Treatment Options for Relapsed or Refractory Lymphoma

An Overview

for Patients and Caregivers

Introduction

Lymphoma, a cancer of the lymphatic system which includes aggressive B-cell lymphomas like Diffuse Large B-Cell Lymphoma (DLBCL), is often treated successfully with first-line therapy- typically R-CHOP chemotherapy (Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone).

However, some patients experience relapse (the cancer returns after treatment) or refractory disease (the cancer does not respond to initial therapy).

If first-line treatment fails, multiple second-line and third-line options are available. These can offer the potential for remission, or long-term disease control. The choice of second- or third-line treatment depends on factors such as the patient's age, overall health, response to previous therapy, and the availability of targeted treatments.

This guide provides an in-depth overview of treatment options for relapsed or refractory (R/R) lymphoma, focusing on aggressive non-Hodgkin lymphomas (NHL) such as DLBCL and follicular lymphoma.

Option 1: Second-Line Chemotherapy

For patients who experience relapse after R-CHOP or another first-line therapy, second-line chemotherapy (also called "salvage therapy") is often recommended. These salvage therapy regimens aim to decrease the amount or size of cancer cells or tumors in the body, and potentially prepare patients for possible autologous stem cell transplant (ASCT). ASCT is a medical procedure where a patient's own healthy stem cells are collected, stored, and then reinfused into their body after they receive chemotherapy.

Key Objectives:

- Disease control
- Shrink the lymphoma enough to make ASCT possible

Common Second-Line Chemotherapy Regimens

These regimens are typically combined with Rituximab (R) for B-cell lymphomas:

Regimen	Drugs Included	Use Case	Common Side Effects
R-ICE	Rituximab, Ifosfamide, Carboplatin, Etoposide	Standard 2nd-line for transplant-eligible patients	Fatigue, myelosuppression, nausea
R-DHAP	Rituximab, Dexamethasone, Cytarabine, Cisplatin	Alternative to R-ICE, especially for chemosensitive lymphoma	Kidney toxicity, neuropathy, nausea
R-GDP	Rituximab, Gemcitabine, Dexamethasone, Cisplatin	Less intense than R-ICE; used for transplant-ineligible patients	Mild fatigue, nausea, lower toxicity
R-ESHAP	Rituximab, Etoposide, Methylprednisolone, Cytarabine, Cisplatin	Similar to R-DHAP but with high-dose steroids	Immunosuppression, infections, kidney risk

Effectiveness:

- 40–60% of patients respond to second-line chemotherapy.
- If there is a good response (tumor shrinkage), the patient may proceed to ASCT.
- Patients who do not respond to salvage chemo are considered for CAR-T therapy or other targeted treatments.

Challenges:

- Toxicity: These regimens can be difficult to tolerate, especially in older patients.
- Relapse Risk: Many patients relapse again after chemotherapy alone, requiring additional therapies.

Seeing my husband go through this again was devastating. I felt helpless watching him struggle with side effects. I wished I could take on some of the pain for him.

Emily, caregiver for spouse

Who is 2nd-line chemotherapy best for?

- Healthy patients whose doctor has determined they can tolerate high-dose chemotherapy and potentially undergo a stem cell transplant.

Goal: Induce disease remission before ASCT.

Effectiveness: Response rates vary (40–60% for some regimens).

Side Effects: Increased risk of infections, fatigue, nausea, and bone marrow suppression.

I have been given a second chance at life!. I cherish it and try to enjoy every minute.

Karen, Lymphoma Survivor

Option 2: Autologous Stem Cell Transplant (ASCT)

ASCT has the potential to provide a cure for patients with relapsed or refractory aggressive lymphoma. "Autologous" means that patient's own cells are used in the transplant process.

Key Objective:

- Long-term disease control

How stem cell transplants are performed:

1. Stem Cell Collection:

- The patient's own stem cells are collected from blood (via a process called "leukapheresis").
- Prior to collection, growth factors (e.g., G-CSF, filgrastim) may be used to stimulate the bone marrow to release stem cells into the bloodstream.

