

Highlights

- Chimeric antigen receptor (CAR) T-cell therapy is a type of immunotherapy that uses a person's own immune cells (T cells) to identify and attack cancer cells.
- In CAR T-cell therapy, T cells are taken from a patient's blood and sent to a laboratory. There, technologies are used to change the genetic makeup of cells. These genetically modified T cells will express a specific receptor that allows them to identify and attack cells that have the target antigen. In the laboratory, the number of engineered T cells is then multiplied and the modified cells are eventually re-infused into the patient.
- The most frequently targeted antigen in CAR T-cell immunotherapy is CD19, a protein expressed on the surface of nearly all healthy and cancerous B cells, including leukemia and lymphoma B cells. Research is also under way that involves using other CAR target antigens in the treatment of other hematologic cancers, as well as solid tumors.
- Tisagenlecleucel (Kymriah™) is approved by the US Food and Drug Administration (FDA) for the treatment of patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse. It is also approved for adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy.
- Axicabtagene ciloleucel (Yescarta™) is FDA approved for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high-grade B-cell lymphoma, and DLBCL arising from follicular lymphoma. It is not indicated for the treatment of patients with primary central nervous system lymphoma.
- CAR T-cell clinical trials for hematologic malignancies have shown promising results, especially for relapsed and refractory B-cell acute lymphoblastic leukemia (B-ALL) and relapsed and refractory diffuse large

B-cell lymphoma (DLBCL), where lasting remissions have been reported.

- CAR T-cell therapy is associated with serious side effects, some of which can be life threatening. Diligent monitoring of a patient's condition after CAR T-cell infusion is critical to minimize the risk of serious side effects. Most side effects associated with CAR T-cell therapy can be managed with supportive care and medication.
- Research is under way to increase the long-term effectiveness and safety of CAR T-cell therapy. Some of the strategies being explored in clinical trials include trying to decrease side effects by improving the design of CAR T cells, identifying additional targets and receptors, combining CAR T cells with other types of immunotherapy and identifying other routes of delivery.

Introduction

Surgery, chemotherapy, and radiation therapy have been the foundation of cancer treatment. Advances in the field of immunology (a branch of science that studies all aspects of the immune system) have led to a greater understanding of the ways in which the body's own defenses can be used for treatment of blood cancers. Cancer researchers are now studying how the immune system can help destroy cancer cells. Chimeric antigen receptor (CAR) T-cell therapy is a type of immunotherapy that uses a patient's own T cells to recognize and attack cancer cells.

This fact sheet provides information on how CAR T-cell therapy may work, the possible side effects of this treatment approach and its potential role in the treatment of blood cancer. A brief overview of the immune system and immunotherapy is included to help patients understand the information provided in this publication.

The Natural Immune System and Immunotherapy

The immune system is the body's defense against infection and cancer. It is made up of a network of cells and organs that defend the body from foreign substances called "antigens." Antigens stimulate the activation of the immune system to target foreign material and kill infected cells.

Lymphocytes are a key part of a complex immune system. They are the cells that respond to foreign organisms and they help to fight cancer. Most lymphocytes are found in the lymph nodes, the spleen, a few other lymphatic organs and the lymphatic channels, but some enter the bloodstream. There are three major types of lymphocytes: T lymphocytes (T cells), B lymphocytes (B cells) and natural killer (NK) cells. B lymphocytes make the antibodies that recognize and target antigens. B lymphocytes are found in the marrow and other parts of the lymphatic system. T lymphocytes have several functions, including helping B lymphocytes to make antibodies against invasive microbes, and directly killing invading or infected cells in the body. Natural killer cells also attack cancer cells and eliminate viruses.

B-cell lymphomas and leukemias arise when normal B cells mutate (change) and become cancerous. These cancerous B cells then multiply and crowd out normal B cells.

Immunotherapy is an active area of clinical research and there are proven immunotherapy treatments for many people with certain types of cancer. Immunotherapies that are either approved for use or are under study in clinical trials to determine their effectiveness in treating various types of cancer include monoclonal antibody therapy, radioimmunotherapy, therapeutic cancer vaccines and CAR T-cell therapy. Immunotherapy improves the body’s ability to detect and attack cancer cells. CAR T-cell therapy is a special type of immunotherapy given to patients to treat cancer.

