UPDATED MAY 2026


What you need to know about...

immunotherapy






LUNGEVITY
Transforming Lung Cancer

foreword

About LUNGevity

LUNGevity is the nation's premier lung cancer-focused nonprofit, changing outcomes for people with lung cancer through research, education, and support.

About the LUNGevity PATIENT EDUCATION SERIES

LUNGevity has developed a comprehensive series of materials for lung cancer patients and their caregivers, focused on understanding how lung cancer develops, how it can be diagnosed, and treatment options. Whether you have recently been diagnosed with lung cancer or someone you care about has been diagnosed or is concerned about lung cancer risk, we have resources to help you.

The medical experts and lung cancer survivors who provided their valuable expertise and experience in developing these materials all share the belief that well-informed patients make their own best advocates.

In addition to this and other booklets in the LUNGevity patient education series, information and resources can be found on LUNGevity's website at www.LUNGevity.org.

This patient education booklet was produced through a charitable donation from:

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introduction

Immunotherapy is a type of biological therapy that harnesses and increases the natural ability of the patient's immune system to fight cancer. Instead of trying to stop or kill the person's cancer cells directly, as most cancer treatments do, immunotherapy trains the person's own natural immune system to recognize cancer cells and selectively target and kill them.

This booklet will help you:

- Learn how the immune system works
- Understand how immunotherapy may boost the immune system to help fight lung cancer
- Find out what immunotherapy options are available now
- Understand whether immunotherapy might be a good treatment option for you

YOU'LL FIND A GLOSSARY TOWARD THE END OF THIS BOOKLET.
Words included in the glossary appear **blue** the first time that they appear.

01 immune system

What is the immune system?

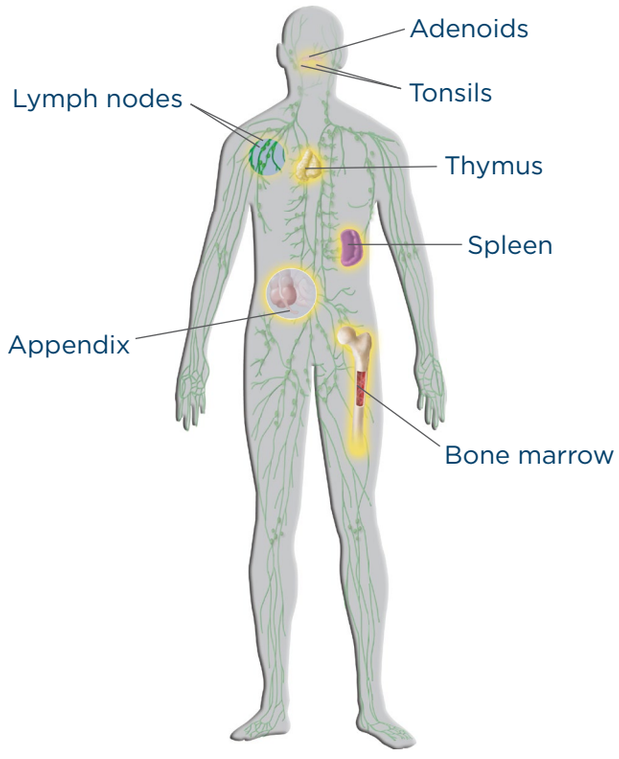
The **immune system** is a network of cells, tissues, and organs that work together to protect the body from **foreign** invaders, such as **bacteria** or **viruses**.

Key players in defending the body include a specific type of **white blood cell (WBC)** called **lymphocytes**. There are three major types of lymphocytes[1]:

- **Natural killer (NK) cells**
- **B cells**
- **T cells**

Lymphocytes grow and develop in the **bone marrow**, **thymus**, and **spleen**. They can also be found in clumps throughout the body, primarily in **lymph nodes**. Lymph nodes in the neck are called **cervical lymph nodes**, and those between the lungs in the middle of the chest are known as **mediastinal** lymph nodes. Clumps of lymphoid tissue are also found in the appendix, tonsils, and **adenoids**. Lymphocytes circulate through the body between the organs and nodes via **lymphatic vessels** and blood vessels. Thus, the immune system works in a coordinated way to monitor the body for germs and other abnormal cells.[2,3]

ORGANS OF THE IMMUNE SYSTEM



How does the immune system work?

A key feature of the immune system is its ability to tell the difference between the body's own normal cells, or "self," and cells and other substances that are foreign to the body, or "non-self." Every cell in the body carries a set of distinct **proteins** on its surface. These identifying surface proteins let the immune system know that they are cells that belong to the body.[4]

Healthy cells display normal proteins on their surface. The immune system has learned to ignore normal proteins. (However, there are people with **autoimmune disorders** in which the immune system inappropriately tries to eliminate healthy cells.) If the surface proteins are abnormal, such as when a virus infects cells or when cells become cancerous, they can be recognized by the immune system. Proteins recognized by the immune system are called **antigens**.[4]

If a foreign substance—such as a bacterium, virus, or **tumor** cell—is recognized, the immune system kicks in to try to deal with it. It is the "non-self" antigens on the surface of these cells that the immune system identifies as abnormal. The immune system is great at recognizing bacteria and virus cells, because they "look" very different from healthy cells. On the other hand, tumor cells started as healthy cells and can look a lot like healthy cells. As a result, the body may have a harder time recognizing tumor cells as foreign.[4]

In other instances, the immune system may recognize a tumor antigen but may be unable to mount a response strong enough to destroy the tumor. As cancers grow, they can evolve ways to escape attack by the immune system. For these reasons, many people with healthy immune systems still develop cancer and cancer still progresses. In many people with cancer, the cancer cells coexist with immune cells capable of killing the cancer, but the cancer cells hold the immune cells back from working the way they should.[3]

What is the role of the immune system in cancer?

