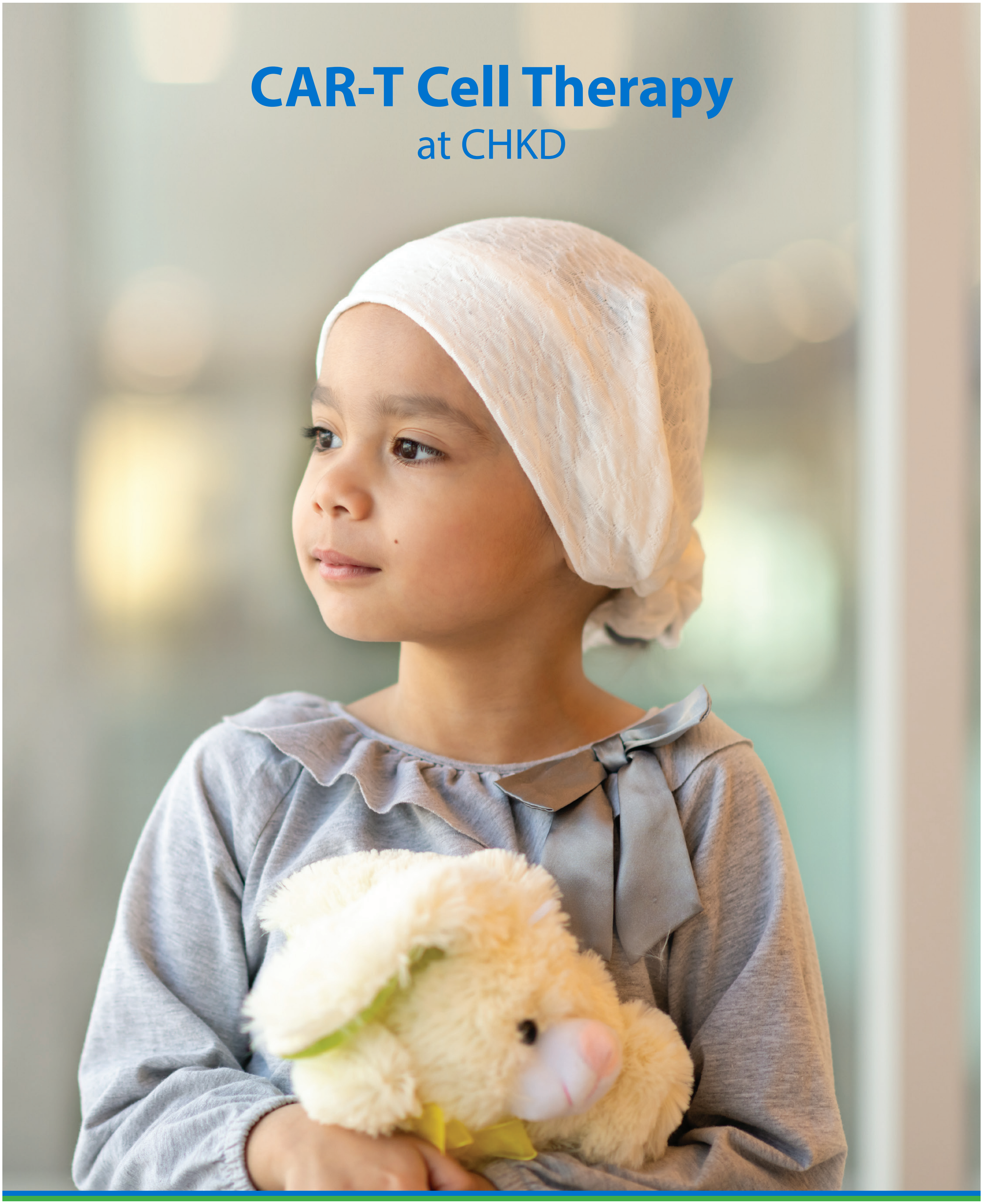
CAR-T Cell Therapy

at CHKD

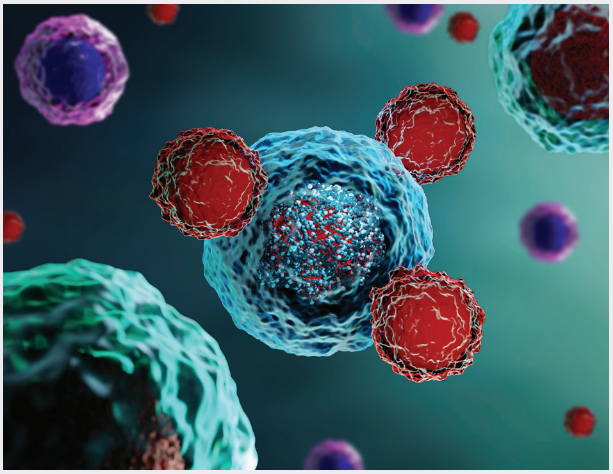


Children's Hospital
of The King's Daughters

What is CAR-T cell therapy?

CAR-T cell therapy is a treatment where the body's own immune cells (T cells) are used to kill cancer cells. T cells are a type of white blood cell whose job is to kill disease cells. Sometimes cancerous B cells look like normal, healthy cells, so T cells do not recognize them. The CAR (chimeric antigen receptors) are like special glasses that help T cells to see these hidden cancer cells.

In this treatment, we collect T cells from the patient's blood and send them to an outside lab to have the chimeric antigen receptor added. After the T cells are modified, they are infused back into the patient to start their work of finding and fighting the cancer cells.



CAR-T cells attach to and destroy rapidly dividing cancerous B cells.

Who can benefit from CAR-T cell therapy?

Currently, CHKD is using CAR-T cell therapy for patients with B cell acute lymphoblastic leukemia (ALL) whose leukemia did not respond to chemotherapy or whose leukemia has come back after treatment. Kymriah, the CAR-T cell therapy treatment used by CHKD, is approved for refractory/relapsed B cell ALL in patients up to 25 years old. Kymriah is also approved for adult patients with relapsed or refractory B cell lymphoma.

How do we decide if CAR-T cell therapy is right for your child?

Prior to collecting T cells, your child will go through a series of tests to make sure they are a candidate for CAR-T cell therapy. Tests may include:

- Chest X-ray to make sure your child's lungs are clear and there are no signs of infection.
- Blood tests to check kidney function, liver function, blood counts, and to determine if your child has been exposed to certain viruses.
- Pulmonary function tests to assess the functioning of the lungs.
- Echocardiogram to assess the functioning of the heart.
- MRI/CT/PET scans to identify changes in disease status and to rule out abnormalities that may increase the risk of side effects.
- Bone marrow biopsies to determine if cancer cells are present. This test may also help predict how well a patient will respond to the treatment.