For more information about immunotherapy treatments, please see the free LLS booklet *Immunotherapy Facts*, available at www.LLS.org/booklets.

Chimeric Antigen Receptor (CAR) T-Cell Therapy

CAR T-cell therapy is a type of immunotherapy that involves engineering patients’ own T cells to recognize and attack cancer cells. White blood cells are taken from a patient in a procedure called “apheresis” and sent to a laboratory or manufacturing facility. There, the T cells are separated and then modified so that they express an artificial receptor on their surface—one that will allow the engineered T cell to find and attack the cancer cell. These artificial receptors are called “chimeric antigen receptors” (CARs). The number of engineered CAR T cells is multiplied in the laboratory or manufacturing facility. When there are enough of these cells, they are frozen and sent to the patient’s treatment center. There, the CAR T cells are thawed and given back to the patient via an intravenous infusion.

The most frequently targeted antigen in CAR T-cell immunotherapy for leukemia and lymphoma is called “cluster of differentiation (CD) 19” (CD19). The CD19

antigen is expressed on the surface of nearly all healthy and cancerous B cells, including lymphoma and leukemia B cells. CD19 is expressed only on B cells and not on other cells; further, patients can tolerate prolonged periods of B-cell depletion (see *B-cell Aplasia* on page 5), so CD19 is considered an ideal target for CAR T-cell immunotherapy. CAR T-cell trials targeting other antigens expressed on various hematologic cancers are also under way (see Table 1).

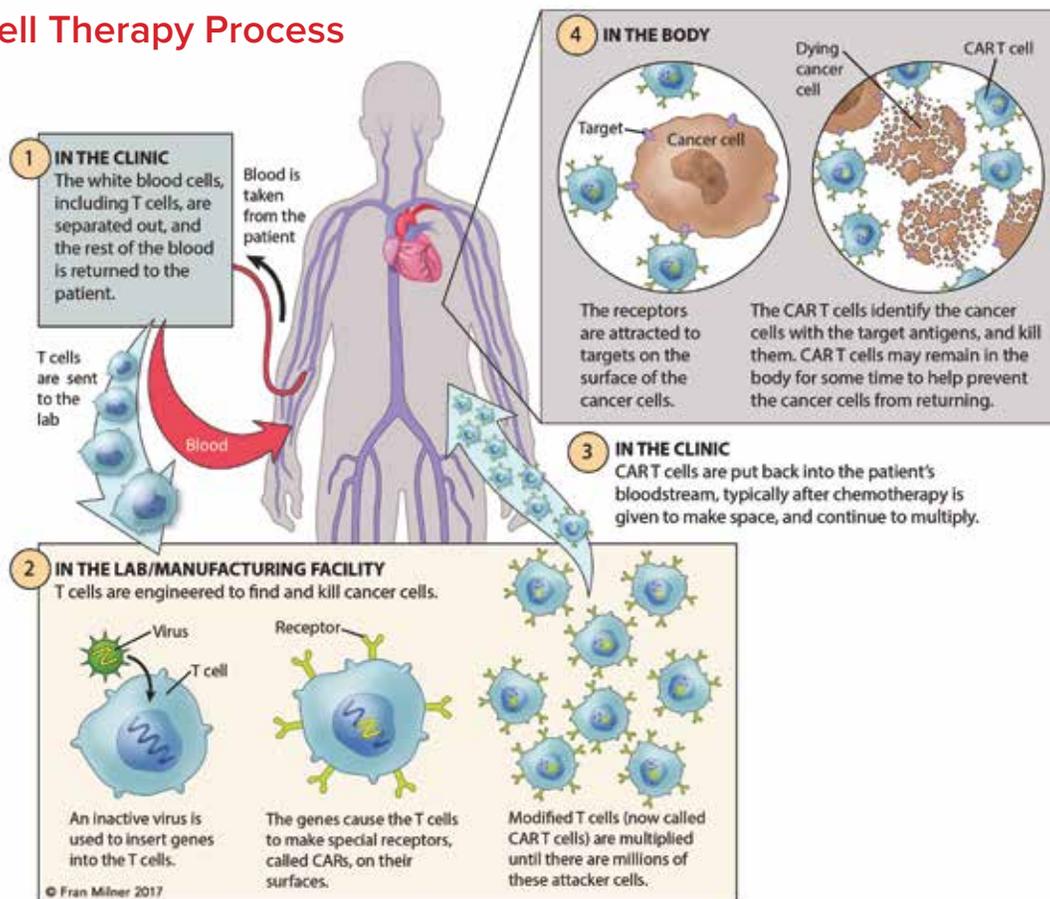
Table 1. CAR target antigens for hematologic malignancies and potential off-tumor targets

