

PATIENT RESOURCE

IMMUNOTHERAPY

for the treatment of

LUNG CANCER

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IMMUNOTHERAPY *for the treatment of* LUNG CANCER

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CO-EDITORS-IN-CHIEF



Charles M. Balch, MD, FACS
Professor of Surgery, The University of Texas MD Anderson Cancer Center
Editor-in-Chief, Patient Resource LLC
Past President, Society of Surgical Oncology



Paul A. Bunn, MD
Distinguished Professor and James Dudley Endowed Professor of Lung Cancer Research, University of Colorado School of Medicine
Past President, American Society of Clinical Oncology



Howard L. Kaufman, MD, FACS
Division of Surgical Oncology, Massachusetts General Hospital
Chief Medical Officer, Replimune, Inc.
Past President, Society for Immunotherapy of Cancer



Rachel E. Sanborn, MD
Co-Director, Thoracic Oncology Program
Phase I Clinical Trials Program
Robert W. Franz Cancer Research Center
Earle A. Chiles Research Institute
Providence Cancer Institute

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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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Understanding the immune system's role in treating lung cancer

Immunotherapy was approved in 2015 to treat advanced lung cancer. It is very different from other types of cancer treatment because it uses the body's own immune system to recognize and attack cancer cells that have been hiding and targets them for destruction. Immunotherapy is a systemic treatment, which means the drugs travel through your bloodstream to all parts of your body to kill cancer cells or keep them from dividing. This guide explains lung cancer, the immune system, immunotherapy and ways to help manage your treatment.

Learning you have lung cancer is life-changing. Give yourself time to digest the news, and then focus on learning as much as you can about your exact diagnosis. Knowing key information, including stage and any biomarkers, will better prepare you to make well-informed decisions with your doctor. If you're unsure of your specific diagnosis, have your doctor or nurse navigator write it down for you, and be sure to ask about any medical terms you don't understand.

EXPLAINING LUNG CANCER

Your lungs are a pair of large, spongy, expandable organs in your chest cavity that are surrounded by a thin layer of protective tissue (pleura). The right lung is a little larger with three parts (lobes), and the left lung has only two (see Figure 1). When you inhale, your lungs absorb oxygen, which is then delivered to the rest of your body. When you exhale, your lungs rid the body of carbon dioxide. Your diaphragm helps your lungs expand and contract when you breathe.

Lung cancer often begins in the lining of the airways when abnormal cells grow out of control, dividing faster and living longer than normal cells. Over time, these cancerous cells accumulate to form a tissue mass (primary tumor). Left untreated, a primary tumor may grow into the pleura and form secondary tumors nearby. The cancer cells can eventually crowd out the normal cells to make breathing increasingly difficult.

In advanced disease, lung cancer cells may break away to form tumors in the opposite lung and distant sites such as the liver, brain or bones. These are known as metastases. Regardless of location, the metastases are still considered lung cancer and are treated as such.

Your doctor will analyze the cancer cells in a biopsy specimen or fluid taken from the lung or elsewhere to define the type of lung cancer, which will help guide treatment decisions.

Adenocarcinoma is the most common subtype diagnosed, especially in never smokers. It generally begins in the mucus-producing cells in the more distal (those that are farthest away) airways. Because it tends to grow more slowly than other types of lung cancer, adenocarcinoma is slightly more likely to be found before it spreads. Adenocarcinomas tend to develop in the peripheral lung and spread to distant sites more often than other types except for small cell lung cancer.

Squamous cell lung cancer (epidermoid carcinoma) is the second most common and starts in the early versions of squamous cells, the thin, flat cells that line the more central airways in the lungs. It most often develops in smokers and in the central lung. It spreads to distant sites less often than adenocarcinomas.

Large cell lung cancer can develop anywhere in the lungs and tends to grow and spread quickly. When it includes neuroendocrine features, it may behave and be treated like small cell lung cancer.

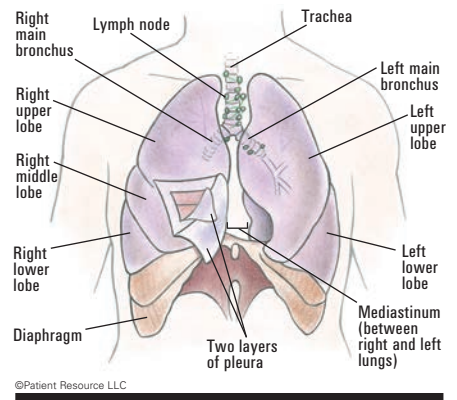
Adenocarcinoma and squamous cell and large cell lung cancers are sometimes collectively referred to as non-small cell lung cancer (NSCLC), which accounts for the majority of lung cancer diagnoses. Each type has distinct characteristics and responses to treatment, which makes it important for your doctor to determine the specific type.

Small cell lung cancer (SCLC), named for its appearance under a microscope, often starts in the central airways (bronchi) in the center of the chest. An aggressive form of lung cancer, it most often spreads to distant parts of the body before it is found. SCLC cells may secrete proteins that cause symptoms such as neurologic weakness or abnormalities in blood electrolytes.

WHAT IS THE IMMUNE SYSTEM?

To understand how your immune system can be used to fight cancer, it's helpful to know it's a complex network of cells, molecules, organs

FIGURE 1
ANATOMY OF THE LUNGS



and lymph tissues working together to defend the body against bacteria, cancer cells and other microscopic invaders.

Its first job is to distinguish between what is part of the body (self) and what is not (non-self). Once it determines that a cell is non-self, or foreign, to the body, it begins a series of reactions to identify, target and eliminate the non-self cells (see Figure 2, page 2).

The lymphatic system, which is made up of lymph nodes, the spleen, thymus, adenoids and tonsils, is a driving force in the immune system. Lymph, a clear fluid, collects and filters bacteria, viruses, toxins and chemicals known as antigens as it circulates in the lymphatic system and bloodstream. Lymph nodes are located throughout the body, with large concentrations near the chest, abdomen, groin, pelvis, underarms and neck.

Lymph contains lymphocytes, a type of white blood cell that attacks infectious agents. Lymphocytes begin in the bone marrow and develop from lymphoblasts (immature cells found in bone marrow). The two main types of lymphocytes are B-lymphocytes (B-cells) and T-lymphocytes (T-cells).

B-cells develop in the bone marrow and mature into either plasma cells or memory cells. Plasma cells make antibodies to fight germs and infection. Memory B-cells help the immune system remember which antigens attacked the body so it can recognize them and respond if they return.

T-cells also develop in the bone marrow and mature into four types: helper, killer, regulatory and memory T-cells. Each responds to non-self antigens in different ways.

HOW THE IMMUNE SYSTEM ELIMINATES CANCER

An immune response begins when B-cells and helper T-cells identify a non-self antigen and tell the rest of the immune system. The body then ramps up its production of T-cells to fight and destroy the antigen.

The immune system uses the same process to recognize and eliminate cancer, but the process is more complicated. Cancer cells are created by the body, so the normal ways to find and fight invading cells aren't always effective. The immune system may have difficulty identifying cancer cells as non-self. It may still see them as part of the body and not coordinate an attack. If the body can't tell the difference between tumor cells and normal cells, the tumor cells may be able to hide from the immune system.

Additionally, cancer cells can change and use multiple methods to escape or confuse the immune system. One way is to produce proteins on their surface to hide from the immune system, like camouflage. Another is to create their own messengers (cytokines), which means that the cancer cells can communicate and confuse other immune cells. This allows the cancer to take control of certain parts of the process that the body uses to regulate the immune response. This means that even if the immune system recognizes the cancer, it may not be able to successfully start or maintain an attack long enough to kill the cancer cells.

The longer the cancer cells face a weakened immune response, the more they're able to adapt, and the easier it is for them to manipulate immune cells inside the tumor's location, sometimes called the tumor micro-

environment area. Immunotherapy offers the immune system reinforcements to keep up its fight.

IMMUNOTHERAPY: YOUR POTENTIAL TREATMENT PATH

You may be a candidate for immunotherapy if you meet certain criteria. If you have a pre-existing autoimmune disorder, be sure to discuss it with your doctor (see *Molecular Testing*, page 7).

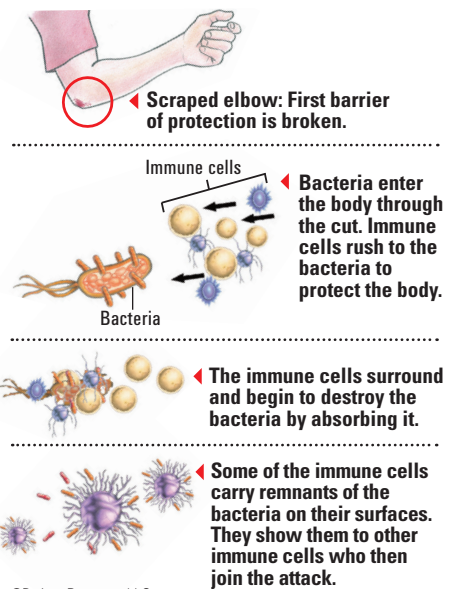
It's important to note that immunotherapy is not effective for every person, even if it is approved for that person's cancer type. Doctors and scientists are involved in clinical trials to learn why, as well as to improve existing therapies and develop new ones.

