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Post-transplant combination
maintenance clinical trial in AML

A Research Study of an Investigational
Drug Combination After Allogeneic
Stem Cell Transplantation in Patients
with Acute Myeloid Leukemia.



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This investigational drug combination is being studied in the clinic for new uses in CLL and AML and is not approved by the FDA or other global regulatory health authorities. Safety and efficacy are under evaluation.

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Vice Presidents, Business Development	Amy Galey Kathy Hungerford
Office Address	8455 Lenexa Drive Overland Park, KS 66214
For Additional Information	prp@patientresource.com
Advisory Board	Visit our website at PatientResource.com to read bios of our Medical and Patient Advisory Board.

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A strong support system is invaluable

Most any challenge is easier to face when you have help, and a cancer diagnosis is no different. You may not realize you already have a built-in support system. A skilled and compassionate health care team is waiting to guide you on your treatment path. And, you have access to a community of cancer survivors and advocates who are committed to making sure you do not face this diagnosis alone.

Support Begins at Home

Start with your inner circle. Think of the people you interact with on a regular basis, such as family, loved ones, friends, neighbors, spiritual community and co-workers. They are your foundation. They are the people who will ask you what you need. Their offers are sincere, so accept them and give serious thought to how they can help. Consider the following suggestions.

Designate a caregiver. This naturally may be your spouse, significant other, parent, child or another loved one. A caregiver takes on many roles, from accompanying you to appointments and being involved in making decisions about your treatment plan to assisting with activities of daily living and simply being a source of comfort. If you can, try to have more than one caregiver to spread out the responsibilities. If you do not have a person to help in this capacity, you can look for other sources of care in your community, such as from your spiritual community, a local caregiving agency or a cancer advocacy group.

Appoint a communicator. Keeping everyone informed about your situation is time-consuming. It can also be inconsistent because it is impossible to update everyone every time a change occurs. Ask someone to take the lead and deliver your updates using email, text or another form of social media. That way, you know the same message is being delivered to everyone at the same time. No one hears it first, and no one hears it last.

Accept offers for meals. Good nutrition is not only crucial for you during cancer treatment, it is important for the other family members living at home. It is easy to slip into a routine of grabbing fast food or ordering in because of convenience, but those are not always the healthiest options. Healthy eating takes planning. When friends ask if they can bring over a meal, say yes, and be sure to mention the types of foods that will be healthiest, or most appetizing, for you and your family.

Coordinate transportation. There may be times when you do not feel well enough to drive. Ask a friend to be your designated driver to take you to appointments or on errands. If you have children, elderly parents or other family members who rely on you to take them to school, sporting events or appointments, look into neighborhood carpools and ask friends for help.

Get to Know Your Health Care Team

A multidisciplinary approach is taken to treat cancer. This team approach combines the wisdom, training and experience unique to



each cancer specialist and enables the specialists to work together to provide you with the best care available. They are also a trusted resource to help you learn the information relevant to your tumor type and stage. Though the members of your team may differ depending on your diagnosis and treatment center, your team will likely include a medical oncologist, radiation oncologist, surgical oncologist, pathologist, oncology nurses, nurse/patient navigator, palliative care specialists and more.

While the medical personnel manage your medical care, the members of your supportive care team will focus on helping you and your family members manage the physical, emotional, practical, spiritual, financial and family-related challenges associated with cancer (see *Supportive Care*, page 6).

Your navigator will be a valuable source of support to you. Nurse navigators are professional registered nurses with oncology-specific clinical knowledge. They offer individual assistance to patients, families and caregivers in the often-complicated world of medical care. Patient navigators help patients set up appointments for doctor visits and medical tests and get financial, legal and social support. They may also work with insurance companies, employers, case managers, lawyers and others who have an effect on a patient's health care needs. They are sometimes called patient advocates.

Discover the Cancer Community

Connect with a local or national cancer advocacy group. Many groups offer peer-to-peer support through programs that match you with a person who has had a similar diagnosis. Talking with someone who knows what you are going through is extremely helpful.

You may also consider joining an in-person or online (virtual) cancer support group. Support groups offer the chance to talk with others who are facing the same challenges, learn what works for them in terms of managing their diagnoses, and share knowledge about your own experiences.

Ask your nurse/patient advocate for a referral, and use the resources beginning on page 37 in this guide.

Lean on and learn from these valuable sources of support, and don't forget to stay hopeful. Treating cancer has come a long way and many people are living longer with a higher quality of life than just a few years ago. Continue to set goals, plan special events and live your best life possible. Find the things that bring you joy and happiness. ■



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Explore your options and move forward with confidence

New and improved strategies continue to offer promise for curing, treating and managing cancer. Many types of treatment are available, but not all types treat every diagnosis. Learn about your options to make you feel more informed and confident as you and your medical team develop a treatment plan uniquely suited to you.

Deciding where to be treated is often a key consideration, as is choosing your oncologist. Depending on your diagnosis, it may benefit you to seek out a specialist, especially if you have a rare type of cancer or one that does not have many available treatments. Specialists are typically leaders in research and more aware of cutting-edge treatments, including clinical trials. If a specialist is not nearby, you can request that one consult with your local oncologist. The second opinion is valuable, and it is wise to gather all the information you can.

Staging is an important part of developing your treatment plan. Doctors commonly use the tumor, node and metastasis (TNM) system developed by the American Joint Committee on Cancer (AJCC). It classifies the tumor (T) according to its dimensions or size, whether cancer cells are found in nearby lymph nodes (N) and whether it has metastasized (M), or spread, to other parts of the body. They are combined to create a stage. Learn how your type of cancer is classified and staged by visiting PatientResource.com and searching by cancer type.

Once you find your medical team, communicate frequently and honestly with them. Do not be afraid to ask questions as you discuss treatment options, possible side effects and expectations for your quality of life. Be sure you understand why it is critical to stay on schedule with appointments for treatments and those you take at home. And, keep in mind that cancer treatment plans are commonly adjusted as the cancer or your response to treatment change. Cancer treatment is a fluid process — patience is a good asset to have. And remember, for most cancer situations it is okay to take the time necessary to get other opinions before making a final decision.

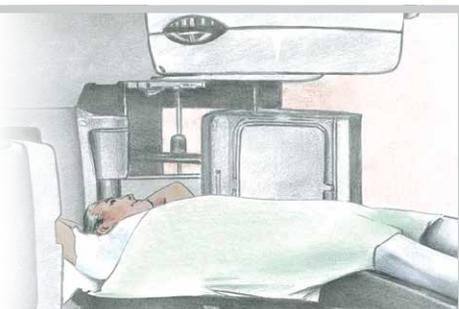
Treatment Types

Treatment plans often include one or more of the following options.

Surgery is the primary method for treating a solid tumor. Removing it may offer the best chance of controlling the disease and preventing it from spreading, especially for people with early-stage disease. Your

FIGURE 1 RADIATION THERAPY

External-beam radiation therapy (EBRT) may be used to treat some types of cancer. EBRT uses a machine to direct high-energy beams of radiation at cancer cells inside the body.



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doctor may also perform a surgical procedure to stage the cancer or to relieve or prevent symptoms that may occur later.

Radiation therapy uses high-energy radiation to destroy cancer cells and shrink tumors. Other uses include targeting specific parts of the body for localized disease or bone pain, and giving it prior to a stem cell transplant. It may also be delivered as neoadjuvant therapy to shrink tumors before surgery and as adjuvant therapy to kill remaining cancer cells after surgery.

External-beam radiation therapy (EBRT) delivers radiation from a machine outside the body (see Figure 1). Types of EBRT include three-dimensional conformal radiation therapy, stereotactic body radiotherapy and intensity-modulated radiation therapy. A newer type of radiation, proton therapy, uses charged particles called protons.

Brachytherapy, also called internal radiation therapy, uses a radioactive substance sealed in needles, seeds, wires or catheters placed directly into or near the cancer. Radiation may be delivered at a high dose rate (over several hours) or at a low dose rate (over a longer period). Alpha emitter radiation therapy uses radiopharmaceuticals, which are drugs that give off targeted radiation, to suppress cancer in the bones and reduce pain.

Drug therapy may be given through an IV into a vein or a port in your body (see Figure 2). It may also be given as an injection (shot), subcutaneously (injection under the skin) or orally as a pill or liquid.

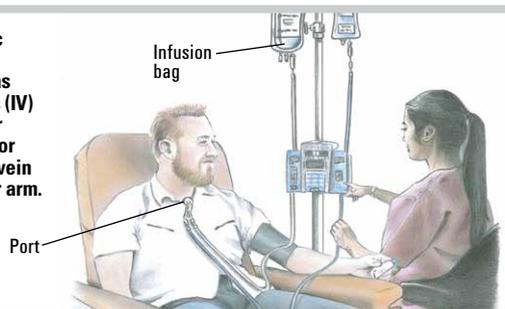
Chemotherapy travels through the bloodstream and affects cells all over the body. It is typically delivered in cycles, with treatment periods followed by rest periods to give your body time to recover. Chemotherapy may be used alone or with other drug therapies and forms of treatment, such as stem cell transplantation or chimeric antigen receptor (CAR) T-cell therapy.

Immunotherapy is designed to use the body's own immune system to recognize and destroy cancer cells. This strategy trains the immune system to respond to cancer, giving it the potential for a response that can extend beyond the end of treatment. Different types of immunotherapy are approved to treat the types of cancer discussed in this guide. Some are used alone or with other therapies.

Targeted therapy uses drugs 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. This

FIGURE 2 DRUG THERAPY

Some systemic treatments are administered as an intravenous (IV) infusion, either through a port or directly into a vein in your hand or arm.



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therapy targets genes, proteins or other substances that support the tumor. Some of these drugs may be given alone or in combination with other drug therapies. Different types of targeted therapy may be available depending on your diagnosis.

Hormone therapy blocks the stimulating effect of hormones. It slows or stops the growth of cancer and is used because hormones that occur naturally in the body promote the growth of some cancers. Both drug treatment and surgery can function as hormone therapy.

Corticosteroids are drugs that can help reduce inflammation and may offer other benefits. They can be used alone or in combination with other drug therapies.

Bone-modifying drugs can treat bone problems caused by some cancers and therapies, such as hormone therapy. These drugs can also prevent further bone damage from occurring.

Active surveillance, also called watchful waiting or watch and wait, may be recommended for cancer that appears to be growing very slowly. Postponing treatment allows you to avoid potential treatment side effects for as long as possible while your doctor closely monitors you for signs that active treatment is necessary. Regularly scheduled imaging tests and blood tests will be necessary. It is very important to make and keep these appointments because treatment should begin if cancer progression occurs.

Stem cell transplantation, also known as bone marrow transplantation, is an infusion of healthy blood stem cells into the body, typically

after high-dose chemotherapy. The two main types are autologous (auto) and allogeneic (allo) transplants. An *auto transplant* uses the patient's own stem cells, which are collected, filtered, processed and frozen. High-dose chemotherapy and sometimes full-body radiation (conditioning) are given to destroy cancer cells. The reserved stem cells are thawed and infused back into the patient's body. An *allo transplant* uses stem cells donated by a family member or unrelated donor. It may be used for patients with a high risk of relapse, those who are not responding fully to other treatments or those who have relapsed disease.

Radiofrequency ablation (RFA) therapy may be used to treat a tumor that is unresectable (inoperable) or when surgery is not an option for another reason. This type of therapy focuses on the cancer's location. The minimally-invasive, image-guided procedure kills cancer cells by inserting a needle through the skin directly into the tumor and running electrical current through it to subject the tumor to extreme temperatures. Other types of therapy include microwave ablation (MWA) and cryoablation, also called cryosurgery or cryotherapy.

Plasmapheresis may be used if the blood becomes too thick. It uses a machine to filter plasma out of the blood.

Clinical trials are medical research studies that may offer access to leading-edge treatments not yet widely available. They may be an option at any stage, even as a first-line treatment. Flip over this guide to learn more in *Cancer Clinical Trials*. ■



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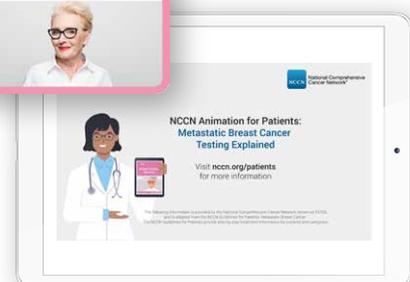
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Proactively prepare for side effects

Knowing the side effects that may occur – and setting expectations for how to manage them if they do – will help you feel more prepared for treatment. The most important thing to remember is to communicate honestly with your health care team about how you feel, both physically and emotionally. The sooner they are aware of changes, the quicker they can help.

To help you maintain the best quality of life possible, your health care team will rely on a group of services known as supportive care. Supportive care addresses the physical, emotional, practical, spiritual, financial and family-related challenges associated with cancer. Many people begin by getting help to manage side effects and pain. Counseling about nutrition, fitness, mental health or spirituality; physical/occupational therapy; speech therapy; complementary medicine and other areas are also available. Supportive care is available to your children, family members, caregivers and others close to you.

You may receive these services from an advanced practice nurse, physical therapist, dietitian or palliative medicine specialist who has extra training in symptom management. These services may be offered at your hospital, cancer center or medical clinic and are often covered by individual insurance plans, Medicare and Medicaid. To learn more, you can talk with the hospital's social worker, financial counselor or your health insurance representative. And, use the resources in this guide beginning on page 33.

Potentially Severe Side Effects

Though serious side effects are rare, they can occur with certain types of treatment. Ask your doctor whether you are at risk from the therapies in your treatment plan, how to identify the symptoms and when to seek emergency care. Report symptoms immediately if they occur so they can be treated promptly. Some potentially severe side effects include the following:

- **Infection** can occur as a result of a low white blood cell count (neutropenia) or other factors. Contact your doctor immediately – do not wait until the next day – if you have any of these symptoms: oral temperature over 100.4 °F, chills or sweating; body aches, chills and fatigue with or without fever; coughing, shortness of breath or painful breathing; abdominal pain; sore throat; mouth sores; painful, swollen or reddened skin; pus or drainage from an open cut or sore; pain or burning during urination; pain or sores around the anus; or vaginal discharge or itching. If you cannot reach your doctor, go to the emergency room.
- **Immune-related adverse events** (irAEs) may occur with certain immunotherapy drugs if the immune system becomes overstimulated by treatment and causes inflammation in one or more organs or systems in the body. Some irAEs can develop rapidly, becoming severe and even life-threatening without immediate medical attention.
- **Cytokine release syndrome** can occur with CAR T-cell therapies if immune cells affected by treatment rapidly release large amounts of cytokines into the bloodstream. Symptoms may include headache, fever, nausea, rash, low blood pressure, rapid heartbeat and difficulty breathing.

