



What you need to know about...

# immunotherapy



# foreword

## About LUNGevity

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LUNGevity is the largest national lung cancer-focused nonprofit, changing outcomes for people with lung cancer through research, education, and support.

## About the LUNGevity PATIENT EDUCATION SERIES

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LUNGevity has developed a comprehensive series of materials for patients/survivors 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, someone you care about has been diagnosed, or you are concerned about your 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, [www.LUNGevity.org](http://www.LUNGevity.org), under "For Patients & Supporters" and "For Supporters & Advocates."

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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 are used in the text.

# 01 immune system

## What is the immune system?

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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**.

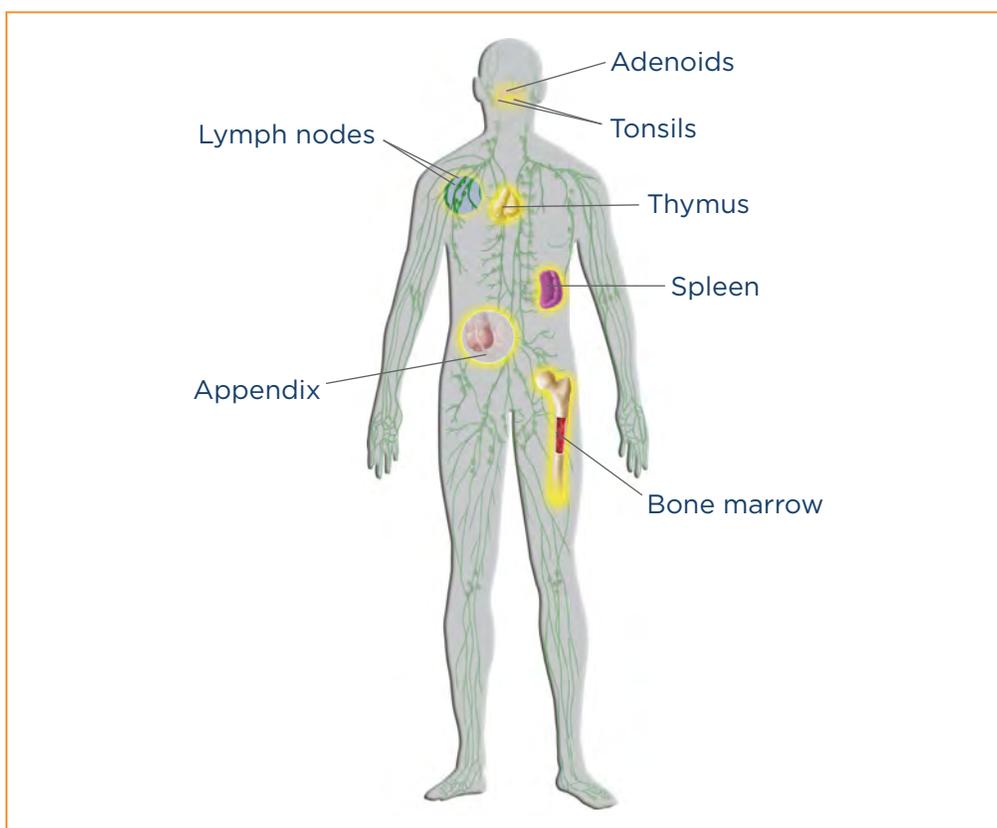
Key players in defending the body include a specific type of **white blood cell (WBC)** called **lymphocytes**. There are three major types of lymphocytes:

- **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 as **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. In this way, the immune system works in a coordinated way to monitor the body for germs and other abnormal cells.

### ORGANS OF THE IMMUNE SYSTEM



## How does the immune system work?

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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 distinctive **proteins** on its surface. These identifying surface proteins let the immune system know that they are cells that belong to the body.

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**.

If a foreign substance—such as a bacteria, 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.

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 from 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 co-exist with immune cells capable of killing the cancer, but the cancer cells hold the immune cells back from working the way they should.

## 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 natural killer (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.

