University Hospitals Bristol and Weston
NHS Foundation Trust

Patient information service
Specialised Services

Chimeric Antigen Receptor T-cell (CAR-T) therapy

This information sheet answers some of the questions you may have about receiving CAR-T therapy at University Hospitals Bristol NHS Foundation Trust. It explains the risks and the benefits of the treatment and what you can expect when you come to hospital before, during and after treatment. If you have any other questions or concerns, please do not hesitate to speak to the doctors or nurses caring for you.

What is Chimeric Antigen Receptor T-Cell (CAR-T) therapy?

CAR-T is a 'personalised cell therapy' that can help treat your cancer. CAR-T is different from most other cancer treatments because it is made from your own white blood cells (T cells), which have been 'reprogrammed' in the laboratory to be able to target and help kill your cancer cells.

T cells destroy bacteria, viruses and cancer cells. However, with some types of cancers your T-Cells have not been doing that job effectively. By manipulating these T-Cells (CAR-T therapy) we may enable the cells to recognise and attack those cancer cells.

Why do I need Chimeric Antigen Receptor T-cell (CAR-T) therapy?

You have been referred to a specialised centre to receive this therapy. There are a small number of CAR-T therapies that are approved for use outside clinical trials.

How does CAR-T therapy work?

Some of your T-cells will be collected using a cell separator (leukapheresis) and then transported to a laboratory to be manufactured into CAR-T cells. This is done by introducing a new gene known as a chimeric antigen receptor (CAR). The addition of this gene helps your own T cells to target the cancer.

The process for receiving CAR-T therapy is broken down into several stages.

Step 1: Work-up

Step 2: Leukapheresis

Step 3: Cell manufacturing

Step 4: Conditioning chemotherapy

Step 5: Infusion

Step 6: Monitoring

Step 7: Follow up

Step 1: Work-up

To ensure you are fit enough to undergo CAR-T therapy you will need to have a number of tests and procedures. This will be discussed with you in detail by your doctor and Clinical Nurse Specialist (CNS). These may include:

- Electrocardiogram (ECG)

- Blood tests

- Infection screening

- CT scan/MRI scan/PET scan

- Echocardiogram (echo)

- Lung function test (LFTs)

- Kidney function tests: EDTA clearance or Glomerular Filtration Rate (GFR)

- Central Venous Catheter insertion

- Bone marrow biopsy

Step 2: Leukapheresis

As the CAR-T treatment is made from your own T cells we need to collect and separate your T cells from the other cells in your body.

Some of your T-cells will be collected using a special process called leukapheresis. They will then be sent to a laboratory where they will be modified by introducing the chimeric antigen receptor (CAR) gene.

We will aim to collect the right amount of T cells but in a small number of patients this is not always possible.

During the leukapheresis process you will be connected to a special machine that separates your blood into its different components. We are then able to identify the T Cell component and collect them, while returning the rest of the cells from your blood to your body. This procedure is usually well tolerated with very few side effects and will be performed by a trained apheresis team. You will be monitored closely during the procedure. The procedure will take 3-5 hours. A more detailed information sheet will be given to you regarding this stage of the process by your team.

Step 3: Cell Manufacturing

When your T cells have been collected, they will be sent away to the specific cell manufacturing laboratory outside of University Hospitals Bristol. This is when your T cells will be modified into CAR-T cells. This is done by introducing a chimeric antigen (CAR) gene. The addition of this gene helps your own T cells target the cancer. The new CAR-T cells are engineered to recognise and kill your cancer cells.

This process of manufacture is tightly controlled by the Human Tissues Authority and because of the rules around this, we are able to track and monitor each step your cells take in this journey. The manufacturing process takes 3-4 weeks and in small proportion of cases it may not be successful.

Once the manufacturing lab have completed their work to modify your T cells, we will arrange a date for them to be sent back to Bristol, where they will be stored in the Stem Cell Laboratory at the NHS Blood and Transplant Centre at Filton until we are ready to infuse them back into you. At this stage, the date for conditioning chemotherapy will be confirmed.

Step 4: Conditioning Chemotherapy (sometimes known as 'lymphodepletion')

Before we are able to infuse the CAR-T cells you will need to receive a number of days of chemotherapy which is referred to as conditioning chemotherapy. This treatment prepares your immune system to receive the CAR-T cells by eliminating other immune cells and creating space for CAR-T cells to grow and do their job.

As with all chemotherapy there are potential side effects. These will be discussed in separate chemotherapy information sheets that your team will give you.

This chemotherapy is likely to be administered on the inpatient ward, D703

Step 5: Infusion

On the day of infusion of your CAR-T cells, if you are not already an inpatient, you will need to attend D703.