The immune system has two responses that work together to detect and destroy cancer cells:

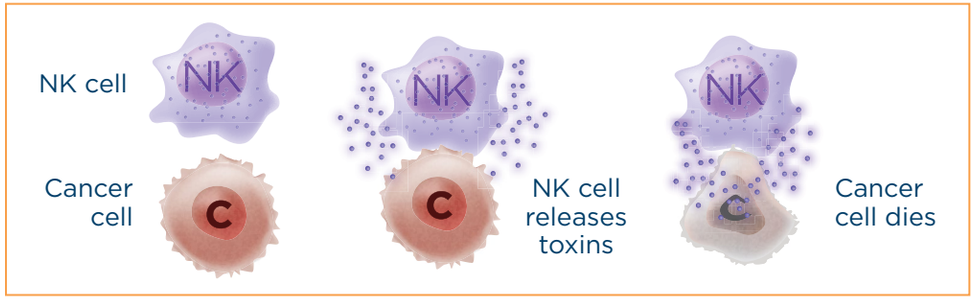
- **Innate immune response**
- **Adaptive immune response**

Innate immune response

Natural killer (NK) cells

The innate immune response is the first line of defense. The innate immune system's normal function is to protect the body from initial invasion by bacteria and viruses, such as when bacteria invade broken skin or viruses land in the throat. The system includes NK cells, a type of lymphocyte that patrols the body and is on constant alert, looking for foreign invaders and abnormal cells. If cells from the innate immune system recognize a cancer cell as abnormal, they can attach to it and immediately release toxic chemicals that kill it. NK cells and other cells of the innate immune system do not need to recognize a specific abnormality on a cell to be able to do their job.[5]

NK CELL RELEASING TOXINS TO CANCER CELL



If bacteria, viruses, or cancer cells evade the innate response, then the adaptive immune response becomes active.

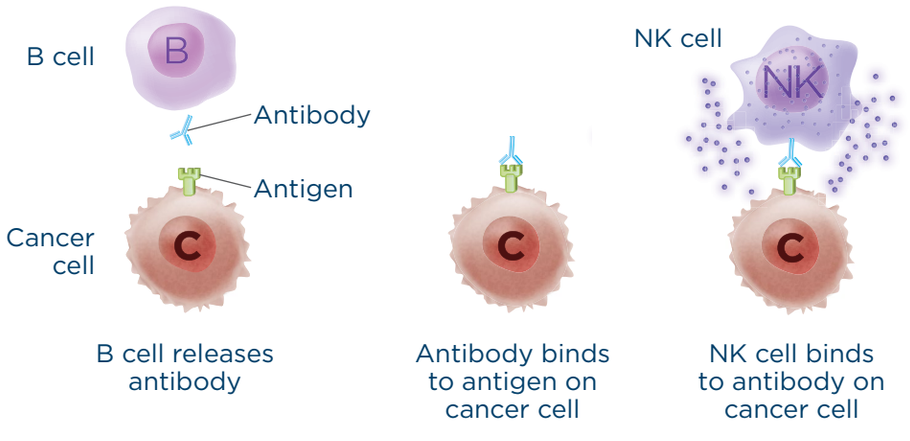
Adaptive immune response

The adaptive immune response recognizes specific abnormalities on cancer cells that make them different from the cells that are naturally found in the body. Though it is more effective than the innate immune response, the adaptive immune response takes longer to become activated. The cells of the adaptive immune response include the other two types of lymphocytes: B cells and T cells.

B cells

B cells are like the body's military intelligence system, seeking out their targets and sending defenses to lock onto them. They react to "non-self" antigens by making proteins called **antibodies**. Antibodies are proteins that can attach to foreign and abnormal cells and let the body know that they are dangerous. Antibodies can kill cancer cells in several ways, including binding NK cells to the cancer. B cells also create "memory": they start to make antibodies quickly when they recognize a past antigen.[6]

