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fighting blood cancers

Immunotherapy Facts

No. 9 in a series providing the latest information for patients, caregivers and healthcare professionals

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Highlights

- Immunotherapy is based on the concept that immune cells or antibodies that can recognize and kill cancer cells can be produced in the laboratory and then given to patients to treat cancer. Several types of immunotherapy are either approved for use or are under study in clinical trials to determine their effectiveness in treating various types of cancer.
- When immunotherapy is used in cancer treatment, it is usually given in combination with chemotherapy or other cancer treatments. It may be used as maintenance therapy following combination chemotherapy, and in some circumstances it is used as a single agent to treat cancer.
- Immunotherapy generally results in fewer short-term side effects than chemotherapy. However, certain side effects are associated with the various types of immunotherapy.
- Types of immunotherapy include monoclonal antibodies, cancer vaccines, radioimmunotherapy, donor lymphocyte infusion, reduced-intensity allogeneic transplantation and chimeric antigen receptor therapy (CAR-T).
- While great strides have been made in understanding the role of the immune system in cancer, the science is still new compared to advances in other cancer treatments. Research in clinical trials is ongoing to develop ways to use immunotherapy in cancer therapy.

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Redefining Cancer Care

Introduction

There have been numerous attempts by cancer researchers, spanning decades, to harness the immune system to destroy cancer cells. Advances in the field of immunology have led to greater understanding of the ways in which the body's own defenses can be manipulated to improve outcomes for patients with blood cancers. Monoclonal antibody therapy, radioimmunotherapy, cancer vaccines and donor lymphocyte infusion (DLI) are types of immunotherapy. These therapies generally result in less severe short-term side effects than chemotherapy.

Immunotherapy is one type of "biologic therapy."

This fact sheet gives an overview of several types of immunotherapy and their role in the treatment of blood cancer. A brief introduction to the natural immune system is included to help patients understand the immunotherapy information in this publication.

The Natural Immune System

The body's natural immune system includes a network of cells and organs that help to defend the body from "antigens." Antigens are substances that are foreign to the body; they stimulate the production of proteins called "antibodies," which target specific antigens. Invading bacteria, viruses, fungi and allergens are examples of antigens. The production of antibodies to attack specific antigens is part of the body's natural immune response. Autoimmune diseases, such as lupus and rheumatoid arthritis, arise from an overactive immune response to substances in the body.

An antigen stimulates the body's immune response (antibody production) when it is ingested or inhaled or comes into contact with the skin or mucous membranes. The antibodies coat, mark for destruction, or inactivate bacteria, viruses, harmful toxins or other foreign particles. Monoclonal antibody therapies, described on page 2, are laboratory-produced proteins designed to mimic the natural antibodies produced during an immune response.

The immune cells that play a role in the body's immune response include

- B lymphocytes (also called "B cells"), which make the antibodies that recognize and target antigens. B lymphocytes are found in the marrow and other parts of the lymphatic system.

- T lymphocytes (also called "T cells"), have several functions, including helping B lymphocytes to make antibodies against invading microbes.
- Natural killer cells (also called "NK cells"), attack cells infected by microorganisms and kill cancer cells. NK cells are called "natural killers" because they do not need to recognize a specific antigen in order to attack and destroy.
- Phagocytes, which swallow and digest microscopic foreign particles, bacteria and dead or dying cells. Neutrophils, macrophages and dendritic cells are all types of phagocytes.

Cancer and the Immune System

In most circumstances, the body's natural immune system does not identify cancer as foreign to the body. One reason for this is that cancer cells are not external invaders, as are viruses and bacteria. Instead, cancer cells are altered (mutated) versions of the body's normal cells. As such, a cancer cell may not present a unique feature (for example, an antigen) that would trigger an immune response.

Cancer cells appear to have almost the same structures as normal cells. One of the challenges facing the researchers who are developing new and better cancer therapies is learning more about the differences between cancer cells and normal cells. Any difference in structure that can be identified as unique to the cancer cell will help researchers to develop treatments that destroy cancer cells but are not toxic to normal cells.