#### NK CELL RELEASING TOXINS TO CANCER CELL



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

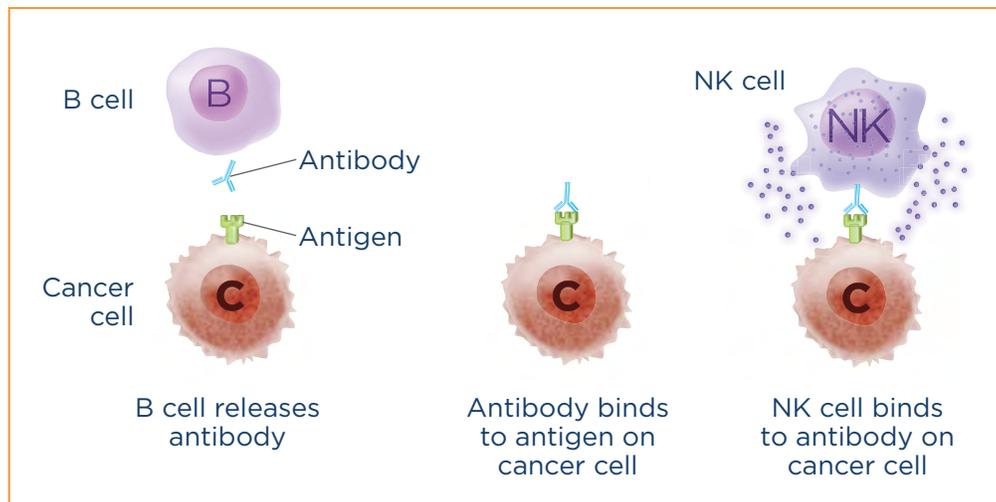
## Adaptive immune response

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 natural killer cells to the cancer. B cells also create "memory"—they start to make antibodies quickly when they recognize a past antigen.

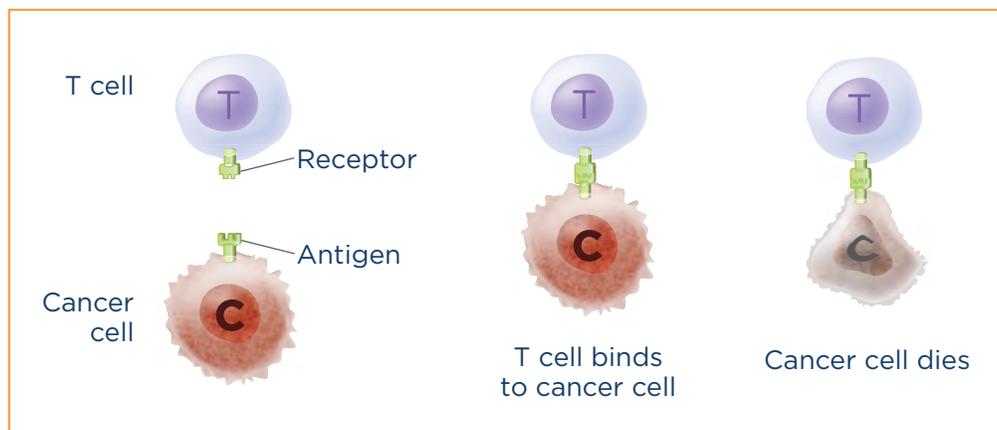
#### B CELL RELEASING ANTIBODY



## 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. The T cells are like soldiers, destroying 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.

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

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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 dampen 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 hard to understand exactly how this happens and how to best turn the T cells back on.

## 02 immunotherapy

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

### 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.

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

There are many different types of immunotherapy. Three main types are currently being studied in people with **non-small cell lung cancer (NSCLC)**:

- **Immune checkpoint inhibitors**
- **Therapeutic cancer vaccines**
- **Adoptive T cell transfer**

Immune checkpoint inhibitors have made the most progress at this time, and the first U.S. Food and Drug Administration (FDA)-approved immunotherapy drugs for lung cancer belong to this group. Immunotherapy is also being studied in **small cell lung cancer (SCLC)**.

## **Immune checkpoint inhibitors**

Many lung cancers co-exist with T cells capable of killing the cancer cells. However, the immune system has many normal mechanisms for dampening 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 tissue. 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. This may allow cancer cells to thrive.

### *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.

### *What immune checkpoint inhibitors are currently available?*

There are currently four FDA-approved immune checkpoint inhibitors for treating patients with lung cancer. Three of them, nivolumab (Opdivo®), pembrolizumab (Keytruda®), and atezolizumab (Tecentriq®), treat patients whose NSCLC has already progressed to **metastatic** disease. One of them, durvalumab (Imfinzi®), treats patients at an earlier **stage** in order to reduce the risk of the lung cancer progressing.

- Durvalumab (Imfinzi®): Approved for patients with stage III NSCLC whose tumors are not able to be surgically removed and whose cancer has not progressed after treatment with concurrent platinum-based **chemotherapy** and **radiation therapy** (sometimes referred to as chemo-radiation or CRT).
- Nivolumab (Opdivo®): Approved for patients with metastatic NSCLC whose lung cancer has progressed on or after platinum-based chemotherapy. Patients with **epidermal growth factor receptor (EGFR)** or **anaplastic lymphoma kinase (ALK)** mutations should have **disease progression** on FDA-approved therapy for these mutations before receiving this drug.