Biomarker testing may be a requirement, particularly in clinical trials, because some types of immunotherapy are approved to treat cancers in people who have specific biomarkers. This helps doctors recommend immunotherapy only to patients who are most likely to respond. One test determines how many of your cancer cells express a protein called programmed death-ligand 1 (PD-L1). If there is a large amount of these proteins, immunotherapy alone may be used. If there are fewer, chemotherapy combined with immunotherapy may be used.

Depending on the cancer's type and stage and unique characteristics, such as previous treatments, age and general health, your doctor may select immunotherapy alone or combined with one of the following therapies.

- Surgery is the removal of the tumor and some surrounding normal tissue.

FIGURE 2
NORMAL IMMUNE RESPONSE



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- Chemotherapy involves drugs to stop the growth of or directly kill cancer cells throughout the whole body. How it is given depends on the type and stage of the cancer.
- Radiation therapy uses high-energy X-rays or other types of radiation to kill cancer cells or stop them from growing.
- Targeted therapy involves drugs or other substances designed to attack cancer cells directly by targeting a specific abnormal gene or protein. Molecular (targeted) therapies are most often used in adenocarcinomas because molecular abnormalities are most common in this type of lung cancer.
- Clinical trials may involve immunotherapy and/or other treatment types. ■

GLOSSARY / These definitions may help you better understand the terms your health care team uses.

IMMUNE SYSTEM

Antibody: A protein B-cells make in response to antigens (foreign substances such as bacteria, viruses and toxins).

Antigen: Any substance that triggers an immune response. Bacteria, viruses, toxins, abnormal proteins in cancer cells and chemicals are all antigens.

B-cell: A type of immune cell that makes antibodies and other proteins to mark specific foreign substances for other immune cells to destroy. A B-cell is a type of lymphocyte or white blood cell.

Immune cells: White blood cells in the immune system that help defend against cancer, infectious disease and other threats to the many cells and tissues in the body.

Immune checkpoint inhibitor: A type of immunotherapy that blocks certain proteins or receptors some immune cells make to turn off an immune response. In effect, these inhibitors "release the brakes" on the immune system so T-cells can destroy cancer cells unchecked.

Immune-related adverse events (irAEs): The immune system's overreaction to immunotherapy. In rare cases, irAEs can rapidly become life-threatening without medical attention.

Lymphocyte: A type of immune cell (white blood cell) in lymph tissue and blood. The main types are B-lymphocytes (B-cells) and T-lymphocytes (T-cells), which both help the immune system fight cancer and infections.

PD-1 (programmed cell death-1): A receptor that binds with another protein (PD-L1) to help keep the body's immune response in check by turning off immune responses.

Receptors (immune receptors): Surface molecules on immune cells that bind to the surfaces of other immune cells. This typically causes the cell to produce signals that help cells communicate and regulate specific functions in the immune system.

T-cells: White blood cells (immune cells) that play a significant role in the immune system's fight against infection and disease. They are a type of lymphocyte that can directly kill cancer cells.

White blood cells: Made in the bone marrow and found in the blood, spleen and lymph tissue, they are part of the body's immune system and help the body fight infection and other diseases.

GENERAL TERMS

Biomarker: Also known as a tumor marker or biological marker, this substance is produced by cancer cells or other cells of the body in response to cancer and may help guide treatment.

Distant: Used to describe cancer that has spread beyond the local or regional area.

In-situ: A group of abnormal cells found only in the place where they first formed in the body. These cells have not spread to distant sites.

Localized: Disease that is limited to a certain part of the body.

Regional: Describes the body area right around the tumor.

Tumor microenvironment: The area that surrounds and sustains a tumor. It is made up of normal cells, molecules and blood vessels.

HEALTH CARE TEAM

Case manager: Your personal advocate who collaborates with health care professionals and non-medical personnel to help overcome various financial, logistical and other common barriers to care.

Medical oncologist: Physician who treats cancer using medications.

Multidisciplinary medical team: A medical team made up of many people, each with a specialized role in your treatment plan. They will work closely together to ensure you receive the best care possible.

Patient navigator: A health care team member who may or may not be licensed (also may be called a lay navigator) who will help guide you through diagnosis and treatment.

Pulmonologist: Physician who specializes in the evaluation and treatment of lung problems.

Some definitions courtesy of the website of the National Cancer Institute (www.cancer.gov)

Ignore statistics and think positive

Melinda and Paul Dunn had plenty in common when they married, including the workplace where they met. Now more than 30 years later, they're survivors of different types of Stage IV cancer, supporting each other every step of the way. Their advice: Ignore statistics and make plans.



Busy taking courses to get into an MBA program in 2012, I noticed I was often short of breath. My dad had died in his 50s of a heart attack, so I saw a cardiologist. To my surprise, the CT scan showed a mass in my left lung. Within a week, I was diagnosed with Stage IV non-small cell lung cancer and told I had maybe another year to live. I was 58.

This news was alarming, but my husband, Paul, and I had been through this before. He had already survived Stage IV melanoma for 22 years after a prognosis as grim as mine. His last recurrence was in 2002.

His experience profoundly changed how I view cancer survival statistics. Those numbers are averages based on groups of people in the past, so they have nothing to do with me personally. By example, my husband taught me how to approach my serious illness: I ignore survival rate statistics, refuse to let cancer consume or define me and look ahead to the future by making plans.

So that's how we've rolled. We plan around my treatment schedule to travel to South America, Scotland, England, San Francisco, New Orleans, wine regions and elsewhere. I planned a different life course to focus on giving back, including volunteering twice a week teaching English to adults new to the country. We also made changes to our house to provide a comfortable, stable home for my elderly mother who had early-stage dementia in her last years.

A major cancer center in a nearby city was familiar territory from Paul's check-ups, so that's where I've established my happy family of caregivers. I began with the "platinum treatment," a combination of three platinum-based chemotherapy drugs that was the standard of care. I responded without progression for two and a half years. I'm what's called a "high responder," meaning I respond well to certain treatments because of the particular makeup of my tumor cells.

When chemotherapy was no longer effective, biomarker testing showed my tumor was positive for the *BRAF* gene mutation. That made me eligible for a clinical trial evaluating a targeted therapy developed for that mutation. I took lots of pills, up to eight a day, through fever spikes and near-crippling muscle pain while my dosage was adjusted. After a few months, my oncologist announced my lungs were clear for the first time since undergoing treatment. Hallelujah! Targeted therapy bought me another two years before cancer returned to the lung and moved farther into my spine.

We turned to immunotherapy, a type called an immune checkpoint inhibitor. I got an IV infusion every other week at first, then after a while, just once a month. It was so easy, and the entire process took less than an hour.

Cancer treatments almost always come with side effects. Getting three chemotherapy drugs at once would wipe me out, and I could barely get out of bed afterward. Immunotherapy damaged my thyroid, so I take thyroid medication. I've been on and off steroids to manage lung inflammation. Acid reflux, which makes my esophagus feel raw, is another side effect. Early-stage heart congestion may or may not be treatment-related.

Being realistic, I knew the immunotherapy drug would run its course, too. That's just the nature of the beast with metastatic cancer. I get scans like clockwork, and if we see progression, we know the treatment has likely done all it can for me. After two and a half years on the checkpoint inhibitor, a scan showed an active spot on my left lung. My doctor recommended moving to a targeted therapy treatment of two different medications taken as pills. I'm so thankful I have options because I figure all I need is something new coming down the pike every two or three years.

As a lung cancer support phone volunteer, I make it my mission to give people hope. Sometimes callers say they just want to cry. I tell them, "Of course you do. You have every right to cry." But then I gently try to move their outlook to a more positive light. The important thing is to have more good days when you're positive than bad days when you cry. Personally, I feel so very fortunate for this gift of additional time, seven years so far. I can spend it being miserable about having cancer, or I can be grateful, positive and hopeful about my life.

We're incredibly lucky to live in an era of rapidly evolving cancer research and expanding treatment options. Researchers and scientists are essentially changing what it means to be diagnosed with lung cancer. ■

Key factors contribute to your treatment plan

Staging is a process that helps your medical team develop a personalized treatment plan based on the extent of disease and how far it has progressed (see Figure 1). To assign a stage, your doctors will evaluate the results of your tissue biopsy, imaging studies, diagnostic tests and physical exams.