2. High-Dose "Salvage" Chemotherapy:

- Patients undergo intensive chemotherapy (e.g., the BEAM regimen) to eradicate cancer cells.
- BEAM regimen includes:
  - B – Carmustine
  - E – Etoposide
  - A – Cytarabine
  - M – Melphalan

3. Stem Cell Infusion & Recovery:

- Healthy, previously-collected stem cells are infused back into the body to rebuild bone marrow.
- Recovery takes 2–4 weeks, with a risk of infections, fatigue, and low blood counts.

> As a transplant patient, you are a living embodiment of courage and hope.
>
> **Joe T, Transplant Patient**

Outcomes of ASCT for Relapsed DLBCL:

40-50% of patients achieve long-term remission.

Best outcomes occur in those who had a complete response (CR) to second-line chemotherapy.

Limitations:

High relapse rate (~50% relapse post-transplant).

Not suitable for frail or elderly patients due to the risks of high-dose chemotherapy.

Alternative for Transplant-Ineligible Patients:

If ASCT is not an option, other treatments such as CAR T-cell therapy or bispecific antibodies may be explored.

Who is ASCT best for?

- Younger or fit patients with relapsed lymphoma who responded to salvage chemotherapy.
- Patients with chemosensitive disease (cancer still responds to chemo).

Best for: Patients who achieve remission or partial response after salvage therapy.

Potential for cure: 40-50% in relapsed DLBCL cases.

Risks: High toxicity, long recovery time, and risk of infection.

> The transplant was challenging, involving a severe reaction to one of the drugs, prolonged hospitalization, and intense fatigue.
>
> **Charlie, ASCT Patient**

Option 3: CAR T-Cell Therapy

CAR T-Cell Therapy, or Chimeric Antigen Receptor T-cell therapy, is an innovative type of immunotherapy that is transforming the treatment landscape for certain types of lymphoma, including Large B Cell Lymphoma (LBCL). This therapy uses a patient's own immune cells, genetically modified in a laboratory, to specifically target and destroy cancer cells. CAR T therapy is often used for patients with relapsed or refractory lymphoma, meaning the lymphoma has returned after treatment or has not responded to traditional therapies.

> CAR T gave my partner a lifeline when we thought we were out of options. The days in the hospital were long, and seeing him so sick from the side effects was heartbreaking, but the outcome made it all worth it. We're hopeful for the future now.
>
> **Lymphoma Caregiver**

What is CAR T-Cell Therapy?

CAR T-Cell Therapy is a form of **immunotherapy**, which means it harnesses the body's immune system to fight cancer. In CAR T therapy, the patient's T cells—a type of white blood cell that plays a critical role in the immune response—are genetically engineered to produce special receptors on their surface called chimeric antigen receptors (CARs).

These CARs allow the T cells to recognize and attach to a specific protein found on the surface of lymphoma cells, such as CD19. Once the modified CAR T Cells are infused back into the patient's body, they seek out and destroy the lymphoma cells.

When Is CAR T-Cell Therapy Used?

CAR T-Cell Therapy is typically considered when other treatments, such as chemotherapy, radiation, or stem cell transplants, have not been successful. It is often used in patients with:

- **Relapsed lymphoma:** When the lymphoma has returned after previous treatments.
- **Refractory lymphoma:** When the lymphoma does not respond to standard treatments.

CAR T-Cell Therapy has been approved for use in several types of lymphoma, including:

- **Diffuse Large B-Cell Lymphoma (DLBCL):** The most common type of Non-Hodgkin lymphoma, DLBCL is a type of B-cell Non-Hodgkin lymphoma that's usually fast-growing.
- **Primary Mediastinal Large B-Cell Lymphoma (PMBCL):** A rare type of B-cell Non-Hodgkin lymphoma that is usually fast-growing. "Primary mediastinal" means that the cancer cells come from B cells in the upper chest area, from an organ called the thymus.
- **Follicular Lymphoma (FL):** A type of B-cell Non-Hodgkin lymphoma that's usually slow growing. The cancer cells tend to grow in clusters called "follicles."
- **Mantle Cell Lymphoma (MCL):** A fast-growing and rare type of B-cell Non-Hodgkin lymphoma. In MCL, cancer cells develop in a part of the lymphatic system called the "mantle zone."

