

## CAR-T cell therapy – Chimeric Antigen Receptor T Cell therapy

# What is CAR-T cell therapy?

CAR-T cell therapy is a new and innovative anticancer treatment. The medicine is manufactured from collecting your own T cells. It is a type of personalised immunotherapy and involves using your own body's immune system to treat your cancer. It provides a promising new approach for the treatment of certain refractory or challenging cancers.

There are currently only a limited number of approved commercial CAR-T products available for use in the UK with specific clinical indications which your consultant will know if you are eligible for.

There are also numerous clinical trials in progress using immune effector cells which have a range of clinical indications including a variety of solid tumour diseases.

Your consultant will know if you are eligible for any of these clinical trial treatments.

## What does our immune system do?

The body's immune system is its defence system against invaders such as bacteria, viruses and unhealthy/ abnormal cells such as cancer cells. Its role is to identify these cells and to destroy them.

Many cells work together to help to make this happen. When the body identifies foreign substances (**antigens**) the immune system will work to try and get rid of them.

2 types of white blood cells – **B lymphocytes** and **T lymphocytes** are very important in how our body's immune system works. Lymphocytes start out in the bone marrow and either stay there and mature into B cells, or go to the thymus gland to mature into T cells.

The role of the B lymphocytes is to find the invader (antigen) and to lock on to it and produce an **antibody**.

The T lymphocytes will then be mobilized to destroy the antigen (infected or changed cell) targeted by the antibody. Some T cells are even known as **killer cells** for the role they play. They also help other immune cells by signalling to them that it is time to do their jobs.

Our bodies are making unhealthy or abnormal cells all the time which the immune system is able to identify and destroy. However in certain situations these cells escape the immune system and continue to multiply to cause a cancer.

CAR-T cell therapy uses your own genetically engineered T cells to try and recognise a specific antigen on your cancer and then to attack and destroy those cancer cells.

The CAR-T cells are programmed to remember the same cancer cell and are designed to continue to expand and attack any new cancer cells over time, thus hopefully safeguarding from further reoccurrence of the disease.

These cells are collected using a process called **apheresis** which will be discussed later on.



## Consent

We will ask you to sign a consent form agreeing to accept the treatment that you are being offered. The basis of the agreement is that you have had The Christie's written description of the proposed treatment and that you have been given an opportunity to discuss any concerns. You are entitled to request a second opinion from another doctor who specialises in treating this cancer. You can ask your own consultant or your GP to refer you.

Your consent may be withdrawn at any time before or during this treatment. Should you decide to withdraw your consent then a member of your treating team will discuss the possible consequences with you.

## Treatment pathway

There are many different steps to this treatment process.

### Step 1: Initial referral

If your consultant thinks this therapy may be suitable for you then you will be offered a consultation with our cellular therapies consultant and cellular therapies co-ordinators in clinic to discuss CAR-T cell therapy.

The treatment process will be outlined 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 cellular therapies coordinators. You will have a physical examination and blood tests including a virology test to look for viruses such as Hepatitis B and C and HIV and syphilis. This test is required legally within 30 days of any blood collection process.

Please let your doctor know if you have any concerns about these tests. You will also require an ECG at this consultation. In addition you will need to complete a data protection/GDPR form for the CAR-T manufacture to enable a request for the product to be made.

Before we are able to collect your T cells you may be required to have a further biopsy of your cancer as well as repeat scans. Following the results of these you will be provided with dates for apheresis (collection of your T cells).

At some point either before or soon after collection (apheresis) you will need to have a heart scan (ECHO) and breathing tests (PFTs), it may be possible for these investigations to be done at your local hospital if you live far away from The Christie.

### Step 2: Apheresis – collecting your T cells

Apheresis is a procedure where blood is passed through a machine that is able to separate out different blood cells using a centrifuge. Your T cells can be collected using this process. It takes approximately 5 - 6 hours and may be done over 1 or 2 days. The cell separator machines are operated by specially trained nurses who will be with you throughout the procedure. It is a safe procedure but as with anything there are some potential side effects and considerations. The machine removes blood from you via a needle in one arm and returns blood to you via a needle (cannula) in the other arm. If you have a central line such as a Hickman line the nurses will be able to use this line. Unfortunately PICC lines cannot be used to carry out this procedure.

On your first visit to the cellular therapies clinic a nurse will examine your veins and if there are any concerns that they would not be suitable to carry out the procedure alternative methods will be discussed with you. This may include the insertion of a temporary line in your groin known as a femoral line so that the procedure can be done smoothly and to maximise the quality of the T cells that are collected.

If needed this type of line is needed it will be inserted by one of the specialist doctors on the cellular therapies team or by one of the specialist interventional radiographers in the hospital, you will give consent for this procedure separately.

Once we have collected your stem cells this line will be removed and you will need to stay on bed rest in the hospital for approximately 4 hours. Although admission post procedure is very rare if you do not require a femoral line we would advise that you still bring an overnight bag with you.