Antigen	Hematologic Malignancy	Potential Normal Tissue Impacted
CD19	ALL, CLL, NHL, HL	Normal B cells
CD20	CLL, NHL	Normal B cells
CD22	ALL, NHL	Normal B cells
Igκ	CLL, NHL, multiple myeloma	Normal B cells
ROR1	CLL, NHL	Pancreas, parathyroid, adipose cells
CD30	NHL, HL	Resting CD8 T cells
CD138	Multiple myeloma	Precursor and plasma B cells, epithelia
CD123	AML	Bone marrow myeloid progenitors, B cells, mast cells, monocytes, macrophages, endothelial cells
NKG2D-L	AML, multiple myeloma	Gastrointestinal lining, endothelial cells
BCMA	Multiple myeloma	B cells
Lewis-Y carbohydrate antigen (CD174)	AML, multiple myeloma	Early myeloid progenitor cells

Table 1. This table lists some of the CAR T-cell therapy antigen targets, currently approved for use or under study in clinical trials for hematologic malignancies, and their potential off-tumor targets.

Key. ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; BCMA, B-cell maturation antigen [also known as “tumor necrosis factor receptor”]; CAR, chimeric antigen receptor; CD, cluster designation; CLL, chronic lymphocytic leukemia; HL, Hodgkin lymphoma; IgK, immunoglobulin kappa light chain; NHL, non-Hodgkin lymphoma; NKG2D-L, natural killer group 2D-ligands; ROR 1, receptor tyrosine kinase-like orphan receptor 1.

CAR T-Cell Therapy Process



T cells are collected from a patient. T cells are collected via apheresis, a procedure during which blood is withdrawn from the body and one or more blood components (such as plasma, platelets or white blood cells) are removed. The remaining blood is then infused back into the body.

T cells are engineered in a laboratory. The T cells are sent to a laboratory or a drug manufacturing facility where they are genetically engineered, by introducing DNA into them, to produce chimeric antigen receptors (CARs) on the surface of the cells. CARs are proteins that allow the T cells to recognize an antigen on targeted cells.

After this engineering, the T cells are known as “chimeric antigen receptor (CAR) T cells.”

The engineered CAR T cells are then multiplied. The number of the patient’s genetically modified T cells is “expanded” by growing cells in the laboratory. When there are enough of them, these CAR T cells are frozen and sent to the hospital or center where the patient is being treated.

At the hospital or treatment center, the CAR T cells are thawed and then infused into the patient. Many

patients are given a brief course of one or more chemotherapy agents, called “lymphodepletion,” before they receive the infusion of CAR T cells. CAR T cells that have been returned to the patient’s bloodstream will multiply in number. These are the “attacker” cells that will recognize, and attack, cells that have the targeted antigen on their surfaces.

The CAR T cells may help guard against recurrence. CAR T cells may eradicate all of the cancer cells and may remain in the body months after the infusion has been completed. The therapy has resulted in long-term remissions for some types of blood cancer.

Tisagenlecleucel (Kymriah™) is FDA approved for the treatment of patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse. Kymriah is also approved for adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, high grade B-cell lymphoma and DLBCL arising from follicular lymphoma. Kymriah is not indicated for treatment of patients with primary central

nervous system lymphoma. Tisagenlecleucel is a CD19-directed genetically modified autologous T cell immunotherapy.

Axicabtagene ciloleucel (Yescarta™) is FDA approved for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high-grade B-cell lymphoma, and DLBCL arising from follicular lymphoma. Yescarta is not indicated for the treatment of patients with primary central nervous system lymphoma. It is a CD19-directed genetically modified autologous T cell immunotherapy.