Another issue is that cancer cells may suppress immune activity. This factor may contribute to the immune system's failure to recognize cancer cells as foreign. Certain cancers, such as lymphoma, may occur in patients whose immune system is depressed by disease or drug therapies.

Immunotherapy, also called "biologic therapy," is a promising treatment and an active area of cancer research for people with certain types of cancer. The development of immunotherapies is based on the concept that immune cells or their products (such as antibodies) that can recognize and kill cancer cells can be made in the laboratory and given to patients to treat cancer. Several types of immunotherapy are either approved treatments or are under study in clinical trials to determine their effectiveness in treating various types of blood cancer.

Immunotherapies generally cause less severe short-term side effects than most chemotherapy or radiation therapies, which not only destroy cancer cells but also affect rapidly dividing normal cells. The effects of chemotherapy on normal cells cause hair loss, mouth sores, nausea, reduced resistance to infection and other side effects.

Types of Immunotherapy

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

- Monoclonal antibody therapy
- Radioimmunotherapy
- Interferons and interleukins
- Donor lymphocyte infusion
- Reduced-intensity allogeneic stem cell transplantation
- Chimeric antigen receptor therapy (CAR-T)
- Therapeutic cancer vaccines.

When immunotherapy is used to treat cancer, it

- Is most often given in combination with other types of cancer treatment
- May be used as maintenance therapy following combination chemotherapy
- Is used as a single agent in some cases to treat individuals with blood cancer.

Monoclonal Antibody Therapy

Monoclonal antibodies (mAbs) are laboratory-made immunoglobulins (proteins that help the body fight infection) that are used to

- Target and attack cancer cells
- Deliver toxins (anticancer drugs or radiation) directly to cancer cells with less harm to healthy cells.

Monoclonal antibody therapy is sometimes referred to as "passive immunotherapy," which means that it does not directly stimulate a patient's immune system to respond to a disease. Instead, a monoclonal antibody mimics a natural antibody made by the body. The monoclonal antibody therapy drug attacks a specific target or marker on the surface of a cancer cell. A monoclonal antibody therapy is also called a "targeted therapy" because it is directed to a single target on the cancer cell.

The monoclonal antibody binds to the target on the cell and, in so doing, blocks or interferes with the activity of the cancer cell. The target for the antibody on the cell surface is referred to by the letters CD ("cluster designation") and a number. For example, the monoclonal antibody rituximab (Rituxan®) targets CD20 on B lymphocytes. The monoclonal antibody alemtuzumab (Campath®) targets CD52 found on T and B lymphocytes, NK cells and monocytes.

All new drugs must show proof that they are safe and effective before they can be approved by the US Food and Drug Administration (FDA). Rituxan, initially FDA approved in 1997, is indicated for non-Hodgkin lymphoma. It is also used to treat patients who have chronic lymphocytic leukemia, Waldenström macroglobulinemia and autoimmune diseases. Campath was first approved by the FDA in 2001 for the treatment of B-cell chronic lymphocytic leukemia. Newer anti-CD20 monoclonal antibodies, ofatumumab (Arzerra®) and obinutuzumab (Gazyva®) that are FDA approved for CLL, appear to be more effective than Rituxan for certain situations.

Monoclonal antibody therapies are usually given to individuals in an outpatient setting. The drug is infused through a needle placed in a vein (an "intravenous infusion," or "IV") in the patient's arm. The doctor may prescribe medicines before each infusion to reduce certain side effects. The doctor will also do regular blood tests to check for other side effects.

Side effects such as fever and chills, tiredness, headache and nausea are among the most commonly reported reactions to Rituxan and Campath. Other less common, but more severe, side effects include shortness of breath, a drop in blood pressure, an irregular heartbeat, chest pain and low blood cell counts.

