

# IMMUNOTHERAPY

*for the treatment of*

# HEMATOLOGIC CANCERS

**FREE** take one

LEUKEMIA  
LYMPHOMA  
MULTIPLE  
MYELOMA



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# HEMATOLOGIC CANCERS

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representatives and industry leaders from around the world. Through educational programs that foster scientific exchange and collaboration, SITC aims to one day make the word "cure" a reality for cancer patients everywhere.

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## ABOUT BLOOD CANCERS AND THE IMMUNE SYSTEM

▲ **Immunotherapy helps** the immune system recognize cancer cells that have been hiding and target them for destruction. The strategy of harnessing the body's natural defense system to fight cancer, which is very different from other types of cancer treatment, holds the potential to positively affect people with every type of cancer. Immunotherapy is among the fastest growing and most promising areas of cancer research and is positively changing the way doctors treat hematologic (blood) cancers.

In general, cancers fall into one of two categories: solid tumors or hematologic cancers. Blood cancers primarily affect blood, bone marrow and lymph nodes and may or may not create an actual tumor (or mass). This guide addresses lymphoma, leukemia and multiple myeloma, which are hematologic cancers, as well as immunotherapy strategies approved to treat certain types of them. As you explore each section on these blood cancers, refer to this article for more information about specific treatments.

Lymphoma starts in the lymphatic system and affects lymphocytes, which are part of the immune system. Lymphoma can be classified into two main categories: Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). NHL is much more common and can be classified as indolent (slow growing) or aggressive (rapidly growing).

Leukemia occurs when white blood cells transform into leukemia cells and grow uncontrollably. As a result, large numbers of these cells accumulate in the bone marrow, which may slow down or prevent normal body functions, including the production of healthy blood cells.

Multiple myeloma begins when the blood's plasma cells multiply uncontrollably. As these abnormal cells multiply, they can affect the body's ability to fight infection. This can result in anemia, bone damage and excessive bleeding from cuts. Plasma cells are produced in the bone marrow and are part of the immune system.

Treatment options will vary depending on which hematologic cancer you have and your unique characteristics, such as previous treatments, age and general health. With many

types of lymphoma and leukemia, identifying the subtype is crucial for developing an effective treatment strategy. Certain types of immunotherapy treat only certain subtypes, making it important to have a specific diagnosis. Biomarker testing helps doctors determine subtypes and whether a patient is a good candidate for immunotherapy.

Common hematologic cancer treatments include watchful waiting, chemotherapy, targeted therapy, radiation therapy, immunotherapy, stem cell transplantation, corticosteroids, bone-modifying agents and surgery. Although surgery is not commonly used for many blood cancers, it may be used to treat a single plasmacytoma (malignant plasma cell tumor) that can occur with multiple myeloma or as palliative treatment to relieve bone pain caused by cancer that has metastasized (spread) to the bone.

### HOW DOES THE IMMUNE SYSTEM WORK?

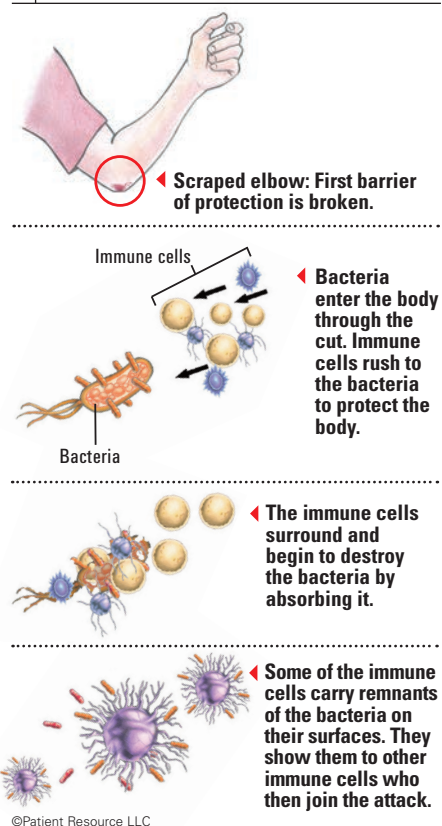
The immune system is a complex network of cells, molecules, organs and lymph tissues working together to defend the body against germs, cancer cells and other microscopic invaders. The first job of the immune system is to distinguish between what is part of the body ("self") and what is not ("non-self"). Once the immune system determines that a cell is non-self, or foreign, to the body, it begins a series of reactions to identify, target and eliminate those non-self cells.

Your immune system constantly identifies and eliminates harmful organisms that could negatively affect your health. For example, when you scrape your elbow, harmful substances can easily enter the body (see Figure 1). A healthy immune system works to destroy viruses and bacteria (non-self antigens) that cause your illness and helps you recover.

A large part of your immune system is the lymphatic system, which is made up of lymph nodes as well as the spleen, thymus, adenoids and tonsils. Lymph nodes are located throughout the body, with large concentrations near the chest, abdomen, groin, pelvis, underarms and neck.

Lymph, a clear fluid, is circulated throughout the body. It collects and filters bacteria, viruses, toxins and chemicals known as antigens, which are circulating in the lymphatic system and bloodstream. Lymph contains lymphocytes, a type of white blood cell that attacks infectious agents. Lymphocytes be-

**FIGURE 1**  
▲ **NORMAL IMMUNE RESPONSE**



gin in the bone marrow and develop from lymphoblasts (immature cells found in bone marrow). Lymphoblasts mature into infection-fighting cells. 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 more quickly if they return.

T-cells also develop in the bone marrow but travel to the thymus to mature into four types, each with its own role in the immune system.

- 1. Helper T-cells** identify foreign, or non-self, antigens and communicate with other immune system cells to coordinate with the B-cells or other T-cells for an attack.
- 2. Killer T-cells** directly attack and destroy cancer cells or normal body cells infected with a virus by inserting a protein that causes them to enlarge and burst. One type of killer T-cell specifically targets cancer cells.



## ABOUT BLOOD CANCERS AND THE IMMUNE SYSTEM

3. **Regulatory T-cells** slow down the immune system after an immune response is finished.

4. **Memory T-cells** can stay alive for years, continuing to fight the same invading cells. Memory is the basis of immune protection against disease in general and explains why we usually don't become infected with some diseases, such as chickenpox, more than once.

The normal process for an immune response begins when B-cells and helper T-cells identify a threat (non-self antigen) and tell the rest of the immune system. The body then ramps up its production of T-cells to fight. Killer T-cells are sent to destroy the non-self cells. Regulatory T-cells are sent to slow down the immune system once the non-self cells have been eliminated to prevent the T-cells from attacking healthy parts of the body. As a result, T-cells return to normal levels. The immune system uses the same process to recognize and eliminate cancer cells as it does to remove other non-self cells, but the process is more complicated.

### IMMUNOTHERAPY FOR HEMATOLOGIC CANCERS

Blood cancer treatment has been revolutionized by various types of immunotherapy. Training the immune system to respond to cancer has the potential for a more lasting response that can extend beyond the end of treatment.

Immunotherapy is not effective for every person, even if it is approved for that person's cancer type. Research is ongoing to find new tests that will help guide doctors to recommend immunotherapy only to patients who are most likely to respond to it.

Different types of immunotherapy may be used alone or in combination with other therapies to treat certain blood cancers.

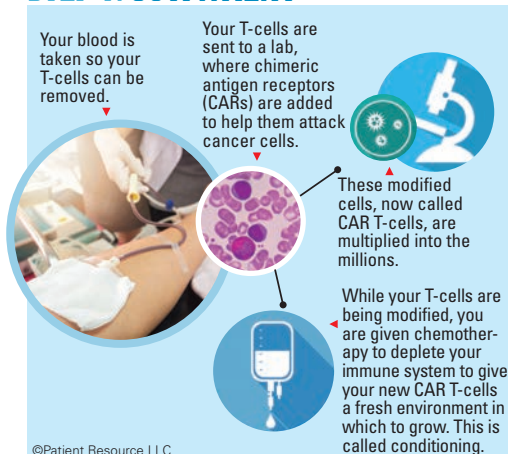
#### Adoptive Cellular Therapy (T-Cell Therapy)

There are two main approaches to adoptive cellular therapy, a treatment that enhances or changes the body's own immune cells to be able to fight cancer. In one strategy, the doctor isolates T-cells that have attached to a patient's tumor (tumor-infiltrating lymphocytes, or TILs), helps the T-cells multiply outside of the body and then administers them back to the patient.

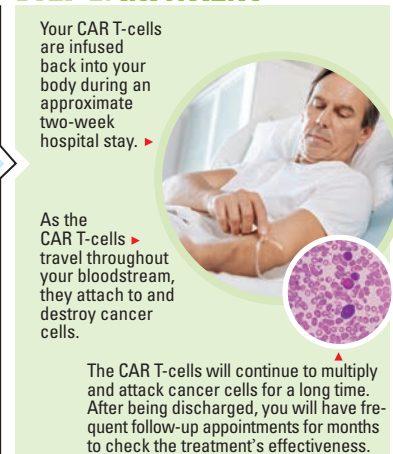
In the second strategy, a patient's T-cells are collected from a blood sample and chimeric antigen receptors (CARs) are added that enable the T-cells to recognize specific

**FIGURE 2**  
**CAR T-CELL THERAPY**

### STEP 1: OUTPATIENT



### STEP 2: INPATIENT



proteins on the surface of cancer cells. These engineered T-cells are called CAR T-cells (see Figure 2). They are multiplied in a laboratory and then infused back into the patient. The goal is for the T-cells to multiply, seek and destroy the cancer cells that carry those specific antigens.