During the procedure your blood is passed through the machine and separated and your T cells collected into a sterile bag. Approximately only 200 - 300mls of blood is taken from you, together with some plasma in a separate bag.

A single use kit is used for each procedure and because we do not want your blood to clot whilst it is in the machine we will mix it with an anticoagulant called ACDA. Occasionally this may cause some side effects, including tingling mainly in your hands feet and around your lips, nausea, light-headedness and central chest pain. You will be monitored very closely during the procedure but if you experience any of these side effects, you should inform the nurse immediately. They can usually be resolved by slowing the machine down and giving you some calcium in a tablet form or by an intravenous drip.

The nurses will check your blood tests on the day of the procedure and will give you any other supplements that you may require to carry out the procedure safely.

Some patients feel light headed and faint when the procedure first starts and the machine is loading but this will normally settle quickly and can be helped by making sure you have had plenty to drink and have eaten before coming to the hospital. If this is the case the nurses will slow the procedure down and allow you to recover, you may also need some extra intravenous fluids and oxygen to help your recovery.

Finally, as with infusions of any fluid through plastic tubing, there is a very small risk of air entering the system. The likelihood of this is extremely low and the machine has multiple sensors and alarms in place. Serious side effects are extremely rare during this procedure.

Once your T cells have been collected they will be sent to the manufacturing site where they can be engineered and expanded for your use.

### **Step 3: What happens whilst my cells are being manufactured?**

In the laboratory your T cells will be re-programmed to produce special receptors on their surfaces 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 or expanded in order to create sufficient numbers for use. They will also go through a very strict quality assurance programme before they are released back to the hospital in a frozen state for your use.

### **This process can take approximately 4 weeks for the commercial licenced products**

As the manufacturing of the CAR-T requires several weeks you may well need to have further treatment or **bridging**. This may be radiotherapy or chemotherapy or both, to keep your disease at bay while you are waiting for admission for CAR-T therapy, this may be done at The Christie or your local hospital.

The cellular therapies team at The Christie will be in close contact with you and your local consultant throughout this time keeping you up-to-date with the progress of the cells organising any investigations you may need and letting you know potential treatment dates.

Once the cells have been manufactured you will be invited back to see the cellular therapies consultant again to consent for your treatment and to further discuss the potential side effects and risks and benefits of going forward with CAR-T therapy and be given an admission date. The duration of your stay will depend on the complications you experience and how quickly you recover but is generally between 2 - 4 weeks.

### **Things for you to consider before your consultation:**

- Do you have a designated friend or relative who can support you after discharge 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 you have been discharged?
- Do you live within an hour's drive of the hospital or have someone who could stay with you in The Christie ambulatory care accommodation?

## Step 4: Inpatient treatment

On the day of your admission you will have a central venous catheter (CVC) line inserted. A CVC is used for the administration of chemotherapy, medications and any other treatment you require and will hopefully minimise the need for you to have needles and cannulas during your treatment. Before you receive your cells back you will need some **lymphodepleting chemotherapy** to help your body accept the CAR-T product and to help prevent your own body's immune system from attacking the CAR-T. This is normally a combination of 2 chemotherapy drugs called fludarabine and cyclophosphamide which will be given over 3 - 4 days followed by a few rest days. In most cases you will be able to have this as an outpatient on our specialist ambulatory care unit.

You will then be admitted on the day that your CAR-T cells are due to be reinfused which will be done using your central line. During your time as an inpatient you will be very closely looked after by a specialist cellular therapy medical and nursing team who are experienced in this treatment.

Once returned to you the CAR-T cells are designed to expand and multiply, attacking your cancer cells. You will remain an inpatient and be very closely monitored for side effects by a specialist cellular therapy medical and nursing team.

Not all patients will experience the same degree of complications. Everyone is different, some side effects will either resolve on their own with close monitoring, others may need closer monitoring and in a small number of patients may require the support of our specialist outreach and critical care team. This is generally only for a short period of time and most patients return back to the ward within a few days.

The ward team are there to support and monitor you throughout your stay until you are able to be sent home safely. Most side effects develop in the first few days after receiving your CAR-T whilst you are in hospital but they can also occur up to 8 weeks later, so it is important to familiarise yourself with these so you are aware of them when you have returned home.

## CAR-T specific side effects

### Cytokine Release Syndrome (CRS)

This is a systemic inflammatory response which happens within the body a few days after the CAR-T has been given back to you. Your immune system may become over activated in the presence of the CAR-T and release an increased number of cytokines (a natural protein involved in fighting infections). This is also known as a **cytokine storm**. This reaction can make you feel quite unwell causing a wide range of potential symptoms such as fever, chills, racing heart, low blood pressure and difficulty breathing. The medical and nursing team have very effective medicines which they can use to help them control the unwanted effects of this cytokine storm but occasionally you may need to be monitored more closely and the ward team may recommend that you spend a few days in the critical care unit until these side effects have resolved and you can then return to the ward.