Monoclonal antibody therapies are sometimes referred to as "naked" or "conjugated." A naked monoclonal antibody therapy does not have another chemical or radioactive material attached to it. Rituxan and Campath are examples of naked monoclonal antibody therapies.

Antibodies Inhibiting Immune "Checkpoints." The body has a complex series of immune "checkpoints" that control the immune system. Some of these checkpoints trigger immune responses and some inhibit immune responses. This regulates the immune system and prevents uncontrolled immune responses. A useful analogy is to consider that the immune system is controlled like a car with a "gas pedal" and a "brake." To make the immune system more effective in recognizing cancer cells, one can either "step on the gas" by providing lymphokines and cytokines that stimulate T lymphocytes and NK cells, or alternatively, one can "remove the foot from the brake" thereby removing inhibiting influences that restrain the activity of T cells and NK cells. If the immune system did not have a "brake" it could get out of control and cause serious damage to normal tissues, as it does in rheumatoid arthritis, Crohn's disease and other "autoimmune diseases." Several "negative regulators" of the immune system have been discovered, including molecules known as PD1, PDL1 and CTLA4. Monoclonal antibody drugs blocking these molecules (e.g., pidilizumab, nivolumab, ipilimumab) have recently been shown to produce dramatic tumor responses in a variety of cancers including lung cancer, melanoma and, more recently, both relapsed Hodgkin lymphoma and non-Hodgkin lymphoma. Combining checkpoint inhibiting antibodies with anti-tumor antibodies (e.g., Rituxan) is one of the most promising avenues of current investigation in the field of immunotherapy.

Antibody Conjugates. A conjugated monoclonal antibody therapy consists of a monoclonal antibody with a radioactive substance, a toxin or another therapeutic agent attached to it. The antibody portion of the conjugate targets the radioisotope, toxin or drug specifically to the cancer cell, and spares normal cells that do not express the target antigen.

Antibody-Drug Conjugates: One example of a conjugated monoclonal antibody is gemtuzumab ozogamicin (Mylotarg®), which was FDA approved in 2000 to treat adults aged 60 years or older with CD33-positive acute myeloid leukemia (AML) in first relapse. This drug was withdrawn from the market in 2010. Gemtuzumab ozogamicin incorporates a powerful chemical toxin called "calicheamicin" and a monoclonal antibody that targets the antigen CD33 on myeloid blast cells.

The monoclonal antibody delivers the calicheamicin to the leukemic cells with the CD33 antigen; then the calicheamicin acts as a chemotherapeutic agent. Calicheamicin is classified as an "antitumor antibiotic." Other drugs in the same class that are used to treat people with AML include daunorubicin (Cerubidine®), doxorubicin (Adriamycin®), idarubicin (Idamycin®) and mitoxantrone (Novantrone®).

A second example of an antibody-drug conjugate is brentuximab vedotin (Adcetris™), which consists of a monoclonal antibody targeting the CD30 antigen attached to the powerful chemotherapy drug, monomethyl auristatin E. The CD30 antigen is highly expressed on the surface of Hodgkin lymphoma cells and T-cell lymphomas. Therefore, it is not surprising that the most impressive results using Adcetris have been observed in patients with Hodgkin lymphoma and anaplastic large T-cell lymphoma, where more than 80% of patients can be expected to show tumor shrinkage.

Radioimmunotherapy

Radioimmunotherapy is another type of conjugated monoclonal antibody therapy in which a monoclonal antibody (mAb) linked to a radioactive isotope is used to deliver radiation therapy directly to the cancer cells. The conjugated mAb, yttrium-90-ibritumomab tiuxetan (Zevalin®), is an example of this treatment. Yttrium-90 is the radioactive isotope, ibritumomab is a CD20 antibody that targets the conjugate to malignant B lymphoma cells and tiuxetan is the linker attaching the radioisotope to the antibody (see Figure 1 and Figure 2 on page 4).