Two CAR T-cell therapies are approved to treat certain blood cancers. These breakthrough therapies are giving hope to people with B-cell lymphoma and B-cell acute lymphoblastic leukemia. Clinical trials are evaluating applications for other types of leukemia as well as for lymphoma and multiple myeloma.

The benefits of CAR T-cell therapy include a high response rate, the possibility of long-term remission, the need for only one infusion (in most cases) and the long-term effectiveness of CAR T-cells, which are designed to work for many years in the bloodstream. Drawbacks include the high cost of the treatment and the risk of dangerous side effects, such as cytokine release syndrome (CRS), neurologic toxicities, B-cell aplasia, tumor lysis syndrome (TLS) and anaphylaxis. Most side effects are reversible, but they should be taken seriously.

#### Cytokines

Cytokines are proteins released by immune cells that communicate with other immune cells. Cytokine immunotherapy aids in communication among immune cells and plays a big role in the full activation of an immune response. This type of immunotherapy works by introducing large amounts of the following laboratory-made cytokines to the immune system to promote specific immune responses.

- *Interleukins* help regulate the activation of certain immune cells.
- *Interferons* boost the ability of certain immune cells to eliminate viral infections and attack cancer cells.
- *Granulocyte-macrophage colony stimulating factors* (GM-CSFs) stimulate the bone marrow, promoting the growth of immune and blood cells and the development of dendritic cells, which become antigen-presenting cells (cells that show the antigens to T-cells).

#### Immune Checkpoint Inhibitors

The immune system must regulate itself, and it only makes enough white blood cells to identify a single germ or abnormal cell present in the body.

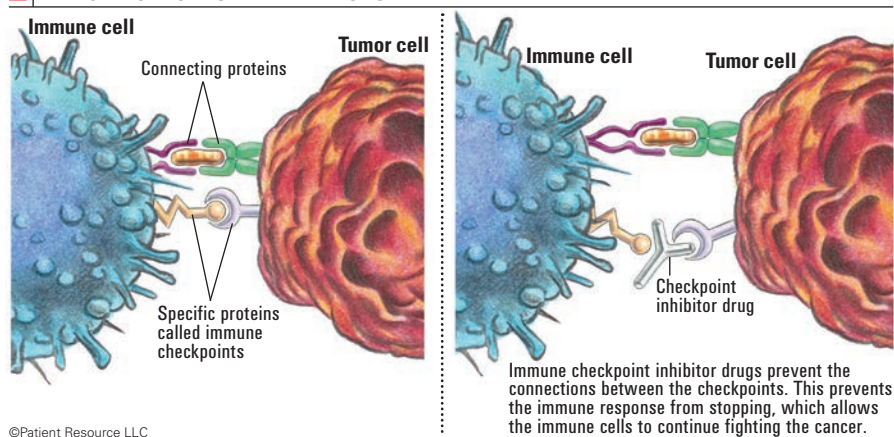
Once a target is identified for destruction by the immune system, killer cells are activated and increase in number to provide an immune response. After an attack, however, the immune system must slow down. It does this through the use of checkpoints.

Checkpoints keep the immune system "in check," preventing an attack on normal cells by using regulatory T-cells. When the correct proteins and cell receptors connect, a series of signals is sent to the immune system to slow down once an immune response is finished, such as when a virus is completely eliminated (see Figure 3). Three checkpoint receptors that slow down the immune system are identified for their roles in cancer treatment.

1. *CTLA-4* (cytotoxic T-lymphocyte-associated protein 4) is a receptor that binds with certain molecules to tell the immune system to slow down.
2. *PD-1* (programmed cell death protein 1) is



**FIGURE 3**  
**IMMUNE CHECKPOINT INHIBITORS**



a receptor involved with telling T-cells to die and to reduce the death of regulatory T-cells (suppressor T-cells). Both slow down an immune response. PD-1 can tell the immune system to slow down only if it connects with PD-L1.

3. *PD-L1 (programmed death-ligand 1)* is a protein that, when combined with PD-1, sends a signal to reduce the production of T-cells and enables more T-cells to die.

Checkpoint-inhibiting drugs prevent connections between checkpoints. This prevents the immune response from slowing down, which allows the immune cells to continue fighting the cancer. Along with keeping the immune response from slowing down, it also helps the immune system recognize cancer cells as foreign cells.

### Immunomodulators

Immunomodulatory agents may stimulate or slow down the immune system in indirect ways. They may boost the immune system and the effects of other therapies on the tumor and the tumor microenvironment, slow or stop the growth of the tumor and its blood vessel formation, improve the bone marrow microenvironment and have an anti-inflammatory effect, slowing the growth of the cancer.

### Monoclonal Antibodies

Also referred to as mAbs, these laboratory-made antibodies are designed to target specific tumor antigens (foreign substances). They can work in different ways, such as flagging targeted cancer cells for destruction, blocking growth signals and receptors, and delivering other therapeutic agents directly

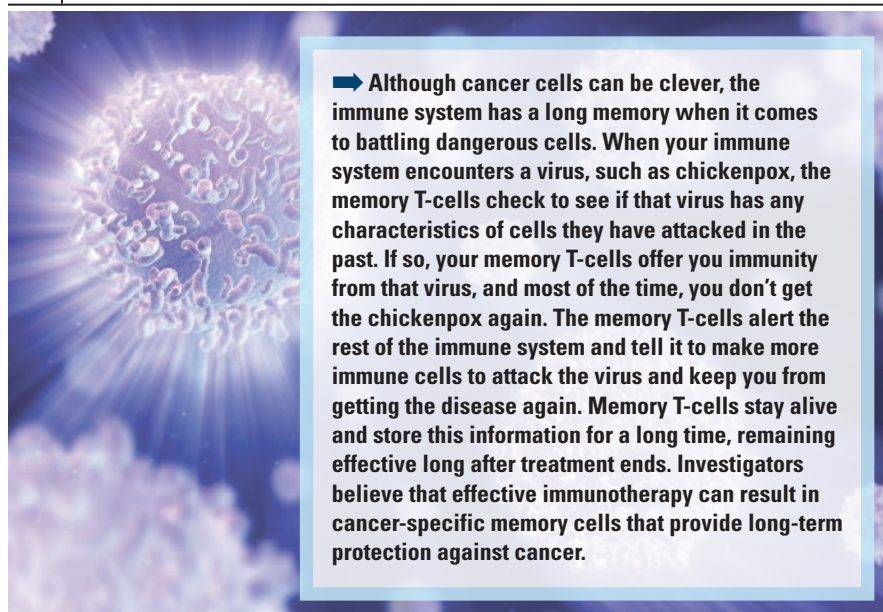
to targeted cancer cells. They can also be created to carry cancer drugs, radiation particles or laboratory-made cytokines (proteins that enable cells to send messages to each other) directly to cancer cells.

When a mAb is combined with a toxin, such as a chemotherapy drug, it travels through the system until it reaches the targeted cancer cell. Then it attaches to the surface, is swallowed by the tumor cell and breaks down inside the cell, releasing the toxin and causing cell death. Combining mAbs with radiation particles, a treatment known as radioimmunotherapy, allows radiation to be delivered in lower doses over a longer period of time. This direct form of radiation delivery typically damages only the targeted cells.

- *Naked mAbs* work by themselves. No drugs or radioactive particles are attached.
- *Conjugated mAbs* have a chemotherapy drug or a radioactive particle attached to them. They are used to deliver treatment to the cancer cells. These also are referred to as tagged, labeled or loaded antibodies.
- *Bispecific mAbs* are made up of two different mAbs and can attach to two different proteins at the same time. In some cases, the two proteins may both be on a cancer cell. In other cases, one protein may be on a cancer cell and one on a T-cell, thereby connecting the T-cell to a cancer cell.

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

## » HOW THE IMMUNE SYSTEM REMEMBERS



➡ 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 the chickenpox again. The memory T-cells alert the rest of the immune system and tell 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.