The TNM classification system developed by the American Joint Committee on Cancer (AJCC) is used to stage non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC) (see Table 1). The T category specifies the primary tumor's size and location. The N category indicates whether lymph nodes show evidence of cancer cells. The location of these lymph nodes is im-

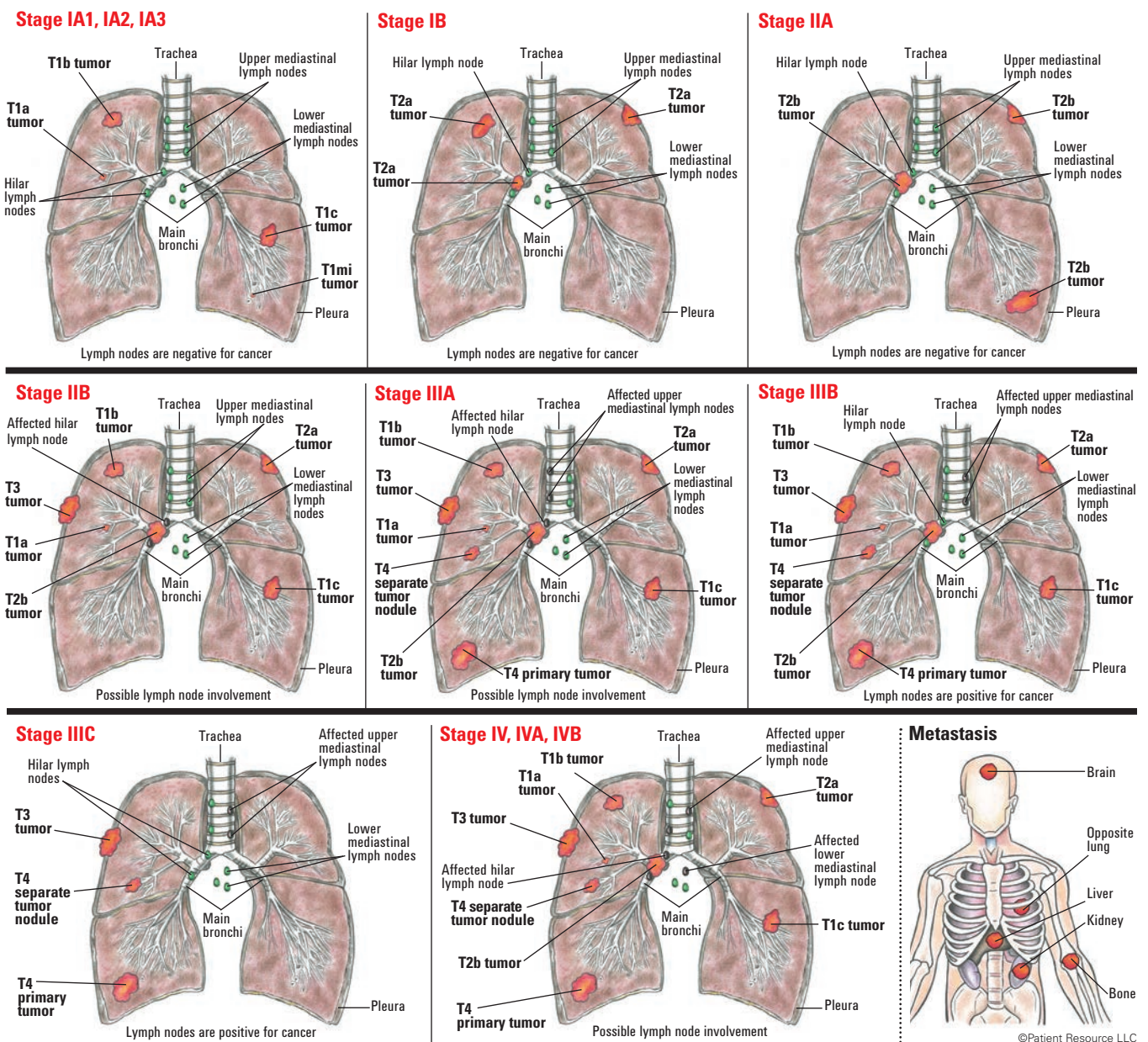
portant because it shows how far the disease has spread. The M category describes distant metastasis, if any. An M subcategory may be added based on the presence of tumor cells that can be detected only by using a microscope or molecular testing.

Lung cancer stages range from 0 through IV (see Table 2). Stage 0 (also known as "in situ") is a precursor of an invasive cancer.

In situ cancers have not spread to other parts of the body. Stages I and II are generally confined to the local area where the cancer is found, and Stage III has spread to regional lymph nodes. Stage IV is locally or regionally advanced disease that has spread to distant sites, such as the brain, liver or bone.

These basic stages group patients who have similar prognoses (outlooks), allowing doctors to more accurately predict survival outcomes depending on the type of treatment they have. The AJCC also recommends tumor genetic testing to help determine which treatments are likely to be most effective.

FIGURE 1
STAGES OF LUNG CANCER



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All lung cancers are staged according to the AJCC TNM system. Sometimes doctors describe SCLC as limited stage (corresponding to Stages I-III) or extensive stage (corresponding to Stage IV) as an additional tool to determine the treatment that may be most beneficial.

- Limited-stage SCLC is confined to one part of the chest, in just one part of the lung and in nearby lymph nodes. Radiation therapy to that area combined with chemotherapy may be a curative treatment option.

- Extensive-stage SCLC has spread to other parts of the body, such as the bone, brain or other lung. Patients with limited-stage SCLC whose tumors are too large to tolerate radiation therapy may be considered as extensive stage.

During staging, your doctors will rely on a pathology report. It is prepared by a pathologist, a doctor with special training in identifying diseases by studying cells and tissues under a microscope. Your report will

describe the results of tissue sample testing and may include results from biomarker testing, tumor molecular analysis or other tests.

With today's emphasis on personalizing treatment for each person's cancer, pathology report results are becoming increasingly important in the diagnosis and treatment of lung cancer (see *Treatment Options*, page 6).

Ask your doctor to discuss the report's findings and how they will affect your treatment options. Request a copy to take with you to medical appointments. ■

TABLE 1
AJCC TNM SYSTEM FOR CLASSIFYING LUNG CANCER

Classification	Definition
Tumor (T)	
TX	Primary tumor cannot be assessed, or tumor proven by the presence of malignant (cancerous) cells in sputum (mucus that has been coughed up) or bronchial washings (cells collected from inside the airways) but not visualized by imaging or bronchoscopy.
T0	No evidence of primary tumor.
Tis	Carcinoma in situ. Squamous cell carcinoma in situ (SCIS). Adenocarcinoma in situ (AIS): adenocarcinoma with pure lepidic pattern (on the alveolar lining), ≤ (not more than) 3 cm in greatest dimension.
T1	Tumor ≤ (not more than) 3 cm in greatest dimension, surrounded by lung or visceral pleura (membrane surrounding the lung), without bronchoscopic evidence of invasion more proximal than the lobar bronchus (i.e., not in the main bronchus).
T1mi	Minimally invasive adenocarcinoma: adenocarcinoma (≤ (not more than) 3 cm in greatest dimension) with a predominantly lepidic pattern (on the alveolar lining) and ≤ (not more than) 5 mm invasion in greatest dimension.
T1a	Tumor ≤ (not more than) 1 cm in greatest dimension.
T1b	Tumor > (more than) 1 cm but ≤ (not more than) 2 cm in greatest dimension.
T1c	Tumor > (more than) 2 cm but ≤ (not more than) 3 cm in greatest dimension.
T2	Tumor > (more than) 3 cm but ≤ (not more than) 5 cm or having any of the following features: • Involves the main bronchus regardless of distance to the carina (ridge at the base of the trachea), but without involvement of the carina. • Invades visceral pleura (membrane surrounding the lung). • Associated with atelectasis (collapse of part of the lung) or obstructive pneumonitis (inflammation of lung tissues) that extends to the hilar region, involving part or all of the lung.
T2a	Tumor > (more than) 3 cm but ≤ (not more than) 4 cm in greatest dimension.
T2b	Tumor > (more than) 4 cm but ≤ (not more than) 5 cm in greatest dimension.
T3	Tumor > (more than) 5 cm but ≤ (not more than) 7 cm in greatest dimension or directly invading any of the following: parietal pleura (outer lung membrane), chest wall (including superior sulcus tumors), phrenic nerve (nerve that helps control breathing), parietal pericardium; or separate tumor nodule(s) in the same lobe as the primary.
T4	Tumor > (more than) 7 cm or tumor of any size invading one or more of the following: diaphragm, mediastinum (area between the lungs), heart, great vessels, trachea (windpipe), recurrent laryngeal nerve (nerve that helps speech), esophagus, vertebral body, or carina (at base of the trachea); separate tumor nodule(s) in an ipsilateral lobe (lobe that is on the same side of the body) different from that of the primary.
Node (N)	
NX	Regional lymph nodes cannot be assessed.
N0	No regional lymph node metastasis.
N1	Metastasis in ipsilateral (on the same side) peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension.
N2	Metastasis in ipsilateral (on the same side) mediastinal and/or subcarinal lymph node(s).
N3	Metastasis in contralateral (on the opposite side) mediastinal, contralateral hilar, ipsilateral (on the same side) or contralateral scalene, or supraclavicular lymph node(s) (located above the collarbone).
Metastasis (M)	
M0	No distant metastasis.
M1	Distant metastasis.
M1a	Separate tumor nodule(s) in a contralateral (on the opposite side) lobe; tumor with pleural or pericardial nodules or malignant pleural or pericardial effusion.
M1b	Single extrathoracic (outside of the lung) metastasis in a single organ (including involvement of a single nonregional node).
M1c	Multiple extrathoracic (outside of the lung) metastases in a single organ or in multiple organs.

