

Cellular therapy programme

Chimeric Antigen Receptor T Cell (CAR T cell) Therapy

What is CAR T cell therapy and how does it work?

CAR T cell therapy is a new treatment. It involves using your own body's immune system to treat your cancer. Our immune systems monitor for unhealthy cells or foreign invaders such as infection or viruses. It uses several kinds of blood cells to destroy anything unfamiliar by recognising the unique protein (antigen) and identifying them as foreign.

One type of blood cells called T cells is particularly good at fighting infection. They move around the body finding defective cells. They have receptors that can attach to foreign cells and trigger the immune system to destroy them. Although they should see all cancer cells as unhealthy it can sometimes be difficult to tell the difference, allowing them to hide and multiply. CAR T cell therapy puts a new gene into your T cells enabling them to recognise a specific antigen on your cancer. This highlights them for the immune system to attack and destroy. The CAR T cells are programmed to remember the same cancer cell and are designed theoretically to safeguard from further reoccurrence if they were to re-emerge.

There are many different components to this treatment process. We have broken down each step describing the patient pathway and what you may expect.

First step - meeting the team

You will have a consultation with our medical team and specialist nurses in clinic to discuss CAR T cell therapy. The treatment process will be discussed in more detail to make sure it is a safe and appropriate option for you. This is an opportunity to raise any concerns or questions you may have. Following this appointment a series of pre-screening tests and investigations will be organised by our transplant co-ordinators. This is to assess your performance status and organ function. These may include physical examination, various blood tests, lung function test and echocardiogram. Following the results of these you will be provided with dates for leukapheresis (collection of your T cells) and admission for CAR T cell treatment. The team will also organise for you to have a central venous catheter (CVC) line inserted. A CVC is used for the administration of chemotherapy, medications and any other treatment you require.

Things for you to consider before your consultation:

- Do you have a designated friend or relative who can support you when at home and can monitor for signs of possible side effects?
- Do you have available transport/ designated driver who could bring you to the hospital if needed once at home?



The next step: Leukapheresis - collecting your T cells

Leukapheresis is a procedure where white cells (some of which are T cells) are separated from the blood. Specially trained nurses operate the apheresis machines. The machine removes blood from you via a needle in one arm. It is then spun in the machine and separated into red cells, white cells and plasma. For this treatment your T cells will be separated out and collected into a sterile bag. The remaining blood is then returned to you via a cannula on your other arm. The whole process can take between 4 and 6 hours and may require 1 to 2 days of collection. After your leukapheresis procedure is complete the collection bag is frozen in our labs and then sent to a designated laboratory to be modified.

What happens in the laboratories?

In the laboratory your T cells will be re programmed to produce special receptors on their cell surface known as CARs (Chimeric Antigen Receptors). These new receptors will enable the T cells to recognise and attach to the antigen on the cancer cell. Your newly modified T cells are reproduced in order to create sufficient numbers. They are then refrozen and stored. This part of the process can take several weeks to complete. When your admission date is finalised the product will be shipped back to our hospital so they are ready for you to receive. Throughout this process, careful measures will be put in place to ensure safety and maintain high levels of quality.

Coming in for treatment

Like any treatment CAR T cell therapy comes with potential side effects. Because of this you will be admitted to the hospital so our team can closely monitor you during this time. Throughout the process they will observe your response and manage any reactions. The duration of your stay will depend on how well you tolerate the treatment and if you experience any complications. During your admission you will first receive a lymphodepleting chemotherapy treatment to prepare your body to receive the CAR T cells. This is used to make 'room' for the cells, improve the chances that they will be accepted by your body and prevent your immune system from attacking them. When you are ready to have the T cells returned they will be thawed on the unit and returned to you via an infusion drip using your central venous catheter (CVC) line.

What happens during treatment?

Once returned to you the CAR T cells are designed to expand and multiply, attacking your cancer cells. It is during this time you will be very closely monitored for side effects. Not all patients will have adverse reactions as each patient experience will differ. The side effects will either resolve on their own or will require expert management from medical and nursing staff. In a number of people this therapy can cause very severe side effects occasionally needing input from our critical care team. You will receive various medications to help prevent and control these side effects and the treatment will depend on their severity. Most side effects develop in the first few days whilst you are in hospital but they can also occur up to 8 weeks after, so it is important to familiarise yourself with these so you are aware of them when you have returned home.

