural boundaries, the cancer cells may spread to areas of the body where they do not belong. This is known as metastasis. Cancer can metastasize (spread) to other organs, tissues, bones or blood, but it is diagnosed according to where in the body it begins. If cancer starts in the lung, it is known as lung cancer. If it spreads to the brain, however, it is still considered lung cancer and is treated as such. It does not become brain cancer.

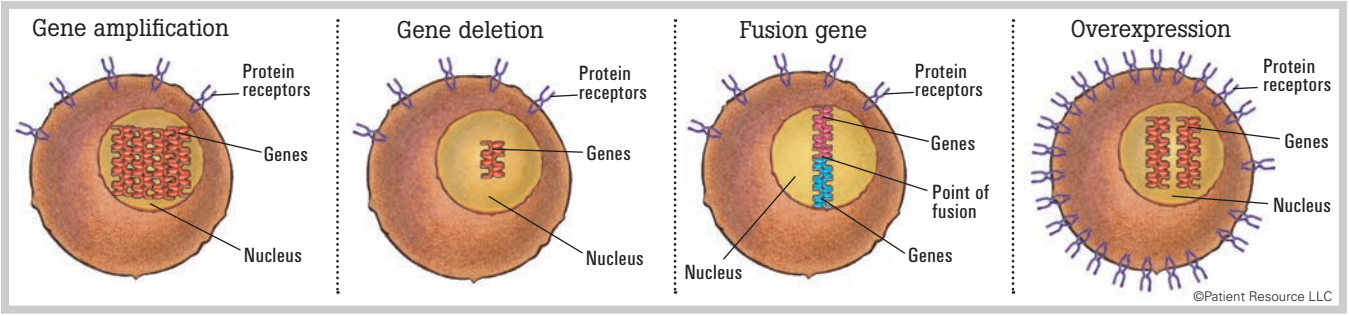
When cells mutate into cancer, the proteins those cells create are also abnormal. Cancer can affect protein production in the following ways:

- Prevent some proteins from being made
- Stop the protein from working the way it should
- Keep the protein from working at all

Many of the genes associated with cancer development fall into three broad categories:

1. Tumor suppressor genes normally control cell growth by monitoring how quickly

FIGURE 2
### GENE MUTATIONS



cells divide into new cells, repairing mismatched DNA and controlling when a cell dies. When these genes mutate, cells can grow out of control and may form a tumor.

2. Oncogenes turn healthy cells into cancerous cells and typically are not inherited. Two common oncogenes are *HER2* and *RAS*.
3. DNA repair genes fix the mistakes a cell makes when it divides and DNA is copied. When a cell cannot fix an error created when a cell is reproducing, mistakes may be copied into the new cell and not corrected. These mistakes can become mutations that lead to cancer.

### UNDERSTANDING MUTATIONS

Research has found that many cancers are caused by mutations (changes) in the DNA. It is common for a cell to have mutations, but it requires multiple mutations before a tumor is formed. A single mutation likely will not cause cancer.

A variety of mutations in a normal gene can increase a person's risk of developing cancer. Mutations can occur in DNA, genes or chromosomes. Some mutations that can occur in genes include the following (see Figure 2):

- Gene amplification — An increase in the number of copies of a gene, which is common in cancer cells. Some amplified genes may cause cancer cells to grow or become resistant to anticancer drugs.
- Gene deletion — The loss of all or part of a gene.
- Fusion gene — A gene made by joining parts of two different genes. Fusion genes, and the fusion proteins that come from them, may be made in the body when part of the DNA from one chromosome moves to another chromosome. Fusion proteins produced by this change may lead to the development of some types of cancer.
- Overexpression — Too many copies of a protein or other substance, which may play a role in cancer development.
- Rearrangement — A mutation that occurs in chromosomes where portions of the chromosome are not in order, which creates a new gene (not shown).

Types of chromosome mutations that can lead to cancer include the following:

- Deletion — Part of a chromosome is missing or deleted.
- Duplication — Part of the chromosome is duplicated, resulting in extra genetic material.
- Inversion — Part of the chromosome has broken off, turned upside down and reattached.
- Rearrangement — A portion of the chromosome has broken off and reattached, creating a different order of its genes, which may create a new gene.
- Rings — Part of a chromosome has broken off and formed a circle or ring.
- Translocation — Part of a chromosome is transferred to another chromosome. ■

## GLOSSARY

### Words to Know

**Adjuvant therapy:** Additional cancer treatment given after primary treatment to lower the risk the cancer will come back.

**Benign:** Not disease-causing

**Cytogenetics:** The study of chromosomes to look for changes, including broken, missing, rearranged or extra chromosomes.

**DNA:** Deoxyribonucleic acid. The molecules inside cells that carry genetic information that is passed from one generation to the next.

**DNA sequencing:** A laboratory process used to learn the exact sequence (order) of the four building blocks, or bases, that make up DNA to find DNA mutations (changes) that may cause diseases, such as cancer.

**First-line therapy:** The first treatment used.

**Fluorescence in situ hybridization (FISH):** FISH can be used to identify where a specific gene is located on a chromosome, how many copies of the gene are present and any chromosome abnormalities.

**Genome:** The complete set of DNA (genetic material) in an organism. In people, almost every cell in the body contains a complete copy of the genome, which contains all of the information needed for a person to develop and grow.

**Genomic sequencing:** This is used to determine the entire genetic makeup of a specific organism or cell type. This can be used to find changes in areas of the genome and to diagnose and treat cancer.

**Histologic grade:** This is a description of a tumor based on how abnormal the cancer cells and tissue look under a microscope. It also helps determine how quickly the cancer cells are likely to grow and spread.

**Liquid biopsy:** A test done on a sample of blood to look for cancer cells or pieces of DNA from a tumor that are circulating in the blood. A liquid biopsy may also be used to help plan treatment, to find out how well treatment is working or to determine whether cancer has come back. Being able to take multiple samples of blood over time may also help doctors understand what kind of molecular changes are taking place in a tumor. It is convenient, can be repeated frequently and does not require a surgical procedure.

**Local treatment:** Directed to a specific organ or limited area of the body, it includes surgery, radiation therapy and topical therapy (a lotion or cream that is applied to the skin).

**Molecular testing:** Checks for certain genes, proteins or other molecules in a sample of tissue, blood or other body fluid. Molecular tests also check for certain changes in a gene or chromosome that may affect the chance of developing cancer. It is done to help diagnose some types of cancer, plan treatment, find out how well treatment is working or make a prognosis (prediction of outcome).

**Mutations:** Also referred to as changes or variants, mutations are the differences between an individual's genetic code when compared to the human reference sequence, which is representative of the sequence (order) of genes in one idealized individual. Some are benign, pathogenic or of unknown significance.

**Neoadjuvant therapy:** Treatment given as a first step to shrink a tumor before the main treatment (usually surgery) is given.

**Next-generation sequencing (NGS):** Tests that detect differences in a patient's genome from a reference genome, which is a representative example of the set of genes in one idealized individual. It identifies sections of DNA that represent changes, including insertions or deletions, in a specific DNA sequence.

**Oncogene:** A mutated form of a gene involved in normal cell growth. Oncogenes may cause the growth of cancer cells. Mutations in genes that become oncogenes can be inherited or caused by exposure to cancer-causing substances.