**Note:** Platinum-based chemotherapies include carboplatin and cisplatin.

- Pembrolizumab (Keytruda®): Approved for patients with metastatic NSCLC in the following situations:
  - As **first-line treatment** for patients whose tumors have a high (greater than or equal to 50%) **Programmed Death Ligand 1 (PD-L1)** expression Tumor Proportion Score (TPS), as determined by an FDA-approved test, with no EGFR or ALK mutation. Approximately 30% of patients with newly diagnosed metastatic NSCLC will have tumors with this high level of PD-L1 expression. (The TPS is the percentage of cancer cells that produce the PD-L1 proteins. The lung cancer tissue is stained with special dyes that mark PD-L1-positive tumor cells. A pathologist counts the number of cells that stain positive and determines the TPS.)
  - For patients whose tumor expresses PD-L1 (TPS greater than or equal to 1%), as determined by an FDA-approved test, with disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK mutations should have disease progression on FDA-approved therapy for these mutations before receiving this drug.
  - As first-line treatment for patients with metastatic non-squamous NSCLC in combination with the chemotherapy drugs pemetrexed and carboplatin, irrespective of PD-L1 expression.
- Atezolizumab (Tecentriq®): Approved for patients with metastatic NSCLC whose lung cancer has progressed during or after being treated with platinum-containing chemotherapy. Patients with EGFR or ALK mutations should have disease progression on FDA-approved therapy for these mutations before receiving this drug.

Patients with pre-existing autoimmune disorders should discuss them with their doctors. Those who go on an immune checkpoint inhibitor should be monitored very carefully for autoimmune side effects.

### *How are immune checkpoint inhibitors administered?*

FDA-approved immune checkpoint inhibitors are given **intravenously**. **Infusion** time and schedules vary, depending on the drug. Immune checkpoint inhibitors are given until disease progression or serious side effects occur.

- Durvalumab (Imfinzi®) is given intravenously over 60 minutes every 2 weeks for no more than 12 months
- Nivolumab (Opdivo®) is given intravenously over 30 minutes every 2 weeks or every 4 weeks
- Pembrolizumab (Keytruda®) is given intravenously over 30 minutes every 3 weeks
- Atezolizumab (Tecentriq®) is given intravenously over 60 minutes every 3 weeks

### *How well do immune checkpoint inhibitors work?*

In **clinical trials** to date with NSCLC patients, approximately 20% have responded to immune checkpoint inhibitors. This includes patients who tested negative for **Programmed Death 1/Programmed Death Ligand 1 (PD-1/PD-L1)**, as well as those who tested positive. The response may continue after treatment is stopped. Some of the responses to date have been long-term. There are many reasons to think that the results will improve as scientists learn how best to use these drugs.

Scientists are looking for ways to increase the number of people who respond to this treatment. In clinical trials, they are combining treatments, boosting the immune system, and using other strategies.

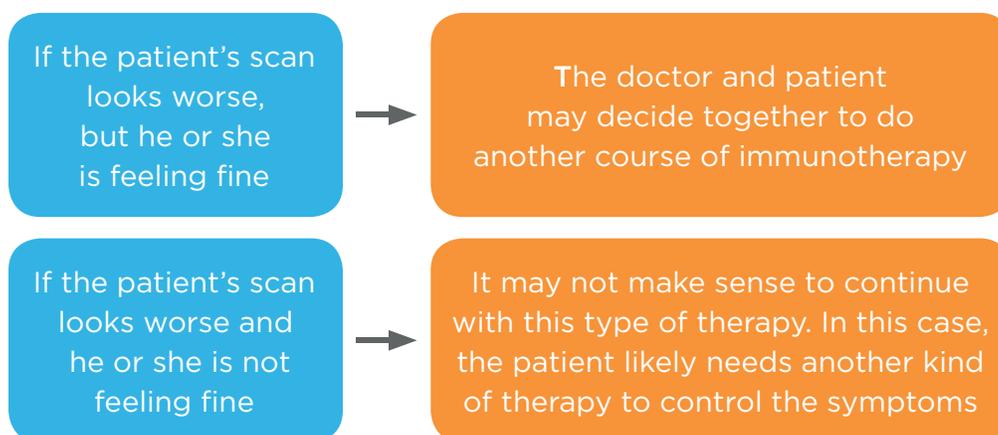
**Note:** Patients whose tumors have high levels of PD-L1 expression are more likely to respond to PD-1/PD-L1 therapies. However, even those with tumors that do not express PD-L1 may respond to these treatments.

### *How long does it take to see results from therapy with immune checkpoint inhibitors?*

Of the approximately 20% of patients in clinical trials with immune checkpoint inhibitors who have responded, most respond within the first couple of months.