CAR T-cell therapy continues to be available to patients who are participating in a clinical trial. Trial protocols vary. Depending on the clinical trial, care may be provided in either a hospital setting or an intensive outpatient treatment center with experience administering cellular immunotherapy. Patients may have to stay at the treatment facility and they may need to plan to stay close by before, during or following treatment. Some trial protocols require patients to confirm the availability of a caregiver before they can enroll in the trial.

Possible Side Effects of CAR T-Cell Therapy

CAR T-cell therapy has shown varying degrees of effectiveness in the treatment of leukemia, lymphoma and myeloma in clinical trials. While many have reported only mild to moderate side effects, this treatment is sometimes associated with significant serious side effects. It is important to speak with your doctor about the potential side effects before starting any treatment.

Most side effects resulting from CAR T-cell therapy will either resolve on their own or can be managed with appropriate treatment. Some of the most common potential side effects of CAR T-cell therapy, as well as the strategies employed to minimize or counteract these effects include cytokine release syndrome, neurologic toxicities, tumor lysis syndrome, anaphylaxis, and B-cell aplasia.

Cytokine-Release Syndrome (CRS). This potentially serious side effect is frequently associated with CAR T-cell therapy. Cytokines (chemical messengers that help the T cells carry out their functions) are produced when the CAR T cells multiply in the body and kill cancer cells. With CAR T-cell therapy, CAR T cells encounter their targets and are rapidly activated. At this point, numerous inflammatory cytokines (including interleukin-6 [IL-6], tumor necrosis factor-alpha [TNF α] and interferon-gamma [IFN γ]) are released. Mild to potentially life-threatening symptoms are

caused by the large amounts of cytokines that are produced and then released by the activated immune system. This collection of symptoms is known as “cytokine-release syndrome.”

CRS symptoms can range from mild flulike symptoms that include nausea, fatigue, headache, chills and fever to more serious symptoms, such as a low blood pressure, tachycardia (abnormally rapid heart rate), capillary leakage (fluid and proteins leak out of tiny blood vessels and flow into surrounding tissues, resulting in dangerously low blood pressure), cardiac arrest, cardiac arrhythmias, cardiac failure, hemophagocytic lymphohistiocytosis (life-threatening immunodeficiency)/macrophage activation syndrome (life-threatening complication of rheumatic disease) (HLH/MAS), hypoxia (lack of oxygen reaching the tissue), renal insufficiency (poor function of the kidneys), poor lung oxygenation and multiple organ failure. Severe CRS requires intensive care treatment. Some patients may also experience neurological symptoms (see *Neurologic Toxicities*). Although most symptoms are reversible, the potential life-threatening risk of CAR T-cell therapy should not be underestimated. Deaths have been reported in CAR-T cell trials.

Depending on its severity, CRS can be self-limited (requiring only supportive care with fever-reducing medication and intravenous (IV) fluids) or it may require rapid intervention with immunosuppressive anticytokine-directed therapy and/or corticosteroids. Researchers have discovered that patients with the most severe reactions expressed high levels of interleukin (IL)-6, and other cytokines, secreted by T cells in response to inflammation. The challenge for researchers has been to find an appropriate therapy that eases the symptoms of uncontrolled inflammation without diminishing the antitumor effectiveness of the engineered T cells. Fortunately, research has shown that CRS can be mitigated by the infusion of the monoclonal antibody tocilizumab (Actemra®), which blocks the action of IL-6 and reduces inflammation without compromising the effectiveness of T cells. Tocilizumab is FDA approved for the treatment of adults and pediatric patients 2 years of age and older with CAR T cell-induced severe or life-threatening cytokine release syndrome.

If severe CRS symptoms do not improve with tocilizumab, or symptoms are rapidly getting worse, corticosteroids are used to reverse CRS. It is not known whether high doses of corticosteroids affect the ability of CAR T cells to completely destroy the cancer cells, but patients who have received corticosteroids have achieved long-lasting remissions. When CRS is life threatening, these drugs may be the only way to stop the worsening symptoms. Another medication approved to treat inflammatory conditions that has been used in CRS management is etanercept (Enbrel®), which blocks tumor necrosis factor (TNF). Your doctor may also prescribe siltuximab (Sylvant®) as a treatment for CRS.