- Lumbar punctures to check for cancer cells in the spinal fluid.

Preparing for CAR-T cell therapy

If you are receiving this information, the doctor has decided that CAR-T cell therapy is a good option for your child. We would like to provide the education and resources you may need during this process. This type of treatment can take some time and will likely require adjustments to your everyday routine.

It is important to choose one person as the designated caregiver who is with your child throughout this process. This can be a parent, but it is important that the person chosen can be present for all education provided. This caregiver will need to attend all appointments before, during, and after treatment and remain with the child. They should be able to monitor symptoms after treatment and identify important changes that may occur.

Because of the nature of this therapy, it is important to talk with your child's oncologist about any changes in status or medication before, during, and after treatment.

The role of the designated caregiver

We understand that other family members and friends may be involved in the care of your child during this time, but it is important that one person takes on the role of the primary caregiver throughout the process. This will provide consistency and understanding in all the steps involved. Some responsibilities of the designated caregiver include:

- Making sure that your child attends all follow-up appointments.
- Understanding the importance of staying within the required distance of the hospital and presenting your wallet card when arriving at the hospital.
- Ensuring that your child does not drive (if they are old enough) or participate in other high-risk activities for eight weeks after CAR-T cell therapy.
- Monitoring your child's medications to ensure all prescriptions are filled and your child takes them as instructed.
- Learning about and watching for new or worsening symptoms and recognizing when to call the care team and return to the hospital.
- Reporting any changes in your child's condition to the care team.
- Protecting your child from sources of infection.
- Providing your child with emotional support throughout the CAR-T cell therapy process.

