Chimeric antigen receptor T-cell (CAR-T) therapy

We have given you this factsheet because your doctor has referred you for chimeric antigen receptor T-cell (CAR-T) therapy. It explains what CAR-T therapy is and what it involves so you know what to expect. We hope it helps to answer some of the questions you may have. If you have any further questions or concerns, please speak to your doctor or contact us using the details at the end of this factsheet.

We understand that CAR-T therapy can sound daunting or even scary. Our specialist team will support you at every stage of the treatment and make sure you have the care you need. You can always tell us if you are feeling worried or ask us any questions, big or small.

What is CAR-T therapy?

CAR-T therapy is a treatment that uses your own immune system to destroy cancer cells.

Why do I need CAR-T therapy?

In the UK, CAR-T therapy is currently used to treat a number of different cancers.

CAR-T therapy has many benefits, including:

- giving you the highest chance of long-term remission (no signs of cancer)
- being an alternative treatment option when other cancer treatments have failed or your cancer has returned

Your doctor has reviewed your treatment options with you and believes CAR-T therapy to be the best treatment option for you.

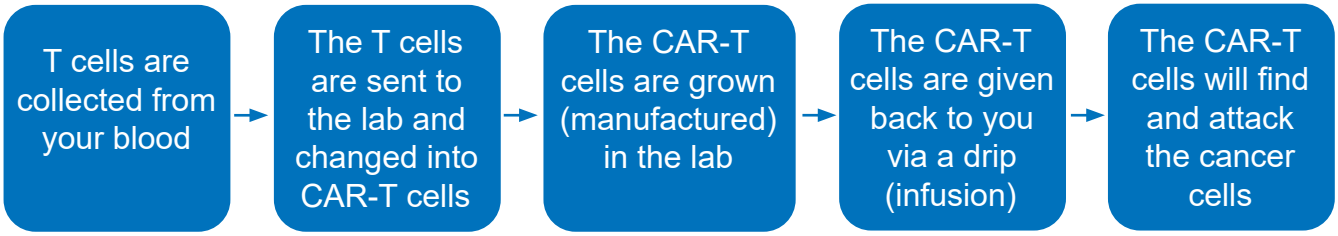
Is CAR-T therapy suitable for everyone?

CAR-T therapy is not suitable for everyone. It is a complex and intensive treatment which can have serious side effects. For this reason, you must meet the eligibility criteria and also be physically fit enough to receive the treatment.

How does it work?

CAR-T therapy works by modifying some of your body's immune cells (known as 'T cells') to become better at fighting cancer cells. T cells are white blood cells which help to protect you from infection, viruses and disease by recognising and killing any abnormal cells such as cancer cells. However, cancer cells are good at tricking your T cells. They do this by looking similar to healthy cells or sending signals to tell your T cells not to attack them.

During CAR-T therapy, we will collect T cells from your blood which we will then send to a laboratory to be genetically modified into cells that recognise and destroy cancer cells (known as 'CAR-T cells'). The laboratory will then manufacture (grow) these specially modified CAR-T cells so that there are enough to treat your disease. When enough CAR-T cells have been grown, we will put these cells back into your bloodstream via an infusion (a drip that is placed into your vein). Please see the flowchart below for a summary of the CAR-T therapy process.



What are the stages of CAR-T therapy?

CAR-T therapy is made up of nine stages:

- **Stage 1 – Initial consultation**
- **Stage 2 – Leukapheresis (T cell collection)**
- **Stage 3 – CAR-T cell manufacturing**
- **Stage 4 – Bridging treatment**
- **Stage 5 – Disease and organ function assessment**
- **Stage 6 – Clinic appointment**
- **Stage 7 – Personalised care and support planning (PCSP) appointment**
- **Stage 8 – Starting CAR-T therapy**
- **Stage 9 – Going home**

Stage 1: Initial consultation

We will arrange a clinic appointment for you to meet with our medical team and specialist nurses to discuss having CAR-T therapy. At this appointment we will:

- explain the treatment process to you in detail
- check you meet the eligibility criteria
- discuss your expectations to make sure that CAR-T therapy is the appropriate treatment option for you
- answer any questions you may have
- discuss the possibility of you having some of your care in an outpatient setting (known as 'ambulatory care'). If you are eligible for ambulatory care, we will give you a separate information sheet about this.

If we think you meet the eligibility criteria to have CAR-T therapy, the next step will be discussing your case at a national panel meeting. If the panel gives their approval for you to have CAR-T therapy, we will send you an appointment letter to have a procedure called leukapheresis (T cell collection).

Stage 2: Leukapheresis (T cell collection)

Leukapheresis is the process of collecting T cells from a person's blood.

We will provide you with a separate information sheet about this stage of the treatment.

Stage 3: CAR-T cell manufacturing

After you have had the leukapheresis procedure, we will send your T cells to a laboratory to be modified into CAR-T cells and manufactured (grown). This process takes approximately four weeks to complete.