**Pathogenic:** Disease-causing

**Pathological stage:** The stage of cancer based on how different from normal the cells in cancer tissue samples look when examined under a microscope.

**Second-line therapy:** Given when the first-line therapy does not work or is no longer effective.

**Standard of care:** The best treatment known for the type and stage of a particular cancer.

**Tumor microenvironment:** The cells, molecules and structures that surround and support a tumor. Abnormal cells, such as cancer cells, can change their microenvironment, which can affect how cancer cells grow and spread.

# The types and purposes of different genomic tests

***Advances in genomic testing technologies*** are allowing scientists to better understand cancer and the mutations that drive it. This is possible through new types of testing that analyze each person's cancer at a deeper level. Doctors use this information to diagnose and stage as well as find treatments that may be approved for those mutations.

Prior to the introduction of genomic testing, doctors diagnosed and determined treatment plans by using general information about the cancer, including its type, where it was located, the grade (how quickly the cancer cells are likely to grow and spread) and whether it had metastasized.

Today, genomic tests go a step further by finding mutations that may be driving the cancer. They do this by looking for biomarkers, changes in chromosomes, circulating tumor cells and gene mutations. The type of test (and the type of tissue used for testing) will vary, depending on the cancer involved and the information your doctor is seeking (see Table 1).

It may not be necessary or beneficial for all patients to have genomic testing, but it should be routine in all younger patients, especially if they have a no-smoking or light-smoking history. During the diagnostic process, your doctor will discuss the possibility of genomic testing with you if your cancer type has known mutations. Testing may be performed multiple times — at diagnosis, if the cancer progresses and sometimes during treatment to determine whether the cancer is responding.

## UNDERSTANDING THE DIAGNOSTIC PROCESS

Obtaining and analyzing a biopsy sample are crucial to diagnosing the type of cancer you have because it will help your doctor determine the most effective type of treatment. In general, your doctor will follow these steps.

**Step 1:** A biopsy of tumor tissue will be taken. It can be done by several methods, and different tests require different amounts of tissue. Ask your doctor how your testing will be done before a biopsy to make sure enough tissue samples will be taken to meet the requirements of all the tests.

**Step 2:** The sample will be sent to a laboratory where a pathologist will look for the presence of cancer cells and document the size and location of the tumor, the number of lymph nodes with cancer cells and other important facts about the cancer. A pathologist is a doctor specially trained to diagnose disease by looking at cells under a microscope.

**Step 3:** If cancer cells are found, they will be extracted from the sample so the pathologist can determine the histologic type of the cancer. The six major histologic types are carcinomas, sarcomas, myelomas, leukemias, lymphomas and mixed types. In some instances, the pathologist may not be able to identify the histologic type because the tissue sample is too small. When this happens, another biopsy may be necessary.

**Step 4:** Specialized equipment will be used to sequence the tumor's DNA and find any abnormalities. DNA sequencing determines the order of the four building blocks – called "bases" – that make up the DNA molecule.

**Step 5:** If abnormalities are found, they will be compared to known mutations.

**Step 6:** Results are returned to your doctor in a pathology report (see *Your Pathology Report*, page 13).

**Step 7:** If a known abnormality is found, your doctor may suggest treatment options that are approved to target the same mutations.

**Step 8:** Genomic testing may be repeated to monitor effectiveness or if your doctor suspects a recurrence or resistance. ■

TABLE 1

## TYPES OF GENOMIC TESTS

| Test | What the test does | Sample type | Purpose |
|---|---|---|---|
| **Comprehensive biomarker testing** | **Looks for known biomarkers** | Tissue | **Determine treatment** |
| **Cytogenetic tests** | **Looks for changes in chromosomes, including broken, missing, rearranged or extra chromosomes** | Tissue, blood or bone marrow | **Diagnose, plan treatment, determine treatment effectiveness** |
| **Fluorescence in situ hybridization** (FISH) | **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** | Tissue | **Diagnose, prognosis and evaluation of remission** |
| **Immunohistochemistry** | **Tests for certain antigens (markers), such as proteins like PD-L1. It may also be used to determine the difference between cancer subtypes** | Tissue | **Diagnose** |
| **Immunophenotyping** | **Tests for and identifies markers on cells** | Blood or bone marrow | **Diagnose and classify blood cell cancers** |
| **Karyotype** | **Looks for abnormal numbers or structures of chromosomes** | Blood, bone marrow or tissue | **Diagnose and identify the Philadelphia chromosome found in chronic myelogenous leukemia** |
| **Liquid biopsy** (also called circulating tumor DNA) | **Looks for cancer cells from a tumor that are circulating in the blood or for pieces of DNA from tumor cells that are in the blood** | Blood | **Detect cancer at an early stage, plan treatment, determine treatment effectiveness** |
| **Microarray** | **Generates a genetic profile for a given tissue sample that reflects the activity of thousands of genes** | Tissue | **Identify cancer subtypes** |
| **Multi-gene panel testing** | **Studies many genes in a sample of tissue to find mutations in certain genes that may increase a person's risk of cancer** | Blood | **Find cancer, plan treatment or determine treatment effectiveness** |
| **Next-generation sequencing** | **Tests multiple genes simultaneously** | Tissue | **Diagnose, prognosis and plan treatment** |
| **Polymerase chain reaction** (PCR) | **Looks for certain changes in a gene or chromosome** | Blood, saliva, mucus or tissue | **Find and/or help diagnose a cancer** |
| **Reverse transcription PCR** (RT-PCR) | **Amplifies traces of DNA sequence so there are adequate quantities for analysis** | Blood, saliva, mucus or tissue | **To look for activation of certain genes, which may also help diagnose cancer** |


***Amy Grove was devastated by a Stage IV non-small cell lung cancer diagnosis at 48. To make matters worse, her cancer was squamous cell carcinoma, which can be difficult to treat. After her first therapy failed, her doctor ordered genomic testing to find a more effective treatment option for her specific type of cancer. Results showed she had a MET amplification, which made her eligible to begin targeted therapy. Today, she is stable and encourages others to ask for genomic testing.***

# Genomic testing unlocked a miracle for this survivor

**Genomic testing saved my life.** I truly believe that if my doctor hadn't ordered it, I wouldn't be here today. I recommend everyone get genomic testing even if your doctor doesn't think your cancer has biomarkers. Mine did, and it gave me the miracle I needed.

Two weeks after I got a flu shot in November 2018, I had a swollen lymph node on the side of my neck. It was in a weird spot, and I figured it was a result of the shot. But when it was still there two weeks later, I decided to get it checked out.

My primary care doctor ordered a CT, which caught the upper part of my lungs. The scan showed a mass on my upper right lung. A PET scan showed a mass in my lung and lymph nodes. I received a Stage IV non-small cell lung cancer diagnosis on my 48th birthday.

I immediately thought I was done for and that there was no hope. I feared I would not see my 50th birthday. I became horribly depressed and anxious. I don't think I slept for the first three weeks after my diagnosis. But sharing my diagnosis with friends and family helped to calm my fears.

At the time, I was put on what was considered the gold standard of treatment, a drug therapy combined with radiation therapy. I was only able to tolerate the drug therapy for a short while, and scans showed the cancer had spread (metastasized) to my skull, shoulder, adrenal glands, hips, ovaries, femur, feet, fingers and ribs.