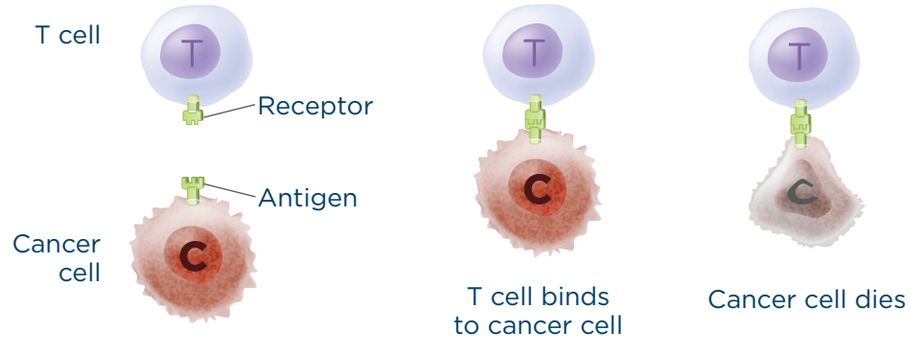
B CELL RELEASING ANTIBODY



T cells

T cells are the major cells the body uses to recognize and destroy abnormal cells. Once a foreign antigen or abnormal cancer protein has been recognized by T cells, the T cells rapidly increase in number. An army of T cells can be formed; these T cells are specifically designed to attack and kill cells that have foreign antigens.[6] The T cells are like soldiers, defending against the invaders. They are responsible for coordinating the entire **immune response** and destroying infected cells and cancer cells.

T CELL ATTACKING CANCER CELL



T cells also develop "memory" after an initial response to an antigen. This memory is meant to ensure that the attack on cancer cells can persist long-term, for months or longer. The memory also allows for future responses against the specific abnormal antigen on cancer cells, if and when the cancer comes back.[6]

How do cancer cells grow despite the innate and adaptive immune responses?

If the immune system recognizes the lung tumor cells and can destroy them, why are lung tumors able to grow?

- Research has shown that tumors enable their own growth by turning off the immune response
- An immune response beyond what is normal or necessary can be toxic, so T cells have many normal methods to tamp themselves down and essentially turn themselves off. This may allow the growth and development of tumor cells despite the presence of T cells with the potential to kill cancer cells

Scientists are working to understand exactly how this happens and how best to turn the T cells back on.[7]

02 immunotherapy

Immunotherapy is a type of **biological therapy.** It aims to enhance the body's immune response and stop lung cancers from escaping the immune system. Biological therapies use substances made from living organisms to treat disease.[8]

What is immunotherapy?

Immunotherapy is a treatment that strengthens the natural ability of the patient's immune system to fight cancer. Instead of targeting the person's cancer cells directly, immunotherapy causes a person's natural immune system to selectively target and kill cancer cells.[9]

Immunotherapies do this in one of two ways:

- By enabling the immune system to mount or maintain a response
- By suppressing factors that prevent the immune response

While there are many different types of immunotherapy, the most progress has been made with immune checkpoint inhibitors. Currently, most U.S. Food and Drug Administration (FDA)-approved immunotherapy drugs for **non-small cell lung cancers (NSCLC)** belong to this group. Several of these are also approved for **small cell lung cancer (SCLC)**.[9]

Another type of immunotherapy, **bispecific T-cell engagers**, is approved for SCLC as well.

Immune checkpoint inhibitors

Many lung cancers coexist with T cells capable of killing the cancer cells. However, the immune system has many normal mechanisms for tamping itself down. The immune system has fail-safe mechanisms that are designed to suppress the immune response at appropriate times to minimize damage to healthy cells. These mechanisms are called immune checkpoint pathways. They are essentially the brakes on the system that can prevent T cells from killing lung cancer cells.

The challenge is that cancers are able to use these immune checkpoint pathways to lessen the immune response at the wrong times.[7]

The **programmed death 1/programmed death ligand 1 (PD-1/PD-L1)** proteins are an example of an immune checkpoint pathway. The PD-1 protein is found on T cells and acts as the brakes that keep the T cells from attacking healthy cells. PD-L1 is a protein on healthy cells, but it can also be found on cancer cells. When the PD-1 on T cells attaches to the PD-L1 on other cells, the T cells know not to attack those other cells. Cancer cells can thus evade detection by T cells, with the result that the T cells' immune response is lessened at a time when it should be active. This allows cancer cells to thrive.[10] **CTLA-4** is another example of a protein on T cells that acts to prevent the immune system from attacking cancer cells.[22]

How do immune checkpoint inhibitors work?

Immune checkpoint inhibitors work by targeting and blocking the fail-safe mechanisms of the immune system. Their goal is to block the immune system from limiting itself, so that the original anti-cancer response works better.[7]

How is biomarker testing used for immune checkpoint inhibitors?

Biomarker testing is the testing of a person's tumor tissue or blood to check for certain **genes,** proteins, or other **molecules** to help determine the optimal treatment plan.[11] Most often, biomarker testing is conducted among those with advanced/**metastatic** NSCLC or **extensive-stage SCLC (ES-SCLC)**, but it can also be conducted among those with earlier-stage lung cancer. To assess the potential value of **immune checkpoint inhibitors** (the drugs that target the pathways that tumor cells use to evade the immune system), biomarker testing primarily determines 1) the level of PD-L1 and 2) the presence of certain **genomic aberrations** (such as in the genes encoding ALK, EGFR, and ROS1) that indicate that an immune checkpoint inhibitor will not be of therapeutic benefit. It may also be used to assess **tumor mutational burden (TMB)** and **microsatellite instability (MSI)**, which are indicators of response to immunotherapy. However, immune checkpoint inhibitors may be prescribed for patients without biomarker testing in certain situations (when prescribed with chemotherapy or for treatment after the cancer progresses). They may also even be prescribed sometimes if the PD-L1 level is low or nonexistent.[12]

For a more comprehensive look at biomarker testing, download the biomarker testing booklet on the LUNGevity website, www.LUNGevity.org.