In a small subset of patients (1%–3%), the tumor on a **CT scan** may seem to get worse at first and then get better, or there may be new areas of tumor. Scientists have coined the term **pseudoprogression** to describe this situation. One theory of why this happens is that, as the lymphocytes come in to attack a tumor, the tumor gets larger, and then, as they kill cancer cells, the tumor gets smaller again. The current scientific thinking is that the tumors get larger because a large number of the patient's T cells move into the tumor to clean it up. Therefore, some tumors that look larger on scans are larger because the immune system is attacking the cancer, not because the cancer cells are growing. **For the great majority of patients whose scans show worsening of disease after at least a couple of months on immunotherapy, the scans are accurately showing that the immunotherapy is not working.**

In cases where the scan looks worse, the best course of action will likely be based on a number of factors:



### *What are the side effects of immune checkpoint inhibitors?*

**The most common side effects reported from immune checkpoint inhibitors as a group include:**

- Nausea
- Fatigue
- Rash
- Musculoskeletal pain
- Cough
- Difficulty breathing
- Constipation
- Decreased appetite

An immune checkpoint inhibitor side effect seen sometimes is **pneumonitis**, which is inflammation of the lung tissue that may lead to difficulty breathing if not treated early and correctly.

Pneumonitis and some of the other side effects seen with immune checkpoint inhibitors are related to “turning on” the immune system, which then may also attack some healthy cells and cause inflammation. Other examples of this include:

- **Arthritis**
- **Colitis**
- **Hepatitis**
- Inflammation of the **endocrine glands**, like the thyroid
- **Nephritis** and **renal dysfunction**

Inflammation of the thyroid can cause either high or low thyroid hormone levels (hyperthyroidism or hypothyroidism, respectively). Inflammation of the liver can also occur, so liver function tests may be run periodically to check for that. Inflammation-related symptoms are usually easy to manage, but sometimes patients may need to take additional medications, including corticosteroids or thyroid hormone replacement.

**Note:** It’s important to let your doctor(s) know if you are experiencing any problems while on treatment, so they can sort out if the side effects are related to the treatment. It is especially important to be very clear with your doctor about the side effects that you are experiencing, because this may impact future treatment plans.

Some patients experience side effects that are severe enough that they need to stop taking the immunotherapy treatment. In general, based on what has been seen with patients in clinical trials to date, these kinds of treatments are well tolerated by most patients.

Because these drugs have only been studied in patients for a few years, we do not know for certain what the long-term side effects are in patients with profound responses, including remission of cancer.

However, doctors have some ideas about what they may be:

- One potential long-term side effect of immunotherapy may be that, if it affects the endocrine gland, a patient may need thyroid hormone supplementation for the rest of his or her life
- Some patients develop diabetes and need to be on medication

**Note:** It's important to tell your doctor(s) if you were ever treated with immunotherapy, even a long time ago, because side effects can show up after long periods of time.



#### RESOURCES FOR MANAGING TREATMENT SIDE EFFECTS:

- LUNGeVity Survivor Resource Center  
[www.LUNGeVity.org/for-patients-caregivers/survivor-resource-center](http://www.LUNGeVity.org/for-patients-caregivers/survivor-resource-center)

#### *Where do immune checkpoint inhibitors fit into the treatment plan for lung cancer?*

Durvalumab (Imfinzi®) is currently FDA-approved for patients with stage III NSCLC.

The other three FDA-approved drugs in this class, nivolumab (Opdivo®), pembrolizumab (Keytruda®), and atezolizumab (Tecentriq®), are currently approved as **second-line treatment or therapy** for patients with metastatic NSCLC who have been or are being treated with platinum-based chemotherapy. In addition, pembrolizumab (Keytruda®) may be used for first-line treatment under certain circumstances.

Numerous immune checkpoint inhibitor drugs are being tested in clinical trials for lung cancer, including:

#### IMMUNE CHECKPOINT INHIBITORS BEING TESTED

Generic Name	Brand Name	Types of lung cancer being tested
Ipilimumab	Yervoy®	NSCLC, SCLC
Durvalumab	Imfinzi®	NSCLC, SCLC
Avelumab	Bavencio®	NSCLC
Tremelimumab	To be determined	NSCLC
PDR001	To be determined	NSCLC
REGN2810	To be determined	NSCLC

Immune checkpoint inhibitors are being used alone and in combination with other therapies in clinical trials, including:

- Chemotherapy
- **Targeted therapy**
- Radiation therapy
- Other checkpoint antibodies
- Other immunotherapies
- Therapies that block blood vessel formation

## Therapeutic cancer vaccines

When most people think of a vaccine, they think of a traditional vaccine given to prevent an infectious disease, such as measles or polio. In addition to traditional vaccines, there are two types of cancer vaccines:

- A preventive cancer vaccine is given to prevent cancer from developing in healthy people. For example, the hepatitis B vaccine is given to children to protect against a hepatitis B viral infection, which can lead to liver cancer.