TABLE 2
STAGES OF LUNG CANCER

Stage	TNM Classification
Occult carcinoma	TX, N0, M0
0	Tis, N0, M0
IA1	T1mi, N0, M0 // T1a, N0, M0
IA2	T1b, N0, M0
IA3	T1c, N0, M0
IB	T2a, N0, M0
IIA	T2b, N0, M0
IIIB	T1a or T1b or T1c, N1, M0 T2a or T2b, N1, M0 T3, N0, M0
IIIA	T1a or T1b or T1c, N2, M0 T2a or T2b, N2, M0 T3, N1, M0 // T4, N0 or N1, M0
IIIB	T1a or T1b or T1c, N3, M0 T2a or T2b, N3, M0 T3, N2, M0 // T4, N2, M0
IIIC	T3, N3, M0 // T4, N3, M0
IV	Any T, Any N, M1
IVA	Any T, Any N, M1a or M1b
IVB	Any T, Any N, M1c

ADDITIONAL RESOURCES

- ▶ **Society for Immunotherapy of Cancer:** www.sitcancer.org
- ▶ **American Cancer Society:** www.cancer.org
Lung Carcinoid Tumor Stages
- ▶ **American Lung Association:** www.lung.org
Lung Cancer Staging
- ▶ **American Society of Clinical Oncology:** www.cancer.net
Lung Cancer Non-Small Cell: Stages
Lung Cancer Small Cell: Stages
Reading a Pathology Report
- ▶ **GO₂ Foundation for Lung Cancer:** go2foundation.org
- ▶ **LUNgevity Foundation:** www.lungevity.org
Staging
- ▶ **National Cancer Institute:** www.cancer.gov
Non-Small Cell Lung Cancer Treatment
Small Cell Lung Cancer Treatment

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Immunotherapy unlocks the power of the immune system

The ability to harness the potential of the immune system to fight cancer is giving new hope to people with lung cancer, improving patient outcomes and offering an enhanced quality of life. Sometimes referred to as biologic therapy or biotherapy, immunotherapy trains the immune system to respond to and attack cancer. This type of treatment is very different from conventional options, such as surgery, chemotherapy and radiation therapy, because it has the potential for a more lasting response that can extend beyond the end of treatment.

Treating lung cancer with immunotherapy is considered a significant leap forward, especially because many cases are diagnosed at an advanced stage. The first immunotherapy approval for a type of lung cancer occurred in 2015. Now, immunotherapy options are available for advanced and metastatic non-small cell lung cancer (NSCLC) and extensive-stage small cell lung cancer (SCLC).

Used alone or in combination with other treatments such as chemotherapy, targeted therapy and radiation therapy, immunotherapy may be used as first- or second-line therapy. A first-line therapy is the first treatment given for a disease. When used by itself, first-line therapy is the one accepted as the best treatment. Second-line therapy is given when the first-line therapy doesn't work or stops working.

INTRODUCING IMMUNE CHECKPOINT INHIBITORS

Immune checkpoint inhibitors are the type of immunotherapy currently approved to treat lung cancer. They target the proteins PD-1 (programmed cell death protein 1) and PD-L1 (programmed cell death-ligand 1) found on cells and boost the immune system's cancer-fighting response. Other types of immunotherapy approved for other cancers are being studied as possible lung cancer treatments (see *Clinical Trials*, page 8).

A primary function of the immune system is to determine which cells or substances are self or non-self (see *Overview*, page 1). The immune system only makes enough white blood cells to fight non-self cells, also called antigens, present in the body. When the immune system is alerted to the threat of antigens, such as bacteria or viruses, it ramps up production of T-cells that attack and destroy the antigens. After an attack, the immune system must slow down so that the T-cells don't begin attacking healthy cells. It does this through the use of checkpoints.

Checkpoints keep the immune system "in check." This process happens between proteins and receptors at the cellular level. To understand how this occurs, it's important to know that the surface of each cell is not completely round and smooth. Cells are covered with receptors and proteins, which work like puzzle pieces. Proteins have "tabs" that stick out, and receptors have "spaces" that curve inward. When the puzzle pieces fit together (known as binding), chemical signals and information are exchanged in a biochemical reaction; this process allows cells to communicate with each other. When the correct proteins and receptors connect, a series of signals is sent to the immune system to slow down once an immune response is finished.

The immune system also can attack and kill cancer cells. In order for a cancer to grow, it must turn off the immune response. This occurs when cancer cells express immune checkpoint proteins. Three checkpoint receptors that slow down the immune system

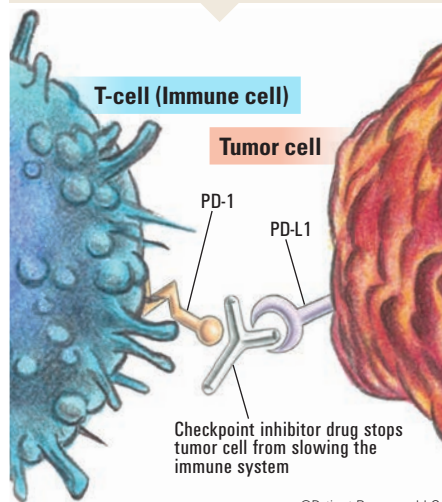
have been identified, and two are present in lung cancer. When they combine, the reaction signals it's time to slow down.

- PD-1 is a receptor involved with telling T-cells to die and to reduce the death of regulatory T-cells, which slow down the immune system after an immune response and inhibit T-cells that attack normal, healthy cells that weren't eliminated before leaving the thymus. PD-1 can tell the immune system to slow down only if it connects with PD-L1.
- PD-L1 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.

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. Checkpoint inhibitor drugs prevent these connections by targeting and blocking PD-1 or PD-L1, and the immune cells continue fighting the cancer. If either checkpoint is blocked, the immune system will not slow down and T-cells can continue to attack antigens and cancer cells.

IMMUNE CHECKPOINT INHIBITORS

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



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QUESTIONS TO ASK YOUR MEDICAL TEAM

- ▶ Would you recommend immunotherapy for my type of lung cancer?
- ▶ Why is immunotherapy the best treatment for me?
- ▶ Have you had success treating patients with immunotherapy?
- ▶ How will we determine what the goals of treatment will be?
- ▶ How will we know if it is working?
- ▶ Will I be able to receive other types of treatment if immunotherapy fails at some point?
- ▶ Will I still be able to work, travel and do regular activities during treatment?
- ▶ Should I consider a clinical trial?
- ▶ What are the side effects of the recommended treatment, and how are these managed?

FDA-APPROVED IMMUNOTHERAPIES FOR LUNG CANCER

Immune checkpoint inhibitors

- ▶ atezolizumab (Tecentriq)
- ▶ durvalumab (Imfinzi)
- ▶ nivolumab (Opdivo)
- ▶ pembrolizumab (Keytruda)

As of 7/11/19

However, cancer is smart and tries to hide from the immune system. One of the ways a cancer cell can outsmart the immune system is by producing PD-L1 on its own surface and using it as camouflage so that T-cells will see it as a normal cell. 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. When an immune checkpoint inhibitor is given, it's as if the immune system develops X-ray vision and sees through the cancer cell's camouflage. This keeps the immune response from slowing down and also helps the immune system recognize cancer cells as foreign cells.

Although cancer cells can be clever, the immune system has a long memory when it comes to battling dangerous cells. When your immune system encounters a virus, such as chickenpox, the memory T-cells check to see if that virus has any characteristics of cells they have attacked in the past. If so, your memory T-cells offer you immunity from that virus, and most of the time you don't get chickenpox again. The memory T-cells alert the rest of the immune system, telling it to make more immune cells to attack the virus and keep you from getting the disease again. Memory T-cells stay alive and store this information for a long time, remaining effective long after treatment ends. Investigators believe that effective immunotherapy can result in cancer-specific memory cells that provide long-term protection against cancer. ■

ADDITIONAL RESOURCES

- ▶ **Society for Immunotherapy of Cancer:**
www.sitcancer.org
- ▶ **American Society of Clinical Oncology:**
www.cancer.net
Lung Cancer Treatment
- ▶ **GO₂ Foundation for Lung Cancer:**
go2foundation.org
- ▶ **LUNGEvity Foundation:**
www.lungevity.org
Immunotherapy
- ▶ **National Cancer Institute:**
www.cancer.gov
Immunotherapy for Cancer Lung Cancer

MOLECULAR TESTING

BIOMARKERS IN IMMUNOTHERAPY FOR LUNG CANCER

→ **Cancer is caused by mutations** in your genes, which are pieces of DNA. Research has found several specific genetic mutations that lead to lung cancer. Doctors can test for these mutations as part of the diagnostic process by looking for biomarkers, which are the molecules produced by the cancer cells or other cells in the body in response to cancer. Testing for biomarkers is known as molecular testing. It may include testing for specific genes, proteins or molecules of the tumor and can be measured in the blood, plasma, urine, cerebrospinal fluid or other body fluids or tissues. Biomarkers are also known as tumor markers, molecular markers, biological markers or serum markers.