- **Infusion-related reactions** most frequently occur with treatment given intravenously (IV) through a vein in your arm, usually soon after exposure to the drug. Reactions are generally mild, such as itching, rash or fever. More serious symptoms such as shaking, chills, low blood pressure, dizziness, breathing difficulties or irregular heartbeat can be serious or even fatal without medical intervention.
- **Tumor lysis syndrome** (TLS) may occur after treatment of a fast-growing cancer, especially certain blood cancers. Symptoms may include vomiting, diarrhea, muscle cramps or twitches, neuropathy and decreased urination. TLS can potentially cause damage to the kidneys, heart, liver or other organs.

Common Side Effects

Every person reacts to treatment differently, even when the diagnosis and the treatment are similar. As you and your doctor review your treatment options, discuss the potential side effects of each type of

▲ **TABLE 1**
SOME COMMON SIDE EFFECTS OF CANCER AND ITS TREATMENT

Side Effects	Symptoms
Anemia	Low energy, weakness, dizziness, light-headedness, shortness of breath, rapid heartbeat
Bleeding & bruising	Hemorrhaging and bruising
Blood clots	Leg discomfort
Bone loss and pain	Weakened bone caused by the cancer or treatment
Chemo brain	Brain fog, confusion and/or memory problems
Constipation	Difficulty passing stools or less frequent bowel movements compared to your usual bowel habits
Decreased appetite	Eating less than usual, feeling full after minimal eating, not feeling hungry
Diarrhea	Frequent loose or watery bowel movements
Fatigue	Tiredness that is much stronger and harder to relieve than the fatigue an otherwise healthy person has
Fever	Raised body temperature that could signal an infection
Hair loss (alopecia)	Hair loss on the head, face and body
Headache	Pain or discomfort in the head
Hypercalcemia	Excessive thirst and/or urination, headaches, nausea/vomiting, severe constipation, confusion, depression or decreased appetite
Lymphedema	Swelling where lymph nodes have been removed or damaged
Nausea and vomiting	The feeling of needing to throw up and/or throwing up
Neuropathy	Numbness, pain, burning sensations and tingling, usually in the hands or feet at first
Neutropenia	Low white blood cell count that increases the risk of infection
Pain	Musculoskeletal and joint pain and aches that occur in the muscles, bones, tendons, ligaments or nerves
Respiratory problems	Shortness of breath (dyspnea) with or without cough, upper respiratory infections
Skin reactions	Rash, redness and irritation, or dry, flaky or peeling skin that may itch
Thrombocytopenia	Low number of platelets in the blood, which can lead to bruising and bleeding
Weight changes	Gaining or losing weight

therapy and how to manage them should they occur, including any that require immediate medical attention (see Table 1).

Along with physical side effects, cancer treatment can bring up a range of emotions. These feelings are normal and should be addressed. Taking care of your emotional well-being will help you cope better and manage physical side effects.

Some emotional side effects may include:

- **Anxiety** can begin as soon as you receive your diagnosis. Moderate to severe anxiety is often treated with medication, therapy or a combination of both.
- **Depression** is not “just part of having cancer.” If these feelings last more than a few days or if you have thoughts of death or of attempting suicide, seek medical attention immediately.
- **Fear** is common, and every ache and pain may trigger a concern. Do your best to stay focused on the present.
- **Scxiety** is the anxiety that can happen when you are awaiting results from imaging scans, laboratory tests or exams. These feelings are normal because every set of results could be life-changing. Talk with your doctor or nurse so you can know when to expect results.
- **Sexuality issues**, such as reduced desire or feeling less desirable, may occur. Sexual health is an important part of life. Share your

concerns with your doctor. If you have a partner, be open with your feelings and about finding new ways to be intimate.

Contact your medical team by phone or the online portal when a physical or emotional side effect or symptom begins so it can be treated or managed immediately. Also, be alert for late effects. They are side effects that can occur months or even years after treatment begins.

Support in All Areas

Supportive care extends to other areas. Use the resources beginning on page 33 of this guide, and ask your health care team for referrals to trusted sources. You do not have to go through this alone.

Social support is available in many forms. You may choose to speak with a therapist or attend an online, telephone or in-person support group. Many advocacy programs offer one-on-one buddy programs that pair you with another person who has the same type of cancer.

Spiritual guidance, even if you do not consider yourself a religious person, is available from a chaplain at the hospital or from your religious community.

Financial counseling can help relieve the stress and anxiety of paying for treatment and other related expenses. Knowing the costs of treatment and related expenses and making a plan may help you feel more in control. ■



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Discovering mutations guides cancer care and prevention

Specialized testing that identifies the presence or absence of cancer-causing mutations offers valuable information. The goal of these genomic and genetic tests is to provide you with the tools you and your medical team need to personalize your care.

Explaining Mutations

Researchers have discovered that cancer stems from changes in our DNA, the unique information plan for the growth and control of an individual's cells. Cancer forms when genes begin to change, or mutate, within the structure of normal cells.

Mutations are generally described as one of two types: acquired (somatic mutations) and inherited (germline mutations). 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. Inherited mutations are inherited from a parent. If you have inherited a mutated gene, it does not mean you will automatically develop cancer; it only means the risk is increased.

Testing for these mutations using advanced technologies is changing how doctors approach cancer treatment. The words genetic and genomic are often used interchangeably, but they have different goals and outcomes.

Genomic Testing

Also known as tumor profiling, genomic testing allows doctors to learn about a 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. Doctors may use genomic testing for any of the following:

- Diagnosing and staging a cancer
- Determining prognosis (outlook)
- Evaluating whether therapies are available to treat mutations in that specific cancer
- Choosing more precise treatments
- 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).

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 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 to check those cells for mutations.

Genomic testing frequently involves testing for biomarkers, which is also known as molecular testing. Biomarkers are substances such as genes or molecules that are produced by cancer cells or other cells of the body in response to cancer. They can be measured in the blood, plasma, urine, cerebrospinal fluid or other body fluids or tissues. Bio-

markers are routinely tested for in certain cancers. Your doctor will let you know if biomarker testing may be beneficial for your treatment strategy (see Table 1).

Not every tumor has known mutations, and some are identified that do not yet have a specialized treatment. In those cases, standard of care treatments and clinical trials are potential options to consider.

Genetic Testing

Several types of cancer are known to run in families, including breast, ovarian, thyroid, prostate, pancreatic, kidney and stomach cancers, as well as melanoma and sarcoma. Genetic testing helps determine whether you have inherited a mutation that increases your risk for developing certain types of cancer.

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

If you have any of these, you may consider genetic testing. If you inherited a mutated gene, you can explore ways to lower your risk, such as surgery, medication, frequent screenings or lifestyle changes.

Genetic testing may be done using a saliva or blood sample. 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 designated laboratories that are regulated to meet standards for accuracy and reliability. And the commercial tests may not screen for all the possible genes and mutations for a particular cancer.

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. ■

▲ 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 a prediction of 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 be tested to 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.

CANCER TYPES



*Treating
cancer
takes a
community*

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Chronic Lymphocytic Leukemia

Chronic lymphocytic leukemia

(CLL) is a generally slow-growing type of hematologic (blood) cancer that develops when a type of white blood cell known as a lymphocyte changes and multiplies uncontrollably. These cells grow at a faster rate than usual, and they do not die when they should, causing them to build up to become cancer cells. They circulate in the bloodstream and can spread through the lymphatic system to other parts of the body.

Except for lymphomas, blood cancers typically do not grow into tumors. But, because lymphocytes make up lymphoid tissue, which is found in the lymph nodes, thymus, spleen, tonsils and other parts of the body, patients with CLL often have larger than normal lymph nodes that can appear as lumps in the neck, armpits or groin regions. This accumulation of cancer cells in the blood, bone marrow, lymph nodes and spleen interferes with the normal production of healthy cells, including red blood cells that carry oxygen, white blood cells that fight infection, and platelets that help blood to clot.

DIAGNOSING & PLANNING

Once you receive your diagnosis, consider contacting a CLL specialist. Advances in CLL treatment are happening so rapidly that not every oncologist has the opportunity to be involved in that progress. If you do not live near a specialist and travel is not an option, ask if the specialist will consult on your case with your local oncologist.

To identify your CLL subtype, your doctor will order molecular profiling on a small sample of fluid or tissue. The results of these tests, including a fluorescence in situ hybridization (FISH) test, your *TP53* gene mutation status, immunoglobulin heavy chain variable (*IGHV*) status, and serum B2-microglobulin concentration, help identify specific gene abnormalities or mutations, proteins and changes in chromosomes.

The Modified Rai Staging System and the Chronic Lymphocytic Leukemia International Prognostic Index (CLL-IPI) further assist your doctor in staging your CLL to determine the best treatment options for you. Modified Rai divides CLL into five stages according to the number of lymphocytes and other cells in the blood and the presence of certain abnormalities noticed on the physical examination. The “risk” characteristic assigned in staging is associated with the

predicted rate of growth for the disease. This offers information about how CLL may progress. CLL-IPI is used to predict the risk of disease recurrence and overall survival, and incorporates the Rai stage.

Along with the results of molecular profiling, your doctor will also consider the clinical stage, your age and other criteria to help determine the treatment that will be most effective for your CLL.

TREATMENT OPTIONS

CLL primarily is managed like a chronic disease. The goal of treatment is to no longer have signs or symptoms of cancer.

Complete remission is when all signs and symptoms of cancer have disappeared, but cancer may still be in the body. Partial remission is when leukemia levels are significantly reduced, but there is still evidence of some leukemia cells. Your doctor may use highly sensitive laboratory tests to look for minimal residual disease (MRD). The testing can find one cancer cell among one million normal cells. This information helps your doctor determine whether the treatment is working or the cancer has returned.

To reach these milestones, your treatments may change as the disease changes. However, researchers continue to discover new ways to treat it, giving many people with CLL more treatment options.

Active surveillance, also called watchful waiting, is an approach used before medical treatment becomes necessary. It is often recommended for early-stage or low-risk CLL when no disease-related symptoms are present. Although delaying active treatment may seem odd, research shows that treating CLL early does not improve the outcome, and it could introduce side effects.

As your medical team monitors you with tests and physical exams, you will be responsible for keeping follow-up appointments and alerting your medical team immediately if you have symptoms that indicate the disease is progressing. Those symptoms include unexplained weight loss, severe fatigue, fevers above 100.4 °F without evidence of infection, drenching night sweats, and spleen or lymph node enlargement.

Clinical trials may be considered as a first-line treatment depending on your diagnosis. A great deal of progress continues to

be made in the way doctors treat CLL, and much of that progress can be traced back to clinical trials.

Targeted therapy is commonly the first treatment given for CLL. It is a personalized strategy that enables your doctor to use the results from your molecular profiling to target specific genes and proteins that are causing cancer cells to grow and multiply. Types of targeted therapy used for CLL include tyrosine kinase inhibitors (TKIs), which block certain substances that control how cells grow and divide; BCL2 inhibitors designed to block the BCL2 protein, which is found inside the leukemia cells; and monoclonal antibodies, laboratory-made immune system proteins that attach to a specific target on cancer cells or other cells that may help cancer grow. The antibodies are then able to kill the cancer cells, block their growth or keep them from spreading. Some may be used alone or in combination with other therapies.

Corticosteroids, anti-inflammatory drugs that appear to help cause the death of cancerous white blood cells, are sometimes given along with other drug therapies.

Chemoimmunotherapy combines chemotherapy with immunotherapy. It may be used for CLL that does not have the *TP53* mutation or deletion in chromosome 17p.

Radiation therapy may be used to shrink an enlarged spleen or swollen lymph nodes, relieve certain symptoms or assist in the conditioning phase of a stem cell transplant.

An **allogeneic stem cell transplant**, which uses stem cells from a volunteer donor, may be used. The goal of transplantation is for your blood counts to return to safe levels and/or remission, which is having no signs or symptoms of cancer.

Chemotherapy is not typically used but may be for specific instances, such as before stem cell transplantation in a process known as conditioning.

Surgery may be recommended in cases where the spleen is enlarged and needs to be removed (splenectomy).

Continued on page 13




CALQUENCE[®]
(acalabrutinib) 100 mg capsules

"...and if you have the opportunity to *support* somebody else, I would encourage you to do that, because it's really gratifying and *appreciated*."

– Jane | Wife and Caregiver of Cliff,
a Real CALQUENCE Patient

YOU ARE NOT ALONE with chronic lymphocytic leukemia (CLL)

The **CALQUENCE Connections Facebook Group** is a community for patients—whether currently taking CALQUENCE[®] (acalabrutinib) or soon to begin treatment—and their caregivers to guide and assist each other throughout treatment.

Join the Facebook group today at
www.facebook.com/groups/calquenceconnections
or scan the QR code with your phone's camera.



Select Safety Information

CALQUENCE is a prescription oral treatment for adults with chronic lymphocytic leukemia or small lymphocytic lymphoma. May cause serious side effects including: serious infections, bleeding problems, decrease in blood cell count, new cancers, and heart rhythm problems. Some may lead to death. Tell your doctor if you experience infections such as flu-like symptoms; unexpected bleeding such as blood in your stool or urine; or heart rhythm problems such as fast or irregular heartbeat. Use sun protection when outside.

Please read Brief Summary of Prescribing Information on adjacent page.

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

If you cannot afford your medication, AstraZeneca may be able to help. Visit AstraZeneca-us.com to find out how.

PATIENT INFORMATION

CALQUENCE® (KAL-kwens) (acalabrutinib) capsules


CALQUENCE[®]
(acalabrutinib) 100 mg capsules

What is CALQUENCE?

CALQUENCE is a prescription medicine used to treat adults with:

- Chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).