- A therapeutic cancer vaccine, in contrast, is given to treat an existing cancer by causing a stronger and faster response from the immune system. Most commonly, this type of vaccine is used in patients in remission in an attempt to prevent likely **relapse**, or the cancer from returning.

### *Where do therapeutic cancer vaccines fit in a lung cancer treatment plan?*

While there are yet no FDA-approved therapeutic cancer vaccines for lung cancer, therapeutic cancer vaccines are being studied in clinical trials for both SCLC and NSCLC.

A number of different therapeutic vaccines are being studied:

#### **THERAPEUTIC CANCER VACCINES BEING STUDIED FOR LUNG CANCER**

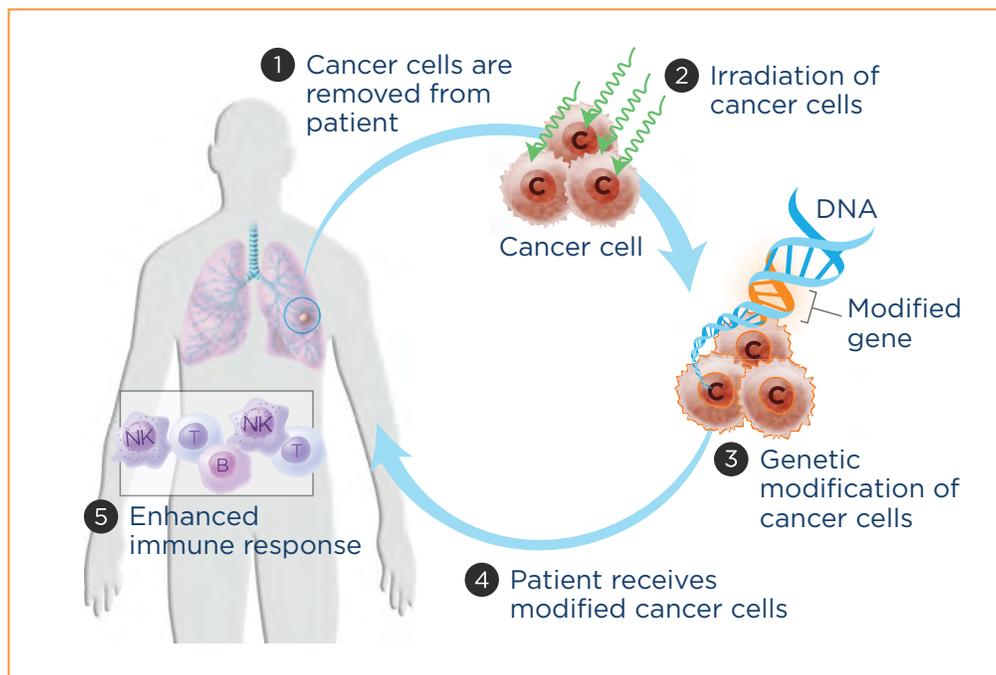
Generic Name	Brand Name	Types of lung cancer being studied
Tergenpumatucel-L	HyperAcute®	NSCLC
BI1361849	To be determined	NSCLC
CIMAvax-EGF	To be determined	NSCLC
GV1001	To be determined	NSCLC
TG4010	To be determined	NSCLC
BEC2	To be determined	NSCLC
INGN	To be determined	SCLC

### How do therapeutic cancer vaccines work?

A therapeutic cancer vaccine is made from a patient's own tumor cells or from substances taken from the tumor cells. They are designed to work by activating the cells of the immune system to recognize and act against the specific antigen on the tumor cell. Because the immune system has special cells for memory, the hope is that the vaccines will also help keep the lung cancer from coming back.

**Note:** There are several ways to receive therapeutic cancer vaccines. The figure below describes one method of receiving therapeutic cancer vaccines.

#### THERAPEUTIC CANCER VACCINE

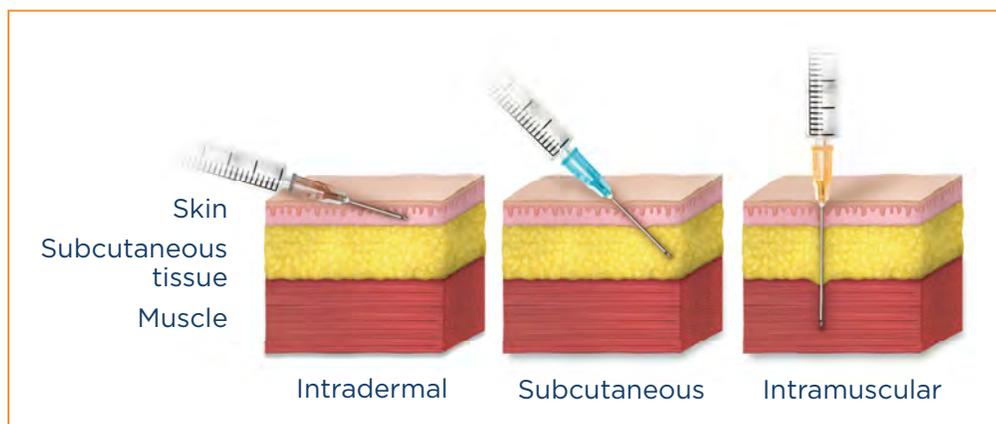


## *How is a therapeutic cancer vaccine administered?*

Therapeutic cancer vaccines are given as an injection either:

- Right below the skin's top layer (**intra**dermally)
- Beneath the skin (**sub**cutaneously)
- Into the muscle (**intra**muscularly)

### TYPES OF INJECTIONS



## *Results of therapeutic cancer vaccine administration*

Several studies have suggested that therapeutic cancer vaccines may be most effective when given in combination with other forms of cancer therapy. In addition, they may even increase the effectiveness of the other treatments. There is also some evidence indicating that surgical removal of the tumor before administration of a cancer vaccine may make it easier for the immune system to develop an effective response.

*What side effects of therapeutic cancer vaccines have been seen in clinical trials?*

**The most common side effect of therapeutic cancer vaccines is inflammation at the site of the injection, including:**

- Redness
- Pain
- Swelling
- Warming of the skin
- Itchiness
- Rash (occasional)

Flu-like symptoms have also been reported after administration of a therapeutic cancer vaccine, including:

- Fever
- Chills
- Weakness
- Dizziness
- Nausea or vomiting
- Muscle ache
- Fatigue
- Headache
- Occasional breathing difficulties

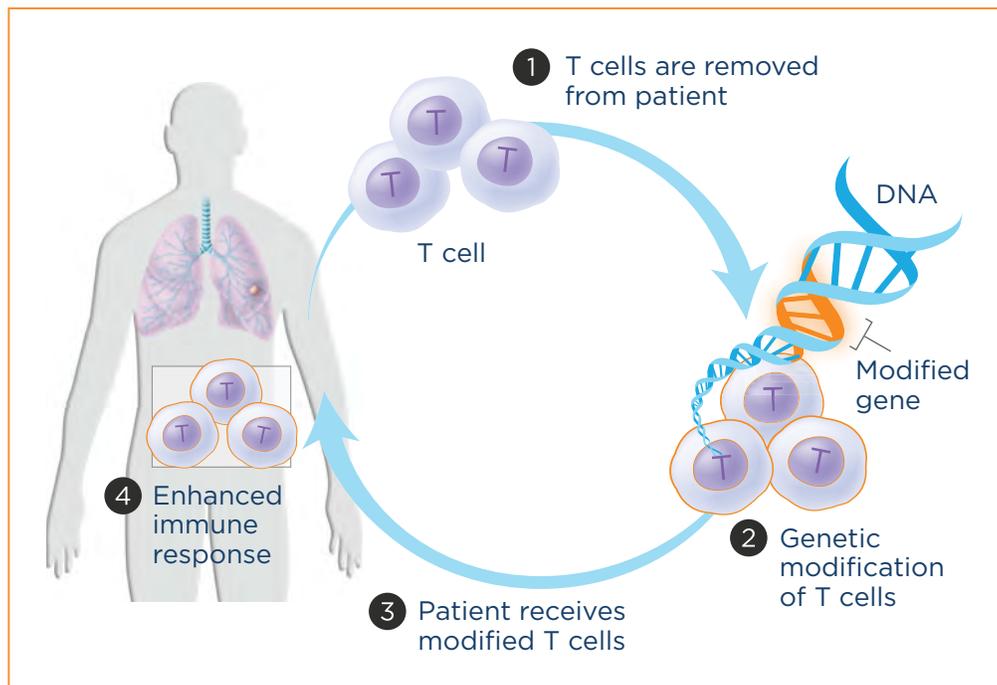
More serious health problems have been reported in a smaller number of people after receiving a therapeutic cancer vaccine, but these may not have been caused by the vaccine.

Rarely, severe allergic reactions to specific vaccine ingredients have been seen following vaccination.

## Adoptive T cell transfer

Adoptive T cell transfer is being developed as a new approach to cancer treatment. The goal is to improve the ability of a person's own T cells to fight cancer. A sample of T cells is removed from the patient and then genetically changed in order to make the T cells more active against specific cancer cells. Scientists can change what is on the surface of the T cells. For example, they can add a receptor to the surface of the T cell that will target a specific antigen on a cancer cell. The receptors work like very specific Velcro that allows T cells to stick to cancer cells and kill the cells. The T cells are then returned to the patient, and the altered T cells quickly home in on their targets.