Once discharged you are very unlikely to experience any symptoms of cytokine release syndrome.

### Neurological toxicities

In some patients the immune activation can affect the neurologic system temporarily. These symptoms can come on while you are an inpatient but can also occur for a few weeks after discharge, which is why it is important that you do not drive for at least 8 weeks after your treatment, operate heavy machinery or undertake any tasks that require a higher level of cognitive functioning. This is also why we ask that for the first 30 days you stay with a friend or family member within an hour's drive of the hospital.

These symptoms may be mild such as inability to find words or make up sentences, impaired attention and memory loss, difficulty in writing, headaches and agitation. In its most severe forms it may affect your movement, cause hallucinations, reduced level of consciousness and cause seizures. It may be that your doctors will arrange an MRI scan if these symptoms occur.

For the first 30 days after the infusion you will be monitored very closely for any of these symptoms and the nursing and medical staff will undertake an **ICANS assessment** including a written and verbal test with you several times in the week to pick up any potential problems that occur.

Even after that point it is very important that you or those supporting you report any changes in your behaviour, speech or mental function to the cell therapy team for investigation.

### **Low blood counts and infection**

It may take many months for your blood counts to return to normal after CAR-T treatment, and you may need support from red cell and platelet transfusions in the first few weeks but these blood levels usually stabilise quickly to acceptable levels. It is important that during this time you report any unusual signs of bleeding or bruising to your cellular therapy team. You will be given a card indicating the requirement for you to have irradiated blood products if needed after your treatment. Please carry this with you at all times.

Full recovery of your white cell, neutrophil and lymphocyte count may longer to occur. The CAR-T has been designed to attack your B cells so longer term drop in these blood counts is not uncommon (B cell aplasia).

This drop 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 daily, and contact The Christie Hotline on **0161 446 3658** if your temperature rises above 37.5°C degrees.

You may also need immunoglobulin replacement after receiving this treatment to boost your immune system or growth factor injections to help boost your neutrophil count and help protect you from infection.

**Not all side effects are listed above, only those specifically related to CAR-T therapy. Please contact the medical team if you experience any unusual symptoms and they will advise you accordingly.**

### **Step 5: Going home/immediate discharge from hospital**

Once are ready to go home and have been discharged you will be reviewed regularly in our ambulatory care department until you have reached 30 days post treatment.

You will need to attend at least 3 times a week for blood tests and ICANS assessments. You will also have a consultation with your consultant at least once a week initially. This may be a telephone consultation or a face to face meeting.

During this time and afterwards please continue to monitor for any signs of infection when at home, and if your temperature rises above 37.5°C, or you experience any of the symptoms outlined as neurological, please contact the cellular therapies team or The Christie Hotline.

It is very important that you report any unusual symptoms or 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, 7 days a week. 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/Christie Hotline Card at all times and the card indicating you require **irradiated** blood products due to the treatment you have received.

### **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. Potential effects on an unborn child are unknown and therefore we recommend that you use effective birth control. If you have any further questions please discuss them with the cellular therapies team or your consultant.

## Step 6: Follow-up monitoring

As well as regular blood tests to assess your response to CAR-T treatment you will also undergo regular assessment of your disease and its response to the CAR-T treatment, using investigations such as PET scans and bone marrow tests.

You may also need to have further investigations such as biopsies and scans in the months post CAR-T therapy, this will depend on your progress and the advice of the cellular therapies consultant.

It may take several months for the full benefit of this treatment to be seen so in general you will have a scan or bone marrow one month after your treatment and again at 3 months and potentially every 3 months for the first year. Your cellular therapy consultant will discuss these results with you and advise you on how the treatment is progressing and if your disease has responded adequately. If there are concerns that the treatment is no longer working or the disease has reoccurred the consultant will discuss with you alternative treatment or trial options if appropriate.

Depending on your response, you may be able to return to your local team/hospital for monitoring long term with interval visits to The Christie continuing at least for the first year post treatment.

### Further information

Blood Cancer UK  
[www.bloodcancer.org.uk](http://www.bloodcancer.org.uk)  
Tel: 0808 169 5155

Lymphoma Action  
[www.lymphoma-action.org.uk](http://www.lymphoma-action.org.uk)  
Tel: 0808 808 5555

### Contact numbers

Apheresis/transplant nurse co-ordinators  
**0161 446 8011** or **0161 918 7219**  
or  
**0161 446 3000** bleep (via switch) **12735**

Out of hours The Christie Hotline: **0161 446 3658**

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.

The Christie is committed to producing high quality, evidence based information for patients. Our patient information adheres to the principles and quality statements of the Information Standard. If you would like to have details about the sources used please contact **[the-christie.patient.information@nhs.net](mailto:the-christie.patient.information@nhs.net)**

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