Most molecular testing for lung cancer looks for epidermal growth factor receptor (*EGFR*) mutations and anaplastic lymphoma kinase (*ALK*) fusions, for which several targeted therapies have been developed. Researchers have identified other biomarkers that are involved in some types of lung cancers. National guidelines currently recommend the following genes be tested if lung cancer is suspected: *ALK*, *BRAF*, *EGFR*, *MET*, *ERBB2 (HER2)*, *NTRK*, *RET* and *ROS1*.

Next-generation sequencing (NGS) is used to test these genes. This technique is capable of processing multiple DNA sequences simultaneously with more speed and accuracy. NGS can be done on both tumor tissue and blood and, at present, can detect abnormalities associated with specific therapies.

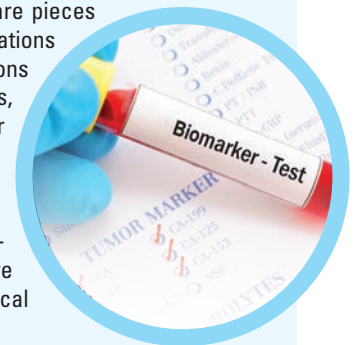
To find out if you are a candidate for immunotherapy, your doctor may also look for the following factors along with molecular testing:

- **PD-L1** expression may be tested to determine if the tumor cells or immune cells in the tumor's microenvironment contain a higher level, which may mean you could be a good candidate for immune checkpoint inhibitors.
- **Tumor mutational burden (TMB)** is an assessment of the number of genetic mutations in a tumor. It can also help doctors determine if you will respond to immunotherapy. It is believed that the higher the TMB level is, the more likely you will be to respond.
- **Microsatellite instability-high (MSI-H)** or deficient mismatch repair (dMMR) may be tested to determine if the cancer is caused by genes that have problems repairing themselves. MSI-H describes cancer cells that have a greater than normal number of genetic markers called microsatellites, which are short, repeated sequences of DNA. Every time a cell reproduces itself, it makes a copy of its genes and DNA. During the process, errors in duplication can be made, much like a misspelled word. The body normally corrects the error, but sometimes it isn't caught and fixed. It then becomes a mutation that is reproduced in later versions of the cell. Cancer cells that have large numbers of microsatellites may have defects in the ability to correct mistakes that occur when DNA is copied. Cancers with MSI-H features appear to respond better to immunotherapy.

Research has shown that people with a high level of PD-L1 expression also typically respond better to immunotherapy. In addition, the level of expression will help your doctor determine whether to give immunotherapy alone or in combination with chemotherapy. People who have tumors with 50 percent or more PD-L1 expression are usually considered good candidates for immunotherapy as a single treatment. If the amount is less than 50 percent, people may be treated with a combination of one or two types of chemotherapy along with an immunotherapy. However, not everyone with a high PD-L1 expression should be given immunotherapy, especially someone with an active *EGFR* mutation.

Not all people who receive immunotherapy respond. In some cases, people with high expressions of PD-L1 do not respond to immunotherapy. Some people with a low PD-L1 expression do respond but less often. Researchers are not sure why this happens and more research is needed so immunotherapy is not given to someone who may not respond to it.

Inform your doctor if you have an autoimmune disorder, such as Crohn's disease, ulcerative colitis or lupus. An autoimmune condition means you have an overactive immune system, and introducing immunotherapy may increase potential safety risks and life-threatening toxicities. Also let your doctor know if you've received immunotherapy before because previous treatments may affect your doctor's treatment decisions. ■



The role of clinical trials for people with lung cancer

Today's strategies available for treating lung cancer are the result of the medical community's commitment to find new and better ways to prevent, diagnose and treat cancer. This is accomplished through structured research studies known as clinical trials.

Some clinical trials investigate whether a new type of treatment, such as a drug, surgery or radiation therapy or a combination of them, is better than the current standard of care. Researchers are also evaluating how various substances in tumors affect the body's immune responses, and are creating ways to reduce treatment side effects. Lung cancer

clinical trials are exploring novel diagnostic tools, additional targeted therapies, improved surgical techniques, more effective radiation therapy and combinations of different approaches for early- and late-stage cancers. Such crucial research fuels advances that continue to transform cancer care, giving more people the chance to live longer and have bet-

ter quality lives after a cancer diagnosis.

Once thought of as a last resort, clinical trials are increasingly becoming the first treatment option for people diagnosed with cancer. Ask your doctor if you should consider a clinical trial. You can also search for them online. However, that can be complicated because thousands of trials are in progress across the country.

The mock search site below explains how to navigate the process. Before you begin, have your exact diagnosis, pathology report and details of previous treatments handy to determine if you qualify. ■

Searching for a clinical trial

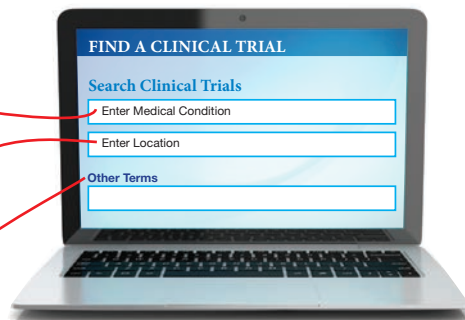
➔ Be an active participant in your own care by looking online at available trials. These step-by-step instructions will help guide you. Once you feel comfortable with the search process, use the list of clinical trial resources below to look for a trial that may apply to you.

STEP 1 FILL IN YOUR INFORMATION

YOUR DIAGNOSIS: For example, enter "lung cancer." To create more options, you can also search for "non-small cell lung cancer" or "NSCLC" and compare results.

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

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



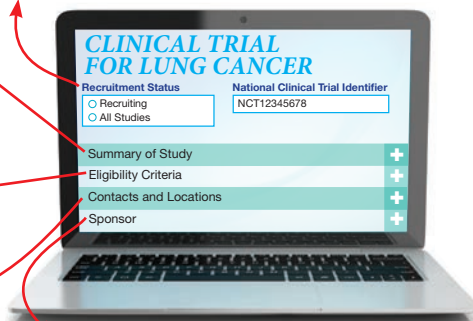
STEP 2 READ YOUR SEARCH RESULTS

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

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

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

CONTACTS AND LOCATIONS: This may contain contact information for the clinical trial investigators, staff or sponsors who may be able to provide more details about the study. Trial locations may be included.



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

What a clinical trial can do for you...

In some situations, a trial may offer the best option among treatments. Additionally, you may benefit from the following:

- ▶ Access to leading-edge treatments that aren't yet available for your type or stage of disease.
- ▶ An alternative strategy if your cancer has become resistant to your current treatment.
- ▶ Another option if your type of cancer is rare and doesn't have as many standard treatments.
- ▶ A higher level of care because you will be closely monitored by your regular oncologist and the clinical trial medical team. This extra attention may help identify and then treat side effects or other problems earlier.
- ▶ The role of being an active partner in your care. It is always your decision to participate. And if the trial doesn't meet your expectations at any time or for any reason, you may leave the trial and return to standard-of-care treatment. A clinical trial will not jeopardize your care.

And what you can do for a clinical trial...

- ▶ Your involvement is an opportunity to help advance cancer treatments. Not all participants have the same experience, even if the treatment is the same, and all the information gathered from a trial is valuable.
- ▶ Many survivors look for opportunities to give back. You may feel a sense of accomplishment at being able to contribute to the future of cancer care.

CLINICAL TRIAL RESOURCES: ACCESS: cantria.com/access / AccrualNet: accrualnet.cancer.gov

ACT (About Clinical Trials): www.learnaboutclinicaltrials.org / Center for Information & Study on Clinical Research Participation: www.searchclinicaltrials.org

CenterWatch: www.centerwatch.com / ClinicalTrials.gov: www.clinicaltrials.gov / Lazarex Cancer Foundation: www.lazarex.org

LIVESTRONG Foundation: www.livestrong.org / LUNGevity Clinical Trial Search: clinicaltrials.lungevity.org / National Cancer Institute: www.cancer.gov/clinicaltrials

National Cancer Institute (NCI) Contact Center (cancer information service): 800-422-6237 / National Institutes of Health (NIH) : 800-411-1222

Discover how case management can work for you

A *valued, and often untapped, resource is case management*, usually a free program designed to help manage the practical issues and problems associated with a cancer diagnosis and treatment. Your case manager is your personal advocate, acting on your behalf by collaborating with medical professionals and non-medical personnel to help overcome various financial, logistical and other common barriers to care.