I was so weak that I had to use a wheelchair. One day I sat down on the couch and broke my left femur and my right foot. I was in so much pain. I was terrified to move for fear I would break something else.

I was already in the middle of radiation therapy to treat the metastases on my hips and femur, so surgery to repair the femur with pins was delayed three weeks.

I had almost lost all hope, but my family stepped up to support me. I had the emotional support of my husband, and my mother moved from Florida to help me for two months. She drove me to my appointments. My brother built a shower in the garage of our two-story house so I could shower without going upstairs. I couldn't have made it through this without my family.

The doctor speculated that the therapy caused hyper progression of my cancer. Although it wasn't the standard approach, my doctor suggested sending out my blood for biomarker testing. Apparently, it is rare for squamous cell lung cancer to have biomarkers, but my doctor was hopeful and took a chance. Thank goodness he did because the results showed I had a *MET* amplification.

My doctor chose a targeted therapy designed to target *MET*. Within two weeks, I felt 90 percent better. I could get out of the wheelchair and walk again. It was like night and day! I truly felt like it was a miracle.

I found a great deal of support online through Facebook groups. I'm not a fan of in-person meetings, so online was perfect for me. With lung cancer, many of the groups are divided by mutation. Together with a friend of mine, who also has lung cancer with a *MET* mutation, we are administrators for a *MET*-specific Facebook group.

Three months after starting the targeted therapy, all of the metastases were gone except for the tumors on the adrenal gland and lung. I had cryoablation to remove the spot on the adrenal gland and stereotactic body radiation therapy (SBRT) on the lung nodule.

Today, I am considered stable and continue to take the targeted therapy. I'll remain on it until it stops working. My doctor says there are other options we can consider when that time comes, and I trust him.

Make sure you advocate for yourself. Speak up and ask for biomarker testing. Don't be afraid of the cost. Most genomic testing companies will help you pay for it if your insurance doesn't. Do not let the cost of genomic testing prevent you from having it because it could save your life.

Advances are being made all the time. Have hope. Lung cancer is no longer a death sentence. Genomic testing could save your life, just as it did mine. ■

# Educate yourself about the therapies used to treat certain mutations

***Treating cancer based on its specific mutations*** is now possible. As a result of years of research, doctors are able to treat some types of cancer with therapies that target genes, proteins and other substances that cause and contribute to the growth of cancer. This more precise way of treating cancer is offering many patients hope for slowing or curing their cancer, often with a better quality of life.

Once the results of your genomic tests are available, you will work closely with your doctor to determine whether you are a good candidate for certain therapies that are approved for specific mutations.

It is important to understand that not all tumors test positive for a mutation. Still others might have a mutation for which an approved therapy does not yet exist. However, clinical trials are underway to find effective treatments for these additional genetic abnormalities and may offer more options soon.

To develop a treatment plan tailored to you, your doctor considers many factors, including the tumor's stage, grade and biomarker status; your general health; and your preferences concerning quality of life in regard to potential treatment side effects.

Following are descriptions of therapies that are available to treat some mutations. These drugs can be given orally, intravenously or subcutaneously (see Figures 1 and 2).

### TARGETED THERAPY

Targeted therapy is a personalized drug strategy that uses the results from genomic testing to select drug therapy that targets specific genes, proteins, mutations, abnormalities or other factors that are involved in the development and support of the tumor. These drugs are designed to kill cancer cells or stop the progression of disease. The drugs travel throughout the body via the bloodstream looking for specific proteins and tissue environments to block cancer cell signals and restrict the growth and spread of cancer.

By targeting specific mutations in proteins, genes and receptors, targeted therapies can attack cancer in the following ways:

- Preventing cancer cells from growing and from living longer than normal
- Blocking or stopping signals that help form blood vessels to the tumor
- Delivering cell-killing substances to cancer cells
- Causing cancer cell death
- Starving cancer of the hormones it needs to grow

Targeted therapies work in different ways and can be classified as small molecule drugs, angiogenesis inhibitors and monoclonal antibodies (mAbs).

**Small molecule drugs** are able to get inside of a cell and affect its internal components. They are used for targets inside cells. Some types of these drugs include the following:

- Apoptosis inducers cause cancer cells to undergo a process of controlled cell death called apoptosis. Apoptosis is one method the body uses to get rid of unneeded or abnormal cells, but cancer cells have strategies to avoid apoptosis. Apoptosis inducers can get around these strategies to cause the death of cancer cells.
- Gene expression modulators modify the function of proteins that play a role in controlling gene expression.
- Histone deacetylase (HDAC) inhibitors affect gene expression inside tumor cells.
- Proteasome inhibitors target enzymes to kill cancer cells.
- Selective inhibitors of nuclear export (SINE) enhance the anticancer activity of certain proteins in a cell.
- Signal transduction inhibitors block signals passed from one molecule to another inside a cell. Blocking these signals can affect many functions of the cell and may kill cancer cells.

**Angiogenesis inhibitors** (also called anti-angiogenic inhibitors) block new blood vessel growth that feeds tumor cells. Tumors need a blood supply to survive and grow.

**Monoclonal antibodies (mAbs)** are laboratory-made antibodies designed to target specific tumor antigens. They can flag targeted cancer cells for destruction, block growth signals and receptors, and deliver other therapeutic agents directly to targeted cancer cells. When a mAb is combined with a toxin, such as a chemotherapy drug, it travels through the system until it reaches the targeted cancer cell.

FIGURE 1
### INTRAVENOUS THERAPY

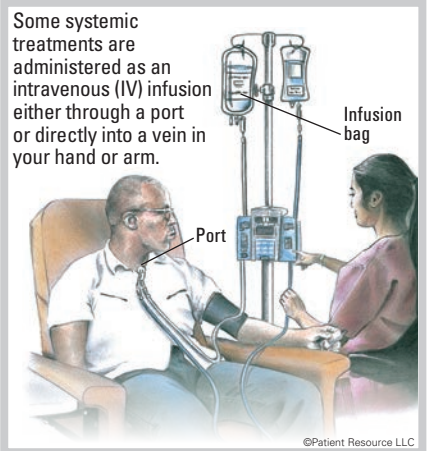



FIGURE 2
### SUBCUTANEOUS INJECTION

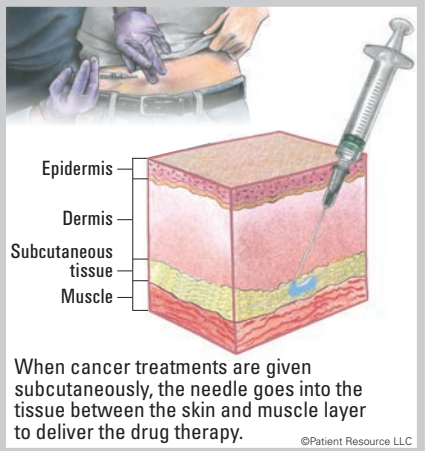
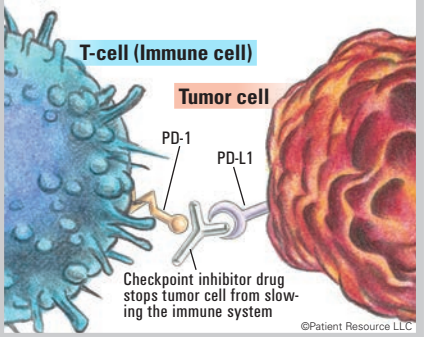



FIGURE 3
### IMMUNE CHECKPOINT INHIBITORS

An immune response is controlled with checkpoints, which are the "brakes" of the immune system. If the checkpoints PD-1 and PD-L1 connect, the immune system slows down and becomes less efficient at finding and attacking cancer cells. Immune checkpoint inhibitors prevent PD-1 and PD-L1 from connecting, enabling the immune system to continue working hard to eliminate cancer cells.