Emotional and financial planning

Our team will provide education and support for the patient and caregiver throughout the entire treatment process. A social worker will meet with you to provide emotional support and address any concerns you may have. You will have several follow-up appointments after the treatment.

It is important that you are prepared to stay within 30 minutes of the hospital for the two weeks after the CAR-T cell infusion. If your home is more than 30 minutes away from the hospital, we will discuss options for where you and your child can stay during the first two weeks.

Your CAR-T team

- **Oncology Physician:** Oversees your child's care throughout treatment.
- **Resident Physicians:** May work with your child during their inpatient stays.
- **Cellular Therapy Nurse Coordinator:** Communicates with you and your child to help organize and schedule any testing and procedures. They will educate you on the process and communicate specific details about your treatment plan.
- **Oncology Nurse Coordinator:** Works with the cellular therapy nurse coordinator to assist in coordination and education for you and your child.
- **American Red Cross Nurse:** A nurse with special experience who will come to collect your child's T-cells through a process called leukapheresis.
- **Registered Nurses (RNs):** Works with your child during their outpatient visits and any inpatient stays. They are trained to care for children before, during, and after their CAR-T cell infusion. Your child will be cared for by infusion nurses, nurses on the inpatient team, and apheresis nurses.
- **Nursing Assistants and Medical Assistants:** Supports the nursing team by helping with care, including vital signs, labs, and activities of daily living.
- **Social Work Team:** Provides families with support throughout the CAR-T cell therapy process. If you need to stay somewhere close to the hospital, they can assist.
- **Child Life Specialist:** Helps your child cope during treatment by explaining the process and procedures in a developmentally appropriate way.
- **Clinical Pharmacists:** Assists with managing the different medications that your child will need. The oncology clinical pharmacist specializes in caring for patients receiving CAR-T cell therapy.
- **Dietician:** Helps you choose safe and healthy foods for your child to eat throughout this process.
- **Case Manager:** Assists if your child is admitted to the hospital. They will also help to obtain home healthcare supplies and work with your insurance company.

What are the steps of the CAR-T cell therapy process?

- Assessment by oncologist to determine if your child is a candidate for CAR-T cell therapy.
- Insurance approval obtained by our team.
- Your child's blood tested to check for certain viruses.
- T cells collected from your child during a short stay in the hospital.
- T cells sent to an outside lab to be modified by CAR.
- Chemotherapy given to help prepare your child's body for the CAR-T cell infusion.
- CAR-T cell infusion. This will likely take place in the Children's Cancer and Blood Disorders Center (CCBDC) outpatient clinic. After observation for adverse reactions, your child will be discharged.
- Patient and caregiver stay within 30 minutes of the hospital for two weeks after the CAR-T cell infusion.
- Follow-up visits to monitor your child for any possible side effects..

How are T cells collected?

Your child's T cells are collected through a process called leukapheresis. Your child will be admitted to CHKD the day before this procedure. During this stay, we will draw blood to send to a lab that will help us decide if your child is ready to have their T cells collected. If the testing shows that your child is ready for T cell collection, they will have a temporary central line put in place to help make it easier for us to collect the cells. Your child's primary oncologist will decide where and when the leukapheresis procedure will take place.

An experienced nurse from the American Red Cross will perform the leukapheresis procedure and your child's oncologist will order any needed labs and medications. The CHKD nurse will monitor your child's vital signs, draw required labs, and give necessary medications.

Depending on age and ability, some patients might need medicine to help them relax. We will provide education and obtain additional consent if this is needed.

Your child will be closely monitored by a team working together to ensure that T cells are collected safely and effectively.