Some studies have proposed C-reactive protein as an indicator of severe CRS since this protein has been associated with the severity of CRS in several studies; however, its use as a predictive biomarker is still being studied. Other methods aiming to reduce the risk of developing severe CRS are being explored in clinical trials. They include

- Using multiple low-dose CAR T-cell therapy infusions (instead of a single high-dose infusion)
- Infusing patients earlier in the course of their disease
- Decreasing the burden of disease prior to CAR T-cell infusion through intensive chemotherapy
- Giving prophylactic (preventative) tocilizumab.

Depending on the patient and the CAR T cells, CRS may occur within 1 to 21 days of CAR T-cell infusion. The duration of CRS is variable and it depends on the type of intervention used to manage it, typically resolving within 1 to 2 weeks after CAR T-cell infusion.

Macrophage activation syndrome (MAS) is closely associated with severe CRS. MAS is a condition caused by the excessive activation and multiplication of T cells and macrophages and it is generally seen in patients with chronic autoimmune and rheumatic diseases. Fortunately, research has shown that MAS (like CRS) can be mitigated by the infusion of the monoclonal antibody tocilizumab (Actemra®). Corticosteroids and anticytokine therapy can be considered as treatment options if MAS is severe and not improving.

Neurologic Toxicities. The connection between CRS, MAS and neurologic adverse events is not yet completely understood. The frequency, severity and nature of neurological effects appear different between CAR-T products. This could be due to differences in the product (eg CD28 versus 4-1BB co-stimulatory domain), or due to a small number of patients, or both. These side effects have been observed in the CAR T-cell treatment of acute lymphoblastic leukemia (ALL), chronic lymphocytic leukemia (CLL), diffuse large B-cell lymphoma (DLBCL) and multiple myeloma. Common symptoms include language impairment (aphasia), confusion, delirium, involuntary muscle twitching, hallucinations, or unresponsiveness. Seizures have also been reported. The underlying cause is unclear and it is not known whether the presence of CAR T cells in the central nervous system is related to the occurrence or severity of neurotoxicity. The cause of neurotoxicity is the subject of intense investigation by researchers.

Neurotoxicity has been reversible in most cases and the symptoms have resolved over several days without intervention or apparent long-term effects. However there can be life-threatening adverse neurological events and there have been fatalities resulting from neurologic complications of CAR T-cell therapy, notably cerebral edema (swelling

in the brain). Although it is sometimes associated with the presence of CRS, the symptoms apparently are neither prevented nor mitigated by IL-6 blocking medication. Some symptoms of neurologic toxicity have been treated with anti-epileptic medication and/or corticosteroids. Some patients may receive prophylactic (preventative) medications, such as levetiracetam (Keppra®, Keppra® XR, Spritam®). More study is needed to understand the mechanism of action, associated risk factors and best management of this potential side effect.

Tumor Lysis Syndrome (TLS). Another known side effect of CAR T-cell therapy is tumor lysis syndrome, a group of metabolic complications that can occur due to the breakdown of dying cells—usually at the onset of toxic cancer treatments. However, TLS can be delayed and may occur one month or more after CAR T-cell therapy. TLS can cause damage to organs, such as the kidney, and can be a life-threatening complication of any treatment that causes breakdown of cancer cells, including CAR T cells. The complication has been managed by standard supportive therapy, including hydration and the use of the medications allopurinol and rasburicase.

Anaphylaxis (Life-threatening Allergic Reaction).

There is potential for a patient receiving CAR T-cell therapy to have an overwhelming immune response against the CAR itself, called “anaphylaxis.” Symptoms associated with anaphylaxis include hives, facial swelling, low blood pressure and respiratory distress. There have been a few reports of acute anaphylaxis. Thorough monitoring and immediate treatment of this life-threatening side effect are critical for patients receiving CAR T-cell therapy.

On-target, Off-tumor toxicity. An important factor in the safe and successful use of CAR T cells is choosing the proper tumor-associated antigen to target. The ideal antigen for CAR T cells has the following key characteristics

- Expression on all tumor cells
- Expression on the tumor cell surface
- Defining role in tumor cell survival
- Lack of expression on healthy tissues.

