Patient Education

Your CAR T-cell Therapy

Information for Patients and Caregivers

Read this guide to learn:

- What is CAR T-cell therapy
- Steps to CAR T-cell therapy
- Side effects of CAR T-cell therapy
- How to choose a caregiver
- Important phone numbers
- Where you can find more information

The Leukemia/Bone Marrow Transplant Program of BC

IMPORTANT PHONE NUMBERS

Leukemia/BMT Inpatient Unit:

Jim Pattison Pavilion, 15th & 16th Floor
Vancouver General Hospital
24-hour care

P: 604-875-4343

Hematology Apheresis Unit (HAU):

Leon Blackmore Pavilion, 6th Floor
Vancouver General Hospital
Monday to Friday 7:00 am – 7:00 pm
Weekends & Holidays Closed

P: 604-875-4626

Leukemia/BMT Daycare (Outpatient Unit):

Leon Blackmore Pavilion, 6th Floor
Vancouver General Hospital

Monday to Friday 7:00 am - 7:30 pm
Holidays 7:00 am - 7:30 pm
Weekends 8:00 am - 6:00 pm

Leukemia/BMT Daycare closes every night. For issues after hours please call the Leukemia/BMT Inpatient unit.

P: 604-875-4073

If you do not have a scheduled appointment, please call the unit and speak to a Triage Nurse prior to showing up to the Leukemia/BMT Daycare unit

Call Us Immediately If You Have:

- Fever: a temperature of 38°C or higher
- Flu-like symptoms
- Chills or shaking
- Shortness of breath or a bad cough
- Rash, blisters, allergic reactions
- Concerns about your Central Venous Catheter (CVC) line
- New bad bruising and/or bleeding
- Difficulty taking your pills
- Diarrhea or vomiting that does not stop
- Dizziness or feeling lightheaded
- New pain or a bad headache
- Fast or irregular heartbeat
- Memory loss or trouble thinking, hallucinations
- Difficulty talking, impaired speech, confusion
- Unable to write properly
- Severe fatigue, weakness, or drowsiness
- Trouble with balance, walking, clumsiness or weakness
- Fallen down
- A seizure

In Case of Emergency – Call 911

If you are having severe chest pain, can't breathe, or require urgent medical care – **You or your caregiver should call 911**. An ambulance will take you to the closest hospital. Tell the staff you are a CAR T-cell patient and are part of the Leukemia/ BMT program and to contact our Doctor on call. These symptoms cannot be managed over the phone.

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About this Booklet

This booklet has been developed to help you and your family prepare for your CAR T-cell therapy. We hope reading this booklet will help you feel more comfortable with your treatment as you learn about what to expect each step of the way.

We welcome your feedback on how we can improve this booklet for other patients and families.

The amount of information available on CAR T-cell therapy and in this booklet can be overwhelming. We know you will not be able to remember everything we tell you. This booklet provides written information to go along with the teaching you will receive from us, your healthcare team.

Read each section of this booklet when you are ready. You will not be expected to know or read everything. We will be here to help you along the way. You may think of questions to ask us as you read through it. We encourage you to write down your questions and bring them, and this booklet, with you to your appointments.

At the end of the booklet there is a section on common medical terms.

What is CAR T-cell therapy?

Chimeric **A**ntigen **R**eceptor T-cell therapy, often shortened to “CAR T-cell therapy” or “CAR T” is a treatment made by taking some of your body’s own white blood cells and genetically modifying them so they recognize and attack your cancer cells. CAR T-cell therapy is a type of immunotherapy.

Immunotherapy (“i-myoo-now-theh-ruh-pee”)

- Uses the body’s own immune system to fight cancer.
- Improves the body’s ability to detect and kill cancer cells.

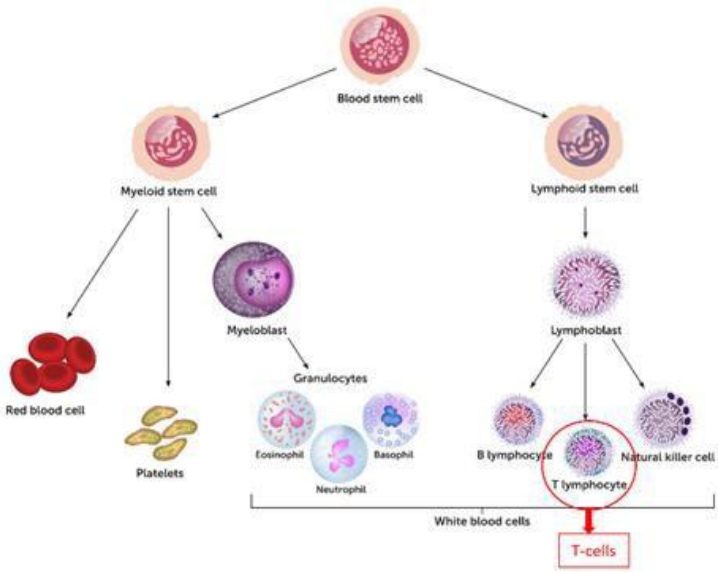


Figure 1. Blood Cells. Adapted from “Figure 2. Blood Cells”, by Healio, 2023.

How does CAR T-cell therapy work?

Your blood will be collected, and CAR T-cells will be made from your own T-cells. These cells will be genetically edited so they target your cancer cells. Your CAR T-cells are then given back to you. In your body they will increase in number and then recognize and attack your cancer cells.

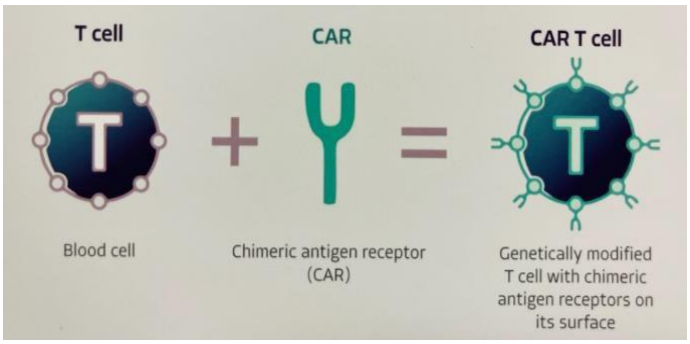


Figure 2. CARS being added to T-cells from “Getting Ready for Treatment with Tecartus,” by Gilead Sciences Canada Inc., 2022.

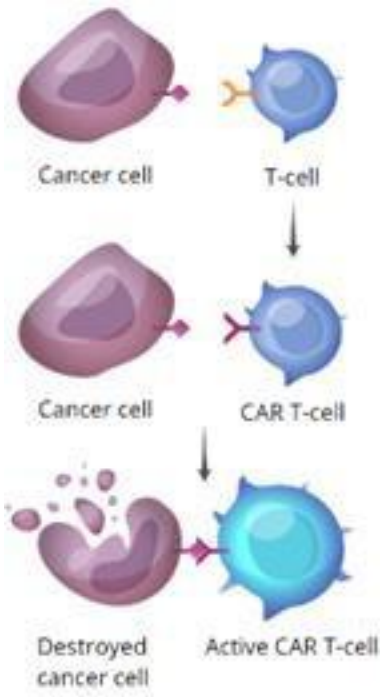


Figure 3. CAR T-cells destroy cancer cells. Adapted from “CAR T-cell Therapy”, by The Princess Margaret Cancer Foundation, n.d

CAR T-cell Therapy

1. Your T-cells are collected and sent to the manufacturing site
2. Your T-cells are genetically modified at the manufacturing site to find and kill cancer cells.
3. These CAR T-cells are then multiplied until there are millions of them.
4. CAR T-cells are put back into your body, where they multiply further and attack your cancer cells.