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

Before taking CALQUENCE, tell your healthcare provider about all of your medical conditions, including if you:

- have had recent surgery or plan to have surgery. Your healthcare provider may stop CALQUENCE for any planned medical, surgical, or dental procedure.
- have bleeding problems.
- have or had heart rhythm problems.
- have an infection.
- have or had liver problems, including hepatitis B virus (HBV) infection.
- are pregnant or plan to become pregnant. CALQUENCE may harm your unborn baby and problems during childbirth (dystocia).
 - If you are able to become pregnant, your healthcare provider may do a pregnancy test before you start treatment with CALQUENCE
 - Females who are able to become pregnant should use effective birth control (contraception) during treatment with CALQUENCE and for at least 1 week after the last dose of CALQUENCE.
- are breastfeeding or plan to breastfeed. It is not known if CALQUENCE passes into your breast milk. Do not breastfeed during treatment with CALQUENCE and for at least 2 weeks after your final dose of CALQUENCE.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Taking CALQUENCE with certain other medications may affect how CALQUENCE works and can cause side effects. Especially tell your healthcare provider if you take a blood thinner medicine.

How should I take CALQUENCE?

- Take CALQUENCE exactly as your healthcare provider tells you to take it.
- Do not change your dose or stop taking CALQUENCE unless your healthcare provider tells you to.
- Your healthcare provider may tell you to decrease your dose, temporarily stop, or completely stop taking CALQUENCE if you develop certain side effects.
- Take CALQUENCE 2 times a day (about 12 hours apart).

(continued)

- Take CALQUENCE with or without food.
- Swallow CALQUENCE capsules whole with a glass of water. Do not open, break, or chew capsules.
- If you need to take an antacid medicine, take it either 2 hours before or 2 hours after you take CALQUENCE.
- If you need to take certain other medicines called acid reducers (H-2 receptor blockers), take CALQUENCE 2 hours before the acid reducer medicine.
- If you miss a dose of CALQUENCE, take it as soon as you remember. If it is more than 3 hours past your usual dosing time, skip the missed dose and take your next dose of CALQUENCE at your regularly scheduled time. Do not take an extra dose to make up for a missed dose.

What are the possible side effects of CALQUENCE?

CALQUENCE may cause serious side effects, including:

- **Serious infections** can happen during treatment with CALQUENCE and may lead to death. Your healthcare provider may prescribe certain medicines if you have an increased risk of getting infections. Tell your healthcare provider right away if you have any signs or symptoms of an infection, including fever, chills, or flu-like symptoms.
- **Bleeding problems (hemorrhage)** can happen during treatment with CALQUENCE and can be serious and may lead to death. Your risk of bleeding may increase if you are also taking a blood thinner medicine. Tell your healthcare provider if you have any signs or symptoms of bleeding, including:
 - blood in your stools or black stools (looks like tar)
 - pink or brown urine
 - unexpected bleeding, or bleeding that is severe or you cannot control
 - vomit blood or vomit that looks like coffee grounds
 - cough up blood or blood clots
 - dizziness
 - weakness
 - confusion
 - changes in your speech
 - headache that lasts a long time
 - bruising or red or purple skin marks
- **Decrease in blood cell counts.** Decreased blood counts (white blood cells, platelets, and red blood cells) are common with CALQUENCE, but can also be severe. Your healthcare provider should do blood tests to check your blood counts regularly during treatment with CALQUENCE.

(continued)

- **Second primary cancers.** New cancers have happened in people during treatment with CALQUENCE, including cancers of the skin or other organs. Your healthcare provider will check you for skin cancers during treatment with CALQUENCE. Use sun protection when you are outside in sunlight.
- **Heart rhythm problems (atrial fibrillation and atrial flutter)** have happened in people treated with CALQUENCE. Tell your healthcare provider if you have any of the following signs or symptoms:
 - fast or irregular heartbeat
 - dizziness
 - feeling faint
 - chest discomfort
 - shortness of breath

The most common side effects of CALQUENCE include:

- headache
- diarrhea
- muscle and joint pain
- upper respiratory tract infection
- bruising

These are not all of the possible side effects of CALQUENCE.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store CALQUENCE?

- Store CALQUENCE at room temperature between 68°F to 77°F (20°C to 25°C).

Keep CALQUENCE and all medicines out of the reach of children.

General information about the safe and effective use of CALQUENCE.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use CALQUENCE for a condition for which it was not prescribed. Do not give CALQUENCE to other people, even if they have the same symptoms you have. It may harm them. You can ask your healthcare provider or pharmacist for more information about CALQUENCE that is written for health professionals.

What are the ingredients in CALQUENCE?

Active ingredient: acalabrutinib

Inactive ingredients: silicified microcrystalline cellulose, pregelatinized starch, magnesium stearate, and sodium starch glycolate.

Capsule shell contains: gelatin, titanium dioxide, yellow iron oxide, FD&C Blue 2, and black ink.

For more information, go to www.CALQUENCE.com or call 1-800-236-9933.

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US-34063 11/19

 AstraZeneca

RELAPSED AND REFRACTORY CLL

CLL may return or not respond to initial treatment.

Refractory CLL: Cancer that does not respond or improve with treatment. Several options are available to treat refractory CLL. Your doctor will consider the options you have already tried and your overall health before recommending another plan, which may include a clinical trial. If your doctor doesn't specialize in CLL, consider getting another opinion as well.

Relapsed (or recurrent) CLL: Cancer that has come back, usually after a period of time during which the cancer could not be detected. If this occurs, your doctor will begin a new cycle of diagnostic tests, which may include another biopsy and laboratory tests. Your doctor will confirm whether the cancer is recurrent and whether it has transformed into a more aggressive subtype, which will affect your treatment plan.

LIVING WITH CLL

Once you are diagnosed with CLL, you will need to consider and adopt management strategies such as the following.

Medication adherence. To be fully effective, every dose must be taken with accuracy, precise timing and safety precautions. Taking the right drug in the right dose at the right time – every time – for as long as prescribed is referred to as medication adherence.

Most cancer therapies are designed to maintain a specific level of drugs in your system for a certain time based on your cancer type and stage, your overall health, previous therapies and other factors. If your medications are not taken exactly as prescribed, or if you miss appointments for IV infusions or injections, the consequences can be serious.

Set yourself up to succeed with these suggestions:

- Talk with your pharmacist about how to take and store the medications properly.
- Track each dose, including missed doses. Download a medication tracking worksheet at PatientResource.com/CLL_Medication_Journal.aspx
- Detail any side effects.
- Use medication reminders and organizers. Set an alarm on your clock or phone, wear a vibrating wristwatch or download a smartphone app.

Contact your doctor if you miss a dose, if side effects interfere with your daily life or if you are having trouble paying for the medication. It is important that you do not skip doses or stop taking your medication without talking with your doctor. Communicating with your health care team is extremely important, and they will rely on you to be open and honest so they can find options that work for you.

Lower your risk of infection. People with CLL often have a weakened immune system, which may make them more susceptible to developing infections. Infections while you are already managing CLL can become serious, making it important to detect and treat them as soon as they start. Your doctor will talk with you about the signs to watch for and what to do if they occur.

Another way to reduce your risk of infections is to stay up to date with your vaccinations and health screenings for other cancers. Vaccinations may include shots for the flu, pneumonia, shingles, COVID-19 and others. Remember to continue to get regular screenings, such as mammograms, colonoscopies, skin exams, Pap tests, HPV testing, prostate specific antigen (PSA) blood tests and any additional testing your doctor recommends.

Make healthy lifestyle choices. Research shows that staying active and following a healthy diet offer many health benefits, including helping you be better prepared for future health issues.

Prepare for physical side effects. Learn about the possible treatment-related side effects before starting treatment. Some may indicate the cancer is progressing, and your treatment plan may need to be re-evaluated.

Severe side effects are not common but can occur with certain types of treatment. Ask if you are at risk, how you can identify the signs and what to do if they occur. Prompt treatment may help prevent more serious complications.

Care for your emotional well-being. It can be an ongoing challenge to stay positive when you are faced with an incurable condition. Find activities that bring you joy. Consider talking to a therapist or trusted friends about your feelings. Join an in-person or online support group. Surrounding yourself

SOME COMMON DRUG THERAPIES FOR CLL

These therapies may be used alone or in combination. For some possible combination therapies your doctor might suggest, go to PatientResource.com/CLL_Treatment.aspx

- ▶ acalabrutinib (Calquence)
- ▶ bendamustine (Bendeka)
- ▶ chlorambucil (Leukeran)
- ▶ cyclophosphamide
- ▶ dexamethasone
- ▶ doxorubicin hydrochloride (Adriamycin)
- ▶ duvelisib (Copiktra)
- ▶ fludarabine phosphate (Fludara)
- ▶ ibrutinib (Imbruvica)
- ▶ idelalisib (Zydelig)
- ▶ methylprednisolone
- ▶ obinutuzumab (Gazyva)
- ▶ ofatumumab (Arzerra)
- ▶ prednisone
- ▶ rituximab (Rituxan)
- ▶ rituximab and hyaluronidase human (Rituxan Hycela)
- ▶ venetoclax (Venclexta)

As of 5/12/22

with support, especially from other CLL survivors, can be very valuable.

Consider telehealth options. Telehealth is accessing medical care from a distance through technology. It may be a way to report symptoms and stay in touch with your doctor between in-person follow-up appointments. Virtual appointments are not designed to replace in-person visits.

Attend follow-up visits. Your doctors will monitor you closely through regularly scheduled appointments. During these visits, you will have exams and lab tests to look for physical signs of CLL and to measure how well the CLL is responding to current treatment. When your treatment is no longer working or is not as effective as it once was, your doctor may try another therapy. ■

STAGING *Staging is an important part of developing your treatment plan. To learn more, visit PatientResource.com and search for CLL under leukemia for details.*

Diagnosed at 69, Marialice Goddard is successfully managing her chronic lymphocytic leukemia (CLL) with the help of a strong support system, a trusted medical team and a clinical trial. Taking a cue from the support group she attends monthly, she shares her story to encourage others with CLL.

Learning to live with CLL takes knowledge and support



▲ Marialice and her daughter, Mary

Five years after being diagnosed with CLL, I began treatment. My doctor and I had been “watching and waiting” until my symptoms really progressed. Believe it or not, those five years were the most difficult part of my CLL diagnosis.

I’d never heard of this type of leukemia, but I assumed I’d take medicine and get rid of it. That was not my treatment plan. I was blessed that the local oncologist I was referred to was a CLL specialist, and I trusted him completely — but I didn’t like this plan and I told him. He said he heard that all the time, and he assured me there was no need to treat before it was necessary.

I was very anxious for about a year. I was sure that every twitch, every pain in my toe, was the CLL. Then my husband was diagnosed with Stage IV colon cancer, and I turned my focus to caring for him. Though we both had cancer, we took care of each other, and it was a nice distraction.

A few years later, fatigue set in. I retired from my role in high school Special Education because it was hard to keep up. When I became so fatigued that I couldn’t get off the couch to get to the bathroom, my daughter Mary took me to the doctor because by that time, my husband had passed away.

My doctor determined it was time to begin treatment. He recommended a research study that consisted of infusion therapy followed by oral therapy. I didn’t have any experience with clinical trials, but I felt so awful and I trusted him, so I followed his advice.

I was 74 when I began the clinical trial. Getting used to treatment wasn’t difficult. I only had minor issues that went away after a few months, and the fatigue resolved fairly quickly. I’ve had consistent, quality care from my doctor and the medical research team. They are excellent communicators, and I get my questions answered right away — even though I tend to have a lot of them!

The representative from the research study has been very involved. At the start, she explained medication adherence and how to track the oral medication on a chart she provided. To stay on schedule, I set the timer on my cell phone and on the stove every night as

a reminder to take the pills. When I go for regularly scheduled monitoring, I turn in my medication tracking chart and get a new, clean one. I also trade in my empty pill bottles for full ones. She contacts me frequently to check on me, and she has become a good friend.

My family has always been a strong source of support. My daughter is my rock, and my sister and her husband are her backups. However, after I began treatment, the research representative talked with me about the benefits of being in a support group. She encouraged me to look into The Leukemia & Lymphoma Society.

I joined a group that meets online monthly. People with all types of leukemia and lymphoma talk about how they deal with having a blood cancer. It doesn’t make having cancer less scary, but it is easier once you realize other people understand. I’ve learned a lot, and it’s really nice to hear the progress that other people are making.

I don’t get down too often anymore — my daughter has a real knack for bringing me up. I do have times when I feel lonely. Before I began treatment, sometimes my fatigue was so intense that it was almost disabling. But because CLL is a blood disease, I didn’t look sick. I got more sympathy after a fall in the driveway left me with a cast on my arm! It’s not that I want sympathy, but the lack of it can sure make you feel as if no one understands what you are going through. That is why I think the ultimate thing to have after a CLL diagnosis is support.

Since I began the research study, the medication being tested has been approved by the U.S. Food and Drug Administration. I’m still on the same regimen, and the only question is really how long I should continue. I know that everyone reacts to treatments differently, but so far, it’s been excellent for me. Regular labwork and CT results will tell me if it stops being effective, and I also get annual preventive checks to make sure I’m healthy otherwise. If it comes time to make a change, I’m sure my doctor will have another suggestion for me.

I am so grateful that the therapy in the clinical trial helps me live a normal life, but I still have hope there will be a cure someday. ■

» My advice to you

- 1 Be well-informed.** It can reduce your stress.
- 2 Ask questions.** If the question is important to you, that’s all that matters.
- 3 Have a support system that is always there for you.** If you can’t find a group, start one.

Lung Cancer

Significant progress is being made in how lung cancer is diagnosed and treated. As a result, lung cancer incidence and mortality rates are declining and new therapies are helping these patients live longer, more fulfilling lives.

Lung cancer occurs when abnormal cells in the lining of the airways accumulate to form a tissue mass. The primary tumor may grow into the lining around the lung and form secondary tumors nearby. The cells may spread through the lymphatic channels to lymph nodes and through the blood to the opposite lung and distant sites such as the liver, brain or bones. These are known as metastases and are still considered lung cancer regardless of where they are found.

For diagnosis and staging, many tests are performed, including biopsies, biomarker tests, routine scans such as a CT of the chest, a CT/PET scan, MRI of the brain, and more. Pathologists identify and examine biopsy tissue to determine the pathologic type of the cancer, then classify the cancer into four main pathologic groups based on the appearance of cells under the microscope and analysis of the proteins they express. The results of the scans and biopsies are used to define the clinical stage. If the patients undergo surgery, a pathologic stage is also assigned.