Then it attaches to the surface, gets swallowed by the tumor cell and breaks down inside the cell, releasing the toxin and causing cell death. Different types of mAbs are used in cancer treatment, but they should not be confused with mAbs that mark cancer cells so the immune system can better see them and destroy them, which is a type of immunotherapy.

### IMMUNOTHERAPY

Immunotherapy harnesses the potential of the body's own immune system to recognize and destroy cancer cells. To determine whether you are a candidate for immunotherapy, doctors test for specific biomarkers, including PD-L1 expression, tumor mutational burden (TMB) and microsatellite instability-high (MSI-H) or deficient mismatch repair (dMMR).

Genomic testing is used specifically to qualify for treatment with immune checkpoint inhibitors and monoclonal antibodies (mAbs).

**Immune checkpoint inhibitors** prevent the immune response from slowing down, which allows the immune cells to continue fighting cancer. They also help the immune system to better recognize cancer cells as foreign cells.

Normally, the immune system is kept in check through the use of biological checks and balances called checkpoints. Checkpoint-inhibiting drugs prevent connections between checkpoints so that the immune system does not slow down and can keep up its fight against cancer (see Figure 3).

Some immune checkpoint inhibitors are also approved as tumor-agnostic treatment, which means they are approved to treat any kind of cancer that has the molecular alterations known as microsatellite instability-high (MSI-H), deficient mismatch repair (dMMR) or tumor mutational burden-high (TMB-H).

MSI-H describes cancer cells that have a greater-than-normal number of genetic markers called microsatellites, which are short, repeated sequences of DNA. Every time a cell reproduces itself, it makes a copy of its genes and DNA. During the process, errors in duplication can be made, much like a misspelled word. The body normally corrects the error, but sometimes it is not caught and fixed (dMMR). It then becomes a mutation that is reproduced in later versions of the cell. Cancer cells that have large numbers of microsatellites may have defects in the ability to correct mistakes that occur when DNA is copied.

When cancer cells have this feature, they are more sensitive to destruction by immune checkpoint inhibitors. MSI is also tested to determine which tumors may have developed because of a deficiency in correcting cellular errors made when it divides.

TMB measures the number of mutations within a tumor to predict a patient's response to immune checkpoint inhibitor treatment. TMB-H describes cancer cells that have a high number of gene mutations.

**Monoclonal antibodies (mAbs)** are laboratory-made antibodies designed to target specific tumor antigens. They can flag targeted cancer cells for destruction, block growth signals and receptors, and deliver other therapeutic agents directly to targeted cancer cells. They can also be created to carry cancer drugs, radiation particles or laboratory-made cytokines (proteins that enable cells to send messages to each other) directly to cancer cells.

When a mAb is combined with a toxin, such as a chemotherapy drug, it travels through the system until it reaches the targeted cancer cell. Then it attaches to the surface, gets absorbed by the tumor cell and breaks down inside the cell, releasing the toxin and causing cell death.

Different types of mAbs are used in cancer treatment, but they should not be confused with mAbs that directly attack certain components in or on cancer cells, a type of targeted therapy.

### HORMONE THERAPY

This treatment blocks the stimulating effect of hormones. It can be used to block the body's ability to produce hormones and interfere with how hormones behave in the body. It is primarily used to treat breast and prostate cancers, which use hormones to grow.

This type of therapy targets specific hormones. For example, in breast cancer, the hormone biomarkers estrogen receptor (*ER*) and progesterone receptor (*PR*) are routinely tested during the diagnostic process and have treatments available to reduce the levels of these hormones that are stimulating the breast cancer.

In prostate cancer, androgen-deprivation therapy (ADT) slows tumor growth by preventing the body from producing androgens or by blocking the effect that the androgens have on the tumor.

### CHEMOTHERAPY

Genomic testing may be used in specific instances to determine whether chemotherapy may be an effective treatment option. Doctors know that some types of cancer respond better to chemotherapy. Genomic tests may be used to choose or avoid chemotherapy in certain circumstances.

### ONGOING MONITORING AND DRUG RESISTANCE

It is common for the treatment strategy you begin with to change. Your doctor will continually monitor your condition and make adjustments for a number of reasons. Sometimes a therapy becomes less effective over time; other times, a new mutation may be discovered and a different therapy may offer more promise; or you may reach remission, among other things. Keep in mind that cancer is a fluid condition, so flexibility and patience are important.

When cancer cells stop responding to a drug, it is known as drug resistance. which is known to happen with some targeted therapies. In some cases, patients will have access to other targeted therapies that are designed for other targets within the cancer. Research is ongoing to identify why resistance occurs and to develop new therapies that target multiple genetic mutations at the same time to avoid the development of resistance. ■

## » NEXT STEPS

1. **Medication Adherence:** Commit to taking your oral medication and keeping your appointments. Taking your drug therapy on time is crucial to maximizing the success of the treatment. Most cancer therapies are designed to maintain a specific level of drugs in your system for a certain time. To be fully effective, every dose must be taken with accuracy, precise timing and safety precautions, whether you receive it via IV, injection or pill form. If your medications are not taken exactly as prescribed, the consequences can be serious, even life-threatening.

2. **Symptom Management:** Before beginning any therapy, it is a good idea to know the potential side effects that may accompany your treatment. There are varying degrees of side effects ranging from minor to severe. Ask about the symptoms to watch for and what you should do if they happen. Some may require alerting the health care team as soon as symptoms begin. Prompt treatment may help prevent more serious complications. Your health care team will rely on you to communicate openly about how you feel.

# Research paves the way for more personalized treatments

***Some clinical trials help researchers better understand*** how genes and biomarkers influence cancer. By learning more about the roles mutations play in causing and affecting certain types of cancer, scientists are able to expand the prevention, diagnosis and treatment options for patients whose cancers have these biomarkers. You may be eligible to participate in a clinical trial based on your risk factors or the results of your biomarker testing.

Some studies called basket trials enroll people based on the biomarkers in their cancer, instead of where in the body the cancer started growing. Others use biomarker tests to match people to treatments based on the genetic changes in their cancers.

Although many advances are being made, it is important to realize that some of the cancer treatments based on these findings may only work for people whose cancers have certain biomarkers. Additionally, some biomarkers may be identified that do not yet have treatments.

### THE BASICS OF CLINICAL TRIALS

Most cancer treatments used today were once therapies or procedures that were developed, tested and evaluated through the clinical trials process to gain approval from the U.S. Food and Drug Administration (FDA). The advances made in these clinical trials give patients more options for preventing, diagnosing and treating cancer.

Many types of cancer clinical trials exist, not just those that study genes and biomarkers. Some evaluate new methods for improving different areas of cancer care, including disease prevention, patient screening, diagnostic tools and procedures. Trials may also evaluate lifestyle or behavioral changes that may improve health.