Your case manager, who may be a social worker, trained financial counselor, nurse or some combination of these areas of expertise, works in various ways to ensure you receive quality services, from screening and assessment to care coordination and discharge planning. Dealing with a serious illness involves much coordination, such as filing insurance claims, paying medical bills and arranging for transportation. It is difficult to focus on these items when you are more concerned with understanding your diagnosis and making treatment decisions. Although these issues may feel secondary, they often become critical. Your case manager helps navigate and address these responsibilities to reduce or eliminate your stress and anxiety so you can focus on healing.

Case management comes in many different forms. It is sometimes very specific and short term, confined to a period of time or specific issue, or it may be a long-term engagement based on a particular patient's needs.

Alan Balch, PhD, Chief Executive Officer at Patient Advocate Foundation (PAF), understands the value of helping patients find solutions to the problems they face during treatment.

“Our case management program is a process of directly assisting patients and their caregivers in finding and securing appropriate resources or dealing with specific barriers. In our experience, the areas in which patients

need help most are transportation, paperwork and finding financial assistance to cover various costs.”

Fran Castellow, MEd, PAF, believes no patient should have to struggle with financial obstacles alone. “Our expert case managers work alongside the patient or caregiver to identify solutions to problems surrounding insurance, medical debt and many other challenges, as well as helping them better afford their out-of-pocket costs.”

Your case manager can help you carefully review your insurance policy, including the items covered by Medicare Parts A, B, C and D, so you know the rules and procedures to follow and what is covered. You are encouraged not to dismiss potential treatment options until you've looked into the financial resources that are available, even if you are uninsured or underinsured.

Case management sometimes offers indispensable services surrounding end-of-life needs. If you choose to be at home at this time, a case manager may be available to arrange for door-to-door transportation from the medical facility to your home and ensure a hospice company, necessary equipment and a nurse are on site before you arrive. The goal is to help you feel secure and comfortable, surrounded by people who care, in the last moments of life. If your health care team doesn't offer case management services, ask for a referral. ■

Myths vs. Facts

→ *If immunotherapy is recommended as a treatment option for your lung cancer, you'll want to know the facts about this leading-edge cancer therapy.*

MYTH: Immunotherapy is a risky treatment because it's so new.

FACT: Immunotherapy is not new. The first immunotherapy to treat cancer was approved more than 30 years ago by the U.S. Food and Drug Administration (FDA). Using the body's immune system to fight disease was first considered in the 1890s.

MYTH: Doctors reserve newer treatments for younger cancer patients.

FACT: Age alone is not a determining factor when considering immunotherapy. A result of a recent research study evaluating the effectiveness of an immune checkpoint inhibitor on more than 530 cancer patients indicated that the responses in people older than 62 were as good as or considerably better than in younger patients; however, side effects may be more severe in the elderly.

MYTH: Doctors recommend immunotherapy only as a last resort.

FACT: Today, immunotherapy is often the first choice of treatment. In 2008, only four immunotherapies were approved to treat six types of cancer. By mid-2019, several FDA-approved immunotherapy agents were available – alone or in combination with other therapies – for a variety of cancer types and any solid tumor with a specific biomarker. Some immunotherapies are now first-line treatments being used before other types of cancer therapy.

MYTH: Immunotherapy is way too expensive for the average person.

FACT: All cancer therapies have associated costs and some are greater than others, so it's essential to know this information before you start treatment. However, your health insurance, Medicare or Medicaid (in some states) may cover or partially cover the costs. Financial resources may also be available through patient assistance programs from pharmaceutical companies, your treatment facility or cancer advocacy groups.



Need help with additional resources?

→ Much of the information available to help you is found online, but not everyone has a computer. If you don't have access to one or if you need assistance searching for information, ask your case manager, nurse navigator, family members or friends to help you. You're not in this alone. A variety of resources are available, from helping you learn more about your specific diagnosis and offering valuable suggestions for caregivers to connecting you with support programs so you can talk with someone who has had a similar experience. To ensure everyone has access to trusted resources, the following organizations also offer phone numbers. Most are staffed weekdays during standard business hours.

American Cancer Society, Cancer Helpline: 800-227-2345 / **American Lung Association:** 800-586-4872
GO₂ Foundation for Lung Cancer, Lung Cancer Helpline: 800-298-2436
LUNGevity, Lung Cancer HELPLINE: 844-360-5864 / **National Cancer Institute:** 800-422-6237
Patient Empowerment Network, Cancer Support Helpline: 888-793-9335

ADDITIONAL RESOURCES

- ▶ **Society for Immunotherapy of Cancer:**
www.sitcancer.org
- ▶ **American Society of Clinical Oncology:**
www.cancer.net
Spotlight On Cancer: Case Managers
- ▶ **LungCancer.org:**
www.lungcancer.org
The Value of Oncology Social Workers
- ▶ **National Cancer Institute:**
www.cancer.gov
Managing Costs and Medical Information
- ▶ **Survivorship A to Z:**
www.survivorshipatoz.org
Social Workers: An Overview

Early care strategies can improve your quality of life

The day-to-day challenges of living with lung cancer are often physically exhausting and emotionally overwhelming. That's why it's important to take advantage of the services referred to as supportive care. They're designed to improve the overall well-being of you and your loved ones from diagnosis through survivorship. Research has shown receiving supportive care as early as possible improves quality of life and may make it easier to stick with and complete scheduled therapies.

A primary focus of supportive care is to help manage treatment-related side effects and cancer symptoms. It also addresses emotional, social, practical and spiritual concerns.

Like most cancer treatments, immunotherapy can have side effects. Some can be prevented and others can be minimized. Ask your health care team for a list of symptoms specific to your treatments and for strategies to help manage them. Learn what to watch for, and how to respond. Find out when to contact your doctor's office, go to an emergency room or call 911. The key is reporting symptoms as soon as they occur – even if they seem trivial – so your doctor can treat them early and prevent serious complications. Let any health care provider you see know if you are receiving or have received immunotherapy.

IMMUNE-RELATED ADVERSE EVENTS

Severe side effects from immunotherapy are

not common but can occur. Called immune-related adverse events (irAEs), they can develop rapidly, becoming severe and even life-threatening without swift medical attention.

These irAEs can result if the treatment overstimulates the immune system. This may cause inflammation, redness or swelling, which can be painful. You may not be able to physically feel these symptoms at first, so it's important to schedule and keep all medical appointments as irAEs may be diagnosed in routine laboratory tests. Be sure to contact your health care team if symptoms occur between appointments. Remain alert to the possibility of irAEs for six months to a year after treatment ends, and report symptoms immediately to your doctor.

Following are body systems that may potentially be affected by certain immunotherapy drugs, along with the irAE and its symptoms.

- Cardiovascular (myocarditis): chest pain,

shortness of breath, leg swelling, rapid heartbeat, changes in EKG reading, impaired heart pumping function

- Endocrine (endocrinopathies): hyperthyroidism, hypothyroidism, diabetes, extreme fatigue, persistent or unusual headaches, visual changes, alteration in mood, changes in menstrual cycle
- Gastrointestinal (colitis): diarrhea with or without bleeding, abdominal pain, bowel perforation
- Liver (hepatitis): yellow skin or eyes (jaundice), nausea, abdominal pain, fatigue, fever
- Nervous system (neuropathies): numbness, tingling, pain, a burning sensation or loss of feeling in the hands or feet, sensory overload, sensory deprivation
- Neurologic (encephalitis): confusion, hallucinations, seizures, changes in mood or behavior, neck stiffness, extreme sensitivity to light
- Pulmonary/lung (pneumonitis): chest pain, shortness of breath, unexplained cough
- Renal/kidneys (nephritis): decreased urine output, blood in urine, swollen ankles, loss of appetite
- Skin (dermatitis): rash, skin changes, itching, blisters, painful sores

Take care of your emotional well-being

You may be feeling intense and unfamiliar emotions as a result of your diagnosis and the uncertainties and challenges you and your loved ones are facing. Various supportive care resources and services are designed to help you and your loved ones cope, including counselors and therapists with expertise in working with people living with cancer. Don't hesitate to ask your health care team for a referral. You can also try these helpful strategies: get regular physical exercise, keep a journal, enjoy nature's beauty, join a local or online cancer support group or participate in phone-based peer-to-peer counseling with other lung cancer survivors.

Following are some emotions you may experience and suggestions for managing them.