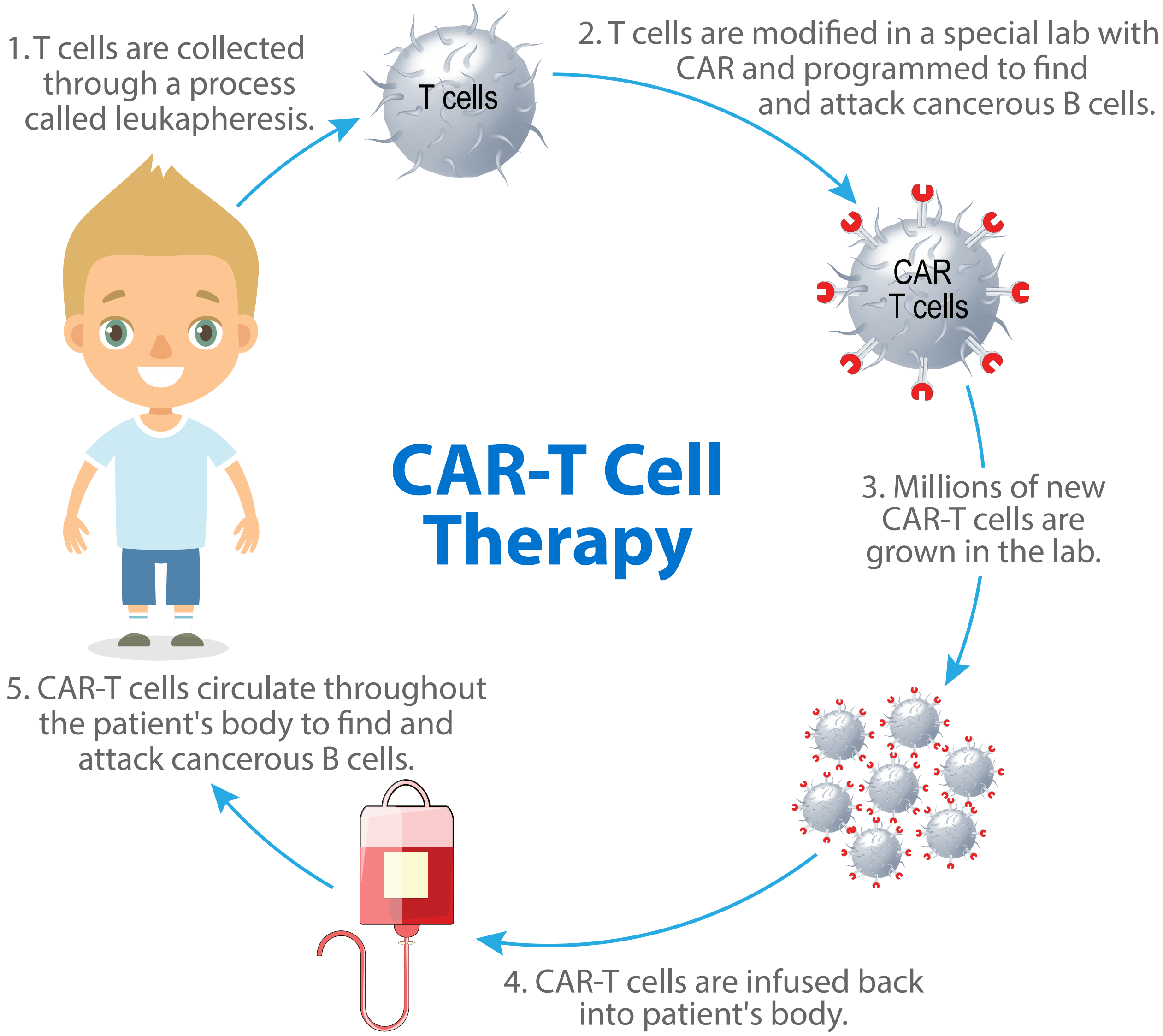
Blood will be drawn and processed through a machine that separates out the T cells. Then, the rest of the blood will be returned to your child's body. The process usually takes four to six hours to complete, but it is unique to each patient.