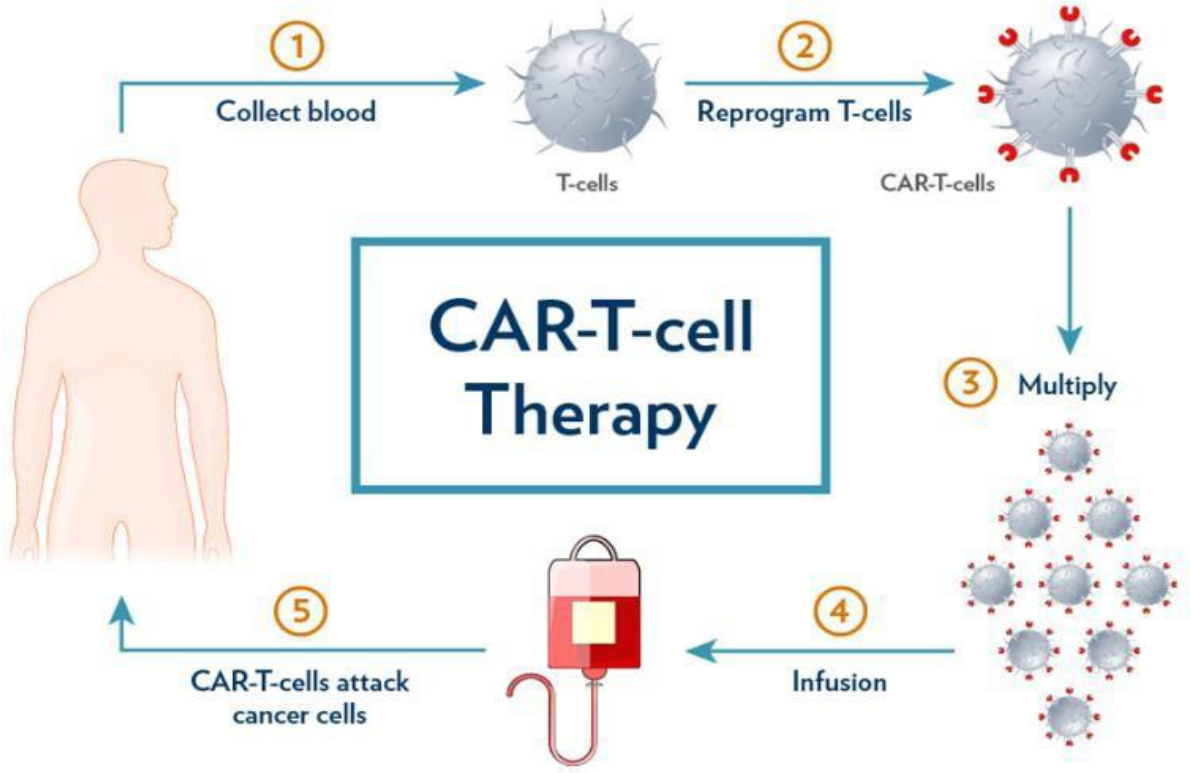


Figure 4. CAR T-cell Therapy. From “CAR-T cell Therapy” by Medical University of South Carolina, 2021.

Steps to CAR T-cell Therapy

CAR T-cell therapy is a long process, and the treatment will take several weeks.

Steps to CAR T-cell therapy	Description	Estimated timeframe
Step 1 **Preparing for CAR T-cell Therapy**	You will have your initial consult with your Hematologist. You will have a phone consultation with your Nurse Navigator.	Initial consult is booked when referral is accepted for CAR T-cell Therapy.
Step 2 **Collecting your cells**	Your T-cells will be collected using an apheresis machine.	2 weeks after initial consult with Hematologist.
Step 3 **Bridging Treatment (If needed)**	While your CAR T-cells are being manufactured, you may have treatments which will help manage your cancer (bridging treatment). This will be decided by your Hematologist and Oncologist.	May occur over approximately 3 weeks
Step 4 **Tunneled Catheter Insertion (If applicable)**	A Hickman line will be inserted. This is a Central Venous Catheter (CVC) line that will be inserted in your chest to help make your treatment more comfortable.	Typically, 1 day prior to Chemotherapy
Step 5 **Lymphodepleting Chemotherapy**	You will be given chemotherapy in the Leukemia/ BMT Daycare unit to prepare the body for the CAR T-cells.	Usually starts 5 days before your Car T-cell infusion and goes over 3 days.
Step 6 **Admission to the Hospital**	You will be admitted to the VGH hospital.	Admission: 1 day before CAR T-cell infusion lasting approximately 7 to 21 days.
Step 7 **CAR T-Cell Infusion**	Your CAR T-cells will be given back to you through your Hickman line. This process is like a blood transfusion and will happen on the second day of your admission.	1 day
Step 8 **Discharge from hospital & Daycare appointments**	When you are ready to be discharged from the hospital, you will be followed up as an outpatient in the Leukemia/BMT Daycare unit.	Approximately 7 to 21 days
Step 9 **Long-term follow-up & managing at home**	It will take time to resume a normal life. You will have follow-up visits with your Hematologist or Oncologist, who will continue to monitor your blood counts.	Up to 12 months

Getting Ready for Your CAR T-cell Therapy

It is helpful to start thinking of the practical, physical, and emotional preparations before CAR T-cell therapy.

What Must I Do Before CAR T-cell Therapy?

1. **Choose a 24-hour Caregiver** – You will need a 24-hour live-in caregiver for at least 30 days after CAR-T therapy. You can have more than one caregiver. Your family and friends can share the caregiver role. Your Social Worker can assist caregivers with navigating leave from work benefits and requesting visa application letters.

2. **Plan Where You Will Stay Before and After Discharge** – You may not be admitted on your expected admission date. It will depend on bed availability. You will need to be within a 45 minute drive from Vancouver General Hospital while undergoing lymphodepleting chemotherapy, while waiting for admission to the hospital, and for 30 days after the CAR T-cell infusion when you are discharged from the hospital.

3. **Register for Fair PharmaCare** – You can register for BC Fair PharmaCare by searching "BC Fair PharmaCare" on your internet browser. Click on the government www2.gov.bc.ca website. Click the square blue box "Register online for Fair PharmaCare." This helps cover the cost of medications.

4. **Arrange Transport** – Patients cannot drive for 8 weeks following infusion of CAR T-cells.

5. **Have a Digital Celsius Thermometer** – You can purchase one from your local pharmacy (if you do not have one already). While receiving CAR T-cell therapy, check your temperature in the morning and evening, and whenever you are feeling unwell.

6. **Arrange for Care of Any Dependents and/or Pets** – Let your Nurse Navigator and Social Worker know if there are any concerns regarding people dependent on you for their care.