### THE DECISION TO PARTICIPATE IS YOURS

As you think about taking part in a clinical trial, you may find it beneficial to talk with your medical team. Also consider the following:

- You may have a rare diagnosis that does not have many approved treatments.
- You could gain access to new tests and treatments before they are widely available.
- Being actively involved in a clinical trial may help you better understand your diagnosis and how current research may guide your treatment options.
- Your involvement will help current and future generations of people with cancer. ■




# Get to know your health care professionals

***Diagnosing and treating cancer*** requires the expertise of many uniquely skilled and dedicated professionals. They will perform a variety of valuable tasks, from testing and treating to educating and comforting. Though your team members may vary depending on the type of cancer you have and the facility at which you receive care, the following specialists will likely be included.

**Case managers** and **social workers** are your personal advocates, acting on your behalf by collaborating with health care professionals and non-medical personnel to help overcome various barriers to care.

**Financial counselors** address cancer-related financial concerns, such as questions about your insurance policy and out-of-pocket expenses, so you can feel more in control and less anxious.

**Genetic counselors** help explain your genetic testing results, which may be difficult to interpret. Understanding how the results can guide treatment may help you make important decisions.

**Genomic/moleculor pathologists** study tissue and blood samples on a molecular level to provide information about the diagnosis, treatment and prognosis for certain conditions, including some types of cancer.

**Medical oncologists** treat cancer patients using drug therapies. Your oncologist will manage your course of treatment.

**Nurse navigators** collaborate with your health care team from diagnosis through survivorship and will be the resource who knows you the best.

**Oncology nurses** may be registered nurses, clinical nurse specialists, advanced practice nurses, radiation therapists, chemotherapy nurses, oncology social workers, case managers, educators or consultants.

**Pathologists** identify diseases by studying cells and tissues under a microscope. They may also be known as genomic or molecular pathologists.

**Pharmacists** prepare and dispense prescriptions, ensure medicines and doses are correct, and prevent harmful drug interactions.

**Radiation oncologists** use radiation therapy to treat and reduce the symptoms of cancer.

**Radiologists** create and interpret pictures of areas inside the body that are made with X-rays, sound waves or other types of energy.

**Surgical oncologists** use surgery to remove tumors or repair a part of the body affected by cancer. ■

# Learn about the components of a pathology report

***Once a biopsy of a tumor is taken,*** the specimen is sent to the pathology department where it is carefully examined by a specially trained doctor called a pathologist, or by a specialist known as a genomic or molecular pathologist. After studying the specimen with and without a microscope, documenting its size, describing its location and appearance, and performing special testing, the pathologist prepares a document that provides all the information about the characteristics of your cancer. This is known as a pathology report.

Most cancer diagnoses are based on the careful examination of tissue obtained during a biopsy of a suspected tumor or of the entire tumor after definitive surgery (removal of the tumor with or without lymph nodes). The pathologist's final diagnosis of your cancer is based on all the findings of the examination.

This important document helps guide your oncologist and other members of your treatment team as they plan the treatment most likely to be effective for your particular type of cancer and your unique characteristics.

### UNDERSTANDING THE RESULTS ON YOUR PATHOLOGY REPORT

The format of a pathology report may look different at different facilities, but most include these general terms.

**Patient information:** Name, birth date and biopsy date.

**Size:** The length, width and weight of the tumor. This is sometimes referred to as the gross description. Prognosis (outlook) is generally better for smaller tumors. Size is a primary factor in staging.

**Location:** Where the tumor is found.

**Histologic grade:** A grade is based on how closely the tumor cells resemble normal cells. The more the cancer cells look like normal cells (lower grade), the better the prognosis.

**Surgical margins:** This indicates whether cancer cells are found in the normal tissue around the edges of the tumor. If they are, additional treatment (surgery or radiation therapy, for example) may be needed.

**Extent of invasion:** This shows the other structures affected by the tumor. This is a factor in staging and determining treatment.

**Lymph node status:** This indicates whether the cancer has spread to lymph nodes. This is important for staging and for determining how extensive the cancer is.

Genomic test results are also included in a pathology report. The results may be considered primary or secondary.

Primary results are directly related to explaining your symptoms or the reason for testing. This includes molecular testing, which tests the tumor sample for genomic mutations or genetic alterations. Types of molecular tests may include cytogenetics studies, flow cytometry and immunohistochemistry. You may also see results for microsatellite instability (MSI) testing, a relatively new test that may guide treatment options in a more personalized way, and tumor mutational burden (TMB), which assesses the number of genetic mutations in a tumor. Often, the report will include information about available clinical trials appropriate for the genetic alterations reported.

Secondary (or incidental) findings are medically meaningful but unrelated to the reason for testing. Secondary findings from molecular testing may include genetic risks for future disease, carrier status (carrying a gene for, but not exhibiting, a condition) and findings related to differences in how you may process medications. ■

## *When to consider a second opinion*

➥ **Identifying all of the characteristics** of the tumor to diagnose cancer is challenging. If the pathologist cannot determine the histologic type for any reason – for example, if the cancer is poorly differentiated – a second opinion from a genomic or molecular pathologist who specializes in cancer and molecular testing may be required. In this case, the pathologist may send a sample of the tumor and prepared microscopic slides to another pathology center for a second opinion.

Sometimes you may choose to seek a second opinion on your own. For example, if your pathology report does not contain a definitive diagnosis, requesting an opinion from another pathologist with extensive expertise in interpreting pathologic findings related to your type and subtype of cancer is strongly encouraged. Or you may have a rare type of cancer that not all oncologists and pathologists are experienced in treating.

Along with determining a diagnosis, a second opinion can confirm the diagnosis or even suggest an alternative one. Some doctors may favor one treatment approach, while others might suggest a different combination of treatments. Doctors in each oncology specialty bring different training and perspectives to cancer treatment planning. Another doctor's opinion may change the diagnosis or reveal a treatment your first doctor was not aware of.

Do not feel awkward or embarrassed about seeking another opinion. You deserve to know about all your treatment options, including clinical trials that you might want to consider. Because the goal is for you to get the best care possible, your pathologist or your oncologist can help you locate another expert to assist.

If you choose to get a second opinion, notes about samples that have been sent for other tests to another expert or hospital will be included on your pathology report.

# Genomic test results offer key input for your treatment path

➥ ***Your doctor may order genomic testing*** *during the diagnostic process or at another time during treatment. Read on to see sample scenarios of when and how genomic testing may occur and how it could help a doctor use those results, combined with other diagnostic results, to create a personalized treatment plan.*

## FICTIONAL CASE STUDY / CHRONIC LYMPHOCYTIC LEUKEMIA (CLL)

**Doug**, age 62, CLL*

***In this fictional scenario, Doug's treatment is guided by the results of his genomic testing.***

**Doug feels fine at his annual physical, but after his bloodwork comes back suspect, his primary care physician refers him to a hematologist who specializes in blood disorders.**

***What is Doug's diagnosis?***

After performing a variety of tests, the doctor confirms a diagnosis of chronic lymphocytic leukemia (CLL). Because the disease is in the early stage and Doug isn't experiencing any symptoms, his doctor recommends active surveillance — watching for signs that treatment should begin.

***Shouldn't his cancer be treated immediately?***

Doug feels physically fit and asks to begin treatment right away. His doctor explains that treating before it is necessary may introduce side effects and other complications. He also tells Doug that early treatment has not been shown to make people live longer with this disease, and it will not be a cure.