Adenocarcinoma, squamous cell and large cell lung cancers are types of non-small cell lung cancer (NSCLC), which account for the majority of lung cancer diagnoses. Each type has unique characteristics and treatment responses. Small cell lung cancer (SCLC) is an aggressive form that most often metastasizes before it is found.

To classify and stage the cancer, doctors use the TNM (tumor, node and metastasis) staging system developed by the American Joint Committee on Cancer (AJCC) and the International Association for the Study of Lung Cancer. Commonly, doctors also use it to stage SCLC. Sometimes SCLC is identified as limited-stage in which the cancer is confined to one part of the chest, in just one part of the lung and in nearby lymph nodes. Extensive-stage SCLC means the cancer has spread to other parts of the body, such as the bone, brain or other lung.

TREATMENT OPTIONS

Your medical team will consider results from pathology, staging and molecular testing to plan treatment. With so many advancements

in lung cancer treatment, it is important to understand the basics of each so you can discuss them with your health care team and, in turn, make the best choices for you and your desired quality of life.

You will be monitored closely so that your therapy can be adapted as needed. As a result, treating your cancer may be a fluid process, changing periodically to offer you the best level of care. Therefore, communicating regularly with your health care team and keeping follow-up appointments are crucial.

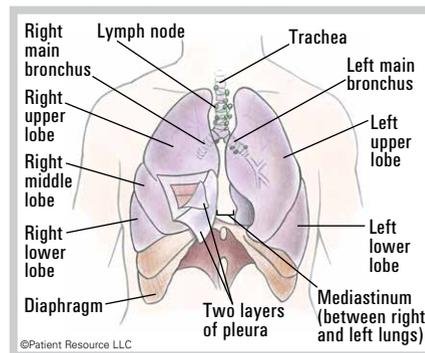
Surgery is typically the primary treatment for Stages I, II and some IIIA lung tumors. Ideally, a board-certified thoracic surgeon experienced in lung cancer should determine whether the tumor(s) can be successfully removed. The procedure will depend on how much of your lung is affected, tumor size and location, and your overall health. The surgery is usually done with video-assisted thoracoscopic surgery (VATS) and is sometimes done robotically. VATS procedures may help preserve muscles and nerves, reduce complications and shorten recovery time. Finding a surgeon with extensive training and experience in robotic surgery is highly recommended. Open surgery with a large chest incision may be necessary:

- Wedge resection removes the tumor with a triangular piece of a lobe of the lung.
- Segmental resection (segmentectomy) removes a larger section of a lobe.
- Lobectomy removes one of the five lobes.
- Pneumonectomy removes an entire lung.
- Sleeve resection (sleeve lobectomy) removes part of the bronchus (main airway) or pulmonary artery to the lung, along with one lobe.

Chemotherapy is typically part of the treatment plan for most stages of NSCLC and is the primary treatment for all stages of SCLC. It may be given alone or in combination with surgery, radiation therapy or immunotherapy. In early stages, it may be used before surgery (neoadjuvant) to help shrink the tumor, after surgery (adjuvant) to kill remaining cells, as maintenance therapy or as palliative care to relieve symptoms.

Immunotherapy is standard first-line therapy for advanced or metastatic NSCLC without specific molecular alterations. It is standard after chemotherapy and radio-

ANATOMY OF THE LUNGS



therapy for unresectable Stage III NSCLC and with chemotherapy for extensive-stage SCLC. Ongoing studies are examining its role before or after surgery in early stages.

Immune checkpoint inhibitors are the type of immunotherapy approved to treat NSCLC and SCLC. These drugs prevent the immune system from slowing down, allowing it to keep up its fight against the cancer.

Checkpoints keep the immune system “in check.” When the correct proteins and cell receptors connect, a series of signals is sent to the immune system to slow down once an immune response is finished. Two checkpoint receptors that slow down the immune system have been identified for their roles in lung cancer treatment:

- PD-1 (programmed cell death protein 1) is a receptor involved with telling T-cells to die and to reduce the death of regulatory T-cells (suppressor T-cells). Both slow down an immune response. PD-1 can tell the immune system to slow down only if it connects with PD-L1.
- PD-L1 (programmed death-ligand 1) is a protein that, when combined with PD-1, sends a signal to reduce the production of T-cells and enable more T-cells to die. When PD-1 (the receptor) and PD-L1 (the protein) combine, the reaction signals that it is time to slow down.

Cancer cells try to outsmart the immune system by producing PD-L1 and using it as camouflage so that the T-cells of the immune system will see them as normal cells. T-cells expect only normal cells to produce PD-L1, so when a T-cell encounters PD-L1 on a cancer cell, it is tricked into signaling the immune system to slow down. This is how cancer can hide from the immune system.

Continued on page 16

The goal of immune checkpoint inhibitors is to prevent PD-1 and PD-L1 from connecting so that the immune system does not slow down. These drugs prevent those connections by targeting and blocking PD-1 or PD-L1, and the immune cells continue fighting the cancer. This treatment is given by IV only.

Molecular therapies are oral agents designed to kill cancer cells with specific genetic (molecular) alterations that are mutations or fusions in cancer-causing genes. They are identified through biomarker tests on blood or biopsy specimens. If your tumor has one of several specific molecular alterations, such a specific oral therapy may be a first-line treatment. Currently, oral drugs target these types: epidermal growth factor receptor (*EGFR*) and *MET*, and certain *BRAF* and *KRAS* mutations; and rearrangements (fusions) in neurotrophic tyrosine receptor kinase (*NTRK*) and anaplastic lymphoma kinase (*ALK*); and *RET* and *ROS1* genes.

Targeted therapies are a systemic treatment that include monoclonal antibodies that are directed at proteins involved in making cancer cells grow but that do not have proven biomarkers. Monoclonal antibodies (mAbs) are laboratory-made antibodies designed to target specific tumor antigens. Antibodies may also be conjugated with cancer-killing drugs (chemotherapies) to direct the chemotherapy to cancer cells. These therapies may be called “antibody drug conjugates.” Angiogenesis inhibitors shut down a protein that is essential for creating blood vessels. With no vessels to supply blood, the tumor eventually “starves” and dies. Angiogenesis inhibitors are often given in combination with chemotherapy.

Radiation therapy, also called radiotherapy, is often used with other therapies and may be used as palliative care to help relieve pain when cancer spreads to the bone. External-beam radiation therapy is the most common form used. Three-dimensional conformal radiation therapy, stereotactic body radiotherapy, intensity-modulated radiation therapy and proton therapy may be used. In some instances, radiation is delivered to persisting sites after response to initial systemic therapy. This is often referred to as consolidative therapy.

Radiofrequency ablation (RFA) may be used to treat small tumors when surgery is

not an option. A needle placed directly into the tumor passes a high-frequency electrical current to the tumor that destroys cancer cells with intense heat.

Cryosurgery, also called cryoablation and cryotherapy, kills cancer cells by freezing them with a probe or another instrument that is super-cooled with liquid nitrogen or similar substances. An endoscope, which is a thin tube-like instrument, is used for this procedure to treat tumors in the lungs’ airways.

Photodynamic therapy kills cancer cells with drugs that become active when exposed to light. A drug that has not yet been exposed to light is injected into a vein. The drug is drawn to cancer cells more than normal cells. Fiber optic tubes are then used to carry a laser light to the cancer cells, where the drug becomes active and kills the cells.

It is used mainly to treat tumors on or just under the skin or in the lining of internal organs. When the tumor is in the airways, it is given directly to the tumor through an endoscope. It may help relieve breathing problems or bleeding in NSCLC and can also treat small tumors.

Clinical trials are studies that help researchers learn more about what causes the various types of lung cancer and how to most effectively treat them. Much of the focus includes identifying biomarkers and applying therapies to treat lung cancer with those specific markers. Research also continues to find treatments for lung cancers that do not exhibit a specific biomarker.

THE BENEFITS OF STOPPING SMOKING

Although you may not see the point of quitting after you receive a lung cancer diagnosis, there are multiple benefits. The most important is that your treatments will be more effective when you no longer use tobacco. The cancer-fighting effects of chemotherapy and radiation therapy are reduced while a person continues to smoke.

Other benefits include:

- Reduces lung inflammation that can lead to cancer progression
- Boosts the immune system so it can better fight disease and infections
- Improves wound healing to accelerate recovery after surgery

SOME COMMON DRUG THERAPIES FOR LUNG CANCER

These therapies may be used alone or in combination. Molecular therapy drugs are approved for specific mutations. For additional combination therapies, go to PatientResource.com/Lung_Cancer_Treatment.aspx

CHEMOTHERAPY

- ▶ carboplatin (Paraplatin)
- ▶ cisplatin (Platinol)
- ▶ docetaxel (Docefrez, Taxotere)
- ▶ etoposide (Etopophos)
- ▶ gemcitabine (Gemzar)
- ▶ lurbinectedin (Zepzelca)
- ▶ methotrexate
- ▶ paclitaxel (Taxol)
- ▶ paclitaxel protein-bound (Abraxane)
- ▶ pemetrexed (Alimta)
- ▶ topotecan (Hycamtin)
- ▶ vinorelbine (Navelbine)

IMMUNOTHERAPY

- ▶ atezolizumab (Tecentriq)
- ▶ cemiplimab-rwlc (Libtayo)
- ▶ durvalumab (Imfinzi)
- ▶ ipilimumab (Yervoy)
- ▶ nivolumab (Opdivo)
- ▶ pembrolizumab (Keytruda)

MOLECULAR THERAPY

Anaplastic lymphoma kinase (ALK) rearrangement

- ▶ alectinib (Alecensa)
- ▶ brigatinib (Alunbrig)
- ▶ ceritinib (Zykadia)
- ▶ crizotinib (Xalkori)
- ▶ lorlatinib (Lorbrena)

BRAF mutation

- ▶ dabrafenib (Tafinlar)/trametinib (Mekinist)

Epidermal growth factor receptor (EGFR) mutation

- ▶ afatinib (Gilotrif)
- ▶ amivantamab-vmjw (Rybrent)
- ▶ dacomitinib (Vizimpro)
- ▶ erlotinib (Tarceva)
- ▶ gefitinib (Iressa)
- ▶ mobocertinib (Exkivity)
- ▶ osimertinib (Tagrisso)

KRAS mutation

- ▶ sotorasib (Lumakras)

MET exon 14 skipping mutation

- ▶ capmatinib (Tabrecta)
- ▶ tepotinib (Tepmetko)

Neurotrophic tyrosine receptor kinase (NTRK) gene fusion

- ▶ entrectinib (Rozylytrek)
- ▶ larotrectinib (Vitrakvi)

RET fusion-positive alteration

- ▶ pralsetinib (Gavreto)
- ▶ selpercatinib (Retevmo)

ROS1 fusion

- ▶ crizotinib (Xalkori)
- ▶ entrectinib (Rozylytrek)

TARGETED THERAPY

Epidermal growth factor receptor (EGFR) mutation

- ▶ necitumumab (Portrazza)

Vascular endothelial growth factor (VEGF) inhibitors (angiogenesis inhibitors)

- ▶ bevacizumab (Avastin)
- ▶ ramucirumab (Cyramza)

As of 5/12/22

- Increases a person’s antioxidant capacity
- Improves the chances of survival after cancer treatment
- Decreases the risk of secondary cancers and other conditions linked to tobacco use
- Lowers blood pressure and decreases heart rate
- May improve senses of smell and taste ■

STAGING Staging is an important part of developing your treatment plan. To learn more, visit PatientResource.com and search for lung cancer to find detailed tables and illustrations.

Nothing put Oswald Peterson's life into perspective like hearing he had an incurable disease and would be kept "comfortable." So, when he was offered a type of immunotherapy for his Stage IV non-small cell lung cancer (NSCLC), he didn't have high expectations. The treatment response surprised him — it was almost like a miracle. He is now no evidence of disease (NED) and is living life to the fullest.

Believe in the power of healing

Teaching your immune system to fight cancer sounds so simple. You'd think someone would have thought of it a long time ago, right? Well, someone had, but when I received my diagnosis, there wasn't a lot known about how immunotherapy would work with Stage IV NSCLC. I was too weak for chemotherapy or radiation therapy, so when my doctor suggested immunotherapy, the goal was not to cure. We simply hoped it'd buy me a few extra months and help others in the future.

I was only 49, but I had resigned myself that it was my time. I had blood clots in my back, fluid around my heart and in my lungs, and the cancer had spread throughout my body.

In addition, I was not in a healthy place emotionally. Two years before, one after the other in a single year, I lost my mom to ovarian cancer, my partner of 26 years, my cat and one of my best friends. Before that, I was Mr. Positive, but those losses were hard.

I was open to trying immunotherapy and began treatment as an inpatient. I had lots of time to reflect on my charmed life. As a first-generation American, a big part of life was going to my family's homeland in Trinidad to participate in the annual Trinidad and Tobago Carnival. I wore heavy costumes — some weighing 200 pounds — and danced and partied in many celebrations. I felt blessed that I could look back and not have any regrets.

Being in a down space was not my natural state, so I chose to take an active part in my healing. Once I focused on my emotional and physical health, my mood soon followed.

Eventually, I was sent home with pain pills and oxygen. I didn't see the oxygen tank as part of my new reality, so I didn't use it. Instead, as I began to feel better, I started to test myself with exercise.

Before I was diagnosed, I could only last two minutes at the gym on the elliptical and stair stepper. After a month, I could do an hour on both. Even before I had cancer, that was a ridiculously long time for me on either of those machines! It became a mind game. If I could do this, the cancer surely must be gone.

I did, however, take the pain pills as directed because I'd seen my mom endure pain from her ovarian cancer, and I thought cancer meant pain. Until I went without the pills because my prescription

couldn't be filled, I didn't realize I wasn't having any pain. I told my doctor and we decided if I had pain, I'd take the pills. As it turns out, I had no pain and no side effects.

Another indication that the immunotherapy was working was when, at a pre-set appointment to have fluid drained from my heart and lungs, the tech told me there was no fluid after performing two ultrasounds looking for it.

A few weeks later, I followed up with another scan, but my doctor wouldn't talk to me about what she saw. She told me not to worry about it, which I assumed was code for "It's NOT working." After the next scan, she said the tumors were shrinking. She'd hesitated to tell me at first in case it was a mistake, but now she was sure. A year later, I was deemed NED.

I'm still on the same treatment, though my infusions are further apart. I'll continue as long as it works.