### Photopheresis

During photopheresis, blood is removed from the body and separated into red blood cells, white blood cells and platelets. The white blood cells are treated with ultraviolet light and drugs. The blood is then returned to the body, and the treated white blood cells boost the immune system in their attack on cancer cells. ■

### ADDITIONAL RESOURCES

- ▶ **Society for Immunotherapy of Cancer:**  
[www.sitcancer.org](http://www.sitcancer.org)
- ▶ **American Society of Clinical Oncology:**  
[www.cancer.net](http://www.cancer.net)  
*Understanding Immunotherapy*
- ▶ **National Cancer Institute:**  
[www.cancer.gov](http://www.cancer.gov)  
*Immunotherapy for Cancer*



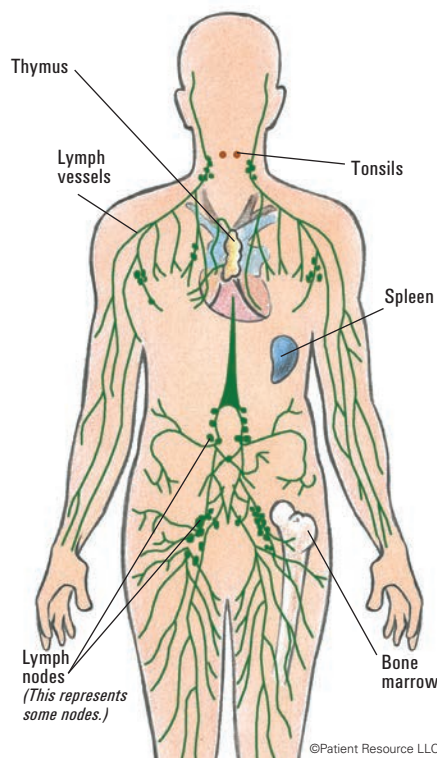
## LYMPHOMA

▲ **Cancer develops** when genes begin to change within the structure of normal cells. These cells – now called cancer cells – grow and push against normal cells. Sometimes they form tumors (or masses); other times, as in the case of most hematologic (blood) cancers, they don't. Hematologic cancers affect the way blood cells are developed and the way they function.

Lymphoma starts in the lymphatic system and affects lymphocytes, which are part of the immune system. It develops when normal lymphocytes transform into abnormal, cancerous cells that reproduce uncontrollably. As they multiply, they collect in the lymph nodes, bone marrow (the spongy center of bones where blood cells are made), spleen, tonsils or other organs, where they can form tumors. These cells eventually begin to outnumber normal cells, which can cause the lymph nodes, spleen or other organs to enlarge.

Sometimes, lymphoma begins outside the lymphatic system, such as in the mediastinum (the area in the chest behind the breastbone), the central nervous system (brain and spinal cord) or on the skin.

**FIGURE 1**  
▲ **THE LYMPHATIC SYSTEM**



To fully understand lymphoma, it helps to have a general knowledge of the lymphatic system. The lymphatic system is a network of tissues and vessels that carry fluid, called lymph, throughout the body. Lymph contains lymphocytes, a type of white blood cells.

The lymphatic system is made up of lymph nodes, as well as the spleen, thymus, adenoids and tonsils (see Figure 1). Lymph nodes are located throughout the body, with larger concentrations near the abdomen, groin, pelvis, underarms and neck.

The main types of lymphocytes that can develop into lymphomas are B-lymphocytes (B-cells) and T-lymphocytes (T-cells).

- **B-cells** produce protein antibodies that attach to infectious organisms, such as bacteria and viruses, marking them for destruction.
- **T-cells** attack infectious organisms directly and can identify and attack body cells infected with a virus or altered by cancer. They also play a part in controlling the immune system.

Both B-cells and T-cells can transform into lymphoma cells. In the United States, B-cell lymphomas are much more common than T-cell lymphomas.

### MORE ABOUT LYMPHOMA

Lymphoma can be classified as Hodgkin lymphoma (HL) or non-Hodgkin lymphoma (NHL).

NHL is much more common than HL and can be classified as indolent (slow growing) or aggressive (rapidly growing). NHL has more than 60 subtypes, and they vary in microscopic appearance and molecular features. They differ in how they affect the body and how they are treated. They also grow and spread at different rates.

If the initial treatment plan does not result in complete remission of your lymphoma, the disease is considered refractory. Immunotherapy is available to treat some types of refractory lymphomas. Different chemotherapy agents or targeted therapy drugs may be additional treatment options.

Relapsed lymphoma occurs when the disease comes back after successful treatment. A relapse can happen weeks, months or even years after initial treatment has ended. Treatments often reduce the amount of cancer cells, but some can remain undetected and continue to grow. Keep your follow-up appointments because finding any recurrence early is important. Your doctor will ask ques-



### QUESTIONS TO ASK YOUR DOCTOR

- ▶ **What type of lymphoma do I have?**
- ▶ **Would you recommend immunotherapy for my type of lymphoma?**
- ▶ **Have you had success treating lymphoma patients with immunotherapy?**
- ▶ **How will we know if the treatment is working?**
- ▶ **Will I be given other treatment options along with immunotherapy?**
- ▶ **What side effects can I expect in the short term and long term, and how will they be managed?**

tions about any ongoing symptoms you may be having, especially those related to recurrence and long-term side effects.

**Hodgkin lymphoma (HL)**, formerly known as Hodgkin disease, typically starts in the lymph nodes in the chest, neck or underarm and may spread to other lymph nodes or to other organs, such as the liver or lungs.

HL is classified as classical or nodular lymphocyte-predominant. The majority of HL cases are classical HL. The cancer cells found in classical HL are Reed-Sternberg cells, which are large, abnormal B-cell lymphocytes. Classical HL has four main subtypes:

1. **Nodular sclerosis HL** is the most common. It occurs most often in the lymph nodes in the mediastinum (central part of the chest) or neck.
2. **Mixed cellularity HL** is the second most common.
3. **Lymphocyte-rich HL** is less common than the first two.
4. **Lymphocyte-depleted HL** is the rarest. It is usually found in lymph nodes in the abdomen and also the spleen, liver and bone marrow. It is more aggressive than other types of HL.



Nodular lymphocyte-predominant HL accounts for the rest of the HL diagnoses. This type of lymphoma has large cells that are variants of Reed-Sternberg cells. Nodular lymphocyte-predominant HL is more similar to indolent B-cell NHL than classical HL and generally grows more slowly than classical HL. It usually begins in lymph nodes in the neck and under the arm.

**Non-Hodgkin lymphoma (NHL)** is one of the more common cancers after solid tumors in the United States. It starts in the lymphatic system, most often in the lymph nodes, liver, spleen or bone marrow, and it can involve the stomach, intestines, skin, thyroid, brain or any other part of the body where lymphatic tissue is found.

NHL is classified as indolent (slow growing) or aggressive (rapidly growing). Because more than 60 different subtypes of NHL exist, it can be difficult to classify. Determining the subtype is important because treatment will vary. Not all treatments will be effective for each subtype. Although the various types of NHL share some common features, they differ in their microscopic appearance, molecular features, growth patterns and effects on the body as well as treatment options.

Overall, the most common form of NHL is diffuse large B-cell lymphoma (DLBCL), which accounts for approximately 30 percent of all newly diagnosed cases of NHL. It is aggressive. The second most common type of lymphoma is follicular lymphoma. This type of lymphoma is indolent. Another indolent lymphoma is marginal zone lymphoma, which begins in the B-lymphocytes.

Most NHL subtypes affect the blood; however, another involves the skin. Cutaneous T-cell lymphoma (CTCL) is typically indolent but can sometimes be aggressive. Two subtypes of CTCL are mycosis fungoides and Sézary syndrome, which often appear as rashes, bumps or scaly patches on the skin.

## IMMUNOTHERAPY FOR LYMPHOMA

Types of immunotherapy that have been approved by the U.S. Food and Drug Administration (FDA) to treat lymphoma include adoptive cellular therapy, cytokines, immune checkpoint inhibitors, monoclonal antibodies and photopheresis. Talk with your doctor about the specific treatments that may be most effective for you.

**Adoptive cellular therapy (T-cell therapy)** is one of the newest types of immunotherapy

to be approved for certain lymphomas. The first two CAR T-cell therapies approved by the FDA were for lymphomas. One treats relapsed or refractory large B-cell lymphoma, including DLBCL, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma and DLBCL arising from follicular lymphoma.

The other approved CAR T-cell therapy is approved for patients up to 25 years of age who have B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse, adults with relapsed or refractory large B-cell lymphoma, including DLBCL not otherwise specified, high grade B-cell lymphoma and DLBCL arising from follicular lymphoma.

The introduction of these two therapies represents a breakthrough in treating lymphomas and is bringing hope to many by offering the possibility of long-term remission. Research in clinical trials continues to explore CAR T-cell therapies alone and in combination with other drugs for additional types of lymphomas as well as other types of cancer.

**Cytokines** are one of the very first immunotherapy strategies approved for any cancer and the first for some lymphomas. The type of cytokine approved for lymphomas includes interferons, which boost the ability of the immune cells to attack cancer cells as well as stimulate the immune system. Although they are not as widely used as they once were, they are still an option for treating certain types of lymphoma.

**Immune checkpoint inhibitors** are not widely used in treating lymphomas, but one is approved for classical HL that has relapsed or progressed after an autologous stem cell transplantation. Another is approved for primary mediastinal B-cell lymphoma. More research is needed to determine if immune checkpoint inhibitors approved for other types of cancer may be appropriate for additional types of lymphoma.

**Monoclonal antibodies (mAbs)** are widely used across many types of lymphoma. They include naked mAbs, conjugated mAbs and bispecific mAbs.

Several lymphoma diagnoses may be treated with mAbs, including anaplastic large cell lymphoma, DLBCL, follicular lymphoma, HL, intravascular B-cell lymphoma, lymphoplasmacytic lymphoma, mantle cell

## FDA-APPROVED CANCER IMMUNOTHERAPIES FOR SOME TYPES OF LYMPHOMA\*

- ▶ axicabtagene ciloleucel (Yescarta)
- ▶ brentuximab vedotin (Adcetris)
- ▶ ibritumomab tiuxetan (Zevalin)
- ▶ interferon alfa
- ▶ interferon alfa-2b (Intron A)
- ▶ lenalidomide (Revlimid)
- ▶ mogamulizumab-kpkc (Poteligeo)
- ▶ nivolumab (Opdivo)
- ▶ obinutuzumab (Gazyva)
- ▶ pembrolizumab (Keytruda)
- ▶ rituximab (Rituxan)
- ▶ rituximab-abbs (Truxima)
- ▶ rituximab and hyaluronidase human (Rituxan Hycela)
- ▶ tisagenlecleucel (Kymriah)
- ▶ venetoclax (Venclexta)

\*Each therapy is prescribed based on specific criteria. Discuss your options with your doctor. As of 3/14/19

lymphoma, marginal zone B-cell lymphoma, mycosis fungoides, Sézary syndrome, NHL, peripheral T-cell lymphoma, primary central nervous system lymphoma, primary cutaneous anaplastic large cell lymphoma and primary mediastinal B-cell lymphoma.

Researchers continue to expand the effectiveness of approved mAbs and discover new types that may be approved for lymphomas in the future. Consider asking your doctor if a clinical trial is an option for you.

**Photopheresis**, a type of immunotherapy first introduced in the 1980s, is used for cutaneous T-cell lymphoma (CTCL), a rare type of NHL, and other blood disorders.

Recent breakthroughs in research have resulted in improved treatment options for people with some types of lymphoma. Multiple drugs are being researched in late-stage clinical trials. Ask your doctor if a trial may be an option for you. ■

## ADDITIONAL RESOURCES

- ▶ **Society for Immunotherapy of Cancer:** [www.sitcancer.org](http://www.sitcancer.org)
- ▶ **Cutaneous Lymphoma Foundation:** [www.clfoundation.org](http://www.clfoundation.org)
- ▶ **Leukemia & Lymphoma Society:** [www.lls.org/Immunotherapy](http://www.lls.org/Immunotherapy)
- ▶ **National Cancer Institute:** [www.cancer.gov](http://www.cancer.gov)  
Adult Hodgkin Lymphoma Treatment—Patient Version  
Adult Non-Hodgkin Lymphoma Treatment—Patient Version
- ▶ **National Comprehensive Cancer Network:** [www.nccn.org](http://www.nccn.org)  
Follicular Lymphoma  
Hodgkin Lymphoma  
Non-Hodgkin's Lymphomas



## LEUKEMIA

▲ **Leukemia is a cancer** that begins in abnormal blood cells within the bone marrow of both children and adults. Normal white blood cells help fight infection as part of the body's immune system. When these cells become old or damaged, they die and are replaced with healthy new cells. But in leukemia, some of the white blood cells behave abnormally. They cannot fight infection properly, they grow uncontrollably and they don't die when they should.

As a result, large numbers of the abnormal cells accumulate in the bone marrow, crowding out healthy blood cells and slowing or preventing new healthy cells from being produced. Unlike many other types of cancer, leukemia does not form solid tumors. Instead, when these abnormal cells continue to grow unchecked, the number of healthy white blood cells, red blood cells and platelets is reduced, putting the individual at increased risk of infection. As leukemia cells spill into the bloodstream, they travel to the lymph nodes, spleen, liver and elsewhere in the body, affecting normal body functions.

Leukemia is most often diagnosed in people older than 55, but it's also the most common cancer diagnosed in children younger than 15 (see *Pediatric Cancer*, page 12).

### BONE MARROW AND TYPES OF BLOOD CELLS

Leukemia begins in the bone marrow, where blood is created, so knowing more about these important structures may help you better understand the disease (see Figure 1).

**Bone marrow** is the soft, spongy center of some bones. It contains immature blood stem cells, more developed blood-forming cells, fat cells and tissues that support cell growth.

**Platelets** are blood cells that gather around wounds, forming clots to stop the bleeding. They also help repair wounds and create blood vessels.

**Red blood cells** (erythrocytes) carry oxygen from the lungs to other parts of the body.

**White blood cells** (leukocytes) are essential to the immune system as the infection fighters of the body. There are several types of white blood cells. These two types are involved in leukemia:

1. **Lymphocytic cells** (lymphocytes) make up lymphoid tissue found in the lymph nodes, thymus, spleen, tonsils and elsewhere in the body. Lymphocytes can be B-lymphocytes (B-cells), T-lymphocytes (T-cells) or natural killer (NK) cells.
2. **Myeloid (myelogenous) cells** begin as immature blood stem cells that develop into red blood cells, white blood cells (excluding lymphocytes) and platelets.

### MORE ABOUT LEUKEMIA

Leukemia is classified by how rapidly the abnormal cells grow, the kind of blood cell in which the disease starts and its response to treatment.

**Acute leukemia** cells grow rapidly. They look similar to immature white blood cells, and as their numbers increase, the bone marrow is prevented from making normal, healthy blood cells.

**Chronic leukemia** cells look similar to healthy, mature white blood cells, but the cells are unable to mature fully. These leukemia cells grow slowly, and the progression of chronic leukemia varies from person to person.

**Lymphocytic leukemia** begins in bone marrow in cells that develop into white blood cells called lymphocytes. Lymphocytic leukemia is also sometimes called lymphoid or lymphoblastic leukemia.

**Myeloid leukemia** begins in early myeloid



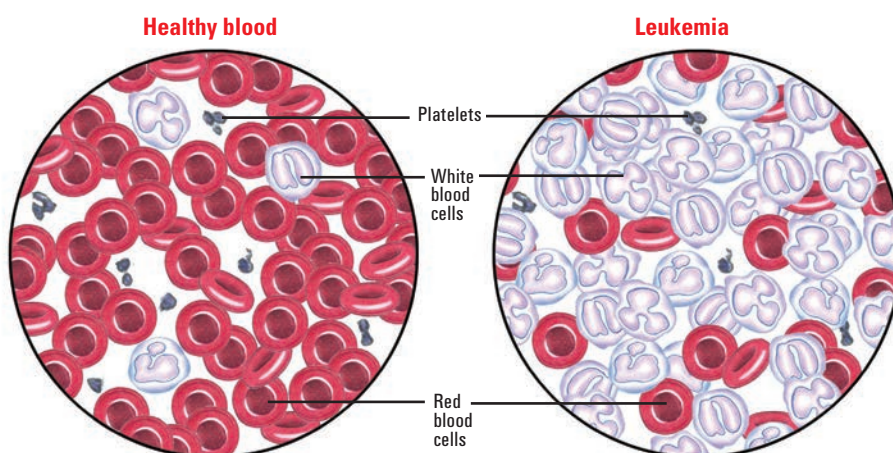
### QUESTIONS TO ASK YOUR DOCTOR

- ▶ What type of leukemia do I have?
- ▶ How does immunotherapy work? Do you recommend it for my type of leukemia?
- ▶ Have you had success treating leukemia with immunotherapy?
- ▶ How and where will I receive treatments, and for how long?
- ▶ What side effects should I expect – short term and long term – and how will we manage them?

blood cells in the bone marrow. Myeloid leukemia is sometimes called myelogenous, myelocytic or myeloblastic leukemia.

**Refractory leukemia** is when leukemia cells are still present after some other treatment has been tried. Immunotherapy is available to treat some types of refractory leukemia. Your doctor will take into account the therapies you have already tried and your overall health before recommending another treatment plan.

**FIGURE 1**  
▲ LEUKEMIA BLOOD CELLS



Leukemia is cancer that starts in blood-forming tissue, such as the bone marrow, and causes a large number of white blood cells to be produced. These cells don't function as expected, meaning they don't fight infection or die as they should. They also overcrowd healthy white blood cells, red blood cells and platelets in the bone marrow, preventing them from functioning properly.

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**Relapsed leukemia** is the name given to leukemia that initially responds to treatment but stops responding after six months or more. Some types of leukemia have multiple relapses, which are also referred to as recurrences. If your cancer relapses, your doctor will begin a new cycle of diagnostic tests. These tests may include another tissue biopsy and laboratory tests. The doctor will confirm if the cancer is recurrent and determine if it has transformed into a more aggressive subtype, which will affect your new treatment plan.

## IMMUNOTHERAPY FOR LEUKEMIA

Immunotherapy and other research advances are enabling more people with leukemia to live longer after treatment. Some types of leukemia are treated with approved immunotherapies, and some are treated in clinical trials. Each type of leukemia responds differently to various therapies, so your medical team will recommend treatment options based on your type of blood cancer and other factors, including your age, overall health and prognosis (predicted outcome from treatment). One or a combination of treatments may be used with immunotherapy, including chemotherapy, targeted therapy and stem cell transplantation.

It's important to find a doctor experienced in treating the type of leukemia you have. A hematologist who specializes in your type of leukemia will be familiar with the most suitable options, including immunotherapy treatments that are being evaluated in clinical trials. If receiving treatment from an expert in the field will involve traveling and that isn't an option, you may find a specialist willing to consult with your local doctor.

Following are some types of leukemia and the immunotherapies available to treat them.

**Acute lymphocytic leukemia (ALL)** progresses rapidly and, if untreated, can spread from the blood and bone to other parts of the body. Treatment is recommended soon after diagnosis because these fast-growing cells can quickly become life-threatening. ALL is the most common type of leukemia diagnosed in children and adolescents.

Biomarker testing can now identify molecular abnormalities associated with ALL. Testing for these abnormalities allows your doctor to choose treatments that target specific biological features. Chromosomal abnormalities have been found with ALL, specifically the Philadelphia chromosome.

Genes that may be tested include *BCR-ABL*, *TEL* and *AML1*.

The first immunotherapy approved to treat a form of ALL was a monoclonal antibody in 2014. In 2017, the first gene therapy was approved in the United States to treat children and young adults with B-cell ALL. This breakthrough treatment is called chimeric antigen receptor (CAR) T-cell therapy (see Figure 2, page 2).

**Chronic lymphocytic leukemia (CLL)** is a slow-growing blood cancer of the lymphatic system and the most common type of leukemia diagnosed in adults. Abnormal white blood cells (lymphocytes) multiply, accumulating over time in the blood, bone marrow, lymph nodes and spleen. This interferes with the production of red blood cells, which carry oxygen; white blood cells, which fight infection; and platelets, which are needed for blood to clot.

Genetic testing, also referred to as molecular profiling, may be done to look for certain gene abnormalities or mutations, proteins and changes in chromosomes that may indicate how the disease may progress. Doctors use these tests to determine whether there are chromosomal or other genetic changes in lymphocytes. Healthy cells in the body contain 23 pairs of chromosomes, but CLL cells often have abnormal chromosome changes, such as deletions or missing parts. In CLL, it is common for parts of chromosomes 11, 13 or 17 to be missing. This is known as a deletion and is often an indication of how slowly or quickly the disease will progress. For example, a deletion in chromosome 13 means that the CLL cells grow slowly, and a deletion in chromosome 17 means the disease will progress quickly and be difficult to treat.

Some monoclonal antibodies, used alone and in combination with other therapies, are approved to treat CLL.

**Chronic myeloid leukemia (CML)** is a slow-growing cancer that develops in abnormal immature myeloid cells, which become white blood cells (other than lymphocytes), red blood cells or cells that make platelets. Biomarkers used to confirm a diagnosis of CML include tests for the *BCR-ABL1* fusion gene and Philadelphia chromosome.

CML may be treated with an interferon, a type of immunotherapy called a cytokine. It is typically not used as a first-line treatment. Ask your doctor if it is appropriate for you.

## FDA-APPROVED CANCER IMMUNOTHERAPIES FOR SOME TYPES OF LEUKEMIA\*

- ▶ alemtuzumab (Campath)
- ▶ blinatumomab (Blinicyto)
- ▶ interferon alfa
- ▶ interferon alfa-2a (Roferon-A)
- ▶ interferon alfa-2b (Intron A)
- ▶ moxetumomab pasudotox-tdfk (Lumoxiti)
- ▶ obinutuzumab (Gazyva)
- ▶ rituximab (Rituxan)
- ▶ rituximab and hyaluronidase human (Rituxan Hycela)
- ▶ tisagenlecleucel (Kymriah)
- ▶ venetoclax (Venclexta)

\*Each therapy is prescribed based on specific criteria. Discuss your options with your doctor. As of 3/14/19

**Hairy cell leukemia** is rare. The unique name comes from the appearance of its cells under a microscope. Hairy cell leukemia begins when certain blood stem cells become abnormal, accumulating in the blood and bone marrow to leave less room for healthy cells and platelets.

One type of immunotherapy approved for this type of leukemia is a cytokine. The approval of alpha interferon in 1986 represented a new advance for treating hairy cell leukemia. Before then, splenectomy (spleen removal) was the only known effective therapy for this disease. Interferon benefited people with active hairy cell leukemia, with or without having a splenectomy. Today, interferon has a relatively limited role in treating this type of leukemia. Ask your doctor if it may be beneficial for you.

It is important to learn as much as possible about your type of leukemia and the available options so you can confidently partner with your medical team to make treatment decisions and manage your disease. ■

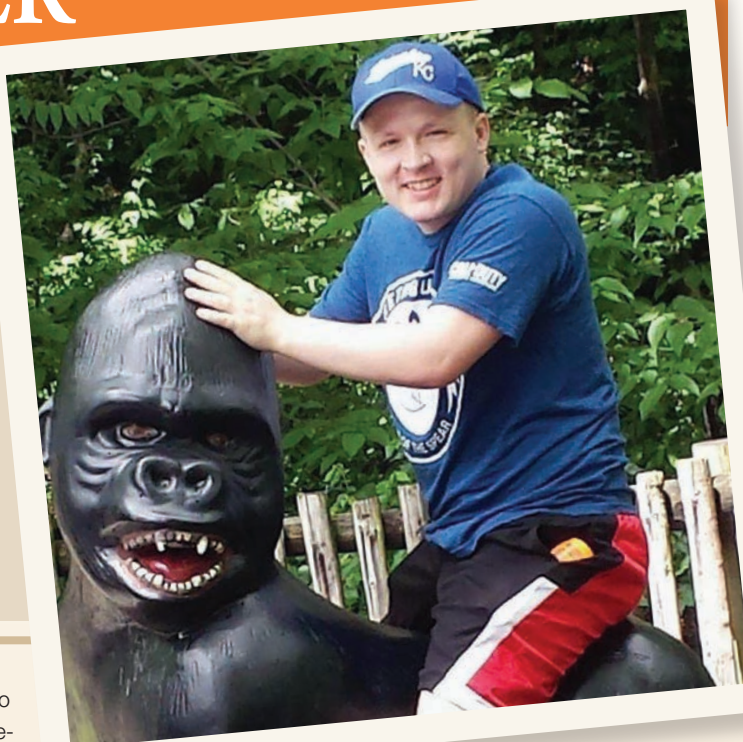
## ADDITIONAL RESOURCES

- ▶ **Society for Immunotherapy of Cancer:**  
[www.sitcancer.org](http://www.sitcancer.org)
- ▶ **American Cancer Society:**  
[www.cancer.org](http://www.cancer.org)  
*Leukemia*
- ▶ **Cancer Research Institute:**  
[www.cancerresearch.org](http://www.cancerresearch.org)  
*Leukemia Immunotherapy*
- ▶ **Cancer Support Community:**  
[www.cancersupportcommunity.org](http://www.cancersupportcommunity.org)  
*Immunotherapy for Leukemia and Lymphoma*
- ▶ **Leukemia & Lymphoma Society:**  
[www.lls.org](http://www.lls.org)  
*Immunotherapy*



# SHOW CANCER WHO'S BOSS

➡ *At 22 years old, Brandon Woods knew something was wrong when he couldn't complete the drill exercises that were part of his weekend requirement for being in the National Guard. The fatigue became worse, and he struggled to breathe. His family rushed him to the hospital, and he was diagnosed with acute lymphocytic leukemia (ALL). He's had several treatments and is grateful for the support he received. He is now focused on giving back and works to raise awareness about blood and stem cell donations.*



▲ Brandon at a local amusement park enjoying a full life after battling cancer

**W**hile I was in the National Guard, I had to go to my drill weekends, which is when reservists resume their military careers once a month. During my February 2016 drill weekend, I noticed I was struggling with exercising. I couldn't do as many sit-ups or push-ups as normal. When I started my 2-mile run, I couldn't run. I could only walk, and it was hard to breathe. I just thought I was tired.

Two weeks later, I noticed a grapefruit-sized bruise on my right leg, followed by one on my left leg. I developed another bruise from my elbow to my wrist on my right side. I also had blood in my nose. During spring break, I played pickleball but my teammates said I had no color in my face and that I looked like I was turning blue. When I went home, my aunt and uncle took one look at me and said they were taking me to the ER.

The first doctor I saw said my blood looked "leukemic." Those words put me on edge. I was scared. I wanted answers yesterday. The doctor ordered a bone marrow biopsy that confirmed I had acute lymphocytic leukemia (ALL).

The doctors started treatment right away, and I spent the next month in the hospital. I received two different chemotherapies, rotated every few days for three months, as the doctors prepared me for a stem cell transplantation.

My brothers and sister were tested to see if one could be a donor. All of my siblings were a 50 percent match to me, but they were 100 percent matches to each other. Even so, my brother, Tyler, donated his stem cells, and I had an allogeneic transplant over the summer using his stem cells.

The chemotherapy caused me to lose my hair and eat a lot. I felt slow and sluggish. Basically, I slept and ate, and I struggled with nausea and vomiting. I did have a bit of Graft-vs-Host Disease, but it wasn't too severe. One of the strangest side effects is the possibility of inheriting conditions from your donor. Tyler had eczema. I'd never had it before, but after the transplant, I started getting it.

Months later, testing showed some cancer had been destroyed, but the doctors wanted to see a better response. They planned for a second stem cell transplant as a preventive measure, but I decided not to get one so I could return to college.

In August 2017, I heard about CAR T-cell therapy being done at a university hospital for people under 25 with ALL. That spring, I asked my oncologist if I could try the treatment. I was enrolled in a clinical trial and received the CAR T-cell therapy later that spring. I spent nine days in the hospital after receiving it. I ran a fever and had the worst headache I've ever had, but I didn't vomit or have other serious complications. The treatment became approved by the U.S. Food and Drug Administration shortly after my trial. Doctors will continue to monitor me, but they hope to see the treatment last for months and, hopefully, years.

Throughout all of this, I relied on my friends and family as well as the nurses and other staff that helped care for me. They were always a phone call or a button press away.

Because of the help and kindness I received, I want to give back and raise awareness for blood and bone marrow donations. I floated the idea for a bone marrow drive at the clinic during one of my checkups. They liked it and helped me work with Be the Match and the community blood center to set it up. The drive took place in the fall of 2018.

I know it's a cliché, but even if the doctors tell you there's a 1 percent chance of surviving, it's still a chance at survival. Don't give up. Reach out to people, don't be afraid to ask questions, learn as much as you can about your cancer so you can make the most educated decisions, and remember — you are the boss of your treatment. ■



## MULTIPLE MYELOMA

▲ **Multiple myeloma** is a hematologic (blood) cancer that develops when the blood's plasma cells transform and grow uncontrollably.

Plasma cells are produced in the bone marrow. As a type of white blood cell that produces antibodies to fight infection when they identify a threat, they are a part of the immune system, a network of cells, organs and tissues that work together to defend your body against germs and infection.

To better understand multiple myeloma, it helps to have a general knowledge of bone marrow and blood cells.

- **Antibodies** are proteins created from plasma cells as a reaction to foreign substances, such as bacteria, in the body.
- **Bone marrow** is the soft, spongy center of some bones that contains immature blood stem cells, more mature blood-forming cells, fat cells and tissues that support cell growth. The immature blood stem cells, known as hematopoietic stem cells, develop into several types of blood cells, including white blood cells, red blood cells and platelets.
- **Lymphocytes** are the primary cells in lymphoid tissue, which is a major part of the immune system. These cells develop from lymphoblasts (immature cells found in bone marrow) into mature, infection-fighting cells. Subtypes of these cells include B-lymphocytes (B-cells) and T-lymphocytes (T-cells).
- **Plasma cells** develop from B-lymphocytes and produce antibodies to fight germs and viruses and stop infection and disease.

### WHAT IS MULTIPLE MYELOMA?

When abnormal plasma cells grow out of control, they can weaken the immune system by preventing healthy plasma cells from producing antibodies. Abnormal, cancerous plasma cells are called myeloma cells, and like normal plasma cells, myeloma cells make antibodies. But myeloma cells are all the same and produce too much of the same antibody. These antibodies are called monoclonal antibody proteins, or M-proteins. M-proteins accumulate in the blood and urine and can lead to damage of the kidneys or other organs.

In people with multiple myeloma, the myeloma cells multiply uncontrollably and accumulate in bone marrow, solid parts of bone and occasionally in other organs. This accumulation of myeloma cells usually occurs in multiple areas of the bones in the body, giving the disease its name, "multiple myeloma" (see Figure 1).

When the cells collect in bone marrow, they slow down the growth of healthy white blood cells, red blood cells and platelets. These cells collect in solid bone, causing holes called lytic lesions. The majority of people with multiple myeloma have these lesions when their disease is diagnosed.

Multiple myeloma is a type of cancer that may return. Because few people who have it are currently cured, doctors now treat it similarly to a chronic condition. Relapsed multiple myeloma occurs when the disease comes back after initial treatment. Refractory myeloma is when the disease does not respond to treatment or it stops responding to a treatment that previously worked.

### IMMUNOTHERAPY FOR MULTIPLE MYELOMA

Recent treatment advances, including those using immunotherapy, are helping make it possible for some people to manage their

### FDA-APPROVED CANCER IMMUNOTHERAPIES FOR MULTIPLE MYELOMA\*

- ▶ daratumumab (Darzalex)
- ▶ elotuzumab (Empliciti)
- ▶ lenalidomide (Revlimid)
- ▶ pomalidomide (Pomalyst)
- ▶ thalidomide (Thalomid)

\*Each therapy is prescribed based on specific criteria. Discuss your options with your doctor. As of 3/14/19

disease and live longer with a better quality of life. Types of immunotherapy approved to treat multiple myeloma include immunomodulatory agents and monoclonal antibodies (mAbs).

To treat multiple myeloma, immunomodulatory agents are often combined with antiangiogenic agents, which may prevent the growth of new blood vessels that tumors need to grow. They are also often combined with a corticosteroid. Immunomodulatory agents are most often used along with other treatments to improve initial response, stimulate the immune system and/or stop disease progression. These drugs can be effective in treating newly diagnosed multiple myeloma and relapsed or refractory disease.

Additionally, mAbs are a treatment option that may be used alone or in combination with other systemic therapies, such as a corticosteroid or an immunomodulatory agent.

These and other types of immunotherapy are also currently in clinical trials, so be sure to discuss this potential treatment option with your health care team. ■

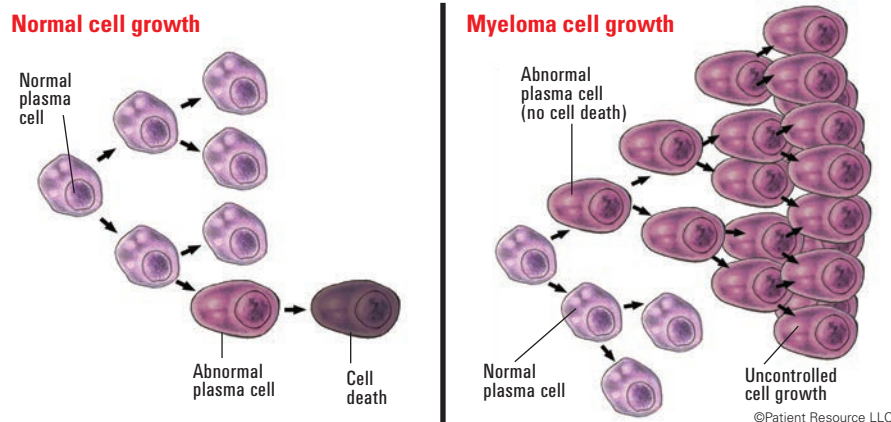
### QUESTIONS TO ASK YOUR DOCTOR

- ▶ Have you had success treating multiple myeloma with immunotherapy?
- ▶ How long will I be on treatment?
- ▶ What short-term and long-term side effects can I expect, and how serious could they be?

### ADDITIONAL RESOURCES

- ▶ **Society for Immunotherapy of Cancer:** [www.sitcancer.org](http://www.sitcancer.org)
- ▶ **American Society of Clinical Oncology:** [www.cancer.net](http://www.cancer.net)  
*Multiple Myeloma: Types of Treatment*
- ▶ **Multiple Myeloma Research Foundation:** [www.themmr.org](http://www.themmr.org)  
*Standard Treatments*
- ▶ **National Cancer Institute:** [www.cancer.gov](http://www.cancer.gov)  
*Plasma Cell Neoplasms (Including Multiple Myeloma) Treatment*  
*T-Cell Transfer Therapy*

**FIGURE 1**  
▲ UNCONTROLLABLE MYELOMA CELL GROWTH





## SUPPORTIVE CARE

▲ **These valuable services** help you and each of your family members maintain a good quality of life from the time you're diagnosed through treatment and survivorship.

A primary focus of supportive care is to help manage any physical and/or emotional distress that stems from your illness and treatment side effects. Your health care team's goal is to successfully treat your cancer while minimizing the discomfort and disruption to your normal activities as much as possible.

As with most cancer treatments, it is natural to expect some side effects. The key is to notice and report symptoms as soon as they begin so your health care team can address them before serious complications occur.

Before you begin immunotherapy, discuss potential side effects with your doctor. They may differ significantly depending on the therapy, so request a list of symptoms specific to the type you'll receive. Learn what to watch for and how to respond.

### IMMUNE-RELATED ADVERSE EVENTS:

#### KNOW WHEN TO CALL YOUR DOCTOR

Severe side effects from immunotherapy aren't common but can occur. Prompt recognition of symptoms and early intervention can often resolve these and allow you to stay on treatment longer. That's why it's very important to report side effects to your doctor or nurse as soon as possible.

Side effects may develop weeks or months after immunotherapy ends. Remain alert to symptoms and report them for at least six to 12 months following treatment. Be sure to contact your health care team if they occur between scheduled appointments.

The most serious side effects from immunotherapy are immune-related adverse events (irAEs). Although rare, irAEs can develop rapidly and potentially be life-threatening without medical attention. They may occur when the immune system is overstimulated by treatment and attacks healthy tissues.

The following describes systems that may be affected, the irAEs and symptoms.

- **Cardiovascular** (cardiomyositis): chest pain, shortness of breath, leg swelling, rapid heartbeat, changes in EKG reading
- **Endocrine** (endocrinopathies): hyperthyroidism, hypothyroidism, extreme fatigue, persistent or unusual headaches, visual changes, alteration in

mood, change 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): tingling, numbness, a burning sensation or a loss of feeling in the hands or feet, pain, sensory overload, sensory deprivation
- **Neurologic** (encephalitis): confusion, hallucinations, seizures, mood or behavior changes, neck stiffness, extreme light sensitivity
- **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)

**Cytokine release syndrome** is an irAE associated with adoptive T-cell therapies and monoclonal antibodies. Reactions are generally mild but can be severe and become life-threatening without medical attention. Symptoms may include headache, fever, nausea, rash, low blood pressure and rapid heartbeat. If you have difficulty breathing, contact your doctor immediately.

### COMMON SIDE EFFECTS

**Constipation** can be very uncomfortable and can also lead to serious medical issues. If dietary changes and over-the-counter solutions don't help, it's important to ask your doctor for help with managing this condition.

## Nurture your emotional well-being

→ **Resources and referrals are available from your health care team to help you manage emotional issues that can arise from your cancer diagnosis, treatment and changing life circumstances.**

**You can also take advantage of proven coping strategies often recommended for people who have cancer. Fresh air, journaling, physical activity and support groups may help you manage your emotions. Consider the following suggestions for dealing effectively with specific emotions.**

► **Anger:** Avoid expressing your anger in unhealthy ways by finding safer alternatives. Punch a pillow or engage in intense physical activity. Yell as loud as you can when you're alone. Talk with a trusted friend about your feelings.

► **Anxiety:** Explore relaxation techniques, such as deep breathing, meditation, yoga, muscle relaxation exercises or massage. Share your anxieties with a good listener. Find out if your treatment facility offers cancer-related informational meetings so you can learn more about what to expect.

► **Depression:** Discuss ongoing feelings of sadness, hopelessness, despair or emotional numbness with your health care team immediately. Depression is a potential side effect of some immunotherapy treatments. It can also occur if your disease symptoms or treatment side effects aren't being relieved. Contact your doctor if depression continues for more than a week. Get immediate medical attention if you have thoughts of suicide.

► **Emotional overload:** Deep breathing



exercises, yoga, meditation or guided imagery may be useful in calming your mind. Make a concerted effort to focus on just one thing at a time. Delegate tasks and chores to friends and loved ones who can lend a hand.

► **Fear:** Knowledge helps alleviate fear. Research your type of cancer and learn as much as possible about your treatment plan so you'll know what to expect. Join a support group or find one online to talk with others who've had similar experiences and challenges.

► **Grief:** It's normal to mourn the loss of your health and a future that didn't include cancer. Your diagnosis may also trigger repressed grief from losing a loved one to cancer in the past. Allow yourself permission to fully grieve. Turn to loved ones or a spiritual community for comfort.

► **Indecisiveness:** Facing such an illness and having your routine upended can make it difficult to focus enough to make clear decisions. Take charge of the things you can control, and ask people close to you to handle day-to-day decisions for now.



**Coughing or difficulty breathing** should be reported to your doctor immediately. Coughing may signal pneumonitis (inflammation of the lungs).

**Diarrhea** is common with immune checkpoint inhibitors and cytokines. It can lead to dehydration and electrolyte imbalance and may signal that the immune system is nearing overload. Contact your health care team immediately if you have four or more bowel movements than usual in a day, episodes that keep you home-bound or severe abdominal cramping.

**Fatigue** is one of the most common side effects of immunotherapy. Cancer-related fatigue can leave you physically and emotionally exhausted. Balance activity with rest each day, focusing only on activities most important to you.

**Flu-like symptoms** may occur with cytokines and include fever, chills, aches, headaches, drowsiness, nausea, vomiting, runny nose, loss of appetite and blood pressure changes.

**Heart palpitations** may occur with certain types of immunotherapy. Contact your doctor immediately about abnormal heart rhythm, dizziness or lightheadedness.

**Infusion-related reactions** usually occur soon after exposure to the drug and may include itching, rash or fever. Serious symptoms are shaking, chills, low blood pressure, dizziness, breathing difficulties and irregular heartbeat. Your doctor may slow the drug's delivery, stop it or recommend analgesics, antihistamines or corticosteroids.

**Injection site reactions** can be painful. Discuss these with your health care team. Your doctor may modify your treatment.

**Mouth sores** may begin as mild pain or burning in the lips, gums, tongue or roof of the mouth, followed by white patches and then large red lesions. Report symptoms right away. Drink plenty of fluids, and brush your teeth with a soft-bristle toothbrush.

**Muscle and joint pain** may occur with immune checkpoint inhibitors. Pain ranges from mild to severe, affecting the whole body or just certain areas. Pain typically resolves when treatment ends. If it persists or worsens, discuss pain management options with your doctor.

**Nausea and vomiting** may occur, particularly when immunotherapy is combined with

other therapies. Avoid unpleasant odors, eat small meals and ask your doctor about anti-emetics (anti-nausea medications).

**Skin reactions**, such as bumpy or itchy red rashes, are common with immune checkpoint inhibitors. Be alert for changes in skin color, inflammation, blistering, hives, dryness, cracking around fingertips, flushing or redness. A corticosteroid, numbing medicine, antihistamine, medicated cream or antibiotic may be recommended.

**Swelling in legs** (edema) results from fluid buildup. The effects may be reversed, so tell your health care team about any recent weight gain or swelling, stiffness or heavy feeling in your legs. ■

#### ADDITIONAL RESOURCES

- ▶ **Society for Immunotherapy of Cancer:** [www.sitcancer.org](http://www.sitcancer.org)
- ▶ **American Society of Clinical Oncology:** [www.cancer.net](http://www.cancer.net)  
*Side Effects of Immunotherapy*
- ▶ **CancerCare:** [www.cancercare.org](http://www.cancercare.org)  
*Coping*
- ▶ **National Cancer Institute:** [www.cancer.gov](http://www.cancer.gov)  
*Immunotherapy for Cancer*



Society for Immunotherapy of Cancer

## SITC Cancer Immunotherapy connectED

*Your free resource for cancer immunotherapy patient education from the Society for Immunotherapy of Cancer (SITC)*

**Access the following free online activities to learn about cancer immunotherapy:**

- Download disease specific resources for patients and caregivers (available in English and Spanish)
- Engage in online companion activities for the *Understanding Cancer Immunotherapy* Patient Resource Guides to learn about cancer immunotherapy side effects, immunotherapy in clinical trials and more
- Hear from a cancer survivor and an expert in the field about how the immune system can be harnessed to fight cancer in *The Global Promise of Immunotherapy* webinar

Sign up for a free SITC connectED account at [sitcancer.org/patient](http://sitcancer.org/patient)





## PEDIATRIC CANCER

▲ **No parent is prepared for** the life-altering words, “Your child has cancer.” But research and treatment advances such as immunotherapy are dramatically improving quality of life and outcomes for children and teenagers diagnosed with blood cancers.

Leukemia is the most common childhood cancer (see *Leukemia*, page 6), and the majority of these diagnoses are acute lymphoblastic leukemia (ALL). Regardless of the diagnosis, knowing where to begin and how to make the important decisions ahead may be overwhelming. These strategies can help you make a plan and move forward logically.

- **Find a pediatric oncologist and/or treatment center.** Treating children is different from treating adults because they aren’t just small adults. It’s essential to work with a pediatric oncologist experienced in treating blood cancers. If this involves travel and temporary lodging,

some treatment centers and hospitals may offer no-cost or reduced-rate family accommodations. Check resources listed on the following page, or ask your nurse navigator for recommendations.

- **Become a student of your child’s disease.** Try to learn as much as possible about your child’s diagnosis and treatment options so you can effectively partner with your medical team to make shared decisions about care. Ask for their insight and informational resources, and research online on your own using listings in this guide (see *Assistance & Support Resources*, page 13).
- **Consider a clinical trial.** Children with cancer often receive treatment through clinical trials to access promising new treatments that aren’t otherwise available. Children younger than 18 cannot legally consent to participate, but your health care team can explain the trial using age-appropriate language and aids in an “assent” process similar to Informed Consent.
- **Access supportive care services early.** Supportive care helps the whole family

maintain a good quality of life throughout your child’s treatment and beyond (see *Supportive Care*, page 10). Ask about it as soon as your child is diagnosed to help manage side effects and to learn about resources for play or music therapy, nutrition advice, counseling, programs for siblings, pediatric oncology camps, spiritual guidance and more.

Remember, your child takes cues from you. Think positively and do your best to forge ahead with confidence, and your child will likely do the same. ■

### ADDITIONAL RESOURCES

- ▶ **American Childhood Cancer Organization:** [www.acco.org](http://www.acco.org)
- ▶ **CancerCare for Kids:** [www.cancercareforkids.org](http://www.cancercareforkids.org)
- ▶ **Leukemia & Lymphoma Society:** [www.lls.org/childhood-blood-cancer](http://www.lls.org/childhood-blood-cancer)
- ▶ **National Cancer Institute:** [www.cancer.gov](http://www.cancer.gov)  
*Children with Cancer: A Guide for Parents Support for Families with Cancer*
- ▶ **National Childhood Cancer Society:** [www.thencs.org](http://www.thencs.org)

## CLINICAL TRIALS

➔ The rapidly increasing number of new and more effective therapies for hematologic cancers is the result of clinical trial research. And although more types of immunotherapy treatments are now approved, a clinical trial may offer an option better suited for your diagnosis.

In addition to asking your doctor about available clinical trials, you can research them on your own. Information about numerous clinical trials is at your fingertips online, but navigating online search tools can be frustrating. To help get you started, these screenshots of a mock search site for clinical trials are shown with step-by-step instructions.

Have your exact diagnosis, pathology report and details of previous treatments handy. If you don’t initially find a good fit, keep checking because new clinical trials are continually added. You can still move ahead with your current treatment plan while you search for clinical trials to discuss with your doctor.

### STEP 1 FILL IN YOUR INFORMATION

**YOUR DIAGNOSIS:** For example, enter “leukemia.” To create more options, you can also search for “acute lymphoblastic leukemia” or “acute lymphocytic leukemia” and compare results.

**DESIRED LOCATION:** For a clinical trial close to home, enter your address. Enter additional locations if traveling for treatment is an option.

**OTHER TERMS:** You can refine your search by including a specific drug, a type of treatment such as “immunotherapy,” or the study’s National Clinical Trial identifier, a unique eight-digit code (preceded by “NCT”) assigned to each trial.

### STEP 2 READ YOUR SEARCH RESULTS

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

**SUMMARY OF STUDY:** The purpose of the trial, the treatment being evaluated and other important information are detailed here. This section is usually written for health care professionals, so it may be difficult to interpret. In that case, print out the information to discuss with your doctor.

**ELIGIBILITY CRITERIA:** This outlines the criteria you must meet to qualify to join the clinical trial, such as cancer type, disease stage, sites of metastasis, general health requirements and previous treatments.

**CONTACTS AND LOCATIONS:** This section may list contact information for people who may be able to provide further details about the study, such as trial investigators, staff or sponsors.

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

### CLINICAL TRIAL RESOURCES

- ▶ **ClinicalTrials.gov** [www.clinicaltrials.gov](http://www.clinicaltrials.gov)
- ▶ **CenterWatch** [www.centerwatch.com](http://www.centerwatch.com)
- ▶ **National Cancer Institute** [www.cancer.gov/clinicaltrials](http://www.cancer.gov/clinicaltrials)
- ▶ **ACT (About Clinical Trials)** [www.learnaboutclinicaltrials.org](http://www.learnaboutclinicaltrials.org)
- ▶ **LIVESTRONG Foundation** [www.livestrong.org](http://www.livestrong.org)
- ▶ **AccrualNet** [accrualnet.cancer.gov](http://accrualnet.cancer.gov)
- ▶ **Jason Carter Clinical Trials Program (blood cancers)** [www.jasoncarterclinicaltrialsprogram.org](http://www.jasoncarterclinicaltrialsprogram.org)
- ▶ **NCI Contact Center (cancer information service)** 800-422-6237
- ▶ **Lazarex Cancer Foundation** [www.lazarex.org](http://www.lazarex.org)
- ▶ **Center for Information & Study on Clinical Research Participation** [www.searchclinicaltrials.org](http://www.searchclinicaltrials.org)
- ▶ **My Clinical Trial Locator** [myclinicaltriallocator.com](http://myclinicaltriallocator.com)



## ASSISTANCE & SUPPORT RESOURCES

### HEMATOLOGIC CANCERS

American Society of Hematology	www.hematology.org
The Angiogenesis Foundation	www.angio.org
Be the Match	www.bethematch.org
Blood & Marrow Transplant Information Network	www.bmtinfonet.org
CLL Advocates Network (CLLAN)	www.clleadvocates.net
CLL Society	www.cllsociety.org
Cutaneous Lymphoma Foundation	www.clfoundation.org
Delete Blood Cancer DKMS	www.dkms.org
Hairy Cell Leukemia Foundation	www.hairycellleukemia.org
HEADstrong Foundation	www.headstrong.org
International Myeloma Foundation	www.myeloma.org
International Waldenström's Macroglobulinemia Foundation	www.iwmf.com
Leukemia & Lymphoma Society	www.lls.org
Lymphoma Foundation of America	www.lymphomahelp.org
Lymphoma Information Network	www.lymphomainfo.net
Lymphoma Research Foundation	www.lymphoma.org
The Max Foundation	www.themaxfoundation.org
Multiple Myeloma Research Foundation	www.themmrf.org
Myeloma Central	www.myelomacentral.com
National Bone Marrow Transplant Link	www.nbmtlink.org
The National CML Society	www.nationalcmlsociety.org
Patients Against Lymphoma	www.lymphomation.org

### IMMUNOTHERAPY

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

### REIMBURSEMENT & PATIENT ASSISTANCE PROGRAMS

Amgen Assist 360	www.amgenassist360.com/patient, 888-427-7478
AstraZeneca Access 360	www.myaccess360.com, 844-275-2360
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
Blincyto Assistance	www.amgenassist360.com/patient/blincyto-cost-assistance, 888-427-7478

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.celgenepatientsupport.com, 800-931-8691
Darzalex Janssen CarePath Savings Program	www.janssencarepath.com/patient/darzalex/patient-support, 844-553-2792
Darzalex Prescription Assistance	www.janssenprescriptionassistance.com/darzalex-cost-assistance, 844-553-2792
Empliciti Patient Support	www.empliciti.com/access, 844-367-5424
Gazyva Access Solutions	www.genentech-access.com/patient/brands/gazyva.html, 866-422-2377
Genentech Access Solutions	www.genentech-access.com/patient, 866-422-2377
Genentech BioOncology Co-pay Card	www.copayassistance.com, 855-692-6729
IncyteCARES	www.incytecares.com, 855-452-5234
Intron A Patient Assistance Program	www.merckhelps.com/intron%20%20a, 800-727-5400
Janssen CarePath	www.janssencarepath.com, 877-227-3728
Janssen Prescription Assistance	www.janssenprescriptionassistance.com
Johnson & Johnson Patient Assistance Foundation, Inc.	www.jjpaf.org, 800-652-6227
Keytruda Patient Assistance	www.merckaccessprogram-keytruda.com/hcc/, 855-257-3932
Kymriah Cares	www.us.kymriah.com, 844-459-6742
Kyowa Kirin Cares	www.kyowakirincares.com/patient, 833-552-2737
Lumoxiti Access 360	www.lumoxiti.com/patient/patient-resources/access360-savings.html, 844-275-2360
Merck Access Program	www.merckaccessprogram.com/hcc/
Merck Helps	www.merckhelps.com, 800-727-5400
Opdivo with You	www.patient-support.bmscustomerconnect.com/opdivo-with-you-registration, 855-673-4861
Pfizer Oncology Together	www.pfizeroncologytogether.com/patient, 877-744-5675
Pfizer RxPathways	www.pfizerxpathways.com, 844-989-7284
Pomalyst Patient Support	celgenepatientsupport.com/pomalyst-patient, 800-931-8691
Revlimid Patient Support	www.revlimid.com/mds-patient/resources, 800-931-8691
Rituxan Hycela Access Solutions	www.genentech-access.com/patient/brands/rituxanhycela.html, 866-422-2377
Rituxan Patient Assistance Programs	www.rituxan.com/hem/patient/rituxan-patient-assistance, 888-249-4918
Seattle Genetics SeaGen Secure	www.seagensecure.com, 855-473-2873
Teva Oncology Core Reimbursement Assistance & Support	www.tevacore.com, 888-587-3263
Thalomid Patient Support	celgenepatientsupport.com/thalomid-patient, 800-931-8691
Xtandi Support Solutions	www.xtandi.com/support-solutions, 855-898-2634
Yescarta Patient Support	www.yescarta.com/support, 844-454-5483
Zevalin Reimbursement Support & Patient Assistance	www.zevalin.com/patient/support-resources-downloads/reimbursement-and-assistance, 888-537-8277

## GLOSSARY

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

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

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

**B-cell:** A type of immune cell (lymphocyte) that makes proteins to mark specific foreign substances for other immune cells to destroy.

**Cytokines:** Proteins secreted by certain immune cells so they can communicate with each other. Cytokines can also be made in a laboratory for cancer-fighting immunotherapies.

**Dendritic cell (DC):** A type of immune cell that increases the immune response. DCs can activate and stimulate other immune cells.

**Immune cells:** White blood cells in the

immune system that help defend against cancer, infectious disease and other invaders.

**Immune checkpoint inhibitor:** An 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.

**Immunomodulating agents:** Various natural and laboratory-made substances that help boost or suppress the immune response. They are used in some types of cancer immunotherapy.

**Interferon:** A substance that interferes with virus replication and cancer cell division and slows tumor growth, boosting the body's immune response. A laboratory version is used as a type of cancer immunotherapy.

**Interleukin:** Part of a group of proteins (cytokines) that some immune cells make. Interleukin helps regulate certain

functions in the immune system. A laboratory version is used in a type of cancer immunotherapy.

**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.

**Monoclonal antibodies (mAbs):** Laboratory-made proteins created to target and bind with specific proteins or molecules on the surface of cancer cells. In cancer immunotherapy, mAbs are meant to stimulate an immune response in the same way naturally produced antibodies do.

**Oncolytic virus:** A naturally occurring virus also manufactured as a cancer immunotherapy. It targets certain cancer or tumor cells, infects them and multiplies to cause cell death. The virus can also induce an immune response.

**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. A type of checkpoint inhibitor blocks PD-1 receptors, in effect "releasing the brakes" on the immune system.

**Radioimmunotherapy:** A combination of radiation therapy and immunotherapy

that links a radioactive substance to a monoclonal antibody and injects it into the body. Radiation from the substance may kill cancer cells.

**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 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.

**Tumor-infiltrating lymphocyte (TIL):** A type of immune cell that invades a tumor mass or microenvironment. A type of immunotherapy removes TIL cells from a patient's tumor and re-engineers them in a laboratory to seek and destroy tumor-specific cancer cells.

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

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



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