> Being by my daughter's side through CAR T was a mix of hope and fear. The treatment sounded amazing, but we didn't know how her body would react. There were a few days when she was very confused and weak, but the doctors knew what to do. The joy of seeing her in remission afterward was indescribable.
>
> • **Lymphoma Parent/Caregiver**

How Does CAR T-Cell Therapy Work?

The process of CAR T therapy involves several steps, spanning from the collection of the patient's T cells to their reinfusion after being modified in a laboratory.

STEP 01

T-Cell Collection (Leukapheresis)

- The first step in CAR T therapy is collecting T cells from the patient's blood. This is done through a process called leukapheresis, where blood is drawn from the patient, and the T cells are separated from the rest of the blood. The remaining blood components are returned to the body.
- This procedure is typically done on an outpatient basis and can take a few hours.

STEP 02

T-Cell Engineering

- After the T cells are collected, they are sent to a specialized laboratory, where they are genetically modified to express chimeric antigen receptors (CARs). These CARs enable the T cells to recognize a specific protein, such as CD19, that is present on the surface of lymphoma cells.
- The modified T cells are then multiplied in the lab to produce millions of CAR T Cells.

STEP 03

Preconditioning Chemotherapy

- Before the CAR T Cells are reinfused, the patient usually receives a short course of low-dose chemotherapy. This chemotherapy, also known as lymphodepleting chemotherapy, helps create space in the immune system for the CAR T-Cells to work more effectively. It reduces the number of normal T cells and other immune cells in the body, allowing the CAR T-Cells to grow and attack the lymphoma more efficiently.

STEP 04

CAR T Cell Infusion

- Once the CAR T-Cells are ready, they are infused back into the patient's bloodstream. This infusion is similar to a blood transfusion and is typically done in a hospital setting.

The CAR T Cells travel throughout the body, recognizing and attaching to lymphoma cells that carry the target protein (eg, CD19), and initiating an immune attack to destroy these cancer cells.

STEP 05

Monitoring and Recovery

- After the CAR T Cells are infused, the patient is closely monitored in the hospital for potential side effects and complications. In many cases, patients will stay in the hospital for several days to weeks, depending on how they respond to the therapy.
- The immune response initiated by the CAR T Cells can be very powerful, so careful monitoring is essential to manage side effects and ensure the therapy is working.

> The hardest part was the waiting. After the T cells were collected, I kept wondering if they would work. But once the treatment started, things moved fast. The side effects were rough, but seeing the cancer shrink was the reward we had been waiting for.

Jerry M., Age 65
Lymphoma Patient

Potential Side Effects of CAR T Therapy

While CAR T therapy has shown remarkable effectiveness in treating relapsed and refractory lymphoma, it can cause significant side effects. The most common and serious side effects include:

Cytokine Release Syndrome (CRS)

- **What it is:** CRS is the most common side effect of CAR T therapy. It occurs when the CAR T Cells activate the immune system, causing a large release of immune molecules called cytokines. While this immune response is a sign that the therapy is working, it can lead to flu-like symptoms or more severe complications.
- **Symptoms:** Fever, low blood pressure, rapid heart rate, difficulty breathing, and confusion. In severe cases, CRS can be life-threatening and may require treatment in the intensive care unit (ICU).
- **Management**: CRS is treated with medications such as tocilizumab (an IL-6 inhibitor) and corticosteroids to reduce inflammation and calm the immune response.