7. **Inform Your Doctor** – If you have seen a Doctor in a separate facility or health care program, ensure your Hematologist (CAR T-cell Doctor) is aware. They are not always informed of all your previous medical records.

8. **Get Your Flu Shot & COVID-19 Vaccine** – During the influenza season (usually October to April), we strongly suggest you and your family receive the flu shot and COVID-19 vaccine. It is free at any local clinic and offered at most pharmacies. While not 100% effective, it is the best way to prevent getting an infection. It will decrease the chances of severe complications. Ask your Hematologist (CAR T-cell Doctor) or Nurse Navigator if you are eligible.

Step 1: Preparing for CAR T-cell therapy

Consultation with Hematologist

Your Hematologist will review your health history, do a physical assessment, and discuss CAR T-cell therapy with you and your caregiver(s). They may ask for additional tests before deciding if CAR T-cell therapy is safe for you.

Please note, a medical consent will be completed during this appointment. If English is not your first language, an interpreter will be needed for informed consent. Family members are not able to be your interpreter for medical consents.

Phone call with BMT Nurse Navigators

Initial phone call: Within a few days of Hematologist consultation

Our Nurse Navigators arrange all the planning, testing, and appointments needed in preparation for your CAR T-cell therapy. They will provide your CAR T-cell collection dates and your CAR T-cell infusion date so you can plan accordingly. Please note these dates can change.

Within a few days of your Hematologist Consultation, your Nurse Navigator will phone you to ask questions about your health history and discuss the tests and appointments you will need. After this 20-30 minute phone call, they will send you an email with more information on your scheduled appointments and tests.

Please tell your Nurse Navigator if you are from out of town and use any mobility aids, raised toilet seats, bedrails, or other assistive devices. They will help you connect with our physiotherapy team to arrange for this type of equipment during your treatment.

Pre CAR T-Cell Therapy Tests

Tests must be done to check how well your heart, lungs and kidneys are working before CAR T-cell therapy. These tests are booked at Vancouver General Hospital during your consultation at the Hematology Apheresis Unit. Depending on appointment availability, we may also arrange for these tests to be done in your local clinic or hospital. You may not need all these tests, and your Hematologist (CAR T-cell Doctor) may order extra testing not listed below. More information on these tests can be found under Common Medical Terms on page 28.

These tests include:

- Blood tests (bloodwork)
- Heart tests: Electrocardiogram (ECG), Radionucleotide Ventriculogram (RVG)
- Lung tests: Pulmonary Function Test (PFT), Chest x-ray
- Kidney tests: 24-hour urine collection
- Lumbar puncture
- Bone Marrow Biopsy

Consultations:

To help you prepare for CAR T-cell therapy, you will meet with members of your healthcare team for personalized teaching in-person or via phone. CAR T-cell therapy can affect every part of your normal routine. Your Hematologist (CAR T-cell Doctor) may refer you for other consultations, depending on the result of certain tests (e.g., cardio-oncologists).

1. Hematology Apheresis Unit (HAU):

The Nurses in the apheresis unit will meet with you to check your veins and teach you about the CAR T-cell collection process. Checking your veins is important because the apheresis machine needs a certain amount of blood flow to work properly. If your arm veins are suitable, we will use them to collect your cells.

2. Social Worker:

You will meet with a Social Worker to discuss how CAR T-cell therapy can affect your family, coping, living arrangements, employment, finances and other practical matters. They can talk with you regarding general steps in creating a will, advance care plan, power of attorney, and temporary substitute decision maker.

3. Dietitian:

If you have had problems with appetite or weight loss in the past, you will meet with a dietician. They will discuss how you can prepare for CAR T-cell therapy and manage side effects through your diet and food choices.

4. Pharmacist:

If you require help with monitoring medications or adjusting medications, you may be referred to one of our Pharmacists.

5. Thrombosis Clinic:

This appointment may be needed if you have had blood clots in your past, or are currently using a blood thinner (e.g., Apixaban®, Dalteparin®, Enoxaparin®, etc.). The thrombosis clinic Doctor and Nurses will teach you how to manage your blood thinner throughout your treatment.

What should I bring to my appointments?

- BC Services Card (CareCard)
- A list of all prescription medications you are taking, including the dose and how often you take them.
- A list of all over-the-counter medications you are taking including:
    - o natural supplements, vitamins, minerals, alternative medicines
- A list of questions you may have about treatment.
- Your caregiver

Step 2: Collecting Your CAR T-cells

Your CAR T-cells are collected by a process called apheresis (“afur-REE-sis”) in the Hematology Apheresis Unit (HAU). During this procedure, your blood will be circulated through an apheresis machine, it will separate and collect your white blood cells. The remaining blood is then returned back to you.

- Your Apheresis Nurse will connect you to an apheresis machine by an intravenous (IV) line in each arm.
- Your blood will be drawn into the machine through one IV line.
- The machine will collect white blood cells, including T-cells, from your blood. The rest of your blood is returned back to your body through the other IV line.
- If your veins are too small to be used, a central intravenous line will be inserted prior to collection. The apheresis process will use two different “ports” on the central venous catheter.
- You will be directly connected to the apheresis machine for 4-6 hours. You may want to bring headphones and music to listen to as you will have limited use of your arms (because of the two IV lines).
- Most patients collect enough white blood cells in a single day. Very rarely a second day is needed to collect enough cells.
- You will be given information on how to prepare for your collection day during your first Hematology Apheresis Unit visit.

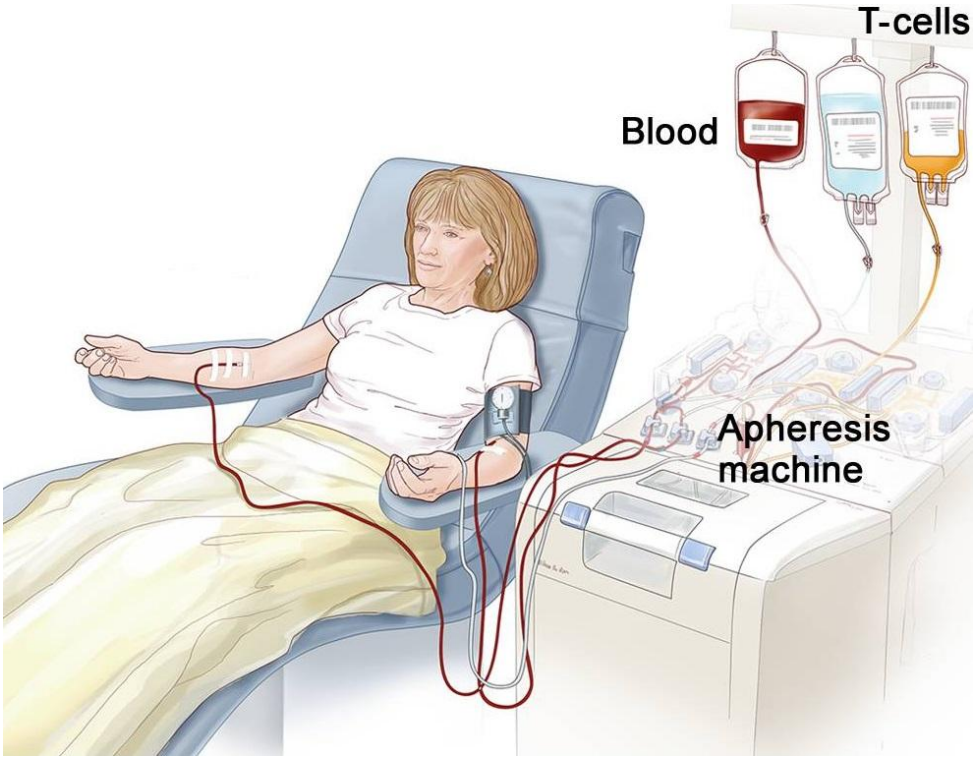


Figure 5. The Apheresis Process, by Winslow, T., 2011.