The CAR-T cells will be delivered frozen to the ward by a member of the stem cell laboratory in a special container. Just before the infusion your nurse will give you some medication into your vein. The medication (an antihistamine) is to help prevent any allergic reaction during the infusion. You will also start an intravenous saline drip (a solution of salt and water) at the same time. Your nurse will also check your observations (blood pressure, pulse and temperature). Several identification checks are performed on your modified cells prior to their infusion. You will be involved in this. The cells are defrosted in a water bath and connected to you via a tube called a giving set. The infusion itself takes no more than 30 minutes.

After the infusion your nurse will flush the drip with saline then take it away.

The T cells have a preservative added to them so that the freezing process does not damage the cells. This preservative carries a smell, often described as 'boiled sweetcorn'. You may not be able to detect this smell but your relatives or visitors may comment on this. You excrete the preservative through your skin and in your bodily fluids for about 24 hours following the infusion.

Step 6: Monitoring

After your CAR-T infusion you will remain an inpatient on D703 for a minimum of 10 days. You will be monitored closely for side effects related to the CAR-T therapy. Once your doctor has decided it is safe to discharge you from the ward it is important that you still remain within 30 minutes of the Bristol Haematology and Oncology Centre for a minimum of 28 days post infusion of CAR-T cells. If you live further away we will provide you with near-hospital accommodation for the required period.

Once you have been discharged from hospital you will require a caregiver to be with you 24/7 up until a minimum of 28 days following infusion of CAR-T cells. This is to ensure your safety, identify symptoms and supervise medications where appropriate. In addition to your primary caregiver it may be useful to identify a backup caregiver. Both your primary and backup caregiver should be at least 18 years old, dependable and in good health.

Step 7: Follow-up

You will have several follow-up appointments to track your progress. Your doctor and team will check to see if your treatment is working by performing blood tests as necessary and to help you with any side-effects you may experience.

It is important that you take care of yourself!

Remember to:

- Call the 24 hour Emergency line immediately if your temperature is 38°C or higher (CALL 0117 342 2011).
- Stay hydrated - drink 2-3 litres of fluid/day unless instructed otherwise.
- Avoid infections.
- Wash your hands with warm water and soap regularly and particularly after using the bathroom and before preparing food.
- Cook meat and eggs all the way through to kill any germs.
- Carefully wash raw fruits and vegetables.
- Avoid gardening, this is because fungus and spores in the ground may be harmful to you.
- Don't clean up after pets.
- Avoid large crowds.
- Practice good oral hygiene by brushing your teeth after every meal.

What are the risks of Chimeric Antigen Receptor T-cell (CAR-T) therapy?

There are some serious side effects that are quite common after receiving CAR-T therapy. It is very important that you are your family/caregivers understand what to look for and notify your hospital team should side effects occur. We understand that these may seem frightening so please take the time to discuss any concerns with your doctor and Clinical Nurse Specialist (CNS).

The most common side effects of CAR-T therapy are:

- Allergic reactions
- Cytokine Release Syndrome (CRS)
- Changes in Immune effector Cell Neurotoxicity Syndome (ICANS)
- Tumour Lysis Syndrome (TLS)
- Reduced immunity

Whilst you are an inpatient at University Hospitals Bristol NHS Foundation Trust you will be monitored closely for these side effects and indeed after the treatment in clinic. You will also need to look out for these side effects after discharge.

Allergic reactions

The infusion of the modified T-cells may cause allergic reactions such as fever, shivers, difficulty breathing, low blood pressure, rash, vomiting. We will give medicines to try to prevent this from happening. The doctors and nurses will monitor you closely during and after the infusion of the cells. If such a reaction does occur, you will be given appropriate medication and monitored until the symptoms resolve.

Tumour Lysis Syndrome (TLS)

CAR T-cell therapy is designed to target your cancer cells. In some cases, this process may destroy large amounts of tumour very quickly. When these cancer cells die they are released into your bloodstream. TLS can occur when the cancer cells break down so quickly that the kidneys can't remove them from the blood.
TLS is a potentially life threatening problem and needs to detected and treated promptly. This involves daily, sometimes twice daily, blood tests to check how your kidneys are functioning in the day following your CAR-T cell infusion. You are likely to need intravenous fluids and in rare circumstances dialysis might be required to effectively treat TLS.

Cytokine Release Syndrome (CRS)

The CAR-T cells may stimulate the release of chemicals called "cytokines" that can cause severe reactions. This is called Cytokine Release Syndrome (CRS). CRS has been seen with most CAR-T products and onset varies depending on which product you are receiving. Your doctor and CNS will be able to discuss this in more detail with you. Side effects associated with the release of cytokines can range from mild (such as fever) to severe (such as low blood pressure and difficulty breathing) and can be life threatening. The team will monitor things closely. CRS can be treated with drugs including antibody therapy and supportive care, e.g. intravenous fluids. Some patients need to be transferred to the intensive care unit (ICU) for extra supportive care during CRS.