> I knew the side effects could be serious, and when I started getting fevers and feeling confused, I was scared. The doctors acted quickly, and within a few days, I was feeling better. After that, my body slowly recovered, and so did my hope.
>
> **Janet B., Age 74**
> **Lymphoma Patient**

Neurotoxicity (Immune Effector Cell-Associated Neurotoxicity Syndrome, ICANS)

- **What it is:** Neurotoxicity is another serious side effect that can occur after CAR T therapy. It involves changes in the patient's brain function due to the immune response triggered by the CAR T Cells.
- **Symptoms:** Confusion, difficulty speaking, memory problems, headaches, seizures, or loss of consciousness.
- **Management:** Neurotoxicity is closely monitored and may be treated with steroids or other supportive therapies. In most cases, these symptoms are temporary and resolve with treatment.

Increased Risk of Infection

- **What it is:** CAR T-Cell therapy can weaken the immune system, particularly in the weeks to months following treatment. This increases the patient's risk of developing infections.
- **Management:** Patients are often given preventive antibiotics, antivirals, and antifungals to reduce the risk of infections. Careful monitoring for signs of infection is essential during recovery.

> When my husband experienced the side effects from CAR T, I was worried we had made the wrong decision. He was disoriented, and I felt helpless. But the medical team was so experienced in handling these reactions, and they got him through it. Now he's in remission, and we're so thankful.
>
> **Lymphoma Caregiver**

Benefits and Effectiveness of CAR T Therapy

CAR T-Cell therapy has shown impressive results in patients with relapsed or refractory lymphoma, particularly for those who have few other treatment options. Some of the key benefits include:

- **High Response Rates:** Many patients who receive CAR T therapy, particularly those with difficult-to-treat lymphomas, experience significant tumor shrinkage or even complete remission.
- **Long-term Remissions:** For some patients, CAR T therapy can lead to durable, long-term remission, meaning they remain cancer-free for extended periods after treatment. This is particularly promising for patients who had previously exhausted all other treatment options.
- **Personalized Treatment:** Because CAR T therapy uses the patient's own immune cells, it is a highly personalized form of treatment. This tailored approach helps maximize the effectiveness of the therapy.

However, it's important to note that not all patients will respond to CAR T therapy, and some may experience a relapse after treatment. Research is ongoing to understand why some patients respond better than others and how to make CAR T therapy more effective for a broader range of patients.

> I didn't know if I'd ever hear the word 'remission' again, but after CAR T, I did. It's still hard to believe. It feels like a second chance, and I'm taking each day as a gift.

William H., Age 61
Lymphoma Patient

> Seeing my wife go from no treatment options to hearing that she's in remission after CAR T is the biggest relief I've ever felt. We're still cautious, but the hope we've gained is priceless."

Lymphoma Caregiver

Who is a candidate for CAR T Therapy

CAR T-Cell therapy is generally reserved for patients with lymphoma who have not responded to standard treatments, including:

- Patients with **relapsed or refractory DLBCL,** meaning the lymphoma has returned or has not responded after two or more lines of treatment, such as chemotherapy or stem cell transplant.
- Patients with **primary mediastinal large B cell lymphoma** or other high-grade B cell lymphomas.

Eligibility for CAR T therapy depends on several factors, including the patient's overall health, the stage of the lymphoma, and how the disease has responded to previous treatments.
Doctors will carefully evaluate whether CAR T therapy is the right option based on these criteria.

> The fear of relapse was always with me, so when I qualified for CAR T therapy, I felt like I had a second chance. It was amazing to think my own cells were reprogrammed to fight the cancer.