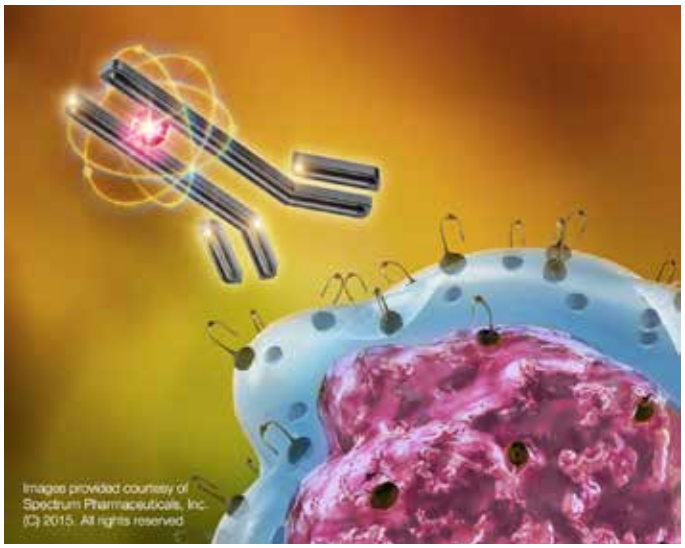

Figure 1. Radiolabeled Yttrium-90-ibritumomab tiuxetan (Zevalin) binds to CD20 molecules on the surface of lymphoma cells.

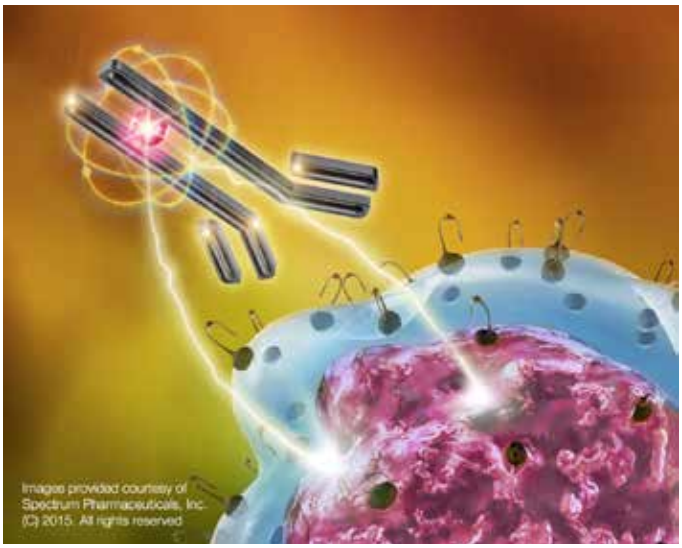

Figure 2. Beta particles emitted from the yttrium-90 irradiate and kill the lymphoma cell.

Zevalin was approved by the FDA in 2002 and is indicated for adults with previously untreated follicular NHL who achieve a partial or complete response to first-line chemotherapy, and for adults with relapsed or refractory, low-grade or follicular B-cell non-Hodgkin lymphoma (NHL), including those with Rituxan-refractory follicular NHL. Its safety and effectiveness in children has not been established.

In most cases, patients are treated with Zevalin in an outpatient facility. The course of treatment can usually be completed in a one- to three-week period. Each treatment can take several hours to complete. Radioimmunotherapy does not cause hair loss, often does not cause nausea and causes only mild degrees of fatigue and lowered blood counts. The recovery period is generally quite brief, except for blood count recovery which generally occurs four to eight weeks after treatment.

One week before receiving the treatment dose of radioimmunotherapy, the patient receives an infusion of Rituxan. Then, on the treatment day, the patient again receives a dose of Rituxan, followed by infusion of ibritumomab radiolabeled with a therapeutic dose of the radioisotope, yttrium-90 antibody (Zevalin) by IV.