- **Anger** is common before, during and after cancer treatment. Allow yourself to express your feelings. To avoid releasing bottled-up anger in unhealthy ways, find safe alternatives. Explain your feelings to a trusted friend or participate in intense physical activity.
- **Anxiety** and worry may interfere with your ability to cope with treatment and function day to day. Explore relaxation techniques, such as meditation, muscle relaxation, yoga or guided imagery. Peer-to-peer cancer support volunteers are good listeners who can offer insight into what to expect — either by phone or online.
- **Depression** is most likely to occur when people with cancer have pain or other unrelieved symptoms. It's extremely important to talk with your doctor about feeling hopeless, helpless, "numb" or worthless. If these feelings last more than a few days or if you have thoughts of death or of attempting suicide, seek medical attention immediately.
- **Emotional overload** is common because so much of what you're experiencing is unfamiliar and beyond your control. Yoga, meditation or guided imagery may help calm your mind. Take charge of things you can control, delegate tasks to others who can lend a hand, and ask loved ones to handle routine decision-making.
- **Fear** occurs because of all the sudden uncertainties, including financial worries, possible changes in your appearance or sexuality and how you'll respond to treatment. Knowledge helps reduce fear. Learn as much as you can about all aspects of your treatment plan so you'll have an idea of what to expect. Share your fears with a friend you trust.
- **Grief** is natural as you may mourn the unexpected changes in your life and the loss of a future without the cloud of recurrence. Your diagnosis may also trigger past grief if you've lost a loved one to cancer. Give yourself permission to grieve, feeling a full range of emotions. Talking with a grief counselor may be helpful.
- **Guilt** may occur if you blame yourself for getting cancer because of actions you did or didn't take, if you feel you're a burden to loved ones or if your prognosis is better than that of others living with lung cancer. Talk with a therapist about these feelings.
- **Loneliness** may occur at various times throughout treatment, especially if you feel no one understands what you're going through or if friends or family members have stopped calling or visiting because they don't know what to say. Consider reaching out for a conversation unrelated to cancer. Be open to meeting other survivors.



MANAGING SIDE EFFECTS

Everyone responds differently to immunotherapy, including combinations of immunotherapy with chemotherapy or other treatments. Following are common side effects and suggestions to help manage them.

Alopecia (hair loss) can affect all parts of the body. Caps, hats, turbans, scarves and wigs are available as head coverings. If you go natural, use a sunscreen with a sun protection factor (SPF) of at least 30. Contact your health insurance provider to see if the cost of a wig is covered with a doctor's prescription for a "cranial prosthesis due to alopecia caused by cancer treatment." Ebeauty (www.eBeauty.com) offers a free wig exchange program. Your nurse navigator may also have information about resources for free wigs.

Bone loss may occur when lung cancer spreads to the bone, which can then become thin, porous and brittle. Your doctor can monitor your bone mass through bone density scans taken before, during and after treatment and may also prescribe bone-modifying agents to help prevent or delay bone fractures. Maintain a healthy weight. Minimize fall risks such as loose rugs, cluttered walkways and poor lighting.

Cognitive dysfunction, often called chemo brain, occurs when people have trouble with memory, concentration or processing information during or after cancer treatment. Though associated with chemotherapy, it can result from other treatments and can last for months or years. Try carrying a daily planner to help stay on track. Use to-do lists, and focus on doing one thing at a time.

Constipation can be very uncomfortable and can lead to serious medical issues. Eat high-fiber foods, drink plenty of clear fluids throughout the day and establish regular bowel habits. It's important to discuss this condition with your doctor, and always check first before taking over-the-counter laxatives.

Coughing is a common symptom of lung cancer and occurs with some types of immunotherapy. A cough may signal pneumonitis (inflammation of the lungs) or a respiratory tract infection. Contact your doctor immediately so the cause of the cough can be determined and managed, especially if the cough is new or changing.

Decreased appetite may occur. To minimize weight loss, try to maintain a nutritious diet during and after treatment, choosing high-calorie, high-protein foods rich in nutrients. If you cannot eat enough to maintain your weight, talk with your doctor.

Diarrhea is uncomfortable when mild. Left untreated, it can quickly become serious. Severe diarrhea can lead to dehydration and electrolyte imbalance. Contact your medical team immediately about severe abdominal cramping, four or more bowel movements than usual per day or episodes that keep you homebound.

Dyspnea is the medical term for difficult or labored breathing or shortness of breath. It can also be a symptom of pneumonitis, a potentially serious irAE. Contact your medical team immediately if you have difficulty breathing so they can determine the cause. If labored breathing comes on suddenly, seek immediate medical attention or call 911.

Fatigue from cancer treatment is more intense and longer-lasting than regular tiredness and can leave you physically and emotionally exhausted. Balance activity with rest, take short naps as needed and save your energy for the activities most important to you. Getting regular exercise, even walking five or 10 minutes daily, is the most effective remedy for treatment-related fatigue.

Infusion-related reactions may occur during or soon after exposure to the drug and may include itching, rash or fever. Serious symptoms are shaking, chills, low blood pressure, dizziness, throat tightness, skin rash or flushing, trouble breathing and irregular heartbeat. Report this immediately. Your doctor may slow the drug's infusion rate or recommend analgesics, antihistamines or corticosteroids.

Injection site reactions can be painful, so discuss solutions with your health care team. Your doctor may modify your treatment.

Muscle and joint pain ranging from mild to severe may affect the whole body or only certain areas. Immunotherapy-related pain typically resolves when treatment ends. If pain persists or worsens, discuss pain management options with your doctor.

Nausea is much easier to prevent than to resolve once it progresses, so ask your doctor about prescribing antiemetic (anti-nausea) medication before you begin treatment. Avoid unpleasant odors. Try eating dry foods such as cereal, crackers or plain toast first thing in the morning. Getting fresh air at the onset of nausea may help.

Pain caused by a tumor pressing on organs, tissues or joints, or by cancer that has metastasized to bone, may occur. Contact your medical team right away to discuss ways to reduce and manage the pain.

Skin reactions may include severe itching and bumpy or itchy red rashes. Be alert to changes in skin color, inflammation, blistering, hives, dryness, cracked fingertips, sun sensitivity, flushing or redness. Moisturize skin twice a day with a thick cream. Avoid detergents, body soap or moisturizers containing alcohol, perfume or dyes. Your doctor may recommend a corticosteroid or numbing medication or prescribe an antihistamine, medicated creams or antibiotics. ■

Being smoke-free reduces risk of complications

➔ **If you're a tobacco user diagnosed with lung cancer**, you may believe there's no reason to quit now. This is not true.

The most important reason to stop smoking if you're undergoing treatment is that your cancer therapy will be more effective. A common and potentially serious side effect of immune checkpoint inhibitors is pneumonitis (inflammation of the lungs), and smoking can further complicate this condition. Additional benefits of quitting follow:

- Decreased heart rate and lower blood pressure
- Less risk of infection
- Faster healing from surgery and a potentially shorter hospital stay
- Less severe side effects from chemotherapy
- Less chance of developing secondary cancers

Quitting is difficult, but you don't have to do it alone. Ask your health care team about local resources and check out these resources that are ready to assist you.



ADDITIONAL RESOURCES

American Cancer Society: www.cancer.org, 800-227-2345 / **BecomeAnEx:** www.becomeanex.org
Freedom from Smoking: www.lung.org/stop-smoking/join-freedom-from-smoking
National Cancer Institute Smoking Quitline: 877-448-7848 / **QuitStart:** teen.smokefree.gov
Smokefree.gov: smokefree.gov, 800-784-8669 / **SmokefreeTXT:** smokefree.gov/smokefreetxt

Support and financial resources available for you

BASIC LIVING EXPENSES

Bringing Hope Home	www.bringinghopehome.org, 484-580-8395
Family Reach Foundation	www.familyreach.org, 973-394-1411
Hugs and Kisses	www.hugsandkissesinc.org, 561-819-9471
Life Beyond Cancer Foundation	www.needhelppayingbills.com, 800-282-5223
Team Continuum	www.teamcontinuum.net, 845-200-7094

CANCER EDUCATION

American Cancer Society	www.cancer.org
American Society of Clinical Oncology	www.cancer.net
CANCER101	www.cancer101.org
CancerCare	www.cancercares.org
CancerQuest	www.cancerquest.org
Centers for Disease Control and Prevention (CDC)	www.cdc.gov
The Gathering Place	www.touchedbycancer.org
Get Palliative Care	www.getpalliativecare.org
Global Resource for Advancing Cancer Education (GRACE)	www.cancergrace.org
The Hope Light Foundation	www.hopelightproject.com
LIVESTRONG Foundation	www.livestrong.org
National Cancer Institute	www.cancer.gov
National Comprehensive Cancer Network (NCCN)	www.nccn.org
National LGBT Cancer Network	cancer-network.org
NCI Contact Center (cancer information service)	800-422-6237
OncoLink	www.oncolink.org
Patient Power	www.patientpower.info
Patient Resource	www.patientresource.com
PearlPoint Nutrition Services	www.pearlpoint.org
Pine Street Foundation	pinestreetfoundation.org
Scott Hamilton Cares Foundation	www.scottcares.org
Triage Cancer	triagecancer.org