Nancy H., Age 70
Lymphoma Patient

Preparing for CAR T Therapy

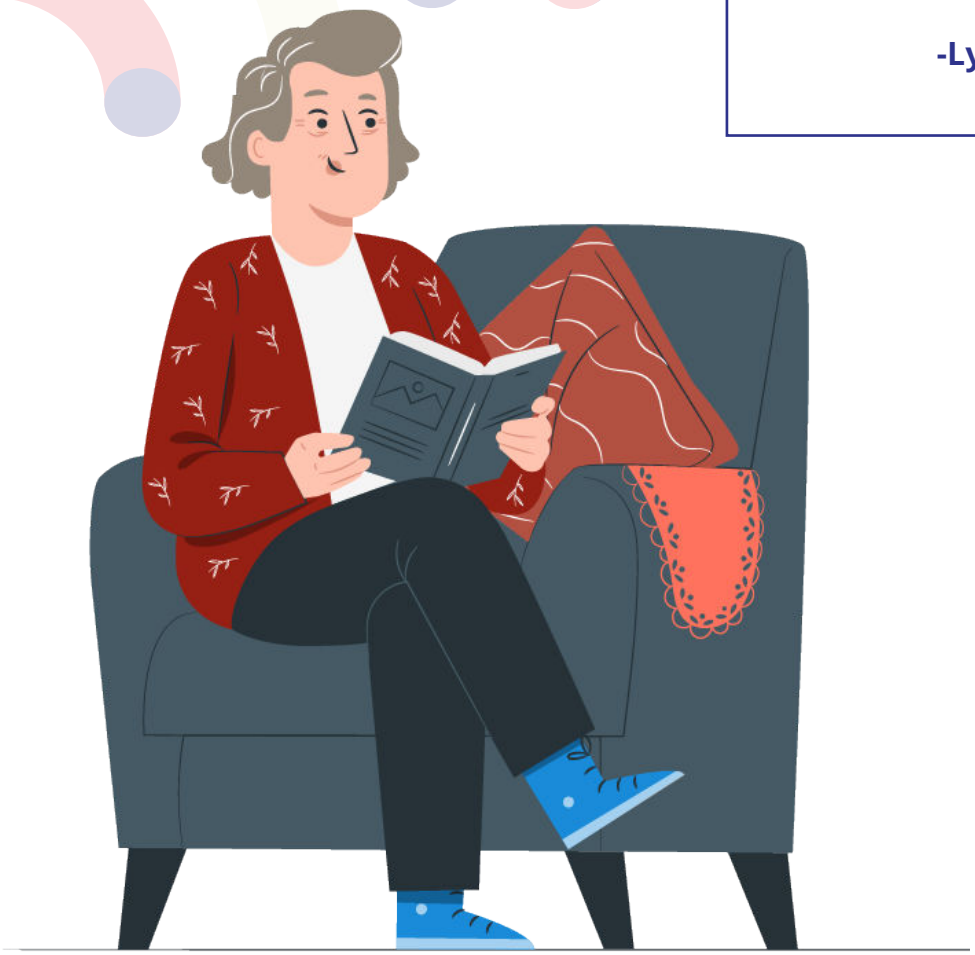
Preparing for CAR T therapy, potential side effects and the recovery process requires a multidisciplinary approach involving healthcare providers, patients, and caregivers. Multiple medical specialists are usually required to help families manage the treatment process, including:

- **Health Assessment:** Before starting the process, patients undergo a thorough medical evaluation, including blood tests, imaging scans, and assessments of heart, lung, and kidney function. This helps ensure the patient is healthy enough to tolerate the therapy.
- **Care Planning:** Because CAR T therapy requires close monitoring, patients will need a strong support system during treatment and recovery. Caregivers play a critical role in providing emotional and physical support during this time.

Recovery and Follow-up After CAR T Therapy

After receiving CAR T therapy, patients will be closely monitored for several weeks or months. The recovery period can vary depending on how the patient responds to treatment and any side effects they experience. Follow-up care typically involves:

- **Frequent Check-ups:** Patients will have regular appointments with their healthcare team to monitor for signs of side effects, infections, or recurrence of the lymphoma.
- **Blood Tests and Scans:** Doctors will use blood tests and imaging scans to check how well the CAR T Cells are working and to ensure the lymphoma is responding to the treatment.
- **Long-term Monitoring:** Because CAR T therapy can have long-lasting effects on the immune system, patients may require long-term follow-up care to monitor for late side effects and ensure that their immune system is functioning properly.



CAR T gave my son a second chance when we thought we were out of options. The treatment was difficult, and there were scary moments, but we are so grateful to be where we are now—looking ahead to a future we thought we might not have."

-Lymphoma Caregiver

I didn't think anything would work after so many relapses, but CAR T turned out to be the miracle I needed. I'm now in remission, and I feel like I have my life back. I wake up every day feeling grateful."