Once the CAR-T cells have completed quality checks, they will be frozen and transported back to our local laboratory, where they will be stored in preparation for starting your treatment (CAR-T cells can be stored for several months if needed).

If it is not possible to successfully manufacture the CAR-T cells, we will contact you to discuss your options.

Stage 4: Bridging treatment

While you are waiting for the CAR-T cells to be manufactured, you may need to have some additional treatment (for example, immunochemotherapy or radiotherapy). Treatment given after having leukapheresis and before starting CAR-T therapy is known as 'bridging treatment'.

Bridging treatment can help to:

- keep your disease under control
- ensure you and your disease are in the best position possible before receiving CAR-T therapy (this gives your CAR-T cells the best chance of working)

In some cases, bridging treatment may not be needed. Your consultant will make the decision as to whether this additional treatment is appropriate for you and will discuss this with you.

Stage 5: Disease and organ function assessment

Your medical team will arrange a number of tests and investigations to make sure you are physically fit enough to have CAR-T therapy. These tests may include:

- an electrocardiogram (ECG) and echocardiogram (ECHO) to check the function of your heart
- blood tests to check your blood count and if you have any viruses or infections
- a CT, MRI or PET scan to assess the status of your disease
- a pulmonary function test (breathing test) to check your lung function
- a creatinine clearance or glomerular filtration rate (GFR) to check your kidney function
- a bone marrow biopsy to check if your bone marrow has been affected by the disease

Your medical and specialist nursing team will explain each of these tests to you in more detail and answer any questions you may have. They will then arrange appointment dates for the necessary tests.

Once all the tests have been completed, your results will be reviewed by our medical team. We will then discuss your results with you at your next clinic appointment.

Stage 6: Clinic appointment

Before starting CAR-T therapy, you will go through a comprehensive consent process. This is to ensure that you have received all the necessary information and had all your questions answered before giving your permission to proceed with CAR-T therapy.

We will invite you to attend a clinic appointment with a CAR-T consultant and other members of our clinical team (for example, a dietitian, physiotherapist or palliative care and symptom management team).

At this appointment, we will:

- discuss CAR-T therapy in detail and explain what the process involves (including the benefits and risks)
- give you lots of information so that you fully understand the procedure (we encourage you to bring a family member or friend with you to the appointment, as well as a notebook, to help you take in all the information)
- answer all your questions
- check you are still well enough to go ahead with CAR-T therapy (if you are not well enough, we may have to delay your treatment or discuss other treatment options with you)

If you are happy to proceed with the procedure, we will then ask you to sign a consent form giving your permission.

Stage 7: Personalised care and support planning (PCSP) appointment

We offer a further specialised appointment, known as a 'personalised care and support planning' (PCSP) appointment, for anyone who is due to receive CAR-T therapy. At this appointment, you will meet with one of our clinical nurse specialists and other members of your wider healthcare team (for example, a dietitian, physiotherapist, occupational therapist, psychologist or palliative care team). We will provide you with a separate factsheet about what will happen at the PCSP appointment and how to prepare for it.

Stage 8: Starting CAR-T therapy

Once your CAR-T cells have been manufactured and you are ready to have the CAR-T cell infusion, we will arrange for you to be admitted to our leukaemia and bone marrow transplant unit (also known as 'C6L') for treatment. We will provide you with a separate factsheet about staying on C6L, so you know what to expect while you are being cared for on the unit.

Lymphodepletion

Before you can receive the CAR-T cell infusion, you must first have something called 'lymphodepletion' (sometimes referred to as conditioning chemotherapy). Lymphodepletion involves receiving a short course of chemotherapy to kill your T cells. This prepares your immune system to receive the CAR-T cells by reducing the number of normal T cells in your blood. By creating space for the modified cells to grow, we are creating the optimal environment ready for your new T cells to be returned into your bloodstream.

The type and duration of chemotherapy you will need may vary and will depend on your underlying condition and the CAR-T cells.

As with any chemotherapy treatment, there are potential side effects. We will give you a separate chemotherapy factsheet with more details.

Some people will need to stay overnight in hospital on C6L for this procedure. Other people may be able to have the procedure as ambulatory care (day-time appointments) on C7 ward (haematology day case unit).

CAR-T cell infusion (day 0)

After you have completed your lymphodepletion chemotherapy, you will have a rest period of at least 24 hours. You will then be ready to receive the CAR-T cell infusion (drip).

Before having the CAR-T cell infusion, we will:

- place a cannula (small plastic tube) into a vein in your hand or arm. If your veins are not suitable for a cannula, we will place a central line (a thin, flexible plastic tube that is inserted into a large vein in the neck, upper chest or groin).
- give you 500ml of fluid via your cannula.
- give you medications (usually paracetamol and antihistamines) to help prevent any reactions to the treatment.
- carry out several identification checks on you and your CAR-T cells