To ease Doug's anxiety, his doctor talks about the benefits of genomic testing and that treatment advances have significantly improved the lives of people with CLL. Through identifying biomarkers or gene mutations, doctors are better able to determine how the cancer will behave and, in turn, create the most effective treatment plan.

The doctor assures Doug that breakthroughs continue to be made, and even more therapies might be available once they are ready to treat.

***What happens in the meantime?***

They will both help monitor the CLL. Follow-up appointments will happen every six months. While the doctor watches for trends in Doug's blood test results that could signal a need to begin treatment, Doug will inform him of any physical symptoms, such as fatigue, swollen lymph nodes or drenching night sweats.

Doug researches reputable sources to learn more about CLL and joins a CLL support group. Both help him better understand how the disease is treated. For example, he discovers that one treatment often is not enough. Sometimes CLL treatments stop working or become less effective.

***Why did treatment become necessary?***

A couple of years later, Doug's blood test results show a trend of decreasing platelet and red blood cell counts. About the same time, he begins having night sweats, feels fatigued and is losing weight. His doctor says it is time to begin treatment.

Genomic tests are ordered to look for biomarkers, and the results are shared with a CLL expert physician. They determine Doug's CLL cells have a mutation in a gene called *TP53* that makes the cancer cells grow rapidly and makes them resistant to chemotherapy. Given his worsening symptoms and blood counts and enlarging lymph nodes, his doctor recommends targeted therapy — a type of treatment that uses drugs or other substances to target the protein that helps his cancer cells grow, divide and spread.

The targeted therapy is very effective. Doug has minimal side effects, feels better and his symptoms and blood counts improve.

Doug's doctor sets up a schedule of follow-up appointments for monitoring purposes. He is confident that if resistance occurs, other approved targeted therapy options and those in clinical trials will be available for Doug. The goal is that they will continue to manage the CLL as a chronic illness.

**Doug is not a real patient.*

## FICTIONAL CASE STUDY / BREAST CANCER

**Rosa**, age 58, Stage IV invasive ductal carcinoma*

***In this fictional scenario, Rosa learns how genomic testing helps determine the most effective treatments for her now and in the future.***

**A swollen lymph node under her arm prompts Rosa to see her doctor. He orders a mammogram, which reveals a tumor in Rosa's left breast. After receiving the results of an ultrasound, tumor biopsy and needle biopsy of the enlarged lymph node, Rosa's doctor sets up an appointment for her with an oncologist.**

***What is Rosa's diagnosis?***

The oncologist sits down with Rosa to discuss her diagnosis of Stage IV invasive ductal carcinoma. It is Stage IV because it involves several of her lymph nodes and has spread to her lungs. Her doctor also discusses the results of the three most common biomarkers tested at diagnosis in breast cancer: estrogen receptor *(ER)*, progesterone receptor *(PR)* and human epidermal growth factor receptor-2 *(HER2)*. Results show Rosa's breast cancer is *ER+*, *PR+*, *HER2-*.

***What is genomic testing, and why is it necessary?***

Because Rosa's cancer is being driven by hormones, blocking these receptors with hormone therapy can decrease tumor growth. The oncologist also orders genomic testing to look for other biomarkers that may indicate which types of drug therapy may work best against her type of breast cancer. It will help her better understand the unique features of Rosa's cancer.

Because breast cancer runs in Rosa's family, she is also a candidate for genetic testing. BReast CAncer genes *(BRCA1* and *BRCA2)*, common breast cancer genetic mutations, are also tested for. Certain targeted therapies are available to treat these mutations.

In addition, she may be a candidate for immunotherapy because her cancer is metastatic. To determine whether immunotherapy may be an

## **Lee**, age 38, Stage IV medullary thyroid cancer*

***In this fictional scenario, Lee is a patient whose genomic testing results give him hope for his advanced cancer diagnosis.***

**During his annual physical, Lee's physician feels a lump on his thyroid gland. He connects Lee with a head and neck cancer specialist who performs a thorough physical examination and medical history. He learns that Lee's father is currently being treated for medullary thyroid cancer. He orders several tests: bloodwork including a complete blood count (CBC) and a comprehensive metabolic panel, a neck ultrasound and a positron emission tomography (PET) scan. He also orders a fine-needle biopsy for diagnostic and genomic testing purposes. Though it is not common, some mutations present with medullary thyroid cancer can be inherited, so he adds genetic testing.**

### *Lee is unfamiliar with genomic testing and asks why it is necessary.*

His doctor explains that he suspects Lee may have thyroid cancer. After the biopsy results are reviewed by a pathologist, he will consider the test results, including those from genomic testing.

Performing genomic testing will help Lee's doctor identify any biomarkers that are present. That information can help him determine the treatment that will be most effective. He thanks Lee for providing his father's cancer history as family medical history is a helpful part of the diagnostic process because some biomarkers are hereditary. Lee volunteers to ask his father for details about his diagnosis.

While Lee waits for his test results, he learns that his father's tumor tested positive for a *RET* gene mutation. *RET* stands for "rearranged during transfection." He shares the news with his doctor.

### *What is Lee's diagnosis?*

The lump on Lee's thyroid is diagnosed as Stage IV medullary thyroid cancer because cancer cells are also found outside his thyroid in nearby lymph nodes.

### *What is Lee's treatment plan?*

In cases of advanced medullary thyroid cancer, it is standard to surgically remove the thyroid. However, that is only one part of the treatment plan recommended by Lee's multidisciplinary health care team. The results of Lee's genomic and genetic tests show that, like his father's, his tumor tests positive for the *RET* gene mutation. Lee's oncologist explains that he is encouraged because *RET* is a known mutation that can be treated with certain therapies designed to stop cancer cells from spreading and shrink the tumor before surgery.

Before moving forward with treatment, Lee's doctor talks with him about his plans to have children as some therapies can affect fertility. He refers him to a fertility specialist to make him aware of his options.

### *Will follow-up appointments be necessary?*

After the surgery and other treatments are complete, ongoing monitoring for recurrence will be necessary. Blood tests will measure his levels of the biomarkers calcitonin or carcinoembryonic antigen (CEA), which generally increase if cancer is present.

### *Should Lee share this information with his family members?*

Yes, because his test results show he inherited the *RET* mutation from his father, and it is important for him to be aware of the risk of passing the *RET* mutation to his children. These results can be complicated to comprehend, so Lee is referred to a genetic counselor who can help him understand how the results may affect his family, including preventive steps that may be available to help reduce the risk of cancer or potentially recognize it before it becomes advanced.

*Lee is not a real patient.

option, the amount of PD-L1 expression on the tumor cells and the tumor mutational burden (TMB) are also assessed. Microsatellite instability-high (MSI-H) and deficient mismatch repair (dMMR) are tested to determine whether the cancer is caused by genes that have problems repairing themselves.

### *What are Rosa's results?*

Genetic testing shows she has a mutation in the *BRCA1* gene. She is referred to a genetic counselor who can explain how the results may affect her and her family members in terms of hereditary mutations, preventive screenings and treatments, and more.

She also has a Ki-67 score greater than 20 percent, which indicates how likely the cancer is to grow and spread, and gives her oncologist information regarding Rosa's prognosis (outcome). Her low TMB levels and lack of MSI-H indicate that she may not respond well to immunotherapy.