Symptoms of CRS include:

- Fever (e.g. Temperature above 38°C)
- Tiredness
- Shortness of breath
- Decreased urine output
- Nausea
- Vomiting
- Diarrhoea
- Irregular heartbeat
- Headache

Changes in neurological status (ICANS)

The immune activation after CAR-T cell infusions can sometimeS alter the brain and nervous system. In most cases this is temporary. Some patients may develop short term symptoms affecting their nervous system causing confusion and drowsiness. These symptoms generally improve on their own and appropriate supportive care will be given, including intensive care if required. You will have a specific neurological assessment each day on the ward looking for subtle changes in your neurological state. You will not be allowed to drive or operate heavy machine for 8 weeks following CAR-T infusion due to the risk of neurological symptoms.

Neurological symptoms include:

- Confusion
- Difficulty speaking
- Difficulty understanding speech
- Tremors (shaking body parts)
- Agitation
- Increased sleepiness
- Dizziness
- Fits
- Loss of consciousness
- Loss of balance or coordination

Reduced Immunity

The protein used to make your CAR-T therapy is present both on the surface of your cancer cells and on normal cells which help you fight infections. Therefore the engineered T cells may target and destroy not only the cancer cells but also some of the normal B cells. The decreased number of normal B cells may lead to low levels of immunoglobulins or antibodies. Persistently low levels of immunoglobulins may cause an increased risk of infection. We will monitor your blood levels of immunoglobulins and if these are persistently low we will give intravenous immunoglobulin replacement as needed.

Risk of developing new cancer after CAR-T therapy

Because the DNA in the CAR-T cells have been modified, there is a risk that these changes could trigger the T cells to divide uncontrollably, in a similar way to blood cancers like leukaemia. There is also a potentially increased risk of other forms of blood cancer as a result of CAR-T therapy. Overall it is thought that the chances of secondary cancers are very small.

What are the alternative treatments?

Your doctors will discuss all alternative treatment options with you. You are likely to have been treated with different cancer medications already which have been unsuccessful in curing your disease completely. One alternative option to consider at this time is supportive or palliative care. The doctors will discuss this with you and there are specialist teams in the hospital and community who help keep patients as well and as comfortable as possible.

Information for women of childbearing potential

Women of childbearing potential must have been tested negative in a pregnancy (blood) test within 7 days prior to starting collection and again prior to conditioning chemotherapy. For patients of child-bearing potential, we will request that from the time of consent and for 12 months after infusion, you and your partner agree to use an effective and DOUBLE method of birth control, i.e. the contraceptive pill or intra-uterine contraception or implants PLUS a condom. This is because we do not know if it could harm unborn babies in the womb.

You should inform your doctor immediately if you or your partner are pregnant and you will be provided with the necessary advice and medical care. Should it occur, we would ask to collect some information about a pregnancy and to follow-up the outcome.

Consent

We must by law obtain your written consent to any procedure beforehand. Staff will explain the risks, benefits and alternatives before they ask you to sign a consent form. If you are unsure of any aspect of the treatment proposed, please do not hesitate to speak with a senior member of the team again.

Contact Details:

24 hour emergency line: **0117 342 2011**

General enquiries about CAR T cells: **0117 342 1118**

Email: **bmtco-ordination@uhbw.nhs.uk**

Notes and queries

As well as providing clinical care, our Trust has an important role in research. This allows us to discover new and improved ways of treating patients.

While under our care, you may be invited to take part in research. To find out more please visit: **www.uhbw.nhs.uk**

Help us prevent the spread of infection in hospital. Please make sure your hands are clean. Wash and dry them thoroughly/use the gel provided. If you have been unwell in the last 48 hours please consider whether your visit is essential.

Smoking is the primary cause of preventable illness and premature death. For support in stopping smoking contact **NHS Smokefree** on **0300 123 1044**.

Drinkline is the national alcohol helpline. If you're worried about your own or someone else's drinking, you can call this free helpline in complete confidence. **Drinkline** on **0300 123 1110.**

For access all patient leaflets and information please go to the following address: **http://foi.avon.nhs.uk/**

Bristol switchboard: 0117 923 0000

Weston switchboard: 01934 636 363

www.uhbw.nhs.uk

For an interpreter or signer please contact the telephone number on your appointment letter.

For this leaflet in large print or PDF format, please email patientleaflets@uhbw.nhs.uk.

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