Unfortunately, it is rare to find such an ideal target. Many tumor antigens are also expressed on healthy cells in tissues. Damage to such noncancerous normal tissue by CAR T cells may pose life-threatening risks, especially when cells in essential tissues such as the heart, lung or liver express the target antigen. B-cell aplasia following CD19-targeted CAR T-cell therapy is an example of on-target, off-tumor toxicity.

B-cell Aplasia. CAR T-cell therapy targeting antigens found on the surface of B cells not only destroys cancerous

B cells but also normal B cells. Therefore, B-cell aplasia (low numbers of healthy B cells or absent B cells) is an expected result of successful CD19-specific CAR T-cell treatment and it has served as a useful indicator of ongoing CAR T-cell activity. This adverse effect also results in the body's reduced ability to make the antibodies that protect against infection. Intravenous or subcutaneous immunoglobulin replacement therapy may be given with the aim of preventing infection, especially in patients with recurrent or severe infections. B-cell depletion has been reported in nearly all patients treated with CD19-targeted CAR T cells and depending on the CAR T-cell configuration, B-cell aplasia can last from months to years. Long-term follow-up study is needed to assess the late effects of B-cell aplasia.

Results, Limitations, and the Future of CAR T-Cell Therapy

Early outcomes from CAR T-cell trials have generated impressive results in patients with blood cancers. With the FDA approval of tisagenlecleucel (Kymriah™), CAR T-cell therapy represents an option for B-cell acute lymphoblastic leukemia (B-ALL) patients who have relapsed after intensive chemotherapy or a stem cell transplant and is also approved for adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy. In some studies, up to 90 percent of children and adults with B-cell acute lymphoblastic leukemia who had either relapsed multiple times, or failed to respond to standard therapies, achieved remission after receiving CAR T-cell therapy. Relapses may be due to the tumor cells losing the expression of the CD-19 antigen, to the limited persistence of CAR T-cells, or inhibition of CAR T-cell activity.

Axicabtagene ciloleucel (Yescarta™) is an FDA-approved therapy for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy.

Studies of CAR T-cell therapy in other blood cancers, including chronic lymphocytic leukemia (CLL), as well as multiple myeloma, also show potential. Research is also under way, exploring the application of CAR T-cell therapy in the treatment of solid tumors.

While data is fast emerging as to the early responses to CAR T-cell therapy, most of the patients participating in these clinical trials have only been followed for a relatively short time. Following these trial participants over the long term will provide information as to the length of their responses. It is important for more pediatric and adult patients to be enrolled in clinical trials. Larger study samples, evaluated over more extended periods, will help researchers further understand the impact of this type of therapy, ways to reduce its toxicity and improve the management of adverse side effects.

Some of the strategies being studied in trials to improve specificity and minimize toxic side effects associated with CAR T-cell therapy include

- **Improved Design**—First-generation CAR T cells included one specific cancer-targeting antibody, a transmembrane component and an intracellular-signaling domain; however, these cells were not effective. Second-generation CAR T-cell designs have an added costimulatory domain to improve the T-cell activity after CAR-to-target binding. Efforts are ongoing to incorporate human-derived (rather than mouse-derived) antigen-binding (ScFv) domains, with the goal of improving safety and long-term efficacy.
- **Standardization of Each Patient's Dose of T cells**—CAR T-cell therapies generally begin with a mixture of various types of T cells, some with very different functions. By creating a better defined “T-cell cocktail,” researchers expect to have better control of dosage and toxicity.
- **Suicide Switches**—If the immune response becomes excessive and toxicity is spiraling out of control, doctors can administer a drug that activates a switch in the cell, triggering the CAR T cells to self-destruct. Other CARs are designed to only be active in the presence of a drug, so they could be turned on and off, depending on toxicities.
- **Multiple Protein Targets**—Finding proteins on cancer cells that are absent from healthy tissues is a great challenge for researchers. Proteins that are only associated with cancer cells could serve as targets for CAR T cells. By focusing on multiple proteins expressed by cancer cells, therapy could attack only the cells that express all of those proteins. This would provide a more precise way to mark malignant cells for destruction. Alternatively, a CAR could target multiple different targets independently to avoid resistance developing by loss of one or the other antigen.
- **Armored CAR T cells**—CAR T cells that have been engineered to express additional costimulatory ligands, soluble cytokines or secretable proteins in order to overcome a hostile tumor microenvironment. Two approaches include using interleukin-12 (IL-12), and 4-1BB ligand (4-1BBL) to enhance CAR-T cell efficacy and persistence.
- **Combining CAR T cells with Other Immunotherapies**—In some studies, CAR T cells have been administered along with other immunotherapy agents, such as the anti-PD-1 monoclonal antibody pembrolizumab or the anti-PD-L1 antibody atezolizumab, in order to enhance the therapeutic effect and/or persistence of CAR T-cell therapy.