After the procedure, the oncologist will decide when the central line can be removed. The line will be removed before your child leaves the hospital. Additional labs may need to be taken before leaving the hospital.

What happens to the T cells after they are collected?

After the T cells are collected, they are sent to a special lab where the CAR is added to turn them into CAR-T cells, making them better able to find and destroy cancer cells. This process can take several weeks.

Once your child's CAR-T cells are ready, they will be frozen and stored until they are used. At that time, we will provide you with a list of appointments and next steps in the process.



CAR-T Cell Therapy

1. T cells are collected through a process called leukapheresis.

2. T cells are modified in a special lab with CAR and programmed to find and attack cancerous B cells.

3. Millions of new CAR-T cells are grown in the lab.

4. CAR-T cells are infused back into patient's body.

5. CAR-T cells circulate throughout the patient's body to find and attack cancerous B cells.

What happens while we are waiting for the CAR-T cells?

Bridging chemotherapy

While the CAR-T cells are being prepared for infusion, your child's oncologist may order additional chemotherapy to continue to fight the cancer cells. Once the plan has been determined, your child's primary oncologist and the nurse coordinator will review the details and help you prepare your child for the treatment plan.

Lymphodepleting chemotherapy

Once the CAR-T cells are ready, a date will be set for the infusion. One week before the infusion, your child will have an additional round of chemotherapy that is usually four to five days long. This chemotherapy is called lymphodepleting chemotherapy. Lymphodepleting chemotherapy lowers your child's white blood cell count to help make room for the new cells that we will infuse. We will review the specific medications that will be used along with their potential side effects, as they may be different from medications used for your child in the past. After the lymphodepleting chemotherapy, we hope to be ready for your child's infusion.

What should be expected on the day of infusion?

On the day of infusion, you will come to the CCBDC outpatient clinic. Your child should already have a central line in place.

To prepare you and your child for the infusion, your child's oncologist and the nurse coordinator will meet with you to review the procedure again and answer any questions you may have. Your child's nurse will draw blood and give your child medications to help prepare their body to receive the CAR-T cells. Your child's nurse and oncologist will assess your child to make sure they are ready for the infusion. For example, if your child has any signs or symptoms of an infection, we may need to reschedule the infusion.

Once the oncologist decides that your child is ready for the infusion, they will receive medications to keep their body from having an allergic reaction to the CAR-T cells. The CAR-T cell infusion will take place in the hospital, where your child will be monitored for any reactions that could occur. The infusion should take less than 30 minutes, but you will need to plan to be at the hospital for most of the day. After the infusion, your child will spend extra time at the hospital so we can watch for any possible reactions. The reaction your child could have will look much like other allergic reactions.

During the infusion, we will monitor for:

- Nausea or vomiting
- Low blood pressure
- Allergic reaction
- Swelling
- Hives
- Pruritis (itchiness)
- Difficulty breathing
- Rash

If your child has any kind of reaction during or after the infusion, the oncologist will assess and treat the symptoms as appropriate. Your child may be given extra medicine to help with the reaction, and they may have to stay in the hospital for longer to receive appropriate treatment. The hope is that your child will not experience a reaction, but it is good idea to be prepared in case your child needs to be admitted to the hospital.

If your child does not have a reaction during or following the infusion, the nurse will review important information with you so your child can be discharged. You will be given phone numbers, guidelines to follow, instructions on when to call and when to return to the hospital, and a wallet card stating that your child has received Kymriah. It is important that you present your wallet card and tell all healthcare providers that your child has received Kymriah, even when coming to CHKD. If you live within 30 minutes of the hospital, you will be discharged to home. If you live farther away from the hospital, you will be discharged to the location determined during your treatment planning.

Infusion side effects and post-infusion monitoring

After infusion, it is important to stay within 30 minutes of the hospital for two weeks and within two hours of the hospital on days 15 through 30. We will monitor your child closely for side effects they may experience, including cytokine release syndrome (CRS), neurotoxicity (often referred to as ICANS), and infection. It is important to recognize the symptoms of these side effects so we can treat them quickly.