Occasionally, patients may have a severe allergic reaction to the infusion. This and other risks should be discussed with the doctor. Fever, chills and aches can occur after the treatment is received. Patients may be given drugs to reduce these effects.

Patients will need to have routine blood work for a few months after receiving the treatment to ensure full blood count recovery. For most patients, the production of blood cells is decreased for a period of time. This is usually a mild to moderate reduction that does not last. Patients who have had chemotherapy and/or external radiotherapy before receiving radioimmunotherapy may experience a greater degree of cytopenias (low blood counts) after radioimmunotherapy.

Other reactions may include low blood pressure, diarrhea or rash. Rash or swelling at the site of the injection affects some patients. These reactions also tend to be mild to moderate and are short-lived. Some patients treated with radioimmmunotherapy may experience nausea and vomiting. However, anti-nausea drugs are given that help to prevent this reaction.

Patients being treated with radioimmunotherapy need to take certain easily understood precautions to protect the people around them from exposure to radiation. The doctor and nurse will explain the precautions. It is important for patients to ask members of their oncology team any questions they may have.

Radioimmunotherapy works gradually, and it may take several months for cancer cells to die and tumors to shrink. The effects of treatment are monitored with physical examinations and imaging tests, such as computed tomography (CT) scans and positron emission tomography (PET) scans.

Zevalin is being studied in clinical trials

- For use with chemotherapy as possible therapy for newly diagnosed patients with follicular lymphoma
- As therapy for aggressive forms of NHL in combination with or following other drug regimens

- As part of high-dose chemotherapy programs along with autologous stem cell support.

Overall, radioimmunotherapy is usually well tolerated.

Interferons and Interleukins

Interferons and interleukins are natural chemicals called "cytokines." These chemicals are secreted by various types of cells and act on other cells to stimulate or inhibit certain actions of the cells. Cytokines that increase production of immune cells can be made in the laboratory and given to patients as part of treatment for infection and cancer. Interferons and interleukins are sometimes referred to as "nonspecific immunotherapies."

Interferons (such as interferon-alpha) are proteins produced by lymphocytes that help the body resist infections and cancers. Interferon-alpha is the most widely used interferon in cancer treatment. High-dose interferon-alpha acts like a chemotherapeutic agent in blocking cancer cell growth. Interferon-alpha may be used to treat some people who have hairy cell leukemia, chronic myeloid leukemia, non-Hodgkin lymphoma or cutaneous T-cell lymphoma.

Interferon-alpha is generally administered every day or several days a week. It is injected subcutaneously (under the skin). Newer formulations of interferon (called "pegylated interferon") are now available with once-a-week dosing. Since interferons stimulate the body's own defenses, researchers are exploring combinations of interferon-alpha and other immune modifiers or chemotherapy.

Interleukins are proteins produced by lymphocytes that activate the growth and activity of many immune cells, such as lymphocytes, that can destroy cancer cells. One of the interleukins, IL-2, is being studied for use in treating patients with leukemia, lymphoma or myeloma.

Side effects of therapy with interferons or interleukins may include high fever, chills, aches and fatigue. IL-2, particularly in high doses, can cause fluid to accumulate in the body so that the person swells up and can feel quite sick. Some patients may need to be hospitalized because of this problem.

Donor Lymphocyte Infusion

Donor lymphocyte infusion is another type of immunotherapy. Lymphocytes from the blood of a donor are collected and then infused into a patient who has already had an allogeneic stem cell transplant from that same donor. The donor and the recipient have a very similar (but not identical) tissue type. As a result, the donor lymphocytes may identify the recipient's cells as targets for attack. The infusion of T lymphocytes from the original stem cell donor may induce another remission. This type of treatment is being studied intensively to learn more about the basis for this immune cell effect and to determine if automatic infusion of donor lymphocytes would be beneficial to prevent relapse for some patients with a very high risk of relapse after transplant.