Are there any side effects with cell collection?

During the collection, you may feel:

- Light-headed or dizzy: This is due to your blood going through the machine.
- Tingling in your lips, fingers and toes, and cramping in your hands and feet. This is caused by a drop in calcium levels in your blood and by the anticoagulant used to prevent your blood from clotting in the apheresis machine. Calcium can be added to your intravenous (IV) and these symptoms should fade.

Tell your Apheresis Nurse at the first sign of any of these side effects, they can help you feel more comfortable.

What happens after the cells are collected?

The bag of cells is sent to the lab where the cells are counted. If there are not enough, you may be asked to come back to the Hematology Apheresis Unit to have the process repeated. This may be the next day or at a later date. If this occurs, your Hematologist will contact you.

Your collected cells are then sent to a manufacturing company where:

- Your T-cells will be genetically modified to have a new special receptor, a CAR, on its surface.
- Modified T-cells are multiplied until there are millions of these CAR-T cells.
- Your cells are then frozen after they are made into CAR T-cells, so they can be preserved and sent back to you.
    - A preservative called DMSO is added to protect your cells.
- It typically takes 3 to 4 weeks to make the CAR T-cells. Please note the timing may vary.
- There is a risk the manufacturing process is unsuccessful in making CAR T-cells or cannot make enough for adequate treatment. If this occurs your, Hematologist will speak to you about your options.

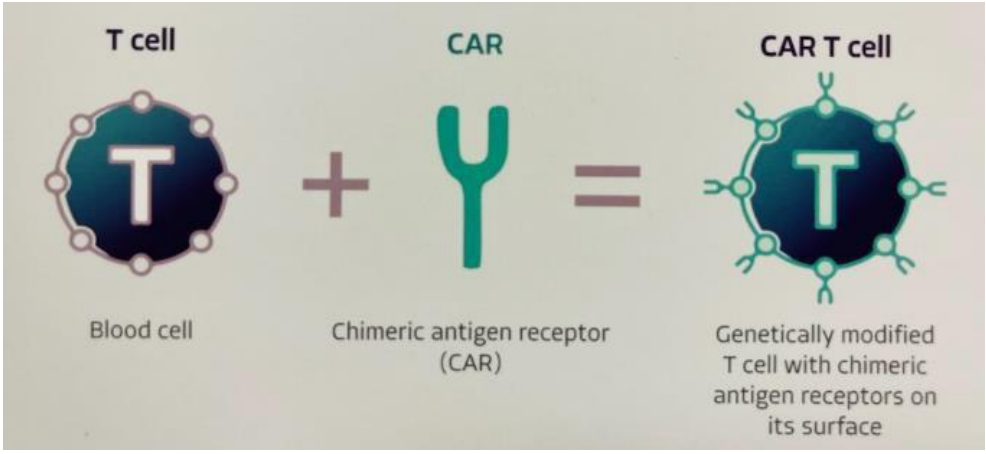


Figure 6. CARS being added to T-cells from “Getting Ready for Treatment with Tecartus,” by Gilead Sciences Canada Inc., 2022.

Step 3: Bridging Treatment

It can take several weeks for the manufacturing company to make your CAR T-cells. While waiting for the CAR T-cells to be ready, you may receive what is referred to as a "bridging treatment". This treatment can include chemotherapy, radiation, or steroid therapy aimed at keeping your cancer under control. Your Doctor will discuss this with you.

Step 4: Central Venous Catheter Insertion

Typically, one day before Lymphodepleting Chemotherapy. Location: Vancouver General Hospital, Jim Pattison Pavilion, Radiology Unit Ground Floor.

If you already have a central venous catheter proceed to Step 5

Before Lymphodepleting chemotherapy, you will need a **C**entral **V**enous **C**atheter (**CVC**) inserted. It is a flexible tube that is put into a large vein in your neck. The other end sits outside of your chest. Having an IV line may sound scary. It will make your CAR T-cell therapy experience much more comfortable.

There are 2 Central Venous Catheters we use in our program. You will have one of the following:

- **Trifusion® Line**;
  - Inserted before CAR T-cell collection for people with small veins.
  - Used for CAR T-cell collection, chemotherapy, CAR T-cell infusion, and recovery.
  - In some cases, a Permcath® CVC is used only for CAR T-cell collection then removed. A Hickman® line would be inserted later.
- or a **Hickman® Line**
  - Inserted a few days prior to the start of Lymphodepleting chemotherapy.
  - Only used for chemotherapy, CAR T-cell infusion, and recovery, not CAR T-cell collection.
  - Most patients have a Hickman line®.

What will my Central Venous Cathater line be used for?

- Giving intravenous (IV) high-dose chemotherapy.
- Giving IV fluids to help keep you hydrated.
- Drawing blood for tests.
- Giving back your CAR T-cells on the infusion day.
- Giving medications.
- Giving blood transfusions, as needed.

Pictures of Central Venous Catheters:

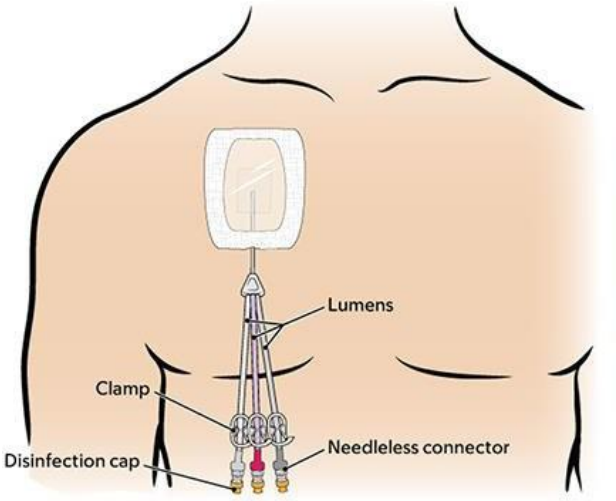


Figure 7. A Hickman line with three lumens. From "Catheter tunneled under your skin, into a vein," by Memorial Sloan Kettering Cancer Center, 2023.

LEFT: A Hickman® line with three lumens. A Trifusion® line is very similar in appearance. A white or clear dressing covers the "exit site" to protect it from infection. Please refer to *All About Your Tunneled Catheter* booklet for more information. Note: you will not have to flush your line, change caps, or change your own dressing as mentioned in the booklet.

RIGHT: The white plastic catheter enters your bloodstream through a neck vein. The tip of the catheter sits above the heart (not in it).