Cytokine release syndrome (CRS)

Cytokines are proteins that are normally released into the immune system. After CAR-T cell therapy, many cytokines are produced and released into the body which can cause CRS. CRS can begin within a few hours, days, or weeks after the infusion. CRS can cause serious and life-threatening side effects. Therefore, it is very important to stay close to the hospital, so we can treat it very quickly.

You will need to check your child's temperature every 4 hours on days 0 through 7 and every 8 hours on days 8 through 15. If your child has a fever or experiences any of the symptoms shown on the following page, it is important to call us at **(757) 668-7243** on your way to the hospital. If this occurs Monday through Friday during CCBDC outpatient clinic hours, and there is space available, you may be directed to the clinic. If you are sent to the emergency room, present your wallet card and be sure to tell staff that your child has received CAR-T cell therapy.

Once arriving at the hospital, whether in the emergency room or CCBDC outpatient clinic, your child's symptoms will be evaluated and treated. It is likely that the nurse will draw labs to check for infection and will monitor vital signs. The oncologist might order different tests depending on the situation. Your child will likely receive medications and care to help alleviate their symptoms. The oncologist will decide if they need a medication called Tocilizumab that helps to treat CRS. Your child will be monitored very closely and will likely stay in the hospital until CRS is resolved. The nurses and doctors in the hospital have specific training in handling CRS after Kymriah to ensure that they provide the best care.

Neurotoxicity (ICANS)

Immune effector cell-associated neurotoxicity syndrome (ICANS) is another condition we will monitor for after CAR-T cell therapy. ICANS is usually temporary and can develop at the same time as CRS. It can also develop after CRS or on its own. ICANS can occur any time within 8 weeks of the CAR-T infusion.

Depending on how severe your child's symptoms are, the doctor may focus on keeping them comfortable until the symptoms resolve. They may also prescribe medications to help. The treatment will depend on the severity and specific symptoms of the neurotoxicity. Your child may be prescribed Tocilizumab, steroids, seizure medications, or other medications to help manage symptoms.

Although the symptoms of neurotoxicity can be scary, they are usually reversible. The symptoms may take some time to resolve. Your child will likely have to stay in the hospital with close observation until their symptoms resolve.

Due to neurological changes, your child should not drive or participate in high-risk activities for 8 weeks following the CAR-T cell infusion.

If your child develops CRS or ICANS, they will need to be admitted to the hospital until their symptoms resolve. They may have to be admitted to the intensive care unit for close monitoring. This can be scary, but our team is trained on what to do for these side effects and will provide the best care for your child during this time.

Symptoms to watch for

Fever
(100.4°F/38°C or higher)

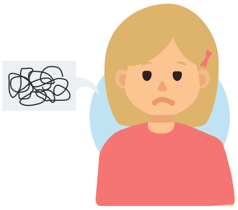
Headaches

Anxiety

Chills

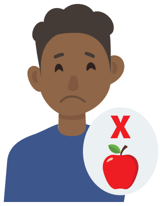
Difficulty breathing

Confusion



Difficulty speaking or slurred words

Severe nausea, vomiting, diarrhea



Loss of appetite

Memory loss

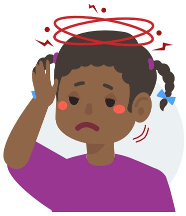
Muscle or joint pain

Agitation

Rash

Sleepiness

Swelling



Dizziness or lightheadedness

Loss of coordination

Weakness

Changes in handwriting

Hallucinations

Seizures

Hemophagocytic lymphohistiocytosis (HLH)

HLH is a rare, but serious complication that can occur after CAR-T cell therapy. HLH can happen at the same time as or shortly after resolution of CRS and needs to be treated quickly. Symptoms usually mimic those of CRS. We will continue to monitor for the symptoms listed in this booklet. You will also need to monitor for these symptoms at home. Additional symptoms may include:

- Enlarged liver
- Swollen lymph nodes
- Skin rashes
- Jaundice (yellowing of skin and eyes)
- Persistent cough
- Stomach pain, vomiting, diarrhea
- Headache, vision changes, or weakness

B cell aplasia

CAR-T cell therapy will reduce your child's white blood cell count. The CAR-T cells will recognize the cancerous B cells but will also destroy the healthy B cells. When the healthy B cells are destroyed, this is called B cell aplasia. B cell aplasia is usually a sign that the CAR-T cells are doing their job. B cell aplasia can last for a long time after the CAR-T cell infusion, and we will monitor for this with a lab called the IgG level. If your child's IgG is below a certain level, we will give them an intravenous immunoglobulin infusion, called IVIG for short.

Reduced white blood counts weaken the immune system and can increase the risk of infection. To help reduce risk of infection, your child will be given antibiotics, anti-viral, and antifungal medications.

Low blood counts

In addition to low white blood cell counts, your child may experience low platelet and red blood cell counts. Having fewer platelets puts your child at risk for bleeding. Having fewer red blood cells can make them tired or weak. Until the counts recover, your child may need blood and platelet transfusions to help boost their counts.

Fatigue

Your child may experience fatigue after CAR-T cell therapy that may take weeks or months to resolve. They may be more tired or weaker than they were before. Your child may be prescribed physical therapy to help regain strength.

Secondary malignancies

Patients treated with CAR-T cell therapy may develop secondary malignancies (cancer) or recurrence of their cancer. This is something your child will need lifelong monitoring for. For all future health visits, it is important to always report that your child has had a CAR-T cell infusion.

Follow-up care

After CAR-T cell therapy, your child will have frequent visits to the CCBDC outpatient clinic. At minimum, we will schedule appointments for one day after the infusion and three days after the infusion. After that, we will schedule appointments at least three times a week until day 14. On days 15 through 29, your child will have weekly visits. Your child's oncologist may decide it is necessary to schedule more frequent visits. This is another reason it's important you stay close to the hospital for the first month.

On or near day 29, we will check to see if the CAR-T therapy worked effectively by conducting a bone marrow biopsy and lab tests. Your child may also have CT scans, depending on their diagnosis. For months two through 12, your child will have monthly appointments to monitor their labs and physical status.

Your child will have check-ups to monitor for:

- CAR-T cell persistence
- Absence of malignancy (cancer)
- Symptoms of CRS and ICANS
- Lab tests to check for low blood counts
- Lab tests to check for electrolyte imbalances
- Infection
- Organ function
- Any other concerns

Long-term monitoring: Five years following CAR-T cell infusion

We will monitor your child for five years following the CAR-T cell infusion. Because your child's risk for infection can be higher for a long time, it is important that we check their IgG levels frequently. IgG is an antibody that protects against viral and bacterial infections. We will follow up every other month, or more often if needed.

In addition, we will check labs every six months. Labs will be monitored for persistence of CAR-T cells, absence of disease, and other organ function.

We will continue to check in and answer any questions that you may have. Education will be provided based on assessment at follow-up appointments, but you are always welcome and encouraged to ask any questions along the way.

Approximate timeline of what to expect after CAR-T cell infusion

DAYS 1–14:

- Appointments on day 1 and day 3 after infusion.
- Appointments at least three times a week for first two weeks.
- Monitoring for CRS, ICANS, HLH, infection, low blood counts, and other possible side effects.

DAYS 15–29:

- Weekly appointments, monitoring for CRS, ICANS, HLH, infection, low blood counts, and other possible side effects.

DAY 29:

- Bone marrow biopsy and labs to assess effectiveness of CAR-T cell therapy.

MONTHS 2–12:

- Monthly visits to monitor labs to check for CAR-T cell persistence, absence of malignancy, low blood counts, infection, and organ function.
- Treatment based off assessment. Patient may need blood and platelet transfusions, medications to prevent infection, IVIG, or other supportive care measures.

1–5 YEARS FOLLOWING INFUSION:

- Monitor IgG levels every other month.
- Additional lab tests every 6 months.