### *What do Rosa's genomic testing results mean?*

The oncologist recommends neoadjuvant chemotherapy to shrink the tumor and a lumpectomy to surgically remove it. Rosa's treatment plan also includes hormone therapy used with targeted therapy, which is designed to target and destroy the cancer cells, lowering the risk of recurrence. Because the tumor is hormone receptor positive, the goal of hormone therapy is to slow or stop the growth of the hormone-sensitive tumor.

### *Are any of these genes or biomarkers hereditary?*

Yes. Rosa's doctor explains that everyone has two copies of the *BRCA1* and *BRCA2* genes, but not everyone has mutations in them. The risk of them leading to cancer increases if a close family member has developed a cancer.

*Rosa is not a real patient.

## **Erika**, age 46, Stage IV non-small cell lung cancer*

***In this fictional scenario, Erika's genomic testing results indicate she may respond best to a specific treatment option.***

**After a series of diagnostic tests and biopsies, Erika learns that what she thought was chronic bronchitis is actually Stage IV non-small cell lung cancer. A marathon runner who had never smoked, Erika asks her doctor two questions: How could I possibly have lung cancer? And what are we going to do about it?**

**Erika's doctor explains that though smoking is the main risk factor for lung cancer, simply having lungs is a risk factor. And though it is difficult to say what caused the cancer, she can be more certain about how to treat it after evaluating the results of her extensive diagnostic tests.**

**The results of the bloodwork, imaging and biopsies determine the pathologic type and subtype of the lung cancer as well as the stage. That information, combined with the results of the biomarker (molecular) testing that may identify the presence of biomarkers and mutations, helps them determine the treatment that is most likely to be effective for Erika. Clinical trials are one option, and these may be specific for a subgroup if a biomarker or mutation is identified.**

### *Why is it important to identify biomarkers or mutations?*

Several mutations are known to be present in non-small cell lung cancer, and many have specific treatments that are designed to target them.

Erika's doctor uses next-generation sequencing (NGS) to test for specific genes. Her physician orders this test from a blood sample with an expectation that a result will be available within 7 to 10 days. Her physician also orders NGS testing on DNA and RNA from her diagnostic biopsy. Results from this analysis should be expected in around 3 weeks. The blood testing is ordered because results should be available in the most rapid timeframe and, if an abnormality is found, it could be used to select therapy because of its accuracy. However, the blood testing is not as sensitive as the tissue testing. Thus, if no actionable abnormalities are found in the blood, a molecular abnormality may still be found in the more sensitive tissue test. This technique is capable of processing multiple DNA sequences simultaneously with more speed and accuracy than single-gene tests.

### *What is the doctor looking for?*

Erika's doctor tests for the following mutations that may be present in non-small cell lung cancer: *ALK, BRAF, EGFR, MET, NTRK, RET, ROS1, KRAS* and *HER2*. Approved targeted therapies are available for all of these; however, Erika's cancer does not test positive for any of the mutations. Erika is disappointed, but her doctor encourages her not to lose hope. More testing could introduce another treatment option.

### *Erika's doctor also considers immunotherapy.*

Certain tests are performed to help determine whether Erika might be a candidate for immunotherapy. One test measures the amount of programmed cell death-ligand 1 (PD-L1) expression on the tumor cells or immune cells in the tumor's microenvironment, which may include the cells, molecules and structures (such as blood vessels) that surround and support the tumor. PD-L1 is a protein that is commonly expressed by cancer cells and this protein inhibits tumor killing by immune cells. Tumor mutational burden, the number of genetic mutations in a tumor, is also assessed. Microsatellite instability-high (MSI-H) and deficient mismatch repair (dMMR) are tested to determine whether the cancer cells have a greater-than-normal number of microsatellites, which are short, repeated sequences of DNA, or if the cancer is caused by genes that have problems repairing themselves.

Test results show that Erika has a high level of PD-L1, which indicates she may respond well to immunotherapy either alone or with chemotherapy.

### *What is Erika's treatment plan?*

Erika's doctor recommends moving forward with a first-line treatment consisting of immunotherapy.

**Erika is not a real patient.*

## *Tips for a Caregiver* / *from Erika's husband**

*In this fictional scenario, Jamal* offers his perspective on caregiving for his wife.*

After we digested the news that Erika had lung cancer, I found myself wanting to be useful and find a way to help my wife. My approach was that this wasn't just her cancer diagnosis, but a challenge for our family to overcome together. I attended all of her appointments with her, and we decided to ask her sister to help us keep our family and friends informed.

***My advice to others when they learn of a loved one's cancer would be....***

- **Learn all you can about the diagnosis, including the type, subtype and any biomarkers.**
- **Meet the health care team, and build a strong relationship with them. This includes the nurse navigator, patient navigator or social worker.**
- **Sign appropriate forms so you can have access to electronic patient records or portals.**
- **Help manage and track medications, and go to appointments with them.**
- **Be a good listener.**
- **Encourage a healthy lifestyle.**
- **Stay alert to physical and emotional changes. Know when to seek professional help.**
- **Don't overhelp. Ask them what type of help they want.**
- **Accept offers of help from loved ones and friends by assigning tasks.**
- **Practice self-care, including keeping up on your medical appointments.**
- **Assist with legal issues. Help your loved one set up an Advance Medical Directive, a Durable Power of Attorney for Health Care (also known as a health care agent or proxy) and a Living Will.**

**Jamal is not a real person.*

# Support and financial resources available for you

## CANCER EDUCATION

Alex's Lemonade Stand Foundation for Childhood Cancer ..... www.alexslemonade.org
American Cancer Society ..... www.cancer.org
American Society of Clinical Oncology ..... www.cancer.net
CANCER101 ..... www.cancer101.org
Cancer*Care* ..... www.cancercare.org
Cancer Support Community ..... www.cancersupportcommunity.org
Centers for Disease Control and Prevention (CDC) ..... www.cdc.gov
The Gathering Place ..... www.touchedbycancer.org
Get Palliative Care ..... www.getpalliativecare.org
Global Resource for Advancing Cancer Education (GRACE) ..... www.cancergrace.org
The Hope Light Foundation ..... www.hopelightproject.com
LLS | PearlPoint Nutrition Services ..... www.pearlpoint.org
National Cancer Institute ..... www.cancer.gov
National Comprehensive Cancer Network (NCCN) ..... www.nccn.org
National LGBT Cancer Network ..... www.cancer-network.org
NCI Cancer Information Service ..... 800-422-6237
OncoLink ..... www.oncolink.org
Patient Resource ..... www.patientresource.com
Scott Hamilton CARES Foundation ..... www.scottcares.org
Triage Cancer ..... www.triagecancer.org
Union for International Cancer Control ..... www.uicc.org
U.S. National Library of Medicine ..... www.nlm.nih.gov