This picture show two lumens, most people will have three.

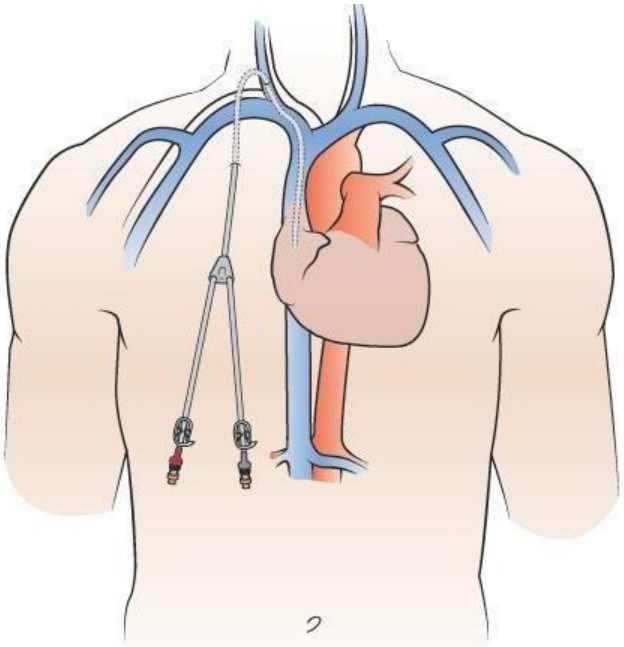


Figure 8. Where the catheter goes in your vein. From "Tunneled Catheter," by Memorial Sloan Kettering Cancer Center, 2023.

Step 5: Lymphodepleting Chemotherapy

~ 5 days before your CAR T-cell infusion day. Location: Leukemia/BMT Daycare unit.

Lymphodepleting chemotherapy, is a type of chemotherapy that aims to reduce the number of T-cells in your body to make room for your new CAR T-cells to grow. This chemotherapy is done to prepare your body for CAR T-cell therapy. In preparation for starting this chemotherapy, your Hematologist may have given you a prescription for anti-nausea medications (Ondansetron®) and medication to protect the kidneys (Allopurinol®). Please bring these to your chemotherapy sessions.

Chemotherapy:

- Will be given through your Central Venous Catheter line (CVC).
- Typically occurs over 3 days.
- Completed at least 48 hours prior to your CAR-T cell infusion.
- Each day of chemotherapy is about ~6 hours long.

Lymphodepleting chemotherapy most often includes:

a. Cyclophosphamide

This chemotherapy is usually given for 3 days.

- Please note this chemotherapy can affect your bladder. Tell you healthcare team of any symptoms such as:
  - o Changes in urination
  - o Burning or pain when peeing
  - o If you see blood in your urine (red or pink coloured pee)
  - o Abdominal pain

b. Fludarabine

This chemotherapy is usually given for 3 days.

***Please note**, different diseases sometimes require different types of lymphodepleting chemotherapy. Your Doctor will speak with you about which chemotherapy you will be receiving.

When you arrive at the BMT/Leukemia Daycare unit for your lymphodepleting chemotherapy, the Nurse will:

- Connect you to intravenous (IV) fluids before you receive chemotherapy to protect your kidneys.
- You will be given medication to prevent you from feeling nauseous.
- Administer your chemotherapy: Cyclophosphamide and Fludarabine.
- Connect you to intravenous (IV) fluids after your chemotherapy has been completed.
- Provide orientation to the BMT/Leukemia Daycare unit.

How does Chemotherapy work?

Chemotherapy targets cells that grow and divide quickly. Chemotherapy also attacks fast growing, healthy cells. The cells in your stomach, hair, skin and bone marrow are examples of cells that grow quickly. Lymphodepleting chemotherapy primarily destroys lymphocytes. Lymphocytes, like T-cells, recognize antigens that are foreign to the body. Without lymphodepleting chemotherapy your body could recognize your new CAR T-cells as foreign and destroy them. Therefore, lymphodepleting chemotherapy is crucial for CAR T-cell therapy.

Nausea and fatigue are common side effects. Lymphodepleting chemotherapy may cause hair thinning. It does not cause full hair loss.

*Please see *Symptom Management Through Treatment* guide for more information*

Hazardous Drug Safety

Chemotherapy is a hazardous medication, meaning it is harmful to cells. It takes 48 hours for chemotherapy medications to slowly leave your body through your urine and stool. Small amounts of the drug can also be found in blood, vomit, semen, and vaginal fluids.

Your body fluids are hazardous every day chemotherapy is given and for 48 hours from when the last dose finishes. While the risk is low, please take precautions to keep you and your family safe while you are hazardous.

You will receive your CAR T-cell infusion at least 48 hours after your last lymphodepleting chemotherapy. Your body will need to get rid of the chemotherapy before your CAR T-cells are infused. If the chemotherapy is still in your body they can destroy your new CAR T-cells.

During the 48 hours that you are hazardous:

About the Leukemia/BMT Daycare Unit:

This is called the **BMT Daycare** for short and is located on the 6th floor of the Leon Blackmore Pavilion. You will be coming to the Leukemia/BMT Daycare unit after Central Line Catheter (CVC) insertion, and for three days of Lymphodepleting Chemotherapy.

Amenities

- There are treatment rooms with beds and chairs for patient use. Private rooms are used for patients with an active infection, symptoms that are infectious, or procedures, such as a bone marrow biopsy or lumbar puncture. Do not take a private room without talking to your Nurse first.
- A small selection of snacks, sandwiches and drinks are available for patients who are unable to come prepared. No hot water is available. Patients or their visitor may come to the snack kitchen or the front desk and wait for a staff member who has a spare moment to get them what they need. Due to infection control, only staff can access the kitchen.
- One family member/caregiver is welcome to assist you and keep you company.
- Wi-Fi connection is available throughout the facility.

What Can I Expect in the BMT Daycare?

On your first visit, your Nurse will give you a tour of the unit. The unit has a “self-care” routine which includes your Nurse teaching you how to check in for each visit, how to take your own vital signs, and where to record symptoms you may be having. At each visit, discuss any side effects you may be experiencing and questions you have with your Nurse and Doctor.

What should I bring to each visit at the BMT Daycare?

Step 6: Admission to the Hospital

Location: 15th or 16th floor, Leukemia/BMT Inpatient unit, Jim Pattison Pavilion, VGH.

I have been given an ideal admission date. What does this mean?

Your ideal admission date is the date we aim to admit you to hospital. We cannot guarantee that a hospital bed on our unit will be available on this date. We make every effort to admit you as close to your ideal admission date as possible.

What should I have ready while I'm waiting to be admitted?

From your ideal admission date onwards, have your hospital bag packed and be ready to come to the hospital as soon as you are contacted by our unit charge Nurse.

What will happen when I am admitted?

When you arrive at the hospital, please check in at the front desk on the 15th floor (T15A).

- You will be assigned a shared room with one other patient or a private room. Private rooms are for patients requiring additional isolation precautions or other circumstances.
- Your Nurse will give you a tour of the unit, take your bloodwork, complete admission forms and perform a physical assessment.
- A Doctor will discuss the CAR T-cell therapy process and treatment with you, perform a physical assessment and go over any consent forms needed.
- After your CAR T-cells are infused, you may experience low blood counts. This is common and the amount of time it takes for your blood counts to return to normal can be unpredictable.
- More information can be found in *The Leukemia/BMT Inpatient Unit* guide.