### ADOPTIVE T CELL TRANSFER



### *Where does adoptive T cell transfer fit into the treatment plan for lung cancer?*

Currently, there are no FDA-approved T cell transfer-based therapies for lung cancer. Adoptive T cell transfer is being studied in clinical trials.

### *How does adoptive T cell transfer work?*

Typically, during an immune response, T cells multiply. After the initial response, most of the newly made T cells are eliminated. This keeps the total T cell number in the body at a normal level. The normal level of T cells is usually not high enough to sustain a response strong enough to effectively fight cancer.

However, there is evidence that T cells have the ability to multiply in abundance when given to someone whose immune system has been weakened. Therefore, in an adoptive T cell transfer, patients are given chemotherapy prior to the adoptive T cell transfer in order to suppress their immune system. Once the chemotherapy is completed and the immune system is weakened, billions of modified T cells are then reintroduced into the patient.

The goal of the T cell transfer is to enable the immune system to attack the tumors in a large number that is otherwise impossible and in a way that it is incapable of doing on its own.

## *How is adoptive T cell transfer administered?*

### *How are T cells removed from a patient?*

The three ways of performing adoptive T cell transfer include:

- Taking T cells from the bloodstream and putting special receptors, called chimeric antigen receptors (CARs), on them. CARs recognize specific proteins found on the surface of cancer cells. The CAR T cells then bind to the cancer cells that have those proteins and destroy them
- Collecting a sample from the tumor and multiplying the T cells in a laboratory
- Taking T cells from the bloodstream, through a procedure called **leukapheresis**, and genetically altering them to attack cancer cells that have specific antigens

### *How are T cells returned to the patient?*

After the T cells are removed from a patient by any of these ways, the T cells are returned to the patient through an infusion.

## *Results of clinical trials involving adoptive T cell transfer*

Clinical trials with very strong patient responses, including lasting responses, have led to FDA approval of two CAR T cell therapies: one for a type of lymphoma and the other for a type of leukemia. Whether T cell therapies will eventually prove to be effective in lung cancer is unknown.

*What side effects have been seen in clinical trials involving adoptive T cell transfer?*

Among the most common side effects of adoptive T cell transfer is the serious cytokine-release syndrome. This is a rapid and large-scale release of **cytokines** into the bloodstream. Cytokines are chemical messengers that help the T cells carry out their duties. Too many cytokines can lead to dangerously high fevers and quick drops in blood pressure. In many patients, this side effect can be managed with standard supportive treatments, including steroids.

Other serious side effects include neurotoxicity—changes in the brain caused by the treatment that can result in a headache, seizures, confusion, infection, low blood cell counts, and a weakened immune system.



### 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 in-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 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?

## What clinical trial options are available?

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Clinical trials are ongoing in lung cancer patients to add to the understanding of these different types of immunotherapy. There have been clear advances in immunotherapy over the last decade, and these advances are based on information learned from patients who were enrolled in clinical trials.

If you are considering whether to participate in a clinical trial, start by asking your doctor whether there is one for which you might qualify in your area. There are several other questions that you should consider asking your healthcare team about participating in a clinical trial.



## QUESTIONS TO ASK YOUR HEALTHCARE TEAM IF YOU ARE CONSIDERING PARTICIPATING IN AN IMMUNOTHERAPY CLINICAL TRIAL:

### About your treatment history:

- What type(s) of treatment(s) for lung cancer have I had so far?
- What line of therapy am I looking for?
  - If you have never been treated before, you are looking for a **first-line clinical trial**
  - If you have had a prior chemotherapy for metastatic disease, you may be looking for a **second-line clinical trial**
  - If you have had multiple lines of therapy, you want a clinical trial that allows for several previous treatments

### About immunotherapy clinical trials:

- What are the benefits and risks of participating in an immunotherapy clinical trial?
- How will I be monitored while participating in a clinical trial?
- What are my responsibilities during the clinical trial?
- Are there any costs associated with my participation in a clinical trial?
- Where can I learn more about clinical trials?
- Who can I talk to if I have questions during the clinical trial?
- What happens if I decide I do not want to participate in the clinical trial at some point?

In addition, below are several resources to help you find a clinical trial that may be a good match for you.