Donor lymphocyte infusion is usually done on an outpatient basis. It has mainly been used to treat patients who have relapsed chronic myeloid leukemia, although those with relapsed acute leukemia, chronic lymphocytic leukemia, Hodgkin lymphoma, non-Hodgkin lymphoma or myeloma may also receive this treatment.

A potential risk of donor lymphocyte infusion is severe graft-versus-host disease (GVHD), in which the recipient's tissues (such as the skin, liver or gastrointestinal tract) are attacked by the donated immune cells.

Reduced-Intensity Allogeneic Stem Cell Transplantation

Reduced-intensity allogeneic stem cell transplantation is another immunotherapy approach. Patients being prepared for a reduced-intensity allogeneic stem cell transplant (also called a "nonmyeloablative transplant") receive less intense conditioning treatment than with a standard allogeneic transplant. While a standard transplant uses the pretransplant treatment to destroy most of the patient's disease cells, a reduced-intensity transplant relies almost exclusively on the donor immune cells to fight disease. The effectiveness of reduced-intensity transplants depends on the graft-versus-tumor (GVT) effect, in which the recipient's new immune system (originating from the donated stem cells) may destroy the bulk of remaining cancer cells. This reduced-intensity dosing is also more tolerable to older patients who would otherwise not do well with high-dose chemotherapy.

The procedure uses low rather than very high doses of either radiation or chemotherapy to condition the patient. Potent immune therapy is given to suppress the recipient's T lymphocytes to avoid rejection of the donor stem cells. The goal is to have the donor stem cells take up residence in the recipient's marrow and produce lymphocytes (immune cells) that attack the patient's blood cancer cells. If the therapy is successful, the immune cells made from the donor's stem cells attack and suppress the recipient's remaining cancer cells.

In addition to older patients, reduced-intensity transplantation may be advantageous for

- Patients with less rapidly progressive blood cancers
- Patients with certain infections where prolonged marrow suppression would be harmful
- Patients with additional serious medical conditions.

Because reduced-intensity transplantation is relatively new, its risks and benefits have not yet been clearly established. As is the case with allogeneic stem cell transplantation, GVHD is a potential concern. Patients interested in exploring the possibilities of a nonmyeloablative transplant should speak to their doctors about whether participating in a clinical trial would be an appropriate step for them.

Chimeric Antigen Receptor Therapy (CAR-T)

Chimeric antigen receptor therapy (CAR-T) is a type of personalized cancer therapy currently being studied in clinical trials for patients with leukemia and lymphoma. Doctors remove T cells (cells of the immune system) from the patient's blood and genetically modify the T cells by introducing DNA into them, which results in the expression of "chimeric antigen receptors (CARs)" on the surface of the T cells. CARs are proteins that allow the T cells to recognize a specific protein (antigen) on tumor cells and attack the cancer cells more effectively. The number of genetically modified T cells are "expanded" by growing them in the laboratory until hundreds of millions of the modified T cells are available. They are then infused back into the patient. Once the CAR-T cells are in the body, the cells multiply and proceed to hunt for cancer cells, helping to guard against recurrence.

Researchers have reported that CAR-T has induced complete remissions in 90 percent of acute lymphoblastic leukemia (ALL) patients and 50 percent of chronic lymphocytic leukemia (CLL) patients, who have failed multiple prior therapies. Dramatic remissions have also been seen in some patients with indolent and aggressive B-cell lymphomas. Although the length of the response is still unknown, some patients have remained in remission for more than two years after therapy.

Therapeutic Cancer Vaccines

Experimental vaccines are being studied to treat certain types of blood cancer. Cancer treatment vaccines under study are intended to induce an immune response against the cancer cells present in the individual.

A vaccine that prevents a disease, such as measles, mumps or tetanus, contains the same antigen (or part of the antigen) that causes the disease, but the vaccine antigen is either killed or very weak. The vaccine antigen is not strong enough to produce the symptoms and signs of the disease, but it is strong enough so that the body reacts by making antibodies. The antibodies prevent infection if a person is exposed to the antigen in the future.