Note: Biomarker testing should be an ongoing part of the discussion with a patient's healthcare team. Any decision to test for biomarkers should be made together.

What immune checkpoint inhibitors are currently approved?

Below are the current FDA-approved immune checkpoint inhibitors for treating patients with lung cancer. They are all administered via injection. The decision about which treatment to use at any time is determined based on the type and stage of lung cancer, the patient's overall health, the current treatment plan, and other factors.

- Atezolizumab (Tecentriq®)[13]:
  - Approved as **adjuvant treatment** following **resection** and platinum-based chemotherapy for adult patients with **Stage** II to IIIA NSCLC whose tumors have PD-L1 expression on ≥ 1% of tumor cells, as determined by an FDA-approved test
  - Approved for the **first-line treatment** of adult patients with metastatic NSCLC whose tumors have high PD-L1 expression (PD-L1 stained ≥ 50% of tumor cells [TC ≥ 50%] or PD-L1 stained tumor-infiltrating immune cells [IC] covering ≥ 10% of the tumor area [IC ≥ 10%]), as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations
  - Approved in combination with bevacizumab, paclitaxel, and carboplatin for the first-line treatment of adult patients with metastatic non-squamous NSCLC with no EGFR or ALK genomic tumor aberrations
  - Approved in combination with paclitaxel protein-bound and carboplatin for the first-line treatment of adult patients with metastatic non-squamous NSCLC with no EGFR or ALK genomic tumor aberrations
  - Approved for the treatment of adult patients with metastatic NSCLC who have **disease progression** during or following platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for NSCLC harboring these aberrations prior to receiving Tecentriq®
  - Approved in combination with carboplatin and etoposide for the first-line treatment of adult patients with ES-SCLC
  - Approved in combination with lurbinectinib for the **maintenance treatment** of adult patients with ES-SCLC whose disease has not progressed after first-line induction therapy with Tecentriq® or atezolizumab and hyaluronidase-tqis, carboplatin, and etoposide
- Atezolizumab and hyaluronidase-tqis (Tecentriq Hybreza™)[14]:
  - Approved as adjuvant treatment following resection and platinum-based chemotherapy for adult patients with Stage II to IIIA NSCLC whose tumors have PD-L1 expression on ≥ 1% of tumor cells, as determined by an FDA-approved test
  - Approved for the first-line treatment of adult patients with metastatic NSCLC whose tumors have high PD-L1 expression (PD-L1 stained ≥ 50% of tumor cells [TC ≥ 50%] or PD-L1 stained tumor-infiltrating immune cells [IC] covering ≥ 10% of the tumor area [IC ≥ 10%]), as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations
  - Approved in combination with bevacizumab, paclitaxel, and carboplatin for the first-line treatment of adult patients with metastatic non-squamous NSCLC with no EGFR or ALK genomic tumor aberrations
  - Approved in combination with paclitaxel protein-bound and carboplatin for the first-line treatment of adult patients with metastatic non-squamous NSCLC with no EGFR or ALK genomic tumor aberrations
  - Approved for the treatment of adult patients with metastatic NSCLC who have disease progression during or following platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for NSCLC harboring these aberrations prior to receiving Tecentriq Hybreza™
  - Approved in combination with carboplatin and etoposide for the first-line treatment of adult patients with ES-SCLC

- Cemiplimab-rwlc (Libtayo®)[15]:
  - Approved in combination with platinum-based chemotherapy for the first-line treatment of adult patients with NSCLC with no EGFR, ALK, or ROS1 aberrations and that is:
    - **locally advanced** where patients are not candidates for surgical resection of definitive chemoradiation or
    - metastatic
  - Approved as a single agent for the first-line treatment of adult patients with NSCLC in which tumors have high PD-L1 expression (tumor proportion score [TPS] ≥ 50%) as determined by an FDA-approved test, with no EGFR, ALK, or ROS1 aberrations, and that is:
    - locally advanced where patients are not candidates for surgical resection or definitive chemoradiation or
    - metastatic
- Durvalumab (Imfinzi®)[16]:
  - Approved in combination with platinum-containing chemotherapy as **neoadjuvant treatment**, followed by Imfinzi® continued as a single agent as adjuvant treatment after surgery, for the treatment of adult patients with **resectable** (tumors ≥ 4 cm and/or node positive) NSCLC and no known EGFR or ALK rearrangements
  - Approved as a single agent for the treatment of adult patients with **unresectable** Stage III NSCLC whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy
  - Approved in combination with tremelimumab-actl and platinum-based chemotherapy for the treatment of adult patients with metastatic NSCLC with no sensitizing EGFR mutations or ALK genomic tumor aberrations
  - Approved as a single agent for the treatment of adult patients with **limited-stage SCLC** whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy

  - Approved in combination with etoposide and either carboplatin or cisplatin for the first-line treatment of adult patients with ES-SCLC
- Opdivo® (nivolumab)[17]:
  - Approved for adult patients with resectable (tumors ≥ 4 cm or node positive) NSCLC in the neoadjuvant setting, in combination with platinum-doublet chemotherapy
  - Approved for adult patients with resectable (tumors ≥ 4 cm or node positive) NSCLC and no known EGFR mutations or ALK rearrangements, for neoadjuvant treatment, in combination with platinum-doublet chemotherapy, followed by single-agent Opdivo® as adjuvant treatment after surgery
  - Approved for adult patients with metastatic NSCLC expressing PD-L1 (≥ 1%) as determined by an FDA-authorized test, with no EGFR or ALK genomic tumor aberrations for the first-line treatment in combination with ipilimumab
  - Approved for adult patients with metastatic or recurrent NSCLC with no EGFR or ALK genomic tumor aberrations as first-line treatment, in combination with ipilimumab and two cycles of platinum-doublet chemotherapy
  - Approved for adult patients with metastatic NSCLC and progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Opdivo®
- Opdivo Qvantig™ (nivolumab and hyaluronidase)[18]:
  - Approved for adult patients with resectable (tumors ≥ 4 cm or node positive) NSCLC in the neoadjuvant setting, in combination with platinum-doublet chemotherapy
  - Approved for adult patients with resectable (tumors ≥ 4 cm or node positive) NSCLC and no known EGFR mutations or ALK rearrangements, for neoadjuvant treatment, in combination with platinum-doublet chemotherapy, followed by single-agent Opdivo Qvantig™ as adjuvant treatment after surgery

- Approved for adult patients with metastatic NSCLC and progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Opdivo Qvantig™
- Note: Not indicated in combination with ipilimumab for the treatment of metastatic NSCLC

• Pembrolizumab (Keytruda®)[19]:
- Approved in combination with pemetrexed and platinum chemotherapy for the first-line treatment of patients with metastatic nonsquamous NSCLC with no EGFR or ALK genomic tumor aberrations
- Approved in combination with carboplatin and either paclitaxel or paclitaxel protein-bound for the first-line treatment of patients with metastatic squamous NSCLC
- Approved as a single agent for the first-line treatment of patients with NSCLC expressing PD-L1 (TPS ≥ 1%) as determined by an FDA-authorized test, with no EGFR or ALK genomic tumor aberrations, and is:
  - Stage III where patients are not candidates for surgical resection or definitive chemoradiation, or
  - metastatic
- Approved as a single agent for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥ 1%) as determined by an FDA-authorized test, with disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Keytruda®
- Approved for the treatment of patients with resectable (tumors ≥ 4 cm or node positive) NSCLC in combination with platinum-containing chemotherapy as neoadjuvant treatment and then continued as a single agent as adjuvant treatment after surgery

- Approved as a single agent for adjuvant treatment following resection and platinum-based chemotherapy for adult patients with Stage IB (T2a ≥ 4 cm), II, or IIIA NSCLC

• Pembrolizumab and berahyaluronidase alfa-pmph (Keytruda Qlex™)[20]:
- Approved in combination with pemetrexed and platinum chemotherapy for the first-line treatment of adult patients with metastatic nonsquamous NSCLC, with no EGFR or ALK genomic tumor aberrations
- Approved in combination with carboplatin and either paclitaxel or paclitaxel protein-bound for the first-line treatment of adult patients with metastatic squamous NSCLC
- Approved as a single agent for the first-line treatment of adult patients with NSCLC expressing PD-L1 (TPS ≥ 1%) as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and that is:
  - Stage III where patients are not candidates for surgical resection or definitive chemoradiation, or
  - metastatic
- Approved as a single agent for the treatment of adult patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥ 1%) as determined by an FDA-approved test, with disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Keytruda Qlex™
- Approved for the treatment of adult patients with resectable (tumors ≥ 4 cm or node positive) NSCLC in combination with platinum-containing chemotherapy as neoadjuvant treatment and then continued as a single agent as adjuvant treatment after surgery

  - Approved as a single agent for adjuvant treatment following resection and platinum-based chemotherapy for adult patients with Stage IB (T2a ≥ 4 cm), II, or IIIA NSCLC
- Tremelimumab-actl (Imjudo®)[21]:
  - Approved in combination with durvalumab and platinum-based chemotherapy for the treatment of adult patients with metastatic NSCLC with no sensitizing EGFR mutation or ALK genomic tumor aberrations

For the most updated list of immunotherapy treatments available for lung cancer, please visit www.LUNGevity.org.

Bispecific T-cell engagers

A **bispecific T-cell engager** is a type of engineered molecule used for the treatment of cancer. These molecules harness and activate T cells, which are involved in the body's immune response, to attack tumor cells.[23]

How do bispecific T-cell engagers work?