-David T., Age 75
Lymphoma Patient

Option 4: Antibody-Drug Conjugates & Targeted Therapies

Antibody-Drug Conjugates & Targeted Therapies

For patients who relapse after ASCT or are ineligible for transplant, targeted therapies provide additional treatment options.

A. Antibody-Drug Conjugates (ADC)

What are ADCs?

- ADCs combine a monoclonal antibody- a laboratory-produced protein that mimics the body's natural antibodies- with a chemotherapy drug.
- The monoclonal antibody targets cancer cells, and the chemotherapy is delivered directly to the tumor, reducing side effects on normal cells.

Key ADCs Used in Lymphoma

1. Polatuzumab Vedotin (Polivy) + Bendamustine + Rituximab (BRP Regimen)
   - Targets CD79b, a protein on B-cell lymphoma cells.
   - Approved for: Relapsed/refractory DLBCL after two prior treatments.
   - Common side effects: Peripheral neuropathy, low blood counts.
2. Brentuximab Vedotin (Adcetris) (for Hodgkin Lymphoma and some T-cell Lymphomas)
   - Targets CD30 (a protein found on the surface of certain immune cells, particularly activated T cells and B cells).
   - Side effects: Neuropathy, fatigue, nausea.

B. Bispecific Antibodies

What are Bispecific Antibodies?

- These bridge T cells to lymphoma cells, helping the immune system destroy cancer cells.
- Typically, bispecific antibodies cause less severe side effects than CAR T-cell therapy and can be used after failure of CAR T-cell therapy.

Examples of Bispecific Antibodies

01

Glofitamab (CD20xCD3)

- Binds to CD20 (on B cells) and CD3 (on T cells) to enhance T cell capability to kill cancer cells.
- Used for: Relapsed DLBCL and follicular lymphoma.
- Side effects: Mild to moderate cytokine release syndrome (CRS), a systemic inflammatory response that occurs when the immune system releases large amounts of cytokines into the bloodstream. Cytokines are proteins that play a role in regulating inflammation and immune function.

02

Epcoritamab (CD20xCD3)

- Subcutaneous injection, more convenient than IV CAR T-cell therapy.
- Used after multiple relapses.

C. Small-Molecule Targeted Therapies

These are oral drugs that target specific pathways in lymphoma cells.

1. Lenalidomide (Revlimid) + Rituximab

   - Used for relapsed follicular lymphoma.
   - Mechanism: Boosts the immune system and directly inhibits cancer cell growth.

2. BTK Inhibitors (Bruton's Tyrosine Kinase Inhibitors)

   - Used in mantle cell lymphoma (MCL) and some aggressive NHL subtypes.
   - Mechanism: Block the B-cell receptor (BCR) signaling pathway to treat B-cell malignancies
   - Drugs: Ibrutinib, Acalabrutinib, Zanubrutinib

Who are ADCs and Targeted Therapies best for?

- Elderly or frail patients who can't tolerate CAR T-cell therapy or ASCT.
- Patients who have previously tried multiple lines of therapy.

ADCs and Targeted Therapy Key Points:

- May be less toxic than CAR T-cell therapy.
- Can be used after failure of CAR T-cell therapy
- Most important side effects: Cytokine Release Syndrome

> It wasn't a pleasant experience, but it could have been a lot worse.
>
> **Hallie, ADC lymphoma patient**

Clinical Trials: Access to Emerging Therapies

For people with relapsed or refractory lymphoma, clinical trials can offer access to treatments that may not yet be widely available. These trials test new drugs, treatment combinations, and innovative therapies.

Why Consider a Clinical Trial?

- Access to the latest therapies before they become standard treatment.
- Potential for better outcomes, especially if standard treatments have failed.
- Close monitoring by a team of specialists.

How to Find a Clinical Trial:

- You can ask your oncologist about available trials or search reputable databases like clinicaltrials.gov or Lymphoma Research Foundation trial resources.
- While clinical trials are not right for everyone, they provide hope and new options for many patients facing difficult treatment decisions.