What are the side effects of CAR T cell therapy?

Things that may occur during CAR T-cell infusion (hours or days after)

- **Cytokine Release Syndrome (CRS).** This is a systemic inflammatory response which happens within the body and is by far the most serious side effect. After receiving the CAR T cells the immune system may become activated as they travel through your body. Substances called Cytokines can be released into your system. This can make you feel unwell causing a wide range of potential symptoms such as fever, chills, racing heart, low blood pressure and difficulty breathing.
- **Neurological toxicities.** In some patients the same immune activation can alter the brain and neurologic system temporarily. These can cause headaches, confusion, drowsiness and difficulty with talking, writing and memory. In severe cases it is possible to experience delirium, difficulty speaking, hallucinations, seizures or loss of consciousness.

Symptoms that may occur days or even weeks after CAR T-cell infusion.

- **B cell aplasia (loss of normal B cells)**

Some cancers involve B cells and CAR T cells are engineered to target this which means there will be a large drop in the number of B cells in your body. This will affect your ability to fight infections. Minor infections can become life-threatening in a matter of hours if left untreated. Symptoms include fever, shivering, sweats, sore throat, diarrhoea, discomfort passing urine, coughing or breathlessness. We recommend you use a digital thermometer so you can check your temperature when you are at home. You may require immunoglobulin replacement after receiving this treatment.

- **Tumor lysis syndrome**

When large numbers of cancer cells die the contents of these cells are released into the blood stream. This can result in a shift of fluids and salts in your body possibly causing damage to your kidneys (acute kidney/renal disorder). If you notice you are passing less urine or have discomfort when going to the toilet, please inform your medical team.

- **Drop in blood counts**

CAR T cell therapy can lower your blood counts. These can include red blood cells, white blood cells and also platelets. Your doctor will test your blood regularly to check for this and may result in you requiring transfusion support. If you experience any bruising or bleeding when you are at home, please contact your medical team/key worker at The Christie or if out of hours The Christie Hotline.

- **Gastrointestinal problems**

The bowel and stomach can be affected by the treatment. You may experience abdominal pain, constipation, diarrhoea, nausea and vomiting. If you develop any of these symptoms please contact The Christie Hotline especially when at home.

- **Skin rash**

You may experience a rash, this can vary from mild to severe. Please inform us of any changes in your skin.

- **Sex, contraception and fertility**

As this is a new therapy there is currently no data available on how this treatment may affect fertility. It is important that you do not get pregnant or father a child during this time. Potential effects on an unborn child are unknown and therefore we recommend that you use effective birth control and women should stop breast feeding as it is unknown if the medication is excreted through breast milk.

Not all side effects are listed above. Please contact the medical team if you experience any unusual symptoms.

Going home/after you leave the hospital

Once you have completed your treatment and are ready to go home you will be reviewed in our outpatient department. Here you will be monitored in relation to your progress following CAR T cell therapy. Please continue to monitor for any signs of infection when at home and phone The Hotline if any symptoms arise. **If your temperature rises above 37.5°C please contact The Christie Hotline on 0161 446 3658.**

Due to the neurological events that can happen, you may be advised to refrain from driving, using machines or taking part in activities where you need to be alert, for up to 8 weeks after. For further information, please refer to your medical team/key worker at The Christie, or if out of hours The Christie Hotline.

Important reminders

- It is very important that you report side effects straight away. Don't delay if you feel unwell please ring The Christie Hotline on **0161 446 3658**. **The lines are open 24 hours a day. Make sure you tell them you have had CAR T cell therapy.**
- Within the first 2-3 months after receiving the treatment if you need to visit any doctor (including A&E) be sure to carry your **Patient Alert Card** at all times.
- If you develop any neurological symptoms similar to the side effects mentioned you must also make contact with your medical team as soon as possible.

If you need information in a different format, such as easy read, large print, BSL, braille, email, SMS text or other communication support, please tell your ward or clinic nurse.

We try to ensure that all our information given to patients is accurate, balanced and based on the most up-to-date scientific evidence. If you would like to have details about the sources used please contact patient.information@christie.nhs.uk

For information and advice visit the cancer information centres at Withington, Oldham or Salford. Opening times can vary, please check before making a special journey.

Contact The Christie Hotline for
urgent support and specialist advice
The Christie Hotline: 0161 446 3658
Open 24 hours a day, 7 days a week