Today I help as many people as I can by speaking at workshops for the Cancer Research Institute and talking with patients. I'm on a patient panel for the hospital where I am treated to improve the patient experience. I also host *O positive*, a podcast for survivors about overcoming great odds and the power of positive thinking.

Two years after being diagnosed, I was in love again and back at Carnival in Trinidad, and my partner Jay got sucked into the fun with me. We have been swimming with the dolphins, parasailing, ziplining and more. I am taking full advantage of being alive. ■

» My advice to you

- **Choose your provider wisely.** Hospitals are not like gas stations. They don't all have the same product.
- **Have a good relationship with your medical team.** If you don't feel that sense of trust, there is no shame in finding a new one. I trust my doctor completely. I often joke that if she told me to stand on my head in the corner for 45 minutes a day, I'd do it. That is how much I trust her.
- **Be open to new treatments.** This includes clinical trials. Medicine changes daily. Timing had a lot to do with my success. I call it a perfect storm because the immunotherapy was available at my hospital right when I needed it.
- **Stay hopeful.** Will yourself to be positive, and surround yourself with people who make you happy.

Bladder Cancer

The bladder is a hollow, expandable muscular organ that collects and stores urine produced in the kidneys. Urine flows from the kidneys to the bladder through two thin tubes called ureters. The urinary tract, which includes the renal pelvis, ureters, bladder and urethra, is lined with urothelial cells that can change shape and stretch without breaking apart.

Bladder cancer develops when genes in normal cells mutate and cause the cells to multiply uncontrollably. The most common type of bladder cancer is urothelial carcinoma, also called transitional cell carcinoma. Other forms include squamous cell carcinoma, adenocarcinoma and small cell carcinoma.

There are two subtypes of bladder cancer: papillary and flat. Papillary tumors grow from the bladder's inner lining toward the center of the bladder, whereas flat tumors grow along the surface of the lining.

Bladder tumors are also described by their invasiveness:

- Noninvasive tumors have not penetrated any other layers of the bladder.
- Non-muscle invasive tumors have grown into the layer of blood vessels and cells that is situated between the bladder lining and the muscle wall but not into the muscle.
- Muscle-invasive tumors have grown into the bladder's wall muscle and sometimes into surrounding tissues or organs outside the bladder.

Bladder cancer is classified and staged according to the tumor, node and metastasis (TNM) system developed by the American Joint Committee on Cancer (AJCC). Doctors categorize the tumor (T) according to its depth of invasion, whether cancer cells are found in nearby lymph nodes (N), and whether it has metastasized (M), or spread, to other

parts of the body. Once the cancer is classified, an overall stage is assigned. Bladder tumors, as with other cancers, are staged in two phases:

- **Clinical stage** — based on the results of a physical examination, evaluation of biopsy specimens, and the results of imaging studies and CT scans.
- **Pathologic stage** — based on more invasive testing, including surgery, to accurately establish how far the disease has spread. Assigning this stage normally includes the removal and testing of bladder tissue and/or nearby lymph nodes for examination. This stage is assigned by a pathologist, a specialist in determining the cause of diseases, including cancer.

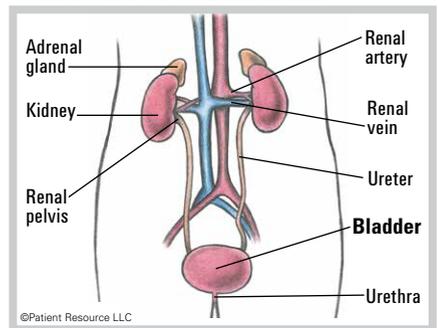
Urothelial cancer is also described by grade (G), which is determined by how much the cancer cells look like healthy cells when viewed under a microscope. The grade may also indicate how likely the cancer is to recur, grow or spread. If cancer has spread beyond the bladder, your doctor may recommend biomarker testing to check for genetic mutations, which may guide treatment.

TREATMENT OPTIONS

To develop a treatment plan tailored to you and the type of cancer you have, your doctor considers many factors, including the tumor's stage, grade and biomarker status; whether the cancer is non-muscle invasive or muscle-invasive; potential side effects; your general health; and your preferences concerning urine control.

Your doctor will continually monitor your condition and make adjustments for a number of reasons. Keep in mind that cancer is an ever-changing condition that presents many challenges, so flexibility and patience are important.

ANATOMY OF THE BLADDER

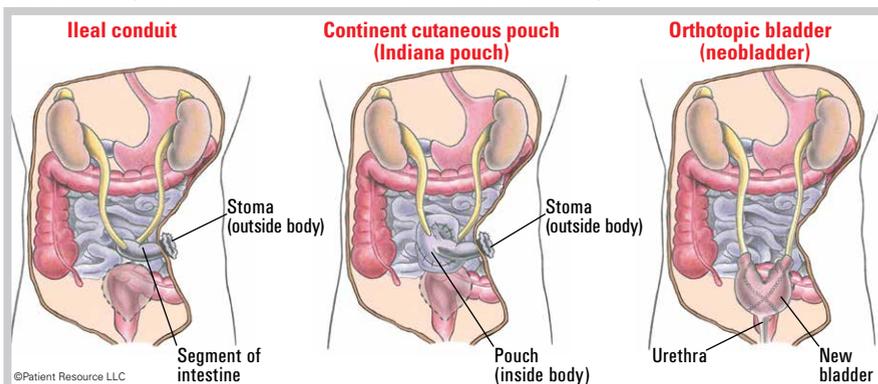


The following treatment options may be used alone or in combination.

Surgery is typically the primary treatment for removing a solid tumor. The type of surgery chosen will depend on the stage and grade of the disease. Removing the tumor may offer the best chance of controlling the disease and keeping it from spreading, especially for people with early-stage disease.

- Transurethral bladder tumor resection (TURBT) may be used to diagnose, stage and treat bladder cancer. A surgeon inserts a cystoscope through the urethra into the bladder and removes the tumor using an instrument with a small wire loop, a laser or high-energy electricity.
- A radical cystectomy removes the entire bladder and possibly nearby tissues or organs. Lymph nodes in the pelvis are also removed. Men may have their prostate and urethra removed, and women may have their uterus, fallopian tubes, ovaries and part of the vagina removed. A partial (segmental) cystectomy may be performed to remove a portion of the bladder, preserving the ability to urinate normally. A cystectomy may be done laparoscopically or robotically.
- If your bladder is removed, a new way to store and pass urine must be created through a urostomy. You and your treatment team will determine which type of urinary diversion will work best for you (see Figure 1).
 - o An ileal conduit involves creating a new tube from a piece of intestine (ileum) to allow your kidneys to drain and urine to exit through a small opening called a stoma.
 - o A continent cutaneous pouch is a pouch inside your body made from a segment of your intestine that is attached to your ureters, allowing urine to be stored

FIGURE 1
UROSTOMY (BLADDER REMOVAL AND RECONSTRUCTION)



internally and then removed through a hole in your abdomen.

- o A neobladder, also referred to as an orthotopic or a substitute bladder, uses a portion of your intestine to connect the ureters and the other end to the urethra.

Chemotherapy may be used alone or with other forms of treatment before surgery (neoadjuvant) or after surgery (adjuvant). In bladder cancer, chemotherapy may be given intravesically or systemically:

- Intravesical (local) chemotherapy delivers drugs into the bladder through a catheter inserted through the urethra. This is local treatment that only destroys superficial tumor cells that come in contact with the chemotherapy solution. It cannot reach tumor cells that have invaded the muscular layer of the bladder wall or tumor cells that have spread to other organs.
- Systemic chemotherapy is given intravenously (IV) through a small tube inserted into a vein or port. It travels through the bloodstream and kills cancer cells located throughout the body.

Immunotherapy harnesses the potential of the body's own immune system to recognize and destroy cancer cells. Several types of immunotherapy are approved for bladder cancer, including cytokines, immune checkpoint inhibitors, modified bacteria and monoclonal antibodies. They may be given intravesically or intravenously.

Cytokines aid in immune cell communication and play a big role in the full activation of an immune response. They are given intravesically.

Immune checkpoint inhibitors are drugs that prevent the immune system from slowing down, allowing it to keep up its fight against the cancer. They are given intravenously through a vein in your arm or a port.

Modified bacteria, such as bacillus Calmette-Guérin (BCG), have been changed to ensure that they will not cause a harmful infection while stimulating an immune response. It is given intravesically over multiple weeks followed by a rest period of several weeks.

Monoclonal antibodies (mAbs) are laboratory-made antibodies designed to target certain tumor antigens, which are specific proteins or other molecules on the surface of tumor cells that may trigger an immune response. In bladder cancer, mAbs target PD-1 or PD-L1 on the surface of the cancer cells.

Targeted therapy uses drugs or other substances to identify and attack specific types of cancer cells. Unlike chemotherapy, which attacks healthy cells as well as cancer cells, targeted therapy is designed to affect only cancer cells. The types of targeted therapy approved for bladder cancer include a kinase inhibitor and monoclonal antibodies (mAbs).

A kinase inhibitor may treat some bladder cancers with the fibroblast growth factor receptor (*FGFR2* or *FGFR3*) gene mutation. Data suggest that tumors with mutated *FGFR3* are less likely to be recognized by the immune system, making targeted therapy an option for this gene mutation.

The mAbs are antibody-drug conjugates, which mean they consist of a monoclonal antibody that is linked to a chemotherapy drug. Each mAb is designed to target a specific protein on the surface of bladder cancer cells. Once the mAb finds the target on a cancer cell, it connects to it and delivers the chemotherapy drug directly into the cell to destroy it.

Chemoradiation therapy combines systemic chemotherapy and pelvic radiation therapy. It may be given after the bladder tumor is removed (using TURBT) or instead of surgery. It is considered a “bladder-preservation” option because removal of the bladder may not be necessary if cancer is not detected after treatment. This may be an option for patients whose tumors appear to have been completely removed by TURBT, invaded no deeper than the muscle wall and have not obstructed the ureter.

Radiation therapy uses high-energy radiation to destroy cancer cells and shrink tumors. It may be given with chemotherapy (chemoradiation therapy) to relieve symptoms or to treat advanced disease. External-beam radiation therapy (EBRT) uses a machine outside the body to send radiation toward the cancer.

Clinical trials are medical research studies that may offer access to leading-edge treatments not yet widely available. Let your team know if you are open to considering a clinical trial. You can also search on your own.

Keep in mind that some may be closed, and you may not qualify for every trial that interests you. Every participant in a specific trial must meet the same eligibility criteria.

SOME COMMON DRUG THERAPIES FOR BLADDER CANCER

These therapies may be used alone or in combination. For some combination therapies your doctor might suggest, go to PatientResource.com/Bladder_Cancer_Treatment.aspx

CHEMOTHERAPY

- ▶ cisplatin
- ▶ doxorubicin (Adriamycin)
- ▶ methotrexate
- ▶ mitomycin (Jelmyto, Mitozytrex, Mutamycin)
- ▶ thiotepa (Tepadina)
- ▶ valrubicin (Valstar)

IMMUNOTHERAPY

Cytokine

- ▶ interferon (Roferon-A, Intron A, Alferon)

Immune checkpoint inhibitors

- ▶ atezolizumab (Tecentriq)
- ▶ avelumab (Bavencio)
- ▶ nivolumab (Opdivo)
- ▶ pembrolizumab (Keytruda)

Modified bacteria

- ▶ bacillus Calmette-Guérin (BCG)

TARGETED THERAPY

Kinase inhibitor

- ▶ erdafitinib (Balversa)

Monoclonal antibodies

- ▶ enfortumab vedotin-efv (Padcev)
- ▶ sacituzumab govitecan-hziy (Trodelyv)

As of 5/12/22

Common criteria include cancer type, subtype, stage, biomarker status and treatment history. Your age, gender and other health conditions may also be factors. For example, if a trial requires that you have already had a certain treatment and you have not, you will not be eligible. Once you find a potential trial, talk with your doctor.

Researchers are evaluating improved ways of performing cystectomies and lymph node dissections, identifying changes to genes or proteins that may lead to bladder cancer, and finding new types of targeted therapy and immunotherapy to use alone or in combination.

RECURRENT BLADDER CANCER

It is possible for bladder cancer to return after treatment. This is known as a recurrence and it can happen weeks, months or even years after treatment stops.

The cancer may return in the same area as the primary cancer or in a different area of the body. Treatment options for recurrent cancer depend on the location and extent of the tumor, treatment history and overall health.

The potential for recurrence is why follow-up care is so important.

If your bladder cancer returns, your doctor will begin a new cycle of testing to determine any changes in your type of cancer and physical symptoms. A new treatment plan may be developed, and you may add finding a clinical trial to your plan. ■

STAGING

Staging is an important part of developing your treatment plan. To learn more, visit PatientResource.com and search for bladder cancer to find detailed tables and illustrations.



Not actual patients.

Setting Our Sights On Living Longer

PADCEV[®] was studied in adults with advanced bladder cancer who had previously received an immunotherapy and platinum-containing chemotherapy. In the study, median overall survival with PADCEV was 13 months versus 9 months with chemotherapy.

Please see Important Safety Information below and talk to your doctor about side effects.

IMPORTANT SAFETY INFORMATION

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

PADCEV may cause serious side effects, including:

 **Skin reactions.** Severe skin reactions have happened in people treated with PADCEV; in some cases severe skin reactions have caused death. Most severe skin reactions occurred during the first cycle (28 days) of treatment but may happen later. Your healthcare provider will monitor you during treatment and may prescribe medicines if you get skin reactions. Tell your healthcare provider right away if you develop any of these signs of a new or worsening skin reaction:

- target lesions (skin reactions that look like rings)
- rash or itching that continues to get worse
- blistering or peeling of the skin
- painful sores or ulcers in mouth or nose, throat, or genital area
- fever or flu-like symptoms
- swollen lymph nodes

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

WHAT IS PADCEV?

PADCEV is a prescription medicine used to treat adults with bladder cancer and cancers of the urinary tract (renal pelvis, ureter or urethra) that has spread or cannot be removed by surgery. PADCEV may be used if you:

- have received an immunotherapy medicine **and** chemotherapy that contains platinum, **or**
- you are not able to receive a chemotherapy that contains the medicine cisplatin and you have received one or more prior therapy.