### **RESOURCES TO HELP YOU NAVIGATE YOUR CLINICAL TRIALS SEARCH:**

- **LUNGeivity Clinical Trial Finder:** <https://clinicaltrials.LUNGeivity.org/index.html>
  - The LUNGeivity Clinical Trial Finder helps you connect with lung cancer trials
  - The screening process locates nearby clinical trials as well as provides information and links to centers performing these studies
- **EmergingMed:** [www.emergingmed.com/networks/LUNGeivity](http://www.emergingmed.com/networks/LUNGeivity)
  - LUNGeivity partners with this clinical trials matching service to help you with the decision of whether to participate in a clinical trial
  - EmergingMed helps you identify lung cancer clinical trials for which you may be eligible
  - Clinical trial navigators are available Monday through Friday from 9:00am to 5:00pm ET at 877-769-4834
- **U.S. National Institutes of Health:** [www.clinicaltrials.gov](http://www.clinicaltrials.gov)
- **National Cancer Institute (NCI):** [www.cancer.gov/clinicaltrials/search](http://www.cancer.gov/clinicaltrials/search)
- **Coalition of Cancer Cooperative Groups:** [www.cancertrials-help.org/cancer-trial-search](http://www.cancertrials-help.org/cancer-trial-search)

## 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

**Adoptive T cell therapy**—Therapy that involves removing some of a patient’s own immune system cells—often altering and increasing their ability to recognize and kill cancer cells—growing billions of them in the laboratory, and infusing the cultured cells into the patient. The idea is to provide an invading force of immune cells that can attack tumors at a level that the immune system is not capable of doing on its own

**Anaplastic lymphoma kinase (ALK)**—A gene that the body normally produces but, when fused with another gene, produces an abnormal protein that leads to cancer cell growth

**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

**Arthritis**—A disease that causes inflammation and pain in the joints

**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

**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

**Chemotherapy**—Treatment with drugs that kill cancer cells

**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

**Colitis**—An illness that causes pain and swelling in the colon

**CT scan**—A procedure that uses a computer linked to an X-ray machine to make a series of detailed pictures of areas inside the body. The pictures are taken from different angles and are used to create 3-dimensional (3-D) views of tissues and organs. A dye may be injected into a vein or swallowed to help the tissues and organs show up more clearly. Also called computed tomography (CAT) scan

**Cytokine**—A type of protein that is made by certain immune and non-immune cells and has an effect on the immune system. Some cytokines stimulate the immune system, while others slow it down

**Disease progression**—Cancer that continues to grow or spread

**Endocrine gland**—A gland (for example, the thyroid or the pituitary) that produces an endocrine secretion

**Epidermal growth factor receptor (EGFR)**—The protein found on the surface of some cells and to which epidermal growth factor (a protein made by many cells in the body and by some types of tumors. It causes cells to grow and differentiate) binds, causing the cells to divide. It is found at abnormally high levels on the surface of many types of cancer cells, so these cells may divide excessively in the presence of epidermal growth factor

**First-line clinical trial**—A clinical trial for a patient who has never been treated before

**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 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

**Hepatitis**—Disease of the liver causing inflammation

**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 only target certain cells of the immune system. Others affect the immune system in a general way

**Infusion**—A method of putting fluids, including drugs, into the bloodstream. Also called intravenous infusion

**Innate immune response**—Immune response to a pathogen that involves the pre-existing defenses of the body; such a response is not specific to a pathogen

**Intradermal**—Within the skin. Also called intracutaneous

**Intramuscular**—Within a muscle

**Intravenous**—Into or within a vein. Intravenous, or IV, usually refers to a way of giving a drug or other substance through a needle or tube inserted into a vein

**Irradiate**—To treat with radiation

**Leukapheresis**—Removal of the blood to collect specific blood cells. The remaining blood is returned to the body

**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

**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 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

**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

**Nephritis**—Acute or chronic inflammation of the kidney caused by infection, degenerative processes, or vascular disease

**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

**Pneumonitis**—Inflammation of the lungs that may be caused by disease, infection, radiation therapy or other therapies, allergy, or irritation of lung tissue by inhaled substance

**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

**Pseudoprogession**—Growth in tumor size that is due to response to treatment and not to growth of cancer cells

**Radiation therapy**—The use of high-energy radiation from X-rays, gamma rays, neutrons, protons, and other sources to kill cancer cells and shrink tumors. Radiation may come from a machine outside the body (external-beam radiation therapy) or it may come from radioactive material placed in the body near cancer cells (internal radiation therapy, or brachytherapy). Also called irradiation and radiotherapy

**Relapse**—The return of a disease or the signs and symptoms of a disease after a period of improvement

**Renal dysfunction**—Reduced ability of the kidneys to filter blood and remove waste products and excess fluid from the body

**Second-line clinical trial**—Clinical trial for patients who have had a prior chemotherapy for metastatic disease

**Second-line treatment or therapy**—Treatment that is usually started after the first set of treatments doesn't work, has stopped working, or has side effects that are not tolerated

**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)

**Subcutaneous**—Beneath the skin

**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

**Targeted therapy**—A type of treatment that uses drugs to attack specific types of cancer cells with less harm to normal cells. Some targeted therapies block the action of certain enzymes, proteins, or other molecules involved in the growth and spread of cancer cells

**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, 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

**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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