Palliative Care: Enhancing Quality of Life

For patients with relapsed or refractory lymphoma who have limited treatment options, palliative care plays a crucial role in improving comfort and well-being. Palliative care focuses on relieving symptoms such as pain, fatigue, nausea, and emotional distress, helping helping patients maintain the best possible quality of life.

Key Benefits of Palliative Care:

- Manages symptoms and side effects of cancer and its treatments.
- Provides emotional and psychological support for patients and caregivers.
- Helps with decision-making about care goals and treatment choices.

Palliative care can be provided alongside active treatment or as part of hospice care for those nearing the end of life. Patients and families should discuss palliative care options with their healthcare team to ensure comprehensive support throughout their journey.

Conclusion

Relapsed or refractory lymphoma presents challenges, but multiple treatment options exist. The choice of therapy depends on factors like prior response to treatment, overall health of the person with lymphoma, and availability of advanced therapies like CAR T-cell therapy and targeted agents.

Key Takeaways:

- Second-line chemotherapy + ASCT is standard for eligible patients.
- CAR T-cell therapy is a promising option for those who fail or are ineligible for ASCT.
- Antibody-drug conjugates and bispecific antibodies are important alternatives.
- Clinical trials provide access to emerging therapies.
- Palliative care can improve quality of life for those with limited treatment options.

Patients and caregivers should work closely with oncologists to create an individualized treatment plan that balances efficacy, quality of life, and personal preferences.

Glossary of Key Terms

This glossary provides simple, easy-to-understand definitions of the key terms related to CAR T therapy, to help patients and caregivers better understand the treatment process and terminology.

A

Antigen: A substance that can trigger an immune response. In CAR T therapy, T cells are engineered to recognize specific antigens, such as CD19, on the surface of lymphoma cells.

B

B Cells: A type of white blood cell involved in the immune system. LBCL originates from abnormal B cells, and CAR T therapy targets specific proteins on these cells to destroy them.

Bone Marrow: The spongy tissue inside bones where blood cells (including T cells and B cells) are produced. CAR T therapy affects the immune system, which is closely related to bone marrow function.

C

CAR (Chimeric Antigen Receptor): A synthetic receptor that is added to a patient's T cells in the laboratory during CAR T therapy. This receptor helps the modified T cells recognize and attack cancer cells. CARs are engineered to bind to specific antigens, such as CD19, which is found on the surface of lymphoma cells.

CAR T-Cell Therapy: A type of immunotherapy where a patient's T cells are modified in a laboratory to express CARs, which target cancer cells. Once these modified T cells are infused back into the patient, they seek out and destroy lymphoma cells.

Cytokine Release Syndrome (CRS): A common and potentially serious side effect of CAR T therapy. CRS occurs when the immune system is activated and releases large amounts of cytokines (proteins involved in immune responses). Symptoms can range from mild (fever, fatigue) to severe (low blood pressure, difficulty breathing).

D

Diffuse Large B Cell Lymphoma (DLBCL): The most common and aggressive subtype of LBCL. DLBCL can sometimes become refractory or relapse after standard treatments, making patients candidates for CAR T therapy.

Donor Lymphocyte Infusion (DLI): A treatment sometimes used after a stem cell transplant where additional T cells from a donor are infused to help fight the cancer. This is different from CAR T therapy, where the patient's own T cells are modified.

E

Eligibility: The criteria that determine whether a patient can receive CAR T therapy. Patients with relapsed or refractory lymphoma who have not responded to other treatments may be eligible.

F

Fevers: A common symptom during CAR T therapy, often related to cytokine release syndrome (CRS). Fevers may indicate that the immune system is reacting to the treatment and attacking cancer cells, but they can also signal complications.

Flow Cytometry: A laboratory technique used to analyze the characteristics of cells, including T cells. Flow cytometry helps monitor the effectiveness of CAR T therapy by tracking the behavior of the modified T cells.

G **Genetic Engineering:** The process used to modify a patient's T cells in CAR T therapy. Scientists alter the genetic material of T cells to express a chimeric antigen receptor (CAR), enabling them to target and destroy cancer cells.