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

 **Before receiving PADCEV, tell your healthcare provider about all of your medical conditions, including if you:**

- are currently experiencing numbness or tingling in your hands or feet
- have a history of high blood sugar or diabetes
- have liver problems
- are pregnant or plan to become pregnant. PADCEV can

harm your unborn baby. Tell your healthcare provider right away if you become pregnant or think you may be pregnant during treatment with PADCEV

- are breastfeeding or plan to breastfeed. It is not known if PADCEV passes into your breast milk. Do not breastfeed during treatment and for at least 3 weeks after the last dose of PADCEV



Females who are able to become pregnant:

- Your healthcare provider should do a pregnancy test before you start treatment with PADCEV.
- You should use an effective method of birth control during your treatment and for at least 2 months after the last dose of PADCEV.



Males with a female sexual partner who is able to become pregnant:

- If your female partner is pregnant, PADCEV can harm the unborn baby.
- You should use an effective method of birth control during your treatment and for at least 4 months after the last dose of PADCEV.



Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Taking PADCEV with certain other medicines may cause side effects.



How will I receive PADCEV?

- PADCEV will be given to you by intravenous (IV) infusion into your vein over 30 minutes.
- You will receive your PADCEV over periods of time called cycles.
 - Each PADCEV cycle is 28 days.
 - You will receive PADCEV on days 1, 8 and 15 of every cycle.

- Your healthcare provider will decide how many treatment cycles you need.
- Your healthcare provider may do blood tests regularly during treatment with PADCEV.

What are the possible side effects of PADCEV?

PADCEV may cause serious side effects, including:

- **Skin Reactions.** See “Skin Reactions” above for more information.

PADCEV is approved to treat your **advanced bladder cancer*** if you have received:

Immunotherapy and platinum-containing chemotherapy

OR

Prior therapy and could not receive cisplatin chemotherapy



Ask your healthcare professional if PADCEV is right for you or your loved one



Visit [PADCEV.com](https://www.padcev.com) or call 1-888-4PADCEV (1-888-472-3238) for more information

***Bladder cancer and cancers of the urinary tract (renal pelvis, ureter or urethra) that has spread or cannot be removed by surgery.**



• **High Blood Sugar (hyperglycemia).** You can develop high blood sugar during treatment with PADCEV. High blood sugar, a serious condition called diabetic ketoacidosis (DKA), and death have happened in people with and without diabetes who were treated with PADCEV. Tell your healthcare provider right away if you have any symptoms of high blood sugar, including: frequent urination, increased thirst, blurred vision, confusion, it becomes harder to control your blood sugar, drowsiness, loss of appetite, fruity smell on your breath, nausea, vomiting, or stomach pain.



• **Lung problems.** PADCEV may cause severe or life-threatening inflammation of the lungs that can lead to death. Tell your healthcare provider right away if you get new or worsening symptoms, including trouble breathing, shortness of breath, or cough.



• **Peripheral neuropathy.** You may develop nerve problems called peripheral neuropathy during treatment with PADCEV. Tell your healthcare provider right away if you get new or worsening numbness or tingling in your hands or feet, or muscle weakness.



• **Eye problems.** You can develop certain eye problems during treatment with PADCEV. Tell your healthcare provider right away if you have dry eyes, blurred vision, or any vision changes. You may use artificial tear substitutes to help prevent or treat dry eyes.



• **Leakage of PADCEV out of your vein into the tissues around your infusion site (extravasation).** If PADCEV leaks from the injection site or the vein into the nearby skin and tissues, it could cause an infusion site reaction. These reactions can happen right after you receive an infusion, but sometimes may happen days after your infusion. Tell your healthcare provider or get medical help right away if you notice any redness, swelling, itching, or discomfort at the infusion site.

The most common side effects of PADCEV include:

- skin rash
- changes in liver and kidney function tests
- increased sugar (glucose) in the blood
- tiredness
- numbness or tingling in your hands or feet, or muscle weakness
- decreased white blood cell, red blood cell, and platelet counts
- hair loss
- decreased appetite
- diarrhea
- decreased sodium, phosphate and protein (albumin) in the blood
- nausea
- itching
- change in sense of taste
- increased uric acid in the blood
- increased lipase (a blood test done to check your pancreas)
- decreased weight
- dry skin

If you have certain side effects, your healthcare provider may decrease your dose or stop your treatment with PADCEV for a period of time (temporarily) or completely.

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

These are not all the possible side effects of PADCEV.



Call your doctor for medical advice about side effects. You may report side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see Brief Summary of full Prescribing Information (Prescription Drug Facts), with an Important Warning of Serious Side Effects on adjacent page.



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Seagen and the Seagen logo are registered trademarks of Seagen Inc.



PADCEV®

enfortumab vedotin-ejfv

Injection for IV infusion 20 mg & 30 mg vials

Prescription Drug Facts

Rx Only

Active Ingredient

Purpose

PADCEV (enfortumab vedotin-ejfv) injection for IV infusion 20mg or 30mg vials Cancer Treatment

Important Warning Severe skin reactions have happened in people treated with PADCEV, in some cases severe skin reactions have caused death. Most severe skin reactions occurred during the first cycle (28 days) of treatment but may happen later. Your healthcare provider will monitor you during treatment and may prescribe medicines if you get skin reactions. Tell your healthcare provider right away if you develop any of these signs of a new or worsening skin reaction: ■ target lesions (skin reactions that look like rings) ■ rash or itching that continues to get worse ■ blistering or peeling of the skin ■ painful sores or ulcers in mouth or nose, throat, or genital area ■ fever or flu-like symptoms ■ swollen lymph nodes
See “Warnings” below for more information about serious side effects of PADCEV.

Uses Treatment of adults with bladder cancer and cancers of the urinary tract (renal pelvis, ureter, or urethra) that has spread or cannot be removed by surgery. PADCEV may be used if you:
■ have received an immunotherapy medicine **and** chemotherapy that contains platinum, **or**
■ you are not able to receive a chemotherapy that contains the medicine cisplatin and you have received one or more prior therapy.
It is not known if PADCEV is safe and effective in children.

Warnings

Ask a doctor before use if you have

■ numbness or tingling in your hands/feet ■ have a history of high blood sugar or diabetes ■ have liver problems

What are the possible serious side effects of PADCEV?

■ skin reactions. See “Important Warning” above ■ high blood sugar (hyperglycemia), including diabetic ketoacidosis (DKA), sometimes resulting in death ■ lung problems ■ nerve problems (peripheral neuropathy) like tingling in your hands or feet or muscle weakness ■ eye problems ■ infusion site reactions if PADCEV leaks out of your veins into tissues around your infusion site (extravasation)

Tell your doctor if you have

■ target lesions (skin reactions that look like rings), rash/itching that continues to get worse, skin blistering or peeling, painful sores in the mouth, nose, throat, or genital area, fever/flu-like symptoms, or swollen lymph nodes ■ frequent urination, increased thirst, blurred vision, confusion, it becomes harder to control your blood sugar, drowsiness, loss of appetite, fruity smell on your breath, nausea, vomiting, or stomach pain ■ trouble breathing, shortness of breath, or cough ■ numbness or tingling in your hands or feet or muscle weakness ■ dry eyes, blurred vision, or any vision changes ■ redness, swelling, itching, or discomfort at the infusion site, or get medical help right away.

If pregnant, able to become pregnant, or have a partner who is able to become pregnant

■ PADCEV can harm your unborn baby, talk to your doctor ■ females should use effective birth control during treatment and for at least 2 months after the last dose of PADCEV ■ males should use effective birth control during treatment and for at least 4 months after the last dose of PADCEV

If breastfeeding

■ do not breastfeed during treatment and for at least 3 weeks after the last dose of PADCEV

Fertility

■ PADCEV may cause fertility problems in males, which may affect the ability to father children



Prescription Drug Facts Continued

Most Common Side Effects

■ Skin rash ■ changes in liver and kidney function tests ■ increased sugar (glucose) in the blood ■ tiredness
■ numbness or tingling in your hands or feet, or muscle weakness ■ decreased white blood cell, red blood cell, and platelet counts ■ hair loss ■ decreased appetite ■ diarrhea ■ decreased sodium, phosphate, and protein (albumin) in the blood ■ nausea ■ itching ■ change in sense of taste ■ increased uric acid in the blood
■ increased lipase (a blood test done to check your pancreas) ■ decreased weight ■ dry skin
If you have certain side effects, your healthcare provider may decrease your dose or stop your treatment with PADCEV for a period of time (temporarily) or completely.

These are not all of the possible side effects of PADCEV. **You may report side effects to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.**

Directions

■ PADCEV will be given by intravenous (IV) infusion over 30 minutes ■ you will receive PADCEV over periods of time called cycles ■ each cycle is 28 days and PADCEV will be given on days 1, 8, and 15 of every cycle ■ your doctor will decide how many treatment cycles you need ■ your doctor may do blood tests regularly during your treatment

Other Information Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Taking PADCEV with certain other medicines may cause side effects.

If you would like more information about PADCEV, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about PADCEV that is written for healthcare professionals (full Prescribing Information) which includes more information about the **Important Warning** with PADCEV.

Inactive Ingredients histidine, histidine hydrochloride monohydrate, polysorbate 20, and trehalose dehydrate.

 **PADCEV**[®]
enfortumab vedotin-ejfv
Injection for IV infusion 20 mg & 30 mg vials

When given the opportunity, be helpful

Angelo Vaccaro is dedicated to helping others. When he was diagnosed at 73 with Stage III bladder cancer and Stage I prostate cancer, he was already volunteering for the American Cancer Society. Today, Angelo is cancer-free, and he shares everything he's learned about his cancer experience with others as a peer navigator at Friend for Life Cancer Support Network.



Helping and educating others is part of my life's work. Following a career in special education, I began volunteering for the American Cancer Society's Road To Recovery program, which provides transportation for cancer patients to get to their treatments free of charge.

I had no symptoms until one day on vacation there was bright red blood in my urine. I made an appointment with my urologist and drove home. At the appointment, as I lay on the table looking at the covered instrument the doctor was going to use, I became very nervous. Then I thought of my youngest grandson who had been born with bladder issues. I knew he had been through this procedure many times. If he could do it, I could, too.

Ten seconds into the procedure, the doctor stood up and said, "You have cancer." Further testing revealed the cancer was aggressive with multiple tumors embedded in the bladder wall, making it a Stage III diagnosis. My first question was, "How fast can you deal with this?"

Within a week, I had a procedure to scrape my bladder and do a chemo wash. Pathology results showed I also had early-stage prostate cancer. The pathologist told me it was unusual to find

a cancer they weren't looking for. Drug therapy started soon after, followed by surgery to remove my bladder and prostate. An ileal conduit system including a stoma was put in place.

I could not have gone through treatment without my wife, my family and my phenomenal care team, including my oncologist, surgeon, nurses and the best ostomy nurse ever.

Even though I'd always been the one to give support, I found I needed it, too. During treatment, I found Reel Recovery, a cancer support group for men that included fly-fishing. I cannot express enough how helpful this support was. After my treatment and surgery, I looked for a support group focused on living successfully with an ostomy. I heard about Friend for Life Cancer Support Network while on a Road To Recovery assignment. I stopped by their office, interviewed and became a peer navigator. What a blessing it has been to talk with men and women locally and nationally about living with an ileal conduit.

I learned so many things along the way that I wished I had known from the beginning — practical things that come from experience. Sharing my knowledge with others as a peer navigator is rewarding, and sometimes I learn things I can pass on to other survivors that make their journeys easier. ■

» Angelo's helpful insights

- ▶ **Listen to and follow the advice of the doctors and nurses.**
- ▶ **Ask for the best ostomy nurse available.** This is your teacher.
- ▶ **Wear your natural clothing when discussing stoma placement.** If possible, the surgeon may be able to place the stoma off your belt line. My stoma was placed right at my belt line, which was challenging.
- ▶ **When ordering supplies, always use the order number,** not just the description. Being specific helps reduce errors or late deliveries.
- ▶ **Ask for samples when ordering.** Sometimes your deliveries may not arrive in time. Those samples can help you get through the gaps.
- ▶ **Recognize that your stoma is a direct opening to your body.** Be careful, and keep the area clean.
- ▶ **Have a day bag or backpack in your vehicle** with a change of appliance, additional supplies and extra clothing if a change is necessary. You never know if an accident will occur.
- ▶ **Be mindful when sitting.** You may place pressure on your appliance when using a seatbelt, sitting too close to the table and getting into a vehicle. Watch for pets that like to jump up on your lap, too.
- ▶ **In the beginning, set your phone alarm** for one hour to check your appliance until you become familiar with your routine.
- ▶ **If you are on a long drive, plan to stop every hour or so.** Some people have found an additional leg bag or a night container helpful.
- ▶ **Put a plastic covering or mat on the bed for nighttime accidents.** Keep extra bed sheets handy in case you have to change them in the middle of the night.
- ▶ **Keep the hair around the stoma clear.**
- ▶ **Make sure the area around the stoma is dry** when you are putting on the appliance.
- ▶ **Be independent as soon as possible.** A partner can be extremely helpful in the beginning.
- ▶ **Speak up and ask questions!** You are your primary advocate.
- ▶ **Reach out for support.** Talking to others who have had cancer is immeasurably valuable.
- ▶ **Be kind and support others.** We all need help.

Prostate Cancer

Prostate cancer starts when healthy cells mutate into abnormal cells, growing uncontrollably and not dying when they should. The prostate is a walnut-sized gland in the male reproductive system that is located below the bladder and in front of the rectum. It makes seminal fluid, which carries and protects sperm in semen.

The TNM system developed by the American Joint Committee on Cancer (AJCC) is used to classify and stage prostate cancer. The tumor (T) is categorized by its size, including how much of the prostate is occupied by cancer and whether it has spread to adjacent structures such as the seminal vesicles, rectum, bladder and/or pelvic wall; whether cancer has affected nearby lymph nodes (N); and whether the cancer has metastasized (M) to other parts of the body. The classification, Gleason grade group, PSA level and other factors are considered in assigning a stage.

TREATMENT OPTIONS

Some prostate cancers may not need to be treated immediately because the cancer is predicted to remain stable for some time and/or other illnesses the patient has reduce the likelihood that the cancer will ever be a problem. One or more of the following therapies may be recommended by your doctor. Some can temporarily or permanently affect sexual function, fertility, and bladder and/or bowel control. Others will have different side effects. Be sure to talk with your doctor.