T cells are activated by the immune system when a foreign antigen or abnormal cancer protein has been recognized in the body. In general, human antibodies are monospecific, which means that they recognize only one antigen. However, bispecific antibodies (bsAbs) are unique molecules that can bind to more than one antigen or protein simultaneously. Bispecific T-cell engagers work by binding directly to a receptor found on the T cell and an antigen found on the cancer cell. The binding of these two cells allows the T cell to recognize and attack the tumor.[24]

What bispecific T-cell engager is FDA-approved?

There is currently one FDA-approved bispecific T-cell engager for treating patients with SCLC:

- Tarlatamab-dlle (Imdelltra™)[25]:
  - Approved for the treatment of adult patients with ES-SCLC with disease progression on or after platinum-based chemotherapy

Do immunotherapy treatments work for all lung cancer patients?

Immune checkpoint inhibitors do not work for all lung cancer patients. Patients whose tumors have high levels of PD-L1 expression are the most likely to respond to PD-1/PD-L1 immune checkpoint inhibitors, but even those with tumors that do not express PD-L1 or express low levels of it may respond. Scientists cannot currently predict who will benefit from immune checkpoint inhibitors. They are working to discover who will respond and on ways to increase the number who do, such as combining treatments and boosting the immune system.[26]

Among those who do respond, the response can begin as early as weeks after the treatment begins and as late as months after it begins. The response may continue after treatment has stopped, and patients may have long-lasting remission.

Likewise, not all patients treated with the bispecific T-cell engager respond to it.

Management of immunotherapy side effects

Immunotherapy treatments can cause side effects. However, just because a side effect is possible does not mean that a patient will experience it. Before beginning treatment with an immunotherapy, the patient should discuss with the healthcare team what side effects, both more common (such as nausea, dizziness, or fatigue) and more rare (such as inflammation of the thyroid), might occur and how to prevent or ease them.

The patient should speak with the healthcare team if and when new side effects begin, as treating them early on is often more effective than trying to treat them once they have already become severe. In some cases, treatment with an immune checkpoint inhibitor might have to be discontinued.

In addition, it needs to be determined whether the symptoms are related to the treatment or not. What side effects are being experienced may impact future treatment plans. Although some side effects go away when treatment is over, some can last a long time.

Note: It is important for a patient to inform the healthcare team if they were ever treated with immunotherapy, even a long time ago, because side effects can show up after long periods of time.

Visit the LUNGevity Survivor Resource Center for information about managing treatment side effects: www.LUNGevity.org/patients-care-partners/survivor-resource-center.

Immunotherapy clinical trials

What immunotherapies are currently being tested in clinical trials?

Apart from immune checkpoint inhibitors and bispecific T-cell engagers that are currently approved, there are many immunotherapy **clinical trials** currently underway. These include, but are not limited to, trials for:

- new immune checkpoint inhibitors
- additional indications for currently approved immune checkpoint inhibitors
- combination treatments
- **a preventative cancer vaccine**
- **therapeutic cancer vaccines**
- **adoptive cell therapy**

Finding a clinical trial that might be right for you

If you are considering participating in a clinical trial, start by asking your healthcare team whether there is one that might be a good match in your geographic area. In addition, there are several resources to help you find one that may be a good match.

RESOURCES TO HELP YOU NAVIGATE YOUR CLINICAL TRIAL SEARCH:

- **LUNGevity Clinical Trial Matching Service:** https://connect.careboxhealth.com/en-US/partner/lcctal
  - Find available clinical trials by type of lung cancer and geographic location
  - Also find information and links to the medical centers at which these clinical trials are taking place
- **National Cancer Institute (NCI):** www.clinicaltrials.gov
- **My Cancer Genome:** www.mycancergenome.org
  - My Cancer Genome gives up-to-date information on what mutations make cancers grow and related treatment options, including available clinical trials
- **Lung-MAP:** www.lung-map.org
  - For patients with NSCLC, Lung-MAP is a collaboration of many research sites across the country. Lung-MAP uses a unique approach to match patients to one of several drugs being developed

QUESTIONS TO ASK YOUR HEALTHCARE TEAM ABOUT IMMUNOTHERAPY AS A TREATMENT OPTION:

- Why do you recommend immunotherapy for me?
- Will immunotherapy be my only treatment, or will it be combined with another treatment?
- Where do I go to get my immunotherapy?
- How will it be administered?
- How often will I get my treatment? How long will it last?
- How often do I need to be seen between treatments for a physical exam and/or lab work?
- What side effects can I expect?
- How will this treatment affect my daily life? Will I be able to work, exercise, and perform my usual activities?
- Are there any tests or procedures I will need to undergo during the treatment?
- When will you know whether or not the immunotherapy has worked?
- What tests will I need after treatment is completed?
- Are there any long-term health issues I should expect from treatment with immunotherapy?
- How much will my treatment cost?