- **Alternative Delivery Routes**—CAR T-cell therapy has been administered intravenously (IV). Some trials have been exploring the use of alternative routes for the delivery of the T cells, such as intratumoral (directly into the tumor), intracerebral (within the brain) and other localized injections, aiming to minimize off-tumor toxicity.
- **Prophylactic Measures**—Studies are exploring ways to reduce the incidence of severe CRS and neurologic toxicities. For example, studies are under way that are combining CAR T-cell therapy with preventative measures, such as administration of tocilizumab before the onset of toxicities.

Studies are also looking at other ways to improve CAR T-cell therapy by enhancing CAR T-cell production, identifying additional targets and receptors, identifying patient risk factors for developing adverse effects and decreasing the side effects of CAR T-cell therapy. Despite its current limitations, CAR T-cell therapy has demonstrated that it has the potential to mark a new era in cancer treatment and personalized immunotherapy.

Enrolling in a Clinical Trial

Clinical trials test new drugs and treatments, many of which are supported by LLS research programs, before they are approved by the Food and Drug Administration (FDA) as standard treatments. Clinical trials are carefully controlled research studies, conducted under rigorous guidelines, to help researchers determine the beneficial effects and possible adverse side effects of new treatments.

Patient participation in clinical trials is important in the development of new and more effective treatments and may provide patients with additional treatment options. Patients interested in participating in a clinical trial involving CAR T-cell therapy are encouraged to talk to their doctors about whether a clinical trial would be appropriate for them.

When you and your doctor discuss CAR T-cell therapy 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 (visit www.LLS.org/whattoask for lists of suggested questions)
- A family member, friend, or another advocate accompany you—both for support and to take notes.

For more information about clinical trials, call an LLS Information Specialist at (800) 955-4572. LLS offers highly personalized clinical-trial search services, which can be accessed through our Information Specialists. Also, see the free LLS booklet *Understanding Clinical Trials for Blood Cancers* at www.LLS.org/booklets.

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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 country 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 various resources are available to you. Use this information to learn more, to ask questions, and to make the most of your healthcare team members' knowledge and skills.

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-trial searches.

Language services are available. For more information, please

- Call: (800) 955-4572 (M-F, from 9 am to 9 pm EST)
- Email: infocenter@LLS.org
- Live chat: www.LLS.org/information specialists
- Visit: www.LLS.org/information specialists.

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

Información en Español (LLS information in Spanish). For more information, please visit www.LLS.org/espanol.

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

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. To join, visit www.LLS.org/community.

Weekly Online Chats. Moderated online chats can provide support and help cancer patients to reach out and share information. To join, please visit www.LLS.org/chat.

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 ongoing. 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 Specialist who can help conduct clinical-trial searches. When appropriate, personalized clinical-trial navigation by trained nurses, is also available.

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.

Resources

The National Cancer Institute (NCI)
www.cancer.gov

(800) 422-6237

The National Cancer Institute, part of the National Institutes of Health, is a national resource center for information and education about all forms of cancer, including CAR T-cell therapy. The NCI also provides a clinical-trial search feature, the PDQ® Cancer Clinical Trials Registry, at www.cancer.gov/clinicaltrials, where patients can look for clinical trials.

National Comprehensive Cancer Network (NCCN)
www.nccn.org

(888) 909-6226

The National Comprehensive Cancer Network®, a not-for-profit alliance of 26 of the world's leading cancer centers devoted to patient care, research, and education, is dedicated to improving the quality, effectiveness, and efficiency of cancer care so that patients can have the best quality of life. Through the leadership and expertise of clinical professionals at NCCN Member Institutions, NCCN develops practice guidelines that are appropriate for use by patients, clinicians, and other healthcare decision-makers.

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