Step 7: CAR T-Cell Infusion

What will happen on my CAR T-cell infusion day?

Your CAR T-cells will be reinfused (put back into your body).

Before the infusion:

- Blood tests and a routine check-up will be completed.
- Pre-medications are medications given to help minimize side effects.
  - Tylenol® and Benadryl®, as needed anti-nausea medications
- Your Nurse will stay with you during the infusion.
- Vital signs will be done at the start, middle, and end of the infusion.
  - Vitals signs are when your temperature, blood pressure, heart rate, breathing rate, and oxygen levels are checked.

Your CAR T-cells:

- Come from the manufacturing company frozen. A technician will thaw your frozen CAR T-cells in a warm water bath.
- Will be infused back to you through your Central Venous Catheter (CVC).
- Typically take less than 15 minutes to be infused (maximum of 30 minutes).

While your CAR T-cells are being given to you:

- You will be sitting up comfortably in a hospital bed. A visitor may be in the room to celebrate and support you.
- You may feel nervous or excited or both; this is normal. You are safe and we are here to support you and can answer any questions you may have.
- You may have an odd taste in your mouth like canned corn or garlic. This is from the DMSO preservative in the bag of CAR T-cells. We will give you a hard candy to suck on through the CAR T-cell infusion to help get rid of this odd taste.
- You may feel a tickle or tightness in your throat or chest. This is normal and you will feel better if you breathe deeply and cough.
- You may feel nauseated (feeling of having to throw up).
- You may feel warm and flushed during the infusion. This is related to the DMSO and is expected.
- You may feel some dizziness, or light-headedness.
- You may feel cold. This feeling is caused by the thawed CAR T-cells.
- All these symptoms will go away once the CAR T-cells are finished being infused.
- Some people have an allergic reaction to the DMSO preservative. Your Nurse and Doctor are ready if this happens and will give you medications to quickly stop the allergic reaction.

After your CAR T-cells have been given back:

- You may feel sleepy from the pre-medication that was given.
- Your Nurse will continue to monitor your vital signs.
- The canned corn taste from the DMSO may stay on your breath 24 hours after the infusion.

What is happening in your body?

- CAR T-cells are put back into your blood stream and they will continue to multiply.
- CAR T-cells identify the cancer cells and kill them.
- CAR T-cells may remain in your body for some time to help prevent the cancer cells from returning.

What are the side effects of CAR T-cell therapy?

Your healthcare team will assess you often to check for side effects of CAR T-cell therapy. Learning about the side effects yourself can help you recognize when they are occurring and know when to notify your Nurse or Doctor. CAR T-cell therapy side effects typically occur 10 to 14 days post-infusion

Everyone is different. It is normal for some people to have more side effects than others. For more detailed information on potential side effects and how to manage them, refer to the *Symptom Management Through Treatment* guide.

Cytokine Release Syndrome (CRS)

What is it?

- CAR T-cell therapy is an immunotherapy. It uses your own immune system to fight your cancer.
- Cytokine Release Syndrome (CRS) occurs when your immune system produces large amounts of cytokines very quickly.
  - Cytokines are chemical messengers that help the T-cells carry out their functions.
  - Cytokines are produced when the CAR-T cells multiple in the body and kill cancer cells.
- CRS results in widespread inflammation throughout the body. This can be harmful and interfere with several body functions.

Timeframe

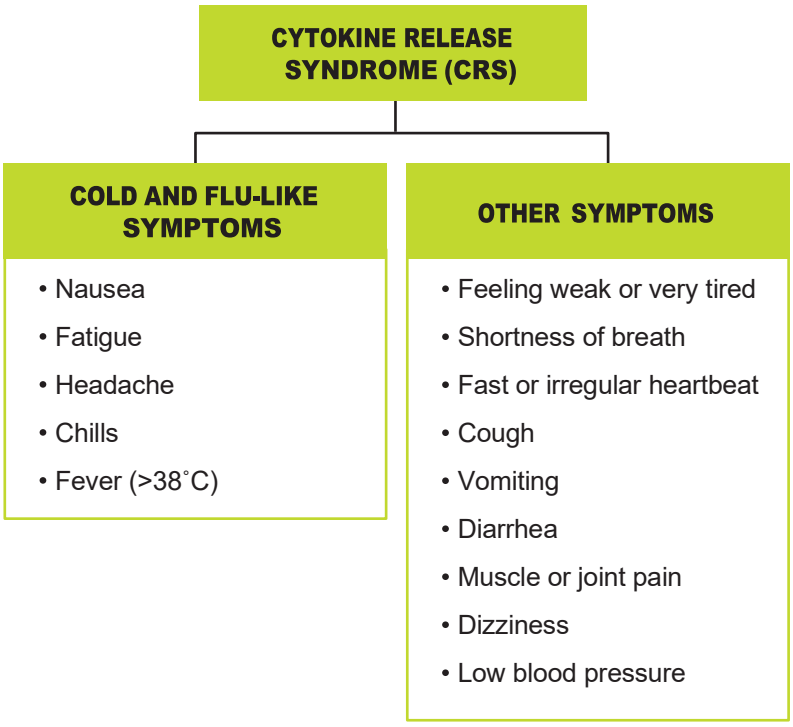
- Typically occurs in the first few days after CAR-T infusion. It can occur up to 30 days after treatment.

When should you contact your healthcare team?

- Have your caregiver immediately contact your healthcare team if you are experiencing CRS symptoms.

Treatment

- Medications can be given to improve symptoms and stop CRS.



Neurotoxicity (ICANS)

- CAR-T therapy can also affect your brain and nervous system.
- During your admission to hospital, your Nurse will complete your CAR-T Toxicity Assessments.
- After discharge from hospital and until Day 30 post CAR T-cell infusion, your caregiver is required to complete your CAR-T Toxicity Assessment (ICE checks) every morning and evening, including days you are seen in Leukemia/BMT Daycare. You will receive the *CAR-T Toxicity Assessment* guide, which includes the ICE check instructions, once you are discharged from the hospital.
- Due to the risk of altered level of consciousness and small risk of seizure, patients treated with CAR T-cell therapy cannot drive for 8 weeks from the day of CAR T-cell infusion. During this time, patients should refrain from driving or operating heavy or dangerous machinery under any circumstances.
- Patients treated with certain CAR T-cell products will receive medications for 30 days after CAR-T cell infusion to prevent seizures.
- Avoid using marijuana or alcohol as these substances can alter your mental state and mimic some symptoms of neurotoxicity.

NEUROTOXICITY

SYMPTOMS

- Changes in ability to write
- Impaired speech
- Difficulty swallowing
- Memory loss
- Hallucinations
- Confusion
- Delirium
- Involuntary muscle twitching
- Tremors
- Loss of balance or coordination
- Dizziness or feeling lightheaded
- Seizures
- Unresponsive

Timeframe:

- Most commonly occurs within the first week after CAR T-cell infusion; however, it can occur up to 8 weeks after.
- Typically, the symptoms resolve over several days without intervention or apparent long-term effects.