Active surveillance delays active treatment while closely monitoring the course of the cancer and its symptoms. This approach may be recommended for early-stage (Stage I or II) cancers, low-risk cancers and some intermediate-risk cancers.

Watchful waiting is similar to active surveillance but usually involves less frequent monitoring and fewer follow-up biopsies. It is often recommended for much older men, particularly those with other serious medical issues.

Surgery may be used alone or with another therapy and is frequently recommended to treat early-stage cancers. It may also be considered for locally advanced disease (Stage III) in some cases. The standard surgery is a radical prostatectomy, which removes the entire prostate, surrounding tissues and the seminal vesicles. A pelvic lymph node dis-

section may be performed along with a prostatectomy to remove lymph nodes. An orchiectomy surgically removes both testicles. It is a surgical form of hormone therapy used to reduce testosterone levels and is not a part of a standard radical prostatectomy.

Radiation therapy may be given to cure the cancer or simply to prevent or relieve symptoms. It may be given as external-beam radiation therapy (EBRT), which involves a large machine that aims radiation at the prostate and surrounding tissues, or brachytherapy, which involves placing tiny radioactive “seeds” or needles directly into the prostate.

Thermal ablation uses extreme cold or heat to treat cancer cells.

Cryoablation, or *cryotherapy*, kills cancer cells by freezing them with a probe that is super-cooled with liquid nitrogen or a similar substance.

Radiofrequency ablation (RFA) places needles in the area of the prostate tumor. High-frequency electric waves generate heat at the tips of the needles, which destroys the tumor. Another option uses high-energy sound waves to create heat to kill cancer cells. This is known as high-intensity focused ultrasound (HIFU).

Hormone therapy adds, blocks or removes hormones. Androgens are male hormones, and prostate cancer cells need them to grow. The main male androgen is testosterone. A type of hormone therapy called androgen-deprivation therapy (ADT) slows tumor growth by preventing the body from producing androgens or by blocking the effect the androgens have on the tumor. Several types of ADT are available and include luteinizing hormone-releasing hormone (LHRH) agonists and LHRH antagonists, antiandrogens, androgen synthesis blockers and an orchiectomy, which surgically removes both testicles to reduce testosterone levels.

Chemotherapy may be used alone or with other forms of treatment.

Targeted therapy uses drugs or other substances to target genes, proteins or other factors that support the tumor. They may be given alone or with other therapies.

SOME COMMON DRUG THERAPIES FOR PROSTATE CANCER

These therapies may be used alone or in combination. For some combination therapies your doctor might suggest, go to PatientResource.com/Prostate_Cancer_Treatment.aspx

CHEMOTHERAPY

- ▶ cabazitaxel (Jevtana)
- ▶ docetaxel (Docefrez, Taxotere)
- ▶ mitoxantrone hydrochloride (Novantrone)

HORMONE THERAPY

Androgen synthesis blocker

- ▶ abiraterone acetate (Zytiga)

Antiandrogens

- ▶ apalutamide (Erleada)
- ▶ bicalutamide (Casodex)
- ▶ darolutamide (Nubeqa)
- ▶ enzalutamide (Xtandi)
- ▶ flutamide (Eulexin)
- ▶ nilutamide (Nilandron)

GnRH receptor antagonists

- ▶ degarelix (Firmagon)
- ▶ leuprolide mesylate (Camcevi)
- ▶ relugolix (Orgovox)

LHRH agonists

- ▶ goserelin acetate implant (Zoladex)
- ▶ histrelin acetate (Vantas)
- ▶ leuprolide acetate (Eligard, Lupron, Lupron Depot)
- ▶ triptorelin pamoate (Trelstar)

IMMUNOTHERAPY

- ▶ sipuleucel-T (Provenge)

RADIOPHARMACEUTICALS

- ▶ lutetium Lu 177 vipivotide tetraxetan (Pluvicto)
- ▶ radium Ra 223 dichloride (Xofigo)

TARGETED THERAPY

- ▶ olaparib (Lynparza)
- ▶ rucaparib (Rubraca)

As of 5/12/22

Immunotherapy in the form of a vaccine may be used. White blood cells are collected, modified in a lab to recognize prostate cancer cells and then infused back into the body to find and destroy the cancer.

Radiopharmaceuticals are drugs that contain a radioactive substance used to kill cancer. One treats castration-resistant prostate cancer (CRPC) and metastatic CRPC that has prostate-specific membrane antigen.

Bone-modifying (strengthening) therapy uses drugs to help relieve bone pain and may reduce the risk of bone problems. This therapy may be recommended when cancer metastasizes (spreads) to the bone or if androgen-deprivation therapy (ADT) is taken for a year or more, as ADT increases the risk of osteoporosis.

Clinical trials may be a valuable option for first- or second-line therapy or at any other time during your treatment. ■

STAGING

Staging is an important part of developing your treatment plan. ▶ To learn more, visit PatientResource.com and search for prostate cancer to find detailed tables and illustrations.

Chuck and Hannah Keels describe their love story as nothing short of miraculous. A self-described Stage IV prostate cancer thriver who shows no evidence of disease, Chuck feels uniquely prepared to help Hannah as she manages a Stage IV breast cancer diagnosis. They offer hope to each other and many cancer survivors as they follow their credo: **→ Get up and live!**



A match made in heaven

People who meet Chuck Keels now have a hard time believing he was diagnosed with Stage IV prostate cancer in 2015 but, at the time, it was a life-threatening diagnosis. He was told he had three months to live and that hospice was the only option.

"I was a 50-year old single dad of two boys," he said. "I gave away all of my belongings in Phoenix and planned to take my two boys back home to Ohio. On the day we were supposed to fly out, I heard 'pop!' and hit the floor. The trip was off."

In the ambulance on the way to the hospital, every bump was excruciating. The ambulance took him to a different hospital – not the one where he'd received his grim diagnosis – and the doctors there ran their own tests.

"I had a compression fracture as a result of the cancer metastasizing to my bones. But along with that bad news came some very good news from a medical team put together just for me. A hospitalist, oncologist and two spinal surgeons told me they wanted to fight my prostate cancer, and they had a plan that started with two surgeries the next day. I would have one to stop the testosterone production in my body and the other to insert a port for chemotherapy."

The surgeries went perfectly, and as he was lying in the recovery room, he remembers it got weirdly cold.

"I thought perhaps someone had left the big double doors open, but they were closed. I looked to the left and saw a man with a white scarf, beard and a brown robe. He put his hand on my shoulder. That day, all my pain stopped. I'd like to say my faith got me through it, but I wasn't a particularly religious person."

After three months of his prescribed six months of chemotherapy, his doctor said his scans looked like those of a healthy guy. His recovery continued, and he focused on healthy eating, juicing,

using essential oils and exercising. He also surrounded himself with loving and supportive people.

"I started getting phone calls from friends, and friends of friends, who wanted to know how I beat Stage IV cancer. I began to share my story on Facebook about how taking an active role in the things I could control helped me mentally and physically. I wrote a book titled *Hi...I'm Chuck*, and even had a business card made that said "Cancer Coach." Before long, I had thousands of followers, something that almost prevented me from meeting Hannah."

"That's where my story begins," Hannah explained.

"Two days after Chuck's recovery room experience, I was moving with my husband and four boys to Phoenix. It was a huge move — new house, new school, new job and all that goes with that. Six months after the move, my husband left me. I cried for three months straight, then found a lump in my breast. I was diagnosed with Stage III breast cancer at 42. A month after being diagnosed, my divorce was final. A month after that, I had a mastectomy and the next month returned to my job as an operating room nurse."

Unfortunately, Hannah's cancer progressed to Stage IV, and she lost her job when she wasn't able to continue working in the same capacity because of the medications she was taking. A year later, her best friend passed away unexpectedly.

"I felt the weight of so much loss," she said. "I was looking for the lessons in it. I prayed about it and began writing a book to help work through my feelings. I'd never published a book, so a friend offered to connect me with her cousin who had just published a book about his cancer journey. I had a hard time connecting with him on Facebook, so I messaged him."

To Chuck's surprise, Facebook capped his friend list at 5,000, so Hannah couldn't friend him. Her message was automatically moved to a different mailbox, and he just happened to check it 30 days later.

He apologized for the delayed response to her message and suggested they get together for coffee. Hannah, however, had just left for an extended vacation in The Netherlands to visit family. She agreed to meet when she returned.

But instead of waiting for her to get home, they began messaging. And texting. And video chatting.

According to Hannah, they hit it off instantly.

"He made me laugh. We had so much in common — our kids, our faith, cancer. One night before we hung up, he hinted that I was the one for him, and he said, 'Goodnight, Mrs. Keels.' We hadn't even met in person!"

That didn't last long. He picked her up at the airport and they were basically inseparable. Six weeks later they were engaged; six weeks after that they were married.

"I wasn't looking for someone," Chuck admitted. "In fact, I was okay with the idea of growing old alone, but when I met Hannah, I just knew I wanted her."

Hannah wasn't looking for a new relationship either.

"The last one was too hard to get over, but our conversations just blew me away. We shared a solid foundation, and I decided I wanted someone to make memories with."

On their honeymoon, Hannah had an epiphany.

"I had lost so much: my home, my marriage, my best friend, my vocation and my health. But I got it all back in Chuck, and my mindset changed. I could dream again." Chuck helped Hannah publish her book, *Faith Like Skin*.

Just one month after their honeymoon, they began thinking of formalizing the coaching Chuck had started. After much research, they created Living Hope Cancer Foundation (getupandlive.org), a 501(c)(3). It's a forum for creating a positive spiritual mindset when you have cancer.

"We use our own experiences to help people make a personal plan that coincides with a medical plan," Chuck explained. "Aside from supporting the need for second opinions, we leave the medical part to the experts. A personal plan is something you need from the minute you get that diagnosis. Even driving home in the car that first day, most people are wondering what they do with this new information they just received."

Hannah is living her personal plan as she actively manages Stage IV breast cancer.

"In the first 14 months of our marriage, I had 5 ambulance rides," she said. "Five months after we got married, a tumor was discovered in my neck and I began to have new symptoms. My heart was racing, I was short of breath and my neck hurt. Those symptoms turned into agonizing pain the next day, and Chuck took me to the ER."

Because it was the beginning of COVID, Chuck couldn't go in with Hannah. He had to drop off her at the door.

"The ER was oddly quiet. It was very dark and nearly silent. After I had scans, I was told my neck was broken. The nurse asked me where my husband was."

Chuck was sitting in his truck in the hospital parking lot, waiting for news.

"I heard a knock on the window," he said, "and the nurse told me Hannah had a fractured neck and would need to be transported to a different hospital for emergency surgery. Watching them drive off in the middle of the night was a scary feeling."

Hannah had two surgeries — one to cut off the blood supply to the tumor and the other to fuse her vertebrae together. Because of the need for space in the ICU, she was able to recover at home. That took about 8 weeks.

"The honeymoon was over!" she laughed. "I came home in a neck brace, and radiation therapy and IV chemotherapy were next. I'd only had oral chemotherapy up until this point, but testing revealed a new treatment was in order for my triple negative diagnosis."

With the new treatment came hair loss. In solidarity, Chuck shaved his head.



"That really moved me because I know it brought back memories of his cancer fight," Hannah said.

Radiation therapy to target a node in Hannah's chest affected her esophagus. "I lost my voice temporarily, and I needed a feeding tube. That was hard for me because I love to sing and I'm a foodie!"

As they'd done in the past, they adapted and did what they could to get the most out of life. Hannah used floaties to stay above water in their pool, and they kayaked with strict instructions from Chuck that she not paddle — only ride and enjoy.

Not long after, Hannah suffered a compression fracture in her spine. She had spinal fusion surgery and spent four months in a wheelchair.

"It's hard to ask for help," she admitted, "and it's hard to lose your independence. Chuck was at my beck and call. He managed my pain meds, brought my toothbrush to my bedside. He did everything."

"It isn't often your caregiver knows exactly how to help," he laughed. "But her fracture was just below where I'd had mine, so I drew from my experience. We are here to help each other at different times in our lives, and I set a goal to be the best caregiver I could be."

Hannah's next challenge centered around the discovery of metastases in her brain and in her hip socket.

"I had radiation therapy to my brain and hip socket. After 26 days of bed rest, I was able to walk just one week after the radiation treatments ended."

Chuck continues to be impressed with Hannah's attitude.

"Every time she has a setback, she views it as temporary and just something to get through."

Using what has helped them through their journeys gives this inspiring couple purpose. Chuck gets the most satisfaction from hearing the hope and excitement in the voices of the people they coach. Before meeting Chuck, Hannah couldn't see past the next couple of years. Today, she sees far into the future, the two of them with gray hair, walking on the beach together.

Their advice to others: Get up and live! ■

Breast Cancer

Breasts are made up of connective, fat and glandular tissues that contain the cells that can make milk. Glandular tissue includes the milk ducts and lobules.

When genes in normal breast cells mutate and cause the cells to multiply uncontrollably, they form a disorganized mass of abnormal cells called a tumor.

Multiple types of breast cancer exist. Non-invasive breast cancer lacks the ability to spread beyond the ductal or lobular walls. Invasive breast cancer spreads beyond the ductal or lobular structures into surrounding fatty and fibrous breast tissue and has the ability to spread to other organs. When cancer cells spread (metastasize) to other parts of the body through the bloodstream or lymphatic system, the cancer cells are still considered breast cancer, regardless of where they spread.

The results of a biopsy, imaging scans, immunohistochemistry and genomic testing are used to classify and stage breast cancer, according to the American Joint Committee on Cancer (AJCC). Immunohistochemistry on the initial biopsy material 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+*) or absence (*ER-/PR-*) of these hormone receptors. Before a final stage is determined, tumor grade, biomarkers and molecular and genetic changes in cancer tissue identified in multigene panels are also considered.

TREATMENT OPTIONS

One or more of these options may be used.

Surgery is the most common treatment for most breast cancers. It removes the tumor in the breast and it may be used to prevent or treat symptoms or complications of breast cancers that have metastasized to distant organs.

Lymph node surgery is usually necessary to stage the cancer (called a sentinel lymph node biopsy) or to control cancer that has spread to the nodes. The underarm (axilla) is the most common site of spread for breast cancer.