03 glossary

Adaptive immune response—Specific response of the immune system; creates T cells to respond to a specific antigen on a cancer cell

Adenoids—A mass of lymphatic tissue located where the nose blends into the throat

Adjuvant treatment—Additional cancer treatment given after the primary treatment to lower the risk that the cancer will come back. Adjuvant therapy may include chemotherapy, radiation therapy, hormone therapy, targeted therapy, or biological therapy

Adoptive cell therapy—A type of immunotherapy in which immune cells are taken from the patient's own blood or tumor tissue, grown in large numbers in the laboratory, and then returned to the patient to help the immune system fight the cancer. Sometimes the T cells are changed in the laboratory to make them better able to target the patient's cancer cells and kill them

Antibody—A protein made by B cells in response to an antigen. Each antibody can bind to only one specific antigen. The purpose of this binding is to help destroy the antigen. Some antibodies destroy antigens directly. Others make it easier for white blood cells (WBCs) to destroy the antigen

Antigen—A protein on the surface of a cell that causes the body to make a specific immune response

Autoimmune disorder—A condition in which the body recognizes its own tissues as foreign and directs an immune response against them

B cell—A type of white blood cell (WBC) that circulates in the blood and lymph, seeking out foreign invaders. Upon meeting a "non-self" antigen, it makes proteins called antibodies, which detect and destroy the antigens. Also called B lymphocyte

Bacteria—A large group of single-cell microorganisms. Some cause infections and disease in animals and humans

Biological therapy—A type of treatment that uses substances made from living organisms to treat disease. These substances may occur naturally in the body or may be made in the laboratory. Some biological therapies stimulate or suppress the immune system to help the body fight cancer, infection, and other diseases. Other biological therapies attack specific cancer cells, which may help keep them from growing or kill them

Biomarker testing—A laboratory method that uses a sample of tissue, blood, or other body fluid to check for certain genes, proteins, or other molecules that may be a sign of a disease or condition, such as cancer. Biomarker testing can also be used to check for certain changes in a gene or chromosome that may increase a person's risk of developing cancer or other diseases. Biomarker testing may be done with other procedures, such as biopsies, to help diagnose some types of cancer. It may also be used to help plan treatment, find out how well treatment is working, make a prognosis, or predict whether cancer will come back or spread to other parts of the body. Also called molecular profiling and molecular testing

Bispecific T-cell engager—A substance made in the laboratory that can bind to two target proteins on the surface of different cells. For example, a bispecific T-cell engager may bind to a certain protein

on healthy T cells (a type of immune cell) and, at the same time, to a different protein on cancer cells. This brings the T cells and cancer cells close together so that the T cells can more effectively kill the cancer cells. Some bispecific T-cell engagers are being used to treat certain types of cancer, including acute lymphoblastic leukemia, multiple myeloma, lymphoma, and small cell lung cancer (SCLC)

Bone marrow—The soft, sponge-like tissue in the center of most bones. It produces white blood cells (WBCs), red blood cells, and platelets

Cervical lymph nodes—Lymph nodes found in the neck

Clinical trial—A type of research study that tests how well new medical approaches work in people. These studies test new methods of screening, prevention, diagnosis, or treatment of a disease. Also called clinical research trial or study

CTLA-4—A protein found on T cells (a type of immune cell) that helps keep the body's immune responses in check. When CTLA-4 is bound to another protein called B7, it helps keep T cells from killing other cells, including cancer cells. Some anti-cancer drugs, called immune checkpoint inhibitors, are used to block CTLA-4. When this protein is blocked, the "brakes" on the immune system are released and the ability of T cells to kill cancer cells is increased

Disease progression—Cancer that continues to grow or spread

Extensive-stage small cell lung cancer (ES-SCLC)—Cancer has spread outside of the lung in which it began to other parts of the body

First-line treatment—The first therapy given for a disease. It is often part of a standard set of treatments, such as surgery followed by chemotherapy and radiation. When used by itself, first-line treatment is the one accepted as the best treatment. If it doesn't cure the disease, or if it causes severe side effects, other treatments may be added or used instead

Foreign—In medicine, this term describes something that comes from outside the body. A foreign substance in the body's tissues, such as a bacterium or virus, may be recognized by the immune system as not belonging to the body. This causes an immune response. Other foreign substances in the body, such as artificial joints, are designed to not cause an immune response

Gene—Pieces of DNA that contain the information for making a specific protein

Genomic aberration—Alteration in the normal structure or number of chromosomes. Sometimes called mutation or alteration

Immune checkpoint inhibitors—Agents that target the pathways that tumor cells use to evade recognition and destruction by the immune system

Immune response—The activity of the immune system against foreign substances (antigens)

Immune system—A complex network of cells, tissues, organs, and the substances they make that help the body fight infections and other diseases. The immune system includes white blood cells (WBCs) and organs and tissues of the lymph system, such as the thymus, spleen, tonsils, lymph nodes, lymph vessels, and bone marrow

Immunotherapy—A type of cancer therapy that uses substances to stimulate or suppress the immune system to help the body fight cancer, infection, and other diseases. Some types of immunotherapy target only certain cells of the immune system. Others affect the immune system in a general way

Innate immune response—Immune response to a pathogen that involves the preexisting defenses of the body; such a response is not specific to a pathogen