Treatment

- Intravenous (IV) medications can be given to improve symptoms and stop neurotoxicity.

When to contact your healthcare team?

- Your caregiver should immediately contact your healthcare team if they suspect you are experiencing neurotoxicity symptoms.

Caregiver instructions if the patient has a Seizure

If you witness a seizure CALL 911. Some things you can do to help reduce harm:

- Make sure the patient is in a safe position.
    - Remove anything around the patient that could potentially harm them, e.g., table corners, glass, hot objects, eyeglasses, long jewelry etc.
- Do not put anything in their mouth.
- Call your healthcare team and report the event.
- Keep track of how long the seizure lasts.
- Once the seizure stops, position the patient on their side, lying down.

Infection

- CAR T-cell therapy can weaken your immune system's ability to fight infection.
- Symptoms of infections can be similar to Cytokine Release Syndrome.
- You will be given medications (e.g., antibiotics, antifungals, antivirals) to prevent infections after receiving CAR T-cell therapy.
- Do not take Tylenol® unless instructed by your healthcare team. Tylenol® can "hide" or "mask" your fever without treating the infection.
- Routinely check your temperature twice per day in the morning and early evening. Check it more if you are feeling unwell.

INFECTION

SYMPTOMS

- Fever (>38˚C)
- Chills or shaking, sweating
- Headache
- Dizziness
- Low blood pressure
- Shortness of breath
- Fast or irregular heartbeat
- Feeling weak or very tired
- Coughing up yellow or green mucus
- Pain, burning, or blood when you pee

Timeframe:

- Typically, your white blood cell counts will improve in the 30 days after CAR T-cell infusion. How quickly these counts improve can vary from person to person. Sometimes low white blood cell counts can persist for months afterward.

When to contact your healthcare team?

- You are advised to contact your healthcare team if any signs of infection are suspected by yourself or your caregiver.
- If you have a temperature of 38°C or higher.

Treatment

- If you have an infection, your healthcare team will treat you with antibiotics, antivirals, and antifungal medications.

Low Hemoglobin

CAR T-cell therapy can lower your hemoglobin. Hemoglobin carries oxygen from the lungs to your body. Hemoglobin is found inside red blood cells.

LOW HEMOGLOBIN

SYMPTOMS

- Feeling tired or weak
- Shortness of breath
- Hearing your heartbeat in your ears when you bend down
- Extreme fatigue with climbing stairs or walking uphill

Timeframe:

- Typically, your blood cell counts will improve in the two weeks after CAR T-cell infusion.

Treatment

- While your blood counts are low you may need a blood transfusion

When to contact your healthcare team?

- You are advised to contact your healthcare team if any symptoms of low hemoglobin are suspected by yourself or your caregiver.

Low Platelets

CAR T-cell therapy can lower your platelets. Platelets help your blood form a clot. Platelets stop or prevent bleeding.

- Do not take Aspirin® or Advil® as it may increase your risk of bleeding
- Clean your nose by blowing gently. Do not pick your nose.

LOW PLATELETS

SYMPTOMS

- Bruising easily
- Bleeding that won't stop
- Gums bleeding
- Nosebleeds
- Blood on your toilet paper when wiping your bum
- For women: increase in bleeding during your period

Timeframe:

- Typically, your blood cell counts will improve in the two weeks after CAR T-cell infusion.

Treatment

- While your blood counts are low you may need a platelet transfusion

When to contact your healthcare team?

- You are advised to contact your healthcare team if any symptoms of bleeding are suspected by yourself or your caregiver.
- If you have any signs of spontaneous bleeding or experience any of the following symptoms:
  - Vomit that looks like coffee grounds
  - Black, tarry stool
  - Bright red blood in your urine

Step 8: Discharge from the Hospital & BMT Daycare Appointments

Before you are discharged:

- You are well enough to be monitored as an outpatient.
- You are able to eat and drink enough to maintain your weight.
- You have enough strength and mobility to attend regular clinic visits.
- You are able to take your medications in pill form.

Once you have been cleared for discharge from the hospital, you will have appointments again at Leukemia/BMT Daycare unit. Caregivers are required to complete CAR-T Toxicity Assessments (ICE Checks) once the patient is discharged from hospital.

What will happen during each visit at the BMT Daycare?

Each visit will vary in length, depending on what your blood tests and symptoms are that day. A typical visit lasts 2-4 hours. You can expect:

- Blood tests taken from your Central Venous Catheter (CVC).
- Your healthcare team to do an assessment.
- Your Nurse to complete a CAR-T Toxicity Assessment (ICE check).
- Close monitoring for fever, infection, and other complications.
- IV fluids and medications for treating symptoms as needed.
- Arrangements for extra tests as needed (e.g, X-ray, CT scan, Ultrasound).

What should I bring to each visit at BMT Daycare?

- Your ID card with your name and medical record number (we will give you this).
- A list of the current medications you are taking.
- Any medications you may need to take throughout the day.
- One family member or friend. You will not be able to drive or take public transportation while you are still recovering from CAR T-cell therapy.
- Snacks, drinks, a reusable water bottle. Bring your own hot water in a thermos. Note: no hot water available.
- Things to occupy your time, although you may prefer to rest or watch TV.

What should I do every day?

- After discharge from hospital and until Day 30 post CAR T-cell infusion, your caregiver is required to complete your CAR-T Toxicity Assessment (ICE check) every morning and evening, including days you are seen in Leukemia/BMT Daycare unit. You will receive the *CAR-T Toxicity Assessment* guide, which includes the ICE check instructions, once you are discharged from the hospital.
- Check your temperature twice a day. Check it more often if you are feeling unwell. Call us immediately if you have a temperature of 38°C or higher.
- Write down questions you have and bring them to your next appointment.

Step 9: Managing at Home after CAR T-cell therapy

In general, it will take 3-6 months for you to return to a normal lifestyle. Adjusting to life after CAR T-cell therapy can feel like a slow recovery. You may still have good days and bad days. It will take time for you to step back into your regular routine. Be patient with yourself as you adjust and recover.

Choosing a Caregiver

When do I need a caregiver?

A caregiver is strongly recommended during lymphodepleting chemotherapy. A caregiver is required for 24 hours a day, after discharge from your inpatient hospital stay, until you reach 30 days post CAR T-cell Infusion. Your caregiver will be monitoring you for CAR-T Toxicity during this time.

How do I choose my caregiver?

- Caregivers can be family, friends, or hired professionals. *Please note that caregivers cannot be provided by hospitals, health authorities, or the Leukemia/BMT Program.*
- Caregivers should be someone 19 years or older, who you are comfortable around, is comfortable around you, who knows you well, and is able to help you through treatment.
- For us to best care for you, your caregiver must be able to communicate with the healthcare team. Translation and interpretation services can be provided.

How many caregivers do I need:

- You need at least one identified caregiver for the duration of your treatment. We understand this can be challenging from a practical and emotional lens for the caregiver. Therefore, rotating caregivers is also an option.
- If one primary caregiver is identified, we suggest arranging visits from family and friends to ensure caregiving tasks do not fall entirely on one person.
- Having rotating caregivers allows each caregiver to rest, relax and have time away from the hospital, and prevent burnout. *For more information on caregiver burnout please connect with one of our Social Workers.*
- Social Workers can assist caregivers who are planning to take time off work, to explore potential financial benefits and request the supporting documentation needed.