## CAREGIVERS & SUPPORT

4th Angel Patient & Caregiver Mentoring Program ..... www.4thangel.org, 866-520-3197
Cactus Cancer Society ..... www.cactuscancer.org
CanCare ..... www.cancare.org, 888-461-0028
CANCER101 ..... www.cancer101.org, 646-638-2202
Cancer and Careers ..... www.cancerandcareers.org, 646-929-8032
Cancer*Care* ..... www.cancercare.org, 800-813-4673
Cancer Connection ..... www.cancer-connection.org, 413-586-1642
Cancer Hope Network ..... www.cancerhopenetwork.org, 877-467-3638
Cancer Really Sucks! ..... www.cancerreallysucks.org
Cancer Support Community ..... www.cancersupportcommunity.org
Cancer Support Community Helpline ..... 888-793-9355
Cancer Survivors Network ..... csn.cancer.org, 800-227-2345
Caregiver Action Network ..... www.caregiveraction.org, 855-227-3640
CaringBridge ..... www.caringbridge.org
Center to Advance Palliative Care ..... www.capc.org
Chemo Angels ..... www.chemoangels.com
The Children's Treehouse Foundation ..... www.childrenstreehousefdn.org
Cleaning for a Reason ..... www.cleaningforareason.org
Connect Thru Cancer ..... www.connectthrucancer.org
Cooking with Cancer ..... www.cookingwithcancer.org, 205-978-3570
Family Caregiver Alliance ..... www.caregiver.org, 800-445-8106
Friend for Life Cancer Support Network ..... www.friend4life.org, 866-374-3634
The Gathering Place ..... www.touchedbycancer.org, 216-595-9546
Guide Posts of Strength, Inc. ..... www.cancergps.org, 336-883-4483
Imerman Angels ..... www.imermanangels.org, 866-463-7626
Livestrong Foundation ..... www.livestrong.org, 855-220-7777
Living Hope Cancer Foundation ..... www.getupandlive.org
LivingWell Cancer Resource Center ..... www.livingwellcrc.org, 630-933-7860
Lotsa Helping Hands ..... www.lotsahelpinghands.com
The Lydia Project ..... www.thelydiaproject.org, 877-593-4212
MyLifeLine ..... www.mylifeline.org, 888-793-9355
National LGBT Cancer Project ..... www.lgbtcancer.org, 917-301-1913
Patient Empowerment Network ..... www.powerfulpatients.org
SHARE Caregiver Circle ..... www.sharecancersupport.org/caregivers-support, 844-275-7427
Stronghold Ministry ..... www.mystronghold.org, 877-230-7674
Triage Cancer ..... www.triagecancer.org, 424-258-4628
Walk With Sally ..... www.walkwithsally.org, 310-322-3900
Well Spouse Association ..... www.wellspouse.org, 732-577-8899
weSPARK Cancer Support Center ..... www.wespark.org, 818-906-3022

## CLINICAL TRIALS

Be the Match | Jason Carter Clinical Trials Program ..... www.ctsearchsupport.org, 888-814-8610
BreastCancerTrials.org ..... www.breastcancertrials.org
Cancer Support Community ..... www.cancersupportcommunity.org/find-clinical-trial, 888-793-9355
Center for Information & Study on Clinical Research Participation ..... www.searchclinicaltrials.org
ClinicalTrials.gov ..... www.clinicaltrials.gov
Fight Colorectal Cancer ..... trialfinder.fightcrc.org
Head and Neck Cancer Alliance ..... www.headandneck.org/clinical-trials, 866-792-4622
Lazarex Cancer Foundation ..... www.lazarex.org, 877-866-9523, 925-820-4517
The Leukemia & Lymphoma Society ..... www.lls.org/treatment/types-of-treatment/clinical-trials/finding-a-clinical-trial
LUNGevity Clinical Trial Search ..... clinicaltrials.lungevity.org
Metastatic Breast Cancer Trial Search ..... www.breastcancer.org/treatment/clinical_trials/metastatic-trials-tool
Multiple Myeloma Research Foundation ..... www.themmrf.org/resources/clinical-trial-finder
National Cancer Institute ..... www.cancer.gov/clinicaltrials, 800-422-6237
NCI Cancer Information Service ..... 800-422-6237
Sarcoma Alliance for Research Through Collaboration (SARC) ..... www.sarctrials.org
ThyCa Thyroid Cancer Survivors' Association, Inc. ..... www.thyca.org/about/clinical-trials
TNBC Foundation Clinical Trials Matching Service ..... www.tnbcfoundation.org/research/clinical-trials
WCG CenterWatch ..... www.centerwatch.com, 866-219-3440

## GOVERNMENT ASSISTANCE

Benefits.gov ..... www.benefits.gov
Centers for Medicare & Medicaid Services ..... www.cms.gov
Disability Benefits Center ..... www.disabilitybenefitscenter.org
Eligibility.com (Medicare resources) ..... www.eligibility.com/medicare
Hill-Burton Program ..... www.hrsa.gov/get-health-care/affordable/hill-burton, 800-638-0742
InsureKidsNow.gov ..... www.insurekidsnow.gov, 877-543-7669
Legal Services Corporation ..... www.lsc.gov, 202-295-1500
Medicare Rights Center ..... www.medicarerights.org, 800-333-4114
National Breast and Cervical Cancer Early Detection Program ..... www.cdc.gov/cancer/nbccedp, 800-232-4636
National Council on Aging ..... www.ncoa.org, 571-527-3900
Social Security Administration ..... www.ssa.gov, 800-772-1213
State Health Insurance Assistance Programs ..... www.shiphelp.org, 877-839-2675
U.S. Department of Veterans Affairs ..... www.va.gov/health

## MENTAL HEALTH SERVICES

American Psychosocial Oncology Society Helpline ..... 866-276-7443

## PATIENT ADVOCACY

American Cancer Society Cancer Action Network ..... www.fightcancer.org
Cancer Legal Resource Center ..... www.thedrlc.org/cancer
Cancer Support Community ..... www.cancersupportcommunity.org
Dream Foundation ..... www.dreamfoundation.org
Firefighter Cancer Support Network ..... www.firefightercancersupport.org
Friend for Life Cancer Support Network ..... www.friend4life.org, 866-374-3634
The Gathering Place ..... www.touchedbycancer.org
Gems of Hope, Inc. ..... www.gemsofhope.com
LivingWell Cancer Resource Center ..... www.livingwellcrc.org
National Coalition for Cancer Survivorship ..... www.canceradvocacy.org
Office of Cancer Survivorship ..... www.cancercontrol.cancer.gov/ocs
Patient Advocate Foundation ..... www.patientadvocate.org
Research Advocacy Network ..... www.researchadvocacy.org

## PATIENT ASSISTANCE RESOURCES

AbbVie ..... www.abbviepaf.org, 800-222-6885
Astellas Pharma ..... www.astellaspharmasupportsolutions.com, 800-477-6472
AstraZeneca ..... www.myaccess360.com/patient, 844-275-2360
Bristol-Myers Squibb ..... www.bmsaccesssupport.com, 800-861-0048
Genentech ..... www.genentech-access.com/patient, 877-436-3683
Janssen ..... www.janssencarepath.com, 877-277-3728
Lilly Oncology ..... www.lillyoncologysupportcenter.com, 866-472-8663
Merck ..... www.merckhelps.com, 800-727-5400
Novartis ..... www.patientassistancenow.com, 800-282-7630
Pfizer ..... www.pfizeroncologytogether.com, 877-744-5675
Sanofi Genzyme ..... www.sanoficareassist.com, 833-930-2273
Takeda Oncology ..... www.here2assist.com, 844-817-6468

➥ *For more resources, go to* PatientResource.com

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*Where information equals hope*