Limited-stage small cell lung cancer—Cancer is found in one lung, the tissue between the lungs, and nearby lymph nodes only

Locally advanced—Spread of cancer from where it started to nearby tissue or lymph nodes

Lymph node—A rounded mass of lymphatic tissue that is surrounded by a capsule of connective tissue. Lymph nodes filter lymph (lymphatic fluid), and they store lymphocytes (white blood cells [WBCs]). They are located along lymphatic vessels

Lymphatic vessels—Thin-walled tubular structures that collect and filter lymph fluid before transporting it back to the blood circulation. Also called lymph vessels

Lymphocyte—A type of white blood cell (WBC) that is made in the bone marrow and is found in the blood and in lymph tissue. The main types of lymphocytes are B cells, T cells, and natural killer (NK) cells

Maintenance treatment—Treatment that is given to help keep cancer from coming back after it has disappeared following the initial therapy. It may include treatment with drugs, vaccines, or antibodies that kill cancer cells, and it may be given for a long time

Mediastinal—Of the area between the lungs. The organs in this area include the heart and its large blood vessels, the trachea, the esophagus, the thymus, and the lymph nodes but not the lungs

Metastatic—Spread of cancer from the primary site, or place where it started, to other places in the body

Microsatellite instability (MSI)—A change that occurs in certain cells (such as cancer cells) in which the number of repeated DNA bases in a microsatellite (a short, repeated sequence of DNA) is different from what it was when the microsatellite was inherited. MSI may be caused by mistakes that don't get corrected when DNA is copied in a cell. It is found most often in colorectal cancer, gastric cancer, and endometrial cancer, but it may also be found in many other types of cancer. Knowing whether a cancer has MSI may help plan the best treatment

Molecule—The smallest particle of a substance that has all of the physical and chemical properties of that substance

Natural killer (NK) cell—A type of white blood cell (WBC) that patrols the body and is on constant alert, seeking foreign invaders. Once NK cells recognize a cell as abnormal, they release granules (small particles) with enzymes that can kill tumor cells or cells infected with a virus

Neoadjuvant treatment—Treatment given as a first step to shrink a tumor before the main treatment, which is usually surgery, is given

Non-small cell lung cancer (NSCLC)—A group of lung cancers that are named for the kinds of cells found in the cancer and how the cells look under a microscope. The three main types of NSCLC are squamous cell carcinoma, large cell carcinoma, and adenocarcinoma. NSCLC is the most common kind of lung cancer

PD-1/PD-L1—See Programmed death 1/programmed death ligand 1

Preventive cancer vaccine—A vaccine that helps the immune system recognize abnormal cells and kill them before they become cancerous

Programmed death 1/programmed death ligand 1 (PD-1/PD-L1)—Part of the immune system mechanism that keeps T cells from functioning

Protein—A molecule, made up of amino acids, that is needed for the body to function properly. Proteins are the basis of body structures, such as skin and hair, and of other substances, such as enzymes, cytokines, and antibodies

Resectable—Able to be removed by surgery

Resection—Surgery to remove tissue or all of an organ

Small cell lung cancer (SCLC)—A fast-growing cancer that forms in tissues of the lung and can spread to other parts of the body. Named "small" for how the cancer cells look under a microscope

Spleen—An organ that is part of the lymphatic system. The spleen makes lymphocytes, filters the blood, stores blood cells, and destroys old blood cells. It is located on the left side of the abdomen near the stomach

Stage—The extent of a cancer in the body. Lung cancer stages range from Stage 0 (the lung cancer has neither invaded nearby tissue nor spread outside the lung) to Stage IV (the lung cancer may or may not have spread to the lymph nodes, but it has metastasized—spread to another part of the body)

T cell—A type of white blood cell (WBC). T cells are part of the immune system and develop from stem cells in the bone marrow. They help protect the body from infection and may help fight cancer. Also called T lymphocyte

Therapeutic cancer vaccine—A type of treatment using a vaccine that is usually made from a patient's own tumor cells or from substances taken from tumor cells. A cancer vaccine may help the immune system kill cancer cells

Thymus—An organ that is part of the lymphatic system and in which T lymphocytes grow and multiply. The thymus is in the chest behind the breastbone

Tumor—An abnormal mass of tissue that results when cells divide more than they should or do not die when they should

Tumor mutational burden (TMB)—The total number of mutations (changes) found in the DNA of cancer cells. Knowing the TMB may help plan the best treatment. For example, tumors that have a high number of mutations appear to be more likely to respond to certain types of immunotherapy. Tumor mutational burden is being used as a type of biomarker

Unresectable—Unable to be removed by surgery

Virus—A very simple microorganism that infects cells and may cause disease

White blood cell (WBC)—A type of blood cell that is made in the bone marrow and found in the blood and lymph tissue. WBCs are part of the body's immune system. They help the body fight infection and other diseases. Types of WBCs are granulocytes (neutrophils, eosinophils, and basophils), monocytes, and lymphocytes (natural killer [NK] cells, T cells, and B cells)

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05 notes

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