H **Hospitalization:** After receiving CAR T therapy, patients often stay in the hospital for several days or weeks to monitor for side effects, particularly for complications like cytokine release syndrome (CRS) or neurotoxicity.

I **Immune System:** The body's defense system against infections and diseases, including cancer. CAR T therapy harnesses the power of the immune system by reprogramming T cells to specifically attack lymphoma cells.

Immunotherapy: A type of cancer treatment that helps the immune system fight cancer. CAR T therapy is a form of immunotherapy where a patient's T cells are genetically modified to attack cancer cells.

Infusion: The process of delivering the modified CAR T Cells back into the patient's bloodstream after they have been engineered in a laboratory. The infusion is typically done in a hospital setting.

L **Leukapheresis:** A procedure used to collect a patient's T cells for CAR T therapy. Blood is drawn from the patient, and the T cells are separated and collected for genetic modification. The remaining blood components are returned to the patient.

Lymphocytes: A type of white blood cell that is part of the immune system. T cells, the immune cells modified in CAR T therapy, are a type of lymphocyte.

M **Monoclonal Antibodies:** Proteins used in some cancer therapies, like rituximab, that target specific proteins on cancer cells. CAR T therapy also targets specific proteins, but it uses modified T cells rather than antibodies to attack lymphoma cells.

N **Monoclonal Antibodies:** Proteins used in some cancer therapies, like rituximab, that target specific proteins on cancer cells. CAR T therapy also targets specific proteins, but it uses modified T cells rather than antibodies to attack lymphoma cells.

O **Outpatient Treatment:** Some parts of the CAR T therapy process, like leukapheresis, may be done on an outpatient basis, meaning the patient does not need to be hospitalized overnight. However, after the CAR T-cell infusion, hospitalization is usually required for monitoring.

P **Preconditioning Chemotherapy:** A low-dose chemotherapy treatment given before CAR T-Cell infusion. This chemotherapy reduces the number of normal immune cells in the body, making space for the modified CAR T Cells to expand and fight the cancer more effectively.

R

Relapsed Lymphoma: Lymphoma that has returned after a period of remission following treatment. CAR T therapy is often used for patients with relapsed LBCL who did not respond to previous treatments.

Refractory Lymphoma: Lymphoma that does not respond to treatment or continues to progress despite therapies like chemotherapy or radiation. CAR T therapy is a treatment option for patients with refractory LBCL.

Remission: The reduction or disappearance of signs and symptoms of cancer. CAR T therapy aims to induce remission in patients whose lymphoma has not responded to other treatments.

S

Side Effects: The symptoms or conditions that occur as a result of CAR T therapy. Common side effects include cytokine release syndrome (CRS), neurotoxicity, fatigue, and an increased risk of infections. These side effects can vary in severity.

Stem Cell Transplant: A procedure sometimes used to treat relapsed or refractory lymphoma. CAR T therapy is an alternative for patients who are not eligible for or have not responded to a stem cell transplant.

T

T Cells: A type of white blood cell that plays a key role in the immune response. In CAR T therapy, a patient's T cells are collected and genetically modified to express chimeric antigen receptors (CARs), allowing them to target and destroy lymphoma cells.

Tocilizumab: A medication used to treat severe cytokine release syndrome (CRS), a common side effect of CAR T therapy. Tocilizumab blocks a specific protein involved in the immune response and helps reduce inflammation and fever.

V

Viral Vector: A tool used to deliver new genetic material into the patient's T cells during CAR T therapy. The viral vector inserts the genetic code for the chimeric antigen receptor (CAR) into the T cells, allowing them to recognize and attack cancer cells.

W

White Blood Cells: Cells in the blood that help the body fight infections and diseases. T cells, a type of white blood cell, are used in CAR T therapy to fight lymphoma.

Z

Zevalin: A type of radioimmunotherapy used to treat some types of lymphoma. While it is not related to CAR T therapy, it is another treatment option for certain patients with relapsed or refractory lymphoma.