CAREGIVERS & SUPPORT

4th Angel Patient & Caregiver Mentoring Program	www.4thangel.org
CanCare	www.cancare.org
CANCER101	www.cancer101.org
Cancer and Careers	www.cancerandcareers.org
CancerCare	www.cancercares.org
Cancer Connection	www.cancer-connection.org
Cancer Hope Network	www.cancerhopenetwork.org
Cancer Information and Counseling Line	800-525-3777
Cancer Really Sucks!	www.cancerreallysucks.org
Cancer Support Community	www.cancersupportcommunity.org
Cancer Support Helpline	888-793-9355
Cancer Survivors Network	csn.cancer.org
Caregiver Action Network	www.caregiveraction.org
CaringBridge	www.caringbridge.org
Center to Advance Palliative Care	www.capc.org
Chemo Angel	chemoangels.com
The Children's Treehouse Foundation	www.childrenstreehousefdn.org
Cleaning For A Reason	www.cleaningforareason.org
Cooking with Cancer	www.cookingwithcancer.org
Cuddle My Kids	www.cuddlemykids.org
Family Caregiver Alliance	www.caregiver.org
Fighting Chance	www.fightingchance.org
Friend for Life Cancer Support Network	www.friend4life.org, 866-374-3634
The Gathering Place	www.touchedbycancer.org
Guide Posts of Strength, Inc.	www.cancergps.org
The Hope Light Foundation	www.hopelightproject.com
Imerman Angels	www.imermanangels.org
Lacuna Loft	www.lacunaloft.org
The LGBT Cancer Project — Out With Cancer	www.lgbtcancer.org
LIVESTRONG Foundation	www.livestrong.org
LivingWell Cancer Resource Center	www.livingwellcrc.org
Lotsa Helping Hands	www.lotsahelpinghands.com
LUNGevity Caregiver Resource Center	www.lungevity.org/caregiver
The Lydia Project	thelydiaproject.org
MyLifeLine	www.mylifeline.org
Patient Empowerment Network	www.powerfulpatients.org
Patient Power	www.patientpower.info

SHARE Caregiver Circle	www.sharecancersupport.org/caregivers-support
Stronghold Ministry	www.mystronghold.org
Support Groups	www.supportgroups.com
Triage Cancer	www.triagecancer.org
Vital Options International	www.vitaloptions.org
Well Spouse Association	www.wellspouse.org
weSPARK Cancer Support Center	www.wespark.org

CLINICAL TRIALS

ACCESS	cantrria.com/access
AccrualNet	accrualnet.cancer.gov
ACT (About Clinical Trials)	www.learnaboutclinicaltrials.org
Center for Information & Study on Clinical Research Participation	www.searchclinicaltrials.org
CenterWatch	www.centerwatch.com
ClinicalTrials.gov	www.clinicaltrials.gov
Lazarex Cancer Foundation	www.lazarex.org
LIVESTRONG Foundation	www.livestrong.org
LUNGevity Clinical Trial Search	clinicaltrials.lungevity.org
National Cancer Institute	www.cancer.gov/clinicaltrials
NCI Contact Center (cancer information service)	800-422-6237

FINANCIAL ASSISTANCE

American Cancer Society (Hope Lodge)	www.cancer.org/treatment/supportprogramsservices/hopelodge
BenefitsCheckUp	www.benefitscheckup.org
Bringing Hope Home	www.bringinghopehome.org
CancerCare	www.cancercares.org/financial
Cancer Financial Assistance Coalition	www.cancerfac.org
HealthWell Foundation	www.healthwellfoundation.org
Medicare.gov	www.medicare.gov
NeedyMeds	www.needymeds.com
Partnership for Prescription Assistance	www.pparx.org
Patient Access Network Foundation	www.panfoundation.org
Patient Advocate Foundation	www.patientadvocate.org
Patient Services, Inc.	www.patientservicesinc.org
RxAssist	www.rxassist.org
RxHope	www.rxhope.com
Social Security Administration	www.ssa.gov
Social Security Disability Resource Center	www.ssdrc.com
State Health Insurance Assistance Programs	www.shiptacenter.org

GOVERNMENT ASSISTANCE

Benefits.gov	www.benefits.gov, 800-333-4636
Centers for Medicare & Medicaid Services	www.cms.gov
Eligibility.com (Medicare resources)	eligibility.com/medicare/resources
Hill-Burton Program	www.hrsa.gov/get-health-care/affordable/hill-burton, 800-638-0742
Legal Services Corporation	www.lsc.gov, 202-295-1500
Medicare Rights Center	www.medicarerights.org, 800-333-4114
National Council for Aging Care	www.ncoa.org, 571-527-3900
Social Security Administration	www.ssa.gov, 800-772-1213
Social Security Disability Resource Center	www.ssdrc.com
State Health Insurance Assistance Programs	www.shiptacenter.org
U.S. Department of Veterans Affairs	www.va.gov/health

IMMUNOTHERAPY

The Answer to Cancer	www.theanswertocancer.org
Cancer Research Institute	www.cancerresearch.org
Immuno-Oncology	www.immunooncology.com
Society for Immunotherapy of Cancer	www.sitcancer.org

LUNG CANCER

American Lung Association	www.lung.org
Caring Ambassadors Lung Cancer Program	www.lungcancerca.org
GO ₂ Foundation for Lung Cancer	go2foundation.org
International Association for the Study of Lung Cancer	www.iaslc.org
Lung Cancer Action Network	www.lungcan.org
Lung Cancer Foundation of America	www.lcfamerica.org
LungCancer.org	www.lungcancer.org
Lung Cancer Research Foundation	www.lungcancerresearchfoundation.org
LUNGevity Foundation	www.lungevity.org

MEDICAL CARE EXPENSES

CancerCare	www.cancer.org, 800-813-4673
Cancer Warrior, Inc.	www.cancerwarriorinc.org, 323-578-5083
Foundation for Health Coverage Education	www.coverageforall.org
Hair to Stay	www.hairtostay.org, 800-270-1897
Patient Access Network Foundation	www.panfoundation.org, 866-316-7263
Patient Advocate Foundation	www.patientadvocate.org, 800-532-5274
Verna's Purse	www.vernaspurse.org, 888-489-8944

MENTAL HEALTH SERVICES

American Psychosocial Oncology Society Helpline	866-276-7443
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NUTRITION

American Cancer Society	www.cancer.org
CancerCare	www.cancer.org
LIVESTRONG Foundation	www.livestrong.org
OncoLink	www.oncolink.org
PearlPoint Nutrition Services	www.pearlpoint.org
Physicians Committee for Responsible Medicine	www.pcrm.org/health/cancer-resources

PAIN MANAGEMENT

American Chronic Pain Association	theacpa.org
American Society of Anesthesiologists	www.asahq.org
LIVESTRONG Foundation	www.livestrong.org
The Resource Center of the Alliance of State Pain Initiatives	www.trc.wisc.edu
U.S. Pain Foundation	uspainfoundation.org

REIMBURSEMENT & PATIENT ASSISTANCE PROGRAMS

AstraZeneca Access 360	www.myaccess360.com, 844-275-2360
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AstraZeneca Patient Savings Programs For Specialty Products	www.astrazenecaspecialtysavings.com, 844-275-2360
AstraZeneca Prescription Savings Program (AZ&ME)	www.azandmeapp.com, 800-292-6363
Bristol-Myers Squibb Access Support	www.bmsaccesssupport.bmscustomerconnect.com/patient, 800-861-0048
Bristol-Myers Squibb Patient Assistance Foundation	www.bmspaf.org, 800-736-0003
Celgene Patient Support	www.celgenepatientssupport.com, 800-931-8691
Genentech Access Solutions	www.genentech-access.com/patient, 866-422-2377
Genentech BioOncology Co-pay Card	www.copayassistanancenow.com, 855-692-6729
Imfinzi Access 360	www.myaccess360.com/patient/patient-branded-imfinzi/home.html, 844-275-2360
IncyteCARES	www.incytecares.com, 855-452-5234
Keytruda Patient Assistance	www.merckaccessprogram-keytruda.com/hcc/, 855-257-3932
Merck Access Program	www.merckaccessprogram.com/hcc/
Merck Helps	www.merckhelps.com, 800-727-5400
Opdivo with You	www.patientsupport.bmscustomerconnect.com/opdivo-with-you-registration, 855-673-4861
Tecentriq Access Solutions	www.genentech-access.com/patient/brands/tecentriq.html, 866-422-2377

STOPPING TOBACCO USE

American Cancer Society	www.cancer.org
BecomeAnEx	www.becomeanex.org
Freedom from Smoking	www.lung.org/stop-smoking/join-freedom-from-smoking
National Cancer Institute Smoking Quitline	877-448-7848
QuitSTART	teen.smokefree.gov
Smokefree.gov	smokefree.gov
SmokefreeTXT	smokefree.gov/smokefreetxt



Society for Immunotherapy of Cancer

Still have questions about cancer immunotherapy?

Whether you are battling cancer or serving as a dedicated caregiver, being informed can be critical to a successful treatment plan.

The Society for Immunotherapy of Cancer's (SITC) free online patient course, Understanding Cancer Immunotherapy provides resources and basic education about cancer and immunotherapy for patients and caregivers. The course's interactive modules offer easy-to-understand information about immunotherapy as a cancer treatment option by covering the following areas:

- Your treatment options and care providers
- Education on cancer and the immune system
- Types of cancer immunotherapy treatments
- The importance of reporting side effects
- Links to other helpful patient and caregiver resources



To access this self-guided course, please visit sitcancer.org/patient#course

This patient education guide was produced with support from:

