

FS9 in a series providing the latest information for patients, caregivers and healthcare professionals.

Highlights

- Immunotherapy is a type of cancer treatment that improves the immune system's ability to fight cancer.
- Immunotherapy includes treatments that work in different ways. Some boost the body's immune system. Others help train the immune system to attack specific cancer cells.
- Immunotherapy is generally better tolerated than chemotherapy. The side effects of immunotherapy are different from those seen with traditional chemotherapies, and some side effect are serious.
- While great strides have been made in understanding the role of the immune system in cancer, the science is still new compared with other cancer treatments such as chemotherapy. Research in clinical trials is ongoing to develop ways to use and improve immunotherapy.

Introduction

Immunotherapy is a type of treatment that improves the ability of the body's own immune system to detect and attack cancer cells. Immunology is a branch of science that studies all aspects of the immune system. Advances in this field have led to a greater understanding of the ways that the body's immune defenses can be harnessed to treat many types of cancer, including blood cancers. Doctors and researchers are working to manage the immune system to attack and destroy cancer cells. These processes can create effective treatments for blood cancers.

This fact sheet gives an overview of several types of immunotherapy and each one's role in the treatment of blood cancers. A brief introduction on the natural immune system and cancer are included, to help patients understand the immunotherapy information in this publication.

The Natural Immune System

The immune system is the body's primary defense against infection and cancer. It is made up of a complex network of cells, molecules, organs and lymph tissues working together to defend the body against microorganisms such as bacteria, viruses and fungi, as well as against cancer cells. To be able to do this, the immune system must be able to distinguish between cells that naturally belong in the body (self) and foreign cells (non-self). Antigens are substances that the immune system recognizes as toxic and stimulate an immune response; in other words, they are non-self organisms. An antigen may be a substance from the environment (such as a bacteria, a virus, or pollen), or it could be formed inside the body (such as a cancer cell).

Once the immune system determines that a cell is foreign (does not belong) in the body, it begins a series of reactions to identify, target and eliminate the foreign cell. The cells in the immune system that fight infection and disease are white blood cells, which are also called lymphocytes. There are three major types of lymphocytes: B lymphocytes (B cells), T lymphocytes (T cells) and natural killer (NK) cells. B lymphocytes make

the antibodies that recognize and target antigens. B lymphocytes are found in the bone marrow and other parts of the lymphatic system. T lymphocytes have several functions: they help B lymphocytes make antibodies that recognize and fight against invasive microbes and they kill invading or infected cells in the body. T cells are the immune system's main cancerfighters. Natural killer cells also attack cancer cells and eliminate viruses.

When the immune system is functioning normally, the lymphocytes travel through the body looking for and getting rid of anything that does not belong, including bacteria, viruses and even cancer cells. These immune cells search for foreign cells by using their receptors to scan for antigens on the surface of the cells. Once the immune system discovers an antigen, it produces antibodies to attack the foreign cells or it activates T cells to destroy them.

Cancer and the Immune System

Many cancers are likely prevented by the immune system's ability to recognize and destroy abnormal cells before they become cancer. Immunosurveillance is a term used to describe the ways that the immune system patrols the body for pre-cancerous conditions such as cancer-causing proteins on the surface of cells. Immunosurveillance removes these cells before they can build up to a critical mass and develop into cancer.

But even a healthy immune system cannot always prevent cancers from forming. Some cancer cells are able to develop and grow even in the presence of a healthy immune system. Immunoediting is the process by which cancers are able to evade the immune system and multiply. The three phases of immunoediting are elimination, equilibrium, and escape.

- Elimination. Also known as immunosurveillance (see above). The immune system finds and destroys cancer cells, eliminating them from the body. But while most of the cancer cells are destroyed in this phase, some of them survive and are able to reach equilibrium with the immune system.
- Equilibrium. The immune system is unable to completely eliminate all the cancer cells and the cells remain present without progressing or multiplying. During equilibrium, the immune system is able to keep the cancer cells in check but unable to completely eliminate them. The interactions between the cancer cells and the immune system may lead

to an ability of the cancer cells to undergo genetic changes that allow them to avoid being detected and destroyed by the immune system.

• Escape. Cancer cells in the escape phase have acquired the ability to avoid immune recognition and destruction. This leads to the growth and progression to cancer. In the escape phase, cancerous cells use a number of methods to alter the body's immune response in a way that allows the cancer to grow.

Immunotherapies seek to activate or reactivate the immune system to attack and destroy cancer cells that have escaped immune detection. There are several types of immunotherapy that are approved by the FDA or are under study (in clinical trials) to determine their effectiveness in treating various types of blood cancer.

Types of Immunotherapy

Immunotherapies for blood cancer that are in use or under study include:

- Immune checkpoint inhibitors
- Adoptive cell transfer/chimeric antigen receptor (CAR) T-cell therapy
- Monoclonal antibodies
- Therapeutic vaccines.

Immune Checkpoint Inhibitors. Checkpoints are proteins found on T cells that regulate how T cells respond to foreign cells. T cells circulate throughout the body looking for signs of infection and diseases including cancer. When a T cell comes close to another cell, it probes certain proteins on the surface of that cell using a T-cell receptor. If the proteins of the inspected cell indicate that the cell is foreign, the T cell stages an attack against it. Checkpoints signal to T cells to multiply themselves to fight the invader. Once the invader is destroyed, checkpoints signal the T cells to turn off and shut down the T-cell multiplication response. If T cells are active for too long or react to things they should not, they will start to destroy healthy cells and tissues, which could result in autoimmune disorders such as Crohn's disease or rheumatoid arthritis. To prevent the immune system from attacking healthy cells, the immune system creates only enough white blood cells to fight foreign cells and decreases the number of white blood cells when they have finished their attack.

Two checkpoint proteins that work together to turn off (stop) the T cells after the multiplication response are

PD-1 and PD-L1. PD-1 is a checkpoint protein found on T cells that helps keep the T cells from attacking other cells that are not meant to be attacked. When PD-1 binds to PD-L1, a protein on normal cells, it sends a message to the immune system to leave the cell alone. As a result, it reduces the production of T cells and enables more T cells to die. PD-1 can only tell the immune system to slow down if it connects with PD-L1. T cells only expect normal cells to produce PD-L1, but sometimes cancer cells can avoid an immune system attack by producing PD-L1 on their surfaces. When the T cells probe the surface of these cancer cells, they believe that they are detecting normal, healthy cells, and they do not start an attack, which then allows the cancer cells to multiply.

There are two immune checkpoint inhibitors that treat blood cancer by binding to the PD-1 receptor on T cells and blocking the interaction of PD-1 and PD-L1. This prevents the immune system from slowing down and allows the T cells to remain active and continue to attack cancer cells. Checkpoint inhibitors include:

- Pembrolizumab (Keytruda[®]) is approved for the treatment of adult and pediatric patients with refractory Hodgkin lymphoma, or those who have relapsed after 3 or more prior lines of therapy.
 Pembrolizumab has also been approved for the treatment of adult and pediatric patients with refractory primary mediastinal large B-cell lymphoma, or those who have relapsed after 2 or more prior lines of therapy.
- Nivolumab (Opdivo[®]) is approved for the treatment of adults with Hodgkin lymphoma that has relapsed or progressed after autologous hematopoietic stem cell transplantation (auto-HSCT) and brentuximab vedotin (Adcetris[®]), or after three or more lines of systemic therapy including auto-HSCT.

Immune checkpoint inhibitors are given intravenously. The treatment period typically lasts 30 to 60 minutes and the number of sessions may vary, depending on the type of cancer and the drug given.

Side Effects. In general, immune checkpoint therapies are better tolerated than chemotherapy. Most side effects are mild to moderate and reversible, if detected early and addressed promptly. It is important for patients to mention their side effects to their treatment team. Side effects of checkpoint inhibitor treatment can arise at any time during treatment—and sometimes may arise months after treatment. Patients should watch and report any of the following symptoms to their treating doctor:

- Fatigue
- Rash
- Diarrhea
- Abdominal pain
- Nausea/vomiting
- Cough
- Shortness of breath
- Headache
- Confusion
- Muscle weakness or muscle pain

Adoptive Cell Transfer. Adoptive cell transfer is a type of immunotherapy that uses a patient's own T cells to help fight cancer. The T cells are taken from the patient's blood or from the tumor itself and treated in the laboratory with substances to make them better able to target and kill cancer cells in their bodies. Several types of adoptive cell transfer therapies have been developed, but to date, the one that has advanced the furthest in clinical development is called chimeric antigen receptor (CAR) T-cell therapy.

In CAR T-cell therapy, a patient's own T cells are collected using a procedure called apheresis. During this procedure, the blood is removed from one of the patient's large veins and circulated through an apheresis machine, which separates the blood into different components. From this blood, only the T cells are removed, and the remaining blood is returned into the patient.

The T cells are sent to a laboratory where they are genetically engineered to produce receptors on their surfaces called chimeric antigen receptors (CARs). These special receptors allow the T cells to recognize and attach to a specific antigen on tumor cells. (The CAR T-cell therapies that are furthest along in development target an antigen found on B cells called CD19). Once the T cells are modified, they are "expanded" in the laboratory into hundreds of millions of cells. These new CAR T-cells are called "attacker" cells. When there are enough of them, these cells are frozen and sent to the hospital where the patient is being treated.

Prior to receiving the CAR T cells, the patient is given chemotherapy to help prepare the body for the incoming CAR T-cells. Once the CAR T-cells have been infused into the patient's bloodstream, they multiply and begin to recognize and attack the cancer cells with the targeted antigen on their surfaces. The CAR T-cells may remain in

the body months after the infusion has been completed and may result in long-term remissions for some blood cancer patients. At this time the CAR-T cells are approved in young patients (younger than age 26) with relapsed B-cell acute leukemia, and in relapsed lymphomas.

There are two CAR T-cell therapies approved by the FDA:

- Tisagenlecleucel (Kymriah[™]) is approved for the treatment of patients age 25 years and younger with B-cell precursor acute lymphoblastic leukemia that is either refractory or in a second or later relapse. It is also approved for adult patients with relapsed or refractory large B-cell lymphoma after 2 or more lines of systemic therapy.
- Axicabtagene ciloleucel (Yescarta®) is approved for the treatment of adult patients with either relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma not otherwise specified, primary mediastinal large B-cell lymphoma, high-grade B-cell lymphoma, and diffuse large B cell lymphoma (DLBCL) arising from follicular lymphoma.

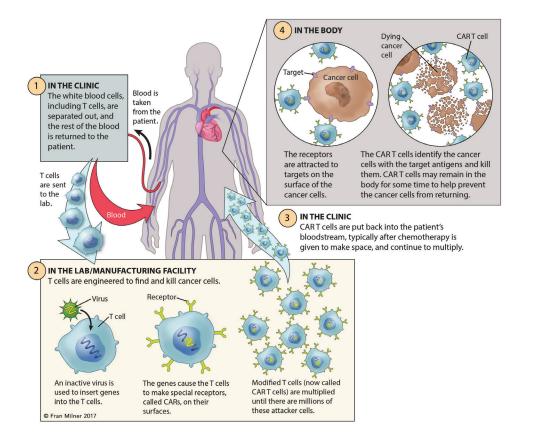
Side Effects. While many patients have reported only mild to moderate side effects, CAR T-cell therapy is sometimes associated with serious side effects that need

to be considered before starting therapy. Serious side effects include:

• Cytokine Release Syndrome. The most common side effect of CAR T-cell therapy is cytokine release syndrome, also known as a "cytokine storm." It is caused by a rapid, large release of cytokines (immune-stimulating molecules) into the blood from immune cells affected by immunotherapy. It typically begins within 24 to 48 hours after the infusion, but may occur up to one week after the infusion. It usually lasts for a week.

Signs and symptoms of cytokine release syndrome include fever, nausea, headache, rapid heartbeat, low blood pressure and difficulty breathing. Most patients have a mild reaction, but severe cytokine release syndrome can be life-threatening. A severe reaction requires intensive medical care, including the use of a ventilator, drugs to increase blood pressure, and seizure medicines.

• Neurologic toxicity, also called CAR-related encephalopathy syndrome (CRES). CAR T-cell therapy can also cause neurologic problems that affect the brain or peripheral nervous system (spinal nerves, cranial/peripheral nerves, etc). Symptoms may include problems remembering words, handwriting



changes, difficulty speaking, difficulty reading time on a clock, hallucinations, being less alert, being confused, and changes in sleep patterns. Neurotoxicity has been reversible in most cases and the symptoms have resolved over several days without intervention or apparent long-term effects. Symptoms can be upsetting for patients and their families, but patients eventually recover all neurologic functions.

For more information about CAR T-Cell therapy, visit www.LLS.org/booklets for the free LLS booklet *Chimeric Antigen Receptor (CAR) T-Cell Therapy Facts.*

Monoclonal Antibodies. One way the immune system attacks foreign invaders is by producing billions of different kinds of antibodies. An antibody is a protein that sticks to an antigen (a substance from the environment, such as a bacteria or virus, or from inside the body, such as a cancer cell). Antibodies circulate throughout the body until they find and attach to a particular antigen for which the antibody has receptors. Once attached, the antibody can recruit other parts of the immune system to destroy the foreign cells that contain the offending antigen. For cancer treatment, researchers can design antibodies in the laboratory that specifically target a certain antigen, such as those found most often on cancer cells. Having the ability to identify and target such antigens would minimize damage to normal cells.

Monoclonal antibodies "mark" cancer cells so that they can be better seen and destroyed by the immune system. Monoclonal antibodies work as target-seeking missiles to find and attach to tumor-specific antigens and then deliver the toxic substance into the cancer cell.

There are three different types of monoclonal antibodies:

Naked monoclonal antibodies. These treatments work by themselves. They have no drugs or radioactive material attached to them. Most naked monoclonal antibodies attach to antigens on cancer cells, but some work by binding to antigens on other, non-cancerous cells. The following are examples of naked monoclonal antibodies.

- Rituximab (Rituxan[®]) is an anti-CD20 antibody. It is used to treat acute lymphoblastic leukemia, chronic lymphocytic leukemia, Hodgkin lymphomas, some non-Hodgkin lymphomas, and Waldenström macroglobulinemia.
- **Obinutuzumab (Gazyva®)** is an anti-CD20 antibody used in the treatment of follicular lymphoma and chronic lymphocytic leukemia (CLL).

- Ofatumumab (Arzerra®) is an anti-CD20 antibody used in the treatment of chronic lymphocytic leukemia.
- Alemtuzumab (Campath[®]) is an anti-CD52 antibody used to treat B-cell chronic lymphocytic leukemia.
- **Daratumumab (Darzalex®)** is an anti-CD38 antibody approved for the treatment of myeloma.
- Elotuzumab (Empliciti[®]) is an anti-SLAMF7 monoclonal antibody approved for the treatment of relapsed or refractory myeloma.

Bispecific monoclonal antibodies. These treatments are composed of two different monoclonal antibodies and can attach to two different proteins at the same time.

Blinatumomab (Blincyto®) is a bispecific T-cell engager (BiTE®) antibody that works by binding with the CD19 protein, which is found on some leukemia cells (especially B-cell acute lymphoblastic leukemia) and on lymphoma cells. Another part of blinatumomab attaches to CD3, a protein found on immune cells called T cells. By binding to both of these proteins, this drug brings the cancer cells and immune cells together, a process that is thought to cause the T cells to be activated and attack the cancer cells. Blinatumomab is FDA-approved for the treatment of B-cell precursor acute lymphoblastic leukemia (ALL) in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1%, and for relapsed or refractory B-cell precursor acute lymphoblastic leukemia.

Conjugated monoclonal antibodies. These drugs have a chemotherapy drug or a radioactive material attached to them. They are used to deliver treatment to the cancer cells. The following are examples of conjugated monoclonal antibodies:

Brentuximab vedotin (Adcetris™) is an antibody drug conjugate that targets the CD30 antigen; this antibody drug is attached to a powerful chemotherapy drug called monomethyl auristatin E. The CD30 antigen is highly expressed on the surface of Hodgkin lymphoma cells and T-cell lymphomas. Brentuximab vedotin is approved for:

- Previously untreated Stage III or IV classical Hodgkin lymphoma (cHL), in combination with doxorubicin, vinblastine, and dacarbazine
- Classical Hodgkin lymphoma (cHL) at high risk of relapse or progression after autologous hematopoietic stem cell transplantation (auto-HSCT) consolidation

- Classical Hodgkin lymphoma (cHL) after failure of auto-HSCT or after failure of at least 2 prior multi-agent chemotherapy regimens in patients who are not auto-HSCT candidates
- Previously untreated systemic anaplastic large cell lymphoma (sALCL) or other CD30-expressing peripheral T-cell lymphomas (PTCL), including angioimmunoblastic T-cell lymphoma and PTCL not otherwise specified, in combination with cyclophosphamide, doxorubicin, and prednisone
- Systemic anaplastic large cell lymphoma (sALCL) after failure of at least one prior multi-agent chemotherapy regimen
- Primary cutaneous anaplastic large cell lymphoma (pcALCL) or CD30-expressing mycosis fungoides (MF) in patients who have received prior systemic therapy

Gemtuzumab ozogamicin (GO) (Mylotarg[™]) is a monoclonal antibody attached to the toxin calicheamicin. Gemtuzumab ozogamicin binds to CD33 and then enters the cell. Once inside the cell, it releases the toxin. Gemtuzumab ozogamicin is FDA-approved for the treatment of adults with newly diagnosed AML and relapsed or refractory AML whose leukemia cells express the CD33 antigen (CD33-positive AML). This medication is slowly injected into a vein through a needle. It is given in cycles consisting of a certain number of treatment days followed by a number of rest days.

Yttrium-90-ibritumomab tiuxetan (Zevalin®) is an example of radioimmunotherapy, a type of conjugated monoclonal antibody therapy in which a monoclonal

antibody linked to a radioactive isotope is used to deliver radiation therapy directly to the cancer cells. Yttrium-90 is the radioactive isotope, ibritumomab is a CD20 antibody that targets the malignant B lymphoma cells and tiuxetan is the "linker" attaching the radioisotope to the antibody. Zevalin is FDA-approved for the treatment of adult patients with relapsed or refractory, low-grade or follicular B-cell non-Hodgkin's lymphoma (NHL) or previously untreated follicular NHL who achieve a partial or complete response to first-line chemotherapy.

Side Effects. Monoclonal antibodies are given by infusion into a vein (called "intravenous" and abbreviated IV). The antibodies are proteins that can sometimes cause allergic reactions. This reaction is most likely to happen during or soon after treatment. Symptoms of an allergic reaction may include fever, chills, rash, dizziness, muscle aches, backaches, headaches, and breathlessness. Naked monoclonal antibodies tend to have fewer serious side effects than chemotherapy drugs. But side effects can occur, depending on which drug is given. Aside from allergic reaction, other more general side effects of monoclonal antibodies may include:

- Fatigue
- Weakness
- Flu-like symptoms
- Headache
- Diarrhea
- Rash
- Dizziness
- Nausea/vomiting

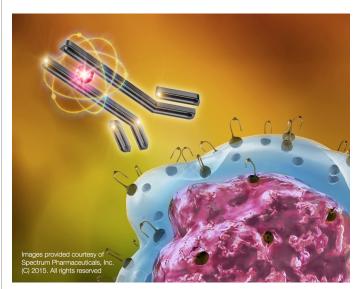


Figure 1. Radiolabeled Yttrium-90-ibritumomab tiuxetan (Zevalin) binds to CD20 molecules on the surface of lymphoma cells.

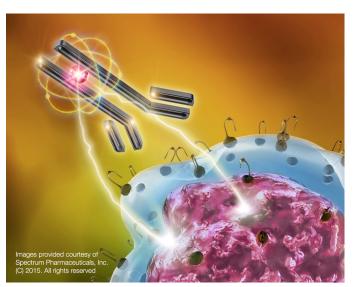


Figure 2. Beta particles emitted from the yttrium-90 irradiate and kill the lymphoma cell.

Therapeutic Cancer Vaccines

Experimental vaccines are being studied to treat certain types of blood cancer. Cancer vaccines train the immune system to recognize cancer cells and protect itself against them. These vaccines are intended to slow down or stop cancer cell growth; to prevent cancer that has been treated from returning; and after treatment, to eliminate the cancer cells that have not been destroyed by treatment. Cancer vaccines expose molecules associated with cancer to the body's immune system, enabling it to destroy them. Researchers continue to focus on developing vaccines for blood cancers.

Side Effects of Immunotherapies

Although many immunotherapies use substances that occur naturally in the body, side effects can occur as a result of an overactivation of the immune system. Each treatment may have side effects specific to the cells that are being affected by the therapy. The doctor should review any potential side effects for each treatment the patient is receiving.

Side effects can sometimes occur weeks or even months after treatment stops. Some patients have a lifetime risk of late side effects caused by immunotherapy. It is important for patients to be vigilant about potential side effects. The organs most susceptible to an overactive immune system caused by immunotherapies are the liver, skin, lungs, kidneys, gastrointestinal tract and endocrine organs. Without diagnosis. along with early recognition and treatment, an autoimmune response could be irreversible or deadly. Many reactions can be reversed with steroids or by temporarily stopping treatment.

If a patient becomes ill at home and needs to be seen by a doctor outside of the patient's cancer team, it is important for the patient or caregiver to alert any doctor seen that the patient is receiving immunotherapy. The Oncology Nursing Society (ONS) provides an "ONS Immunotherapy Patient Wallet Card" online at https:// www.ons.org/sites/default/files/2019-01/IO%20Card%20 1-sided_Vertical.pdf. This Wallet Card form can be printed, filled in and carried by the patient in a wallet or purse at all times. When completed (by the patient, with help from the primary oncologist-hematologist, if needed), the ONS card is intended to communicate information about the patient's immunotherapy treatment with healthcare providers who are not involved with a patient's cancer treatment. See Other Resources on page 9 for more information.

Enrolling in a Clinical Trial

Clinical trials test new drugs and treatments, many of which are supported by LLS research programs.

Clinical Trials. Every new drug or treatment regimen goes through a series of studies called "clinical trials" before it becomes part of standard therapy. Clinical trials are carefully designed and reviewed by expert clinicians, researchers and patient advocates to ensure safety and scientific accuracy. Participation in a carefully conducted clinical trial may be the best available treatment option and should be considered each time the doctor and patient discuss treatment options. The outcomes of patient participation in past clinical trials have resulted in the therapies we have today.

LLS Information Specialists, available at (800) 955-4572, offer guidance on how patients can work with their doctors to determine if a specific clinical trial is an appropriate treatment option. The Leukemia & Lymphoma Society offers help for patients and caregivers in understanding, identifying and accessing clinical trials. When appropriate, patients and caregivers can work with Clinical Trial Nurse Navigators at LLS who will help patients find appropriate clinical trials and then personally assist them throughout the entire clinical-trial process. Please visit www.LLS.org/CTSC for more information.

When you and your doctor discuss immunotherapy as a potential treatment option for you, it may be helpful to have

- A list of questions to ask concerning risks versus benefits of such a trial (see page 8 and visit www.LLS.org/WhatToAsk for lists of suggested questions)
- A family member, friend, or another person to accompany you—both for support and to take notes.

Visit www.LLS.org/booklets to see the free LLS booklet Understanding Clinical Trials for Blood Cancers.

Emerging Immunotherapies

Promising areas of research and emerging immunologic treatments include tumor-specific T-cell–directed therapies, new immune checkpoint targets, macrophage checkpoint antibodies, and therapeutic vaccines. Researchers are trying to fine-tune the treatments they have already developed to determine the most effective treatment combinations and to maximize the efficacy of these treatments, while maintaining acceptable safety for the patient. Researchers are also exploring why some patients do not respond to immunotherapies and why some patients relapse after treatment.

Feedback. Visit www.LLS.org/PublicationFeedback to give suggestions about this booklet.

Questions to Ask Your Doctor About Immunotherapy

People living with blood cancers can use the following questions as a guide to discuss immunotherapy with members of their oncology team:

- Why are you recommending this type of therapy?
- What are the benefits and risks of this therapy?
- How does this therapy work to treat this disease?
- How will this treatment be given and how often?
- How long will I need to be on this treatment?
- How will you know if this therapy is working?
- What side effects should be expected during and following my therapy?
- Will changes need to be made to my daily routine, work or exercise?
- Will health plans cover this therapy?
- Will immunotherapy be my only treatment?
 - Will other cancer treatments be needed?
 - If so, will these therapies be given together or at different times?
- Are there any clinical trials involving this therapy that are suitable for this diagnosis?

A printable list of questions about treatment is available at www.LLS.org/WhatToAsk.

Acknowledgement

The Leukemia & Lymphoma Society appreciates the review of this material by

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We're Here to Help

LLS is the world's largest voluntary health organization dedicated to funding blood cancer research, education and patient services. LLS has chapters throughout the

United States and in Canada. To find the chapter nearest to you, visit our website at www.LLS.org/ChapterFind or contact:

The Leukemia & Lymphoma Society 3 International Drive, Suite 200 Rye Brook, NY 10573

Contact an Information Specialist at (800) 955-4572 Email: infocenter@LLS.org

LLS offers free information and services for patients and families touched by blood cancers. The following entries list various resources available to you. Use this information to learn more, to ask questions, and to make the most of your healthcare team.

Consult with an Information Specialist. Information Specialists are master's level oncology social workers, nurses and health educators. They offer up-to-date disease, treatment and support information. Language services (interpreting and translation) are available. Please contact our Information Specialists or visit our website for more information.

- Call: (800) 955-4572 (Monday through Friday, from 9 am to 9 pm EST)
- Email: infocenter@LLS.org
- Live chat: www.LLS.org/InformationSpecialists
- Visit: www.LLS.org/InformationSpecialists

Clinical Trials (Research Studies). Research is ongoing to develop new treatment options for patients. LLS offers help for patients and caregivers in understanding, identifying and accessing clinical trials. When appropriate, patients and caregivers can work with Clinical Trial Nurse Navigators who will help find clinical trials and personally assist them throughout the entire clinical trial process. Visit the Clinical Trial Support Center at www.LLS.org/CTSC for more information.

Free Information Booklets. LLS offers free education and support booklets that can either be read online or ordered. Please visit www.LLS.org/booklets for more information.

Financial Assistance. LLS offers financial support including insurance premium and medication co-pay assistance, as well as travel and other needs, to eligible individuals with blood cancer. For more information, please

- Call: (877) 557-2672
- Visit: www.LLS.org/finances

LLS Health Manager App. This free mobile app helps you manage your health by tracking side effects, medication, food and hydration, questions for your doctor, and more. Export the information you've tracked in a calendar format and share it with your doctor. You can also set up reminders to take medications, hydrate, and eat. Visit www.LLS.org/HealthManager to download for free.

Información en Español. (LLS information in Spanish). Please visit www.LLS.org/espanol for more information.

Telephone/Web Education Programs. LLS offers free telephone/Web and video education programs for patients, caregivers and healthcare professionals. Please visit www.LLS.org/programs for more information.

LLS Community. The one-stop virtual meeting place for talking with other patients and receiving the latest blood cancer resources and information. Share your experiences with other patients and caregivers and get personalized support from trained LLS staff. Visit www.LLS.org/community to join.

One-on-One Nutrition Consultations. Access free oneon-one nutrition consultations provided by a registered dietitian with experience in oncology nutrition. Dietitians assist callers with information about healthy eating strategies, side effect management and survivorship nutrition. They also provide additional nutrition resources. Please visit www.LLS.org/nutrition to schedule a consultation or for more information.

Weekly Online Chats. Moderated online chats can provide support and help cancer patients to reach out and share information. Please visit www.LLS.org/chat for more information.

Podcast. *The Bloodline with LLS* is here to remind you that after a diagnosis comes hope. Listen in as patients, caregivers, advocates, doctors and other healthcare professionals discuss diagnosis, treatment options, quality-of-life concerns, treatment side effects, doctor-patient communication and other important survivorship topics. Visit www.LLS.org/TheBloodline for more information and to subscribe.

LLS Chapters. LLS offers support and services in the United States and Canada including the *Patti Robinson Kaufmann First Connection Program* (a peer-to-peer support program), in-person support groups, and other great resources. For more information about these programs or to contact your chapter, please

- Call: (800) 955-4572
- Visit: www.LLS.org/ChapterFind

Other Helpful Organizations. LLS offers an extensive list of resources for patients and families. There are resources that provide help with financial assistance, counseling, transportation, patient care and other needs. Please visit www.LLS.org/ResourceDirectory for more information.

Advocacy. The LLS Office of Public Policy (OPP) engages volunteers in advocating for policies and laws that encourage the development of new treatments and improve access to quality medical care. For more information, please

- Call: (800) 955-4572
- Visit: www.LLS.org/advocacy

People Suffering from Depression. Treating depression has benefits for cancer patients. Seek medical advice if your mood does not improve over time—for example, if you feel depressed every day for a 2-week period. For more information, please

- Call: The National Institute of Mental Health (NIMH) at (866) 615-6464
- Visit: NIMH at www.nimh.nih.gov. Enter "depression" in the search box

Other Resources

The National Cancer Institute (800) 422-6237 cancer.gov

The National Cancer Institute is part of the National Institutes of Health and is a national resource center for information and education about all forms of cancer. The NCI also provides a clinical-trials search feature, the PDQ® Cancer Clinical Trials Registry, at the website cancer.gov/clinicaltrials/search-form-help, where patients can look for clinical trials for their own diagnosis.

Oncology Nursing Society www.ONS.org

The Oncology Nursing Society created a wallet card for patients to carry and that helps communicate to doctors and nurses that the patient is being treated with immunotherapy. The ONS Immunotherapy Patient Wallet Card can be accessed online at https://www.ons. org/sites/default/files/2019-01/IO%20Card%201-sided_ Vertical.pdf and printed and completed to carry in a wallet or purse.

References

Anderson MH. The targeting of immunosuppressive mechanisms in hematological malignancies. *Leukemia*. 2014;28(9):1784-1792.

Avigan D, Rosenblatt J. Vaccine therapy in hematologic malignancies. *Blood.* 2018;131(24):2640-2650.

Dolan DE, Gupta S. PD-1 pathway inhibitors: changing the landscape of cancer immunotherapy. *Cancer Control.* 2014;21(3): 231-237.

Heymach J, Krilov L, Alberg A, et al. Clinical Cancer Advances 2018: Annual Report on Progress Against Cancer from the American Society of Clinical Oncology. *Journal of Clinical Oncology.* 2018;36(10):1020-1044.

Im A, Pavletic SZ. Immunotherapy in hematologic malignancies: past, present, and future. *Journal of Hematology & Oncology*. 2017;10(1):94.

Jena B, Moyes JS, Huls H, et al. Driving CAR-based T-cell therapy to success. *Current Hematologic Malignancy Reports.* 2017:9(1):50-56.

Kamta J, Chaar M, Ande A, et al. Advancing cancer therapy with present and emerging immuno-oncology approaches. *Frontiers in Oncology*. 2017;7:64.

Marin-Acevedo JA, Soyano AE, Dholaria B, et al. Cancer immunotherapy beyond immune checkpoint inhibitors. *Journal of Hematology & Oncology*. 2018;11(1):8. National Comprehensive Cancer Network.[®] Management of immunotherapy-related toxicities. In: NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]). Version 1.2019. https://www.nccn.org/professionals/ physician_gls/pdf/immunotherapy.pdf. Accessed November 27, 2018.

Ogba N, Arwood NM, Bartlett NL, et al. Chimeric antigen receptor T-cell therapy. *Journal of the National Comprehensive Care Network: JNCCN.* 2018;16(9):1092-1106.

Palanca-Wessels MC, Press OW. Advances in the treatment of hematologic malignancies using immunoconjugates. *Blood.* 2014;123(15):2293-2301.

Tsirigotis P, Shimoni A, Nagler A. The expanding horizon of immunotherapy in the treatment of malignant disorders: allogeneic hematopoietic stem cell transplantation and beyond. *Annals of Medicine*. 2014;46(6): 384-396.

Velasquez MP, Bonifant CL, Gottschalk S. Redirecting T cells to hematological malignancies with bispecific antibodies. *Blood.* 2018;131(1):30-38.

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