If you or your caregiver show signs of a cold or flu (such as a cough, fever or sore throat) 1 week before or any time during your CAR T-cell therapy, tell your healthcare team right away.

Caregiver Responsibilities:

Caregiver duties and responsibilities depend on what your loved one needs. You can help by:

- Coordinating services, such as transportation to and from the clinic.
- Attending appointments, taking notes, asking questions, keeping track of the patient's schedule.
- Providing emotional support.
- Providing support at home:
  - *Reminding the patient to take oral medications.*
  - *Identifying changes in the patient's condition to the clinical team.*
  - *Calling the BMT triage nursing line or obtaining urgent medical care, if needed.*
- Maintaining the home environment (e.g., household cleaning, pet care, laundry).
- Activities of daily living (e.g., grocery shopping, preparing food, picking up prescriptions).
- Serving as a communication link with other family members and friends.

Caregiver Resources

- Go to **www.bloodcancers.ca** Search "Caring for a loved one with a blood cancer" or "Learning to be a caregiver" or "Taking care of yourself". Click on the result that matches the title.
- Go to **www.cancer.ca** Search "caregiver". Click on any of the results you feel apply to your situation.

Common Medical Terms

Anemia: A condition in which the blood has too few red blood cells, or not enough hemoglobin in these cells.

Antibiotics: Medications used to fight bacterial infections.

Antigens: Molecules, such as proteins, found on the outside of cancer cells, bacteria, viruses, etc. T-cells notify your immune system about antigens within the body. Antibodies are created in the body to help target antigens.

Apheresis: A painless procedure where blood is run through a machine that removes T-cells and then returns the remaining cells back to the bloodstream.

Biopsy: Removal of small piece of tissue for microscopic examination.

Blood Tests: You will have many blood tests before and throughout your treatment. Blood tests tell us about your blood cells levels (white blood cells, hemoglobin, platelets). They can also tell us about your general health, how well your organs are working (i.e. kidneys, liver, pancreas), electrolyte imbalances (i.e. potassium, magnesium) and if you have any possible infections.

Bone Marrow: Spongy tissue inside the bones where the blood cells are produced.

Bone Marrow Biopsy: In this procedure, a needle is used to remove a small amount of liquid bone marrow tissue and bone fragment (biopsy) from the pelvic bone. Doctors use these samples to diagnose and monitor blood and marrow disease and cancers.

CAR T-cell therapy: Chimeric **A**ntigen **R**eceptor T-cell therapy, is a treatment made by taking some of your body's own white blood cells and genetically modifying them so that recognize and attack your cancer cells.

Chemotherapy: Anticancer drugs or combination of drugs designed to kill cancer cells.

Chest X-Ray: This is a picture of the organs, bones and tissue inside your chest. It takes about 30 minutes to complete.

Cytokines: Are small proteins that act as chemical messengers that help your body's immune system (such as T-cells) carry out their functions.

Cytokine Release Syndrome: is a collection of symptoms that can develop as a side effect of certain types of immunotherapies, such as CAR T-cell therapy. Having high levels of cytokines may cause increased inflammation throughout the body. This can be harmful and interfere with a number of body functions.

DMSO (dimethyl sulfoxide): A drug used to protect frozen T-cells.

Electrocardiogram (ECG): A heart test to check your heart's electrical activity. Electrode stickers are placed on your chest to measure your heart's rhythm.

Hematologic: Relating to blood and blood forming tissues. A Hematologist is a Doctor that treats diseases and disorders related to the blood.

Immune system: It is the body's defense against infection and disease.

Immunotherapy: refers to treatments that use a person's own immune system to fight cancer.

Infection: Infections are illnesses you get from "germs" (bacteria, viruses, or fungus)

Infusion: The introduction of a liquid into the body through a vein.

Intravenous (IV): A therapy that delivers liquid substances directly into a vein.

Infections: The invasion and spread of harmful organisms (bacteria, viruses, fungus, parasites) that are not normally present in your body.

Leukemia/BMT: Leukemia/Bone Marrow Transplant Program of BC, formed in 1981.

Lumbar Puncture: In this procedure, a needle is used to remove a small amount of cerebrospinal fluid (CSF) from between the lower back bones (vertebrae). CSF is the fluid that surrounds and cushions the brain and spinal cord and can sometimes contain cancer cells. Chemotherapy may be administered into the fluid around the spinal cord to kill cancer cells in the CSF and prevent relapse.

Neurotoxicity (or Neurological Toxicities): Can occur when your brain and nervous system are affected after CAR T-cell therapy. This is sometimes called ICANS by the healthcare team which stands for **I**mmune Effector **C**ell-**A**ssociated **N**eurotoxicity **S**yndrome.

Neutrophils: A type of white blood cell that protects you from infections. They are the first cells to arrive when you have a bacterial infection.

Platelets: Cells that are needed for blood to clot.

Pulmonary Function Test (PFT): A test to check your lung health. A clip will be placed on your nose, and you will be asked to breathe in and out of a mouthpiece.

Red Blood Cells: Cells that carry oxygen from the lungs to the rest of your body.

Radionucleotide Ventriculogram Scan (RVG or MUGA): A nuclear medicine scan used to look at how well your heart is pumping. A series of images of the heart are taken after injections of radioactive solution are given in your arm. The scan takes about 90 minutes.

Receptors: Are proteins that are found on your body's T-cells. These receptors are able to attach to foreign antigens, which can then trigger your immune system to destroy the foreign substance.

T-cell: Are also called T lymphocytes. They are a type of white blood cell. They help control the immune system, make antibodies to fight infections, and can destroy infected or defective cells.

White Blood Cells: A group of blood cells in your body that are a major part of your immune system. White Blood Cells fight infection.

Where Can I Get More Information?

Suggested readings:

- Symptom Management Through Treatment (Leukemia/BMT Program of BC)
- Resources and Support (Leukemia/BMT Program of BC)
- Chemotherapy and Other Drug Therapies (Canadian Cancer Society)
- Coping When You Have Cancer (Canadian Cancer Society)
- Eating Well When You Have Cancer (Canadian Cancer Society)
- Sex, Intimacy and Cancer (Canadian Cancer Society)

Find booklets, videos, and more information at:

The Leukemia Bone Marrow Transplant Program of BC
"Resources"
https://www.leukemiabmtprogram.org/

BC Cancer
"Patient Handout Search"
http://www.bccancer.bc.ca/

The Leukemia & Lymphoma Society of Canada
"Resource Library"
https://www.bloodcancers.ca/

The Canadian Cancer Society
"Cancer information" → "Resources"
www.cancer.ca/en/

Princess Margaret Cancer Foundation
Princess Margaret Cancer Classes "CAR T-cell Therapy"
https://pmcancerclasses.ca/

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This document was created with the intent to help patients enrolled in the Leukemia/ Bone Marrow Transplant Program of BC undergoing CAR T-cell Therapy.

Please note the information contained in this manual is not intended to replace the advice of your healthcare team. Use this as a reference and educational guide. Consult with your Doctor if you have any questions or concerns.

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