A lumpectomy, also called breast-sparing or breast-conserving surgery, removes the tumor along with a small margin of normal-appearing tissue around it. It is used for early-stage breast cancers detected as small tumors. A lumpectomy is usually followed by radiation treatments, which are designed to kill microscopic cancer cells hiding in other

parts of the breast.

A mastectomy involves removal of the entire breast. Total mastectomy is the surgical removal of the entire breast without removing muscle. In a modified radical mastectomy, a total mastectomy is performed along with removal of a block of underarm (axillary) lymph node tissue (axillary dissection). Drains may be placed to collect fluid and assist in healing. Reconstructive surgery may be an option (see PatientResource.com/Breast_Cancer_Treatment.aspx).

Survival rates for breast-conserving surgery plus radiation therapy compared to total mastectomy (with or without reconstruction) are essentially the same. Ongoing follow-ups after both types of surgery are important and recommended.

Radiation therapy is almost always delivered after lumpectomy to destroy hidden cancer cells. Post-mastectomy radiation therapy is sometimes necessary. For patients with a high risk of the cancer growing back on the chest wall area (after mastectomy and/or axillary surgery), radiation can lower this risk.

Chemotherapy drugs may be used as neoadjuvant (preoperative) therapy to shrink a large, bulky tumor so it can be removed surgically or to reduce the tumor's size to offer more surgical options. Neoadjuvant chemotherapy also offers the advantage of helping your doctor determine how well the chemotherapy drugs work against the tumor, and to identify whether additional therapy is needed post-operatively. Adjuvant (after surgery) chemotherapy is given to destroy cancer cells that may remain in the body.

Targeted therapy uses drugs or other substances to identify, attack and destroy specific types of cancer cells or to slow disease progression. Types include anti-*HER2* drugs, kinase inhibitors and monoclonal antibodies. It can be given before or after surgery.

Hormone therapy is used to treat *ER+/PR+* tumors. Several types may be used depending on the stage of the cancer and menopausal status of the female patient. Drugs that lower or block estrogen may be used, or the ovaries may be removed with surgery or suppressed

SOME COMMON DRUG THERAPIES FOR BREAST CANCER

These therapies may be used alone or in combination. For some combination therapies your doctor might suggest, go to PatientResource.com/Breast_Cancer_Treatment.aspx

CHEMOTHERAPY

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

HORMONE THERAPY

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

IMMUNOTHERAPY

- ▶ pembrolizumab (Keytruda)

TARGETED THERAPY

- ▶ abemaciclib (Verzenio)
- ▶ ado-trastuzumab emtansine (Kadcyla)
- ▶ alpelisib (Piqray)
- ▶ entrectinib (Rozlytrek)
- ▶ everolimus (Afinitor, Afinitor Disperz)
- ▶ fam-trastuzumab deruxtecan-nxki (Enhertu)
- ▶ lapatinib (Tykerb)
- ▶ larotrectinib (Vitrakvi)
- ▶ margetixumab-cmkb (Margenza)
- ▶ neratinib (Nerlynx)
- ▶ olaparib (Lynparza)
- ▶ palbociclib (Ibrance)
- ▶ pertuzumab (Perjeta)
- ▶ pertuzumab, trastuzumab and hyaluronidase-zzxf (Phesgo)
- ▶ ribociclib (Kisqali)
- ▶ ribociclib and letrozole (Kisqali Femara Co-Pack)
- ▶ sacituzumab govitecan-hziy (Trodelyv)
- ▶ talazoparib (Talzenna)
- ▶ trastuzumab (Herceptin)
- ▶ trastuzumab and hyaluronidase-oysk (Herceptin Hylecta)
- ▶ tucatinib (Tukysa)

As of 5/12/22

with medication or radiation therapy.

Immunotherapy is designed to stimulate the body's own immune system to treat certain breast cancers.

Clinical trials may be another option. ■

STAGING

Staging is an important part of developing your treatment plan. To learn more, visit PatientResource.com and search for breast cancer to find detailed tables and illustrations.

Colorectal Cancer

Cancer that begins in the colon or rectum is referred to as colorectal cancer. You may hear “colon cancer” and “rectal cancer.” Each is correct depending on where in the body the cancer started.

Part of the digestive system, the colon makes up about the first six feet of the large intestine, and the rectum and anal canal are about the last six inches.

Colorectal cancers typically begin as benign polyps that may become cancerous. During a screening procedure called a colonoscopy, polyps are removed (polypectomy).

The tumor, node and metastasis (TNM) system developed by the American Joint Committee on Cancer (AJCC) is used to classify and stage colorectal cancer. Doctors categorize the tumor (T) according to its depth of invasion in the bowel wall, whether cancer cells are found in nearby lymph nodes (N) and whether the cancer has metastasized (M) – or spread – to other parts of the body. Once the cancer is classified, an overall stage is assigned. Staging provides essential information for describing the extent of the cancer, predicting treatment outcomes and helping guide the treatment plan.

TREATMENT OPTIONS

Your treatment plan will be based on many factors. Ask your doctor to explain each treatment’s risks and benefits to help you decide which one is best for you.

Surgery is the most common treatment for early-stage colorectal cancer. Nearby lymph nodes may be removed (lymphadenectomy) to allow a pathologist to determine whether the cancer has spread, and if so, how far. Different procedures are used to remove the part of the colon or rectum containing the tumor and to reattach the ends. Removing the entire colon is called a colectomy, and removing the entire rectum is a proctectomy. Types of surgery include the following:

- Open surgery involves a large incision in the abdomen.
- Laparoscopic surgery uses a special lighted instrument with a tiny video camera attached that is inserted into a few small incisions in the abdomen.
- Robotic-assisted laparoscopic surgery uses robotic arms that operate surgical tools controlled by a surgeon who has specialized training.

Your surgeon will try to preserve normal bowel function whenever possible. However, sometimes a different pathway for bowel function must be created. The surgeon attaches one end of the small intestine or colon to an opening created in the abdomen called a stoma. A pouch is attached to the stoma to collect waste. This procedure is called a colostomy, ileostomy or simply an ostomy, depending on the part of the intestine used to form the stoma. An ostomy can be temporary or permanent.

Chemotherapy may be given before surgery (neoadjuvant — usually applies to rectal cancer) to shrink a tumor for easier removal and/or after surgery (adjuvant) to kill any remaining cancer cells. Chemotherapy drugs may be used alone or combined with targeted therapies.

Hepatic arterial infusion (HAI) may be used when colon or rectal cancer has spread to the liver. It is chemotherapy delivered directly into the liver through its main blood vessel, the hepatic artery.

Targeted therapy may be used if certain mutations are present in the tumor. Types include angiogenesis inhibitors to prevent the tumor from making new blood vessels, monoclonal antibodies for epidermal growth factor receptor (*EGFR*) and vascular endothelial growth factor (*VEGF*) inhibitors to slow the cancer’s growth, protein kinase inhibitors for the *BRAF V600E* gene mutation, and tumor-agnostic treatment for the *NTRK* gene fusion.

Immunotherapy in the forms of immune checkpoint inhibitors and monoclonal antibodies are approved for colorectal cancer. Single immunotherapy drugs or a combination of two immune checkpoint inhibitors are approved for people who have microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal tumors.

Radiation therapy is typically given to treat rectal cancer and cancer that has metastasized to a localized area of the body, such as a liver lesion or bone lesion. It may

SOME COMMON DRUG THERAPIES FOR COLORECTAL CANCER

These therapies may be used alone or in combination. Possible combination therapies are listed below.

CHEMOTHERAPY

- ▶ capecitabine (Xeloda)
- ▶ fluorouracil (5-FU)
- ▶ irinotecan (Camptosar)
- ▶ trifluridine and tipiracil (Lonsurf)

IMMUNOTHERAPY

- ▶ ipilimumab (Yervoy)
- ▶ nivolumab (Opdivo)
- ▶ pembrolizumab (Keytruda)

TARGETED THERAPY

- ▶ cetuximab (Erbix)
- ▶ entrectinib (Rozlytrek)
- ▶ larotrectinib sulfate (Vitrakvi)
- ▶ panitumumab (Vectibix)
- ▶ regorafenib (Stivarga)

SOME POSSIBLE COMBINATIONS

- ▶ bevacizumab (Avastin) with fluoropyrimidine and irinotecan (Camptosar)
- ▶ bevacizumab (Avastin) with fluoropyrimidine and oxaliplatin (Eloxatin)
- ▶ bevacizumab (Avastin) with fluorouracil (5-FU)
- ▶ cetuximab (Erbix) with irinotecan (Camptosar)
- ▶ cetuximab (Erbix) with leucovorin calcium, fluorouracil (5-FU) and irinotecan (Camptosar)
- ▶ encorafenib (Braftovi) with cetuximab (Erbix)
- ▶ ipilimumab (Yervoy) with nivolumab (Opdivo)
- ▶ irinotecan (Camptosar) with fluorouracil (5-FU) and leucovorin
- ▶ levoleucovorin (Fusilev, Khapzory) with fluorouracil (5-FU)
- ▶ oxaliplatin (Eloxatin) with fluorouracil (5-FU) and leucovorin
- ▶ panitumumab (Vectibix) with leucovorin, fluorouracil (5-FU) and oxaliplatin (Eloxatin)
- ▶ ramucirumab (Cyramza) with leucovorin, fluorouracil (5-FU) and irinotecan (Camptosar)
- ▶ ziv-aflibercept (Zaltrap) with fluorouracil (5-FU), leucovorin and irinotecan (Camptosar)

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be delivered as neoadjuvant therapy and as adjuvant therapy (usually for rectal cancer). It is frequently given with chemotherapy (chemoradiation).

Radiofrequency ablation (RFA), microwave ablation (MWA) or cryoablation may be used to treat colorectal cancer that has spread to the liver or lungs. RFA uses radio-frequency waves to heat the tumor; MWA uses microwave energy to heat the tumor; and cryoablation freezes the tumor.

Clinical trials may be an option. Researchers continue exploring new treatment options or combinations of treatments for all stages of colorectal cancer. A clinical trial may be your best treatment option. Ask your doctor if a clinical trial is right for you. ■

STAGING

Staging is an important part of developing your treatment plan. To learn more, visit [PatientResource.com](https://www.patientresource.com) and search for colorectal cancer to find detailed tables and illustrations.

Bryan Wenger knew cancer ran in his family, and he freely admits he should have had genetic testing earlier because it might have saved him from a Stage IIIB colorectal cancer diagnosis at 26. Although treatment was successful, he later developed Stage III prostate cancer and beat it as well. Today, with the support of his wife and family, he remains diligent about follow-up tests.

CHOOSE POSITIVITY

Multiple people in my family have had cancer, but it wasn't until a great aunt had genetic testing that we realized Lynch syndrome ran in our family. It had contributed to many members of my family having several types of cancer: stomach, pancreatic, colon, breast, ovarian, endometrial, large bowel, small bowel and kidney. In hindsight, I realize I should have had genetic testing once I turned 18 to confirm whether I had Lynch syndrome. I am now very proactive with preventive scans and tests.

By the time I was 26, I noticed blood in my stools. I asked my doctor for a colonoscopy, fearing the worst, but he was reluctant because it was practically unheard of for someone to have colorectal cancer at 26. After discussing my family medical history, he agreed.

He found a tumor that was about the size of a Nerf football. Part of it was two inches within my rectum and five to six inches outside the rectum. The doctor could not complete the colonoscopy because he couldn't get past the tumor. After I woke up, he told me I needed to see an oncologist.

Even with Lynch syndrome running in my family, I still didn't think I would get cancer in my 20s. No one expects that. And most people don't develop colorectal cancer until they are 50 or older.

The oncologist diagnosed the colorectal cancer as Stage IIIB. At the time, I hadn't had genetic testing, but the doctor treated me as if I had Lynch syndrome because the odds were good that I did. I had a partial colectomy and a colostomy followed by eight weeks of chemotherapy and radiation therapy. After all of that, I remained free and clear for almost 10 years.

I had colonoscopies every year, but after several years, my insurance didn't want to pay for them because it was unusual for someone my age to have that many before age 50. This prompted me to bite the bullet and have genetic testing, which confirmed I was positive for Lynch syndrome.

A few years later, my doctor noticed my PSA level rising during my checkups. He grew concerned and ordered a prostate biopsy.



I was diagnosed with Stage III prostate cancer that had spread to my seminal vesicles, and I chose to have a radical prostatectomy.

This cancer was particularly aggressive and returned almost immediately after surgery. I requested to have radiation therapy but the doctor was reluctant because I'd already had radiation to my pelvic area for the colorectal cancer. I wouldn't take "no" for an answer because surgery was no longer an option and I was out of effective treatment options. The doctor finally agreed and, later, I started hormone therapy.

Knowing about Lynch syndrome is a bad news/good news situation. The bad news is that I'm at a higher risk for many other cancers. The good news is that now that I'm aware of it, my doctors and I can be proactive with screenings and monitoring so we can catch future cancers early. We know it's highly likely I will develop future cancers, but knowledge is power. And, as a result of my testing, more members of my family have had testing, too.

Sharing genetic information with family is so important, and I encourage others to do it especially if cancer runs in your family. When I did the genetic testing, I sent in the results of my mother's tests along with mine, which provided more information.

Throughout everything, I've leaned on my family a lot. It also helps that my wife is a therapist. I needed her counsel especially when the hormone therapy had my emotions swinging from one end to the other. I also found support from Friend for Life Cancer Support Network. Now I volunteer to help others and give back.

After being diagnosed at 26, I wasn't sure I would see 40. But with good doctors and genetic testing I'm looking forward to seeing 50. A positive attitude is absolutely necessary. I choose to look cancer in the face and say, "I'm going to beat you." ■

» Bryan's suggestions

- ▶ **Get genetic testing.** If you have several members of your family who have had multiple cancers or developed cancer at a young age, it's a good idea to determine whether you carry the gene.
- ▶ **Find a specialist** that has experience with your type of cancer and genetic mutations.
- ▶ **Don't be afraid to reach out for help.** Cancer isn't something you can do alone.
- ▶ **You have to have hope.**
- ▶ **Plan to know your limitations** with your activities during chemotherapy. It takes a lot out of you, and you can't do what you normally do while on it.
- ▶ **Ginger helps with nausea.** Try ginger snaps and ginger ale.
- ▶ **Don't take "no" for an answer.**
- ▶ **It's your life and your body.** No one can tell you what your quality of life is for you.