Unlike conventional vaccines that are used to prevent infectious diseases, cancer vaccines are designed to treat cancer. Vaccines for leukemia, lymphoma and myeloma are still in development and are only available through clinical trials. Most cancer vaccine studies involve giving a patient chemotherapy or other standard cancer therapy to reduce the amount of disease in the body before administering the vaccine.

Ideally, therapeutic cancer vaccines will destroy any remaining cells after other types of cancer treatment and help prevent the disease from returning. Some therapeutic cancer vaccines are also being studied in patients who are being monitored with "watch and wait." The objective of such studies is to see if early vaccine treatment is more beneficial than waiting until the disease shows evidence of progression before beginning treatment.

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?
- Are there any risks with this therapy?
- How does this therapy work to treat my disease?
- How will this treatment be given to me?
- How often will I get this treatment?
- What is the period of time that I need to be on this treatment?
- How will you know if this therapy is working?
- What side effects should I expect during and/or following my therapy?
- Will the treatment cause pain?
- Will I need to make changes to my daily routine, work or exercise?
- Will my health plan cover this therapy?
- Will I need other cancer treatment? If so, will I receive these therapies together or at different times?
- Are there any clinical trials involving this therapy that are suitable for me?

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

Treatment Under Clinical Trials

Patients are encouraged to explore clinical trials. Clinical trials test new drugs and treatments, many of which are being supported by LLS research programs, before they are approved by the FDA as standard treatments.

Clinical trials are designed to be accurate and very safe. There are clinical trials for newly diagnosed patients and for patients who have already been treated. Sometimes, a clinical trial is the best option for a patient. Clinical trials hold great promise to increase remission rates and find a cure for blood cancers.

Emerging Immunotherapies. Promising areas of research and emerging immunologic treatments also include tumor specific T-cell directed therapies, immune checkpoint targets and small molecule immunomodulatory drugs.

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. Information Specialists can search for clinical trials on behalf of patients, family members and healthcare professionals. This search service is also available at www.LLS.org/clinicaltrials.

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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 or contact

The Leukemia & Lymphoma Society

1311 Mamaroneck Avenue
White Plains, NY 10605
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 lists 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 can answer general questions about diagnosis and treatment options, offer guidance and support and assist with clinical-trials searches. Language services are available. For more information, please:

- Call: (800) 955-4572 (M-F, 9 a.m. to 9 p.m. EST)
- Email: infocenter@LLS.org
- Live chat: www.LLS.org
- Visit: www.LLS.org/informationspecialists.

Free Materials. LLS offers free education and support publications that can either be read online or downloaded. Free print versions can be ordered. For more information, please visit www.LLS.org/publications.

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

Co-Pay Assistance Program. LLS offers insurance premium and medication co-pay assistance for certain eligible patients. For more information, please

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

Online Blood Cancer Discussion Boards and Chats. Online discussion boards and moderated online chats can help cancer patients reach out, share information and provide support. For more information, please visit www.LLS.org/getinfo.

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.

Clinical Trials (Research Studies). New treatments for patients are under way. Patients can learn about clinical trials and how to access them. For more information, please:

- Call: (800) 955-4572 to speak with our LLS Information Specialists who can help conduct clinical-trial searches
- Visit: www.LLS.org/clinicaltrials.

Advocacy. LLS enlists volunteers to advocate for policies and laws to speed new treatments and improve access to quality medical care. For more information, please:

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

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 diagnosis.

References

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

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

Gyurkocza B, Sandmaier BM. Conditioning regimens for hematopoietic cell transplantation: one size does not fit all. *Blood*. 2014;124(3):344-353.

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.

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

Schmeel FC, Schmeel LC, Gast SM, et al. Adoptive immunotherapy strategies with cytokine-induced killer (CIK) cells in the treatment of hematological malignancies. *International Journal of Molecular Science*. 2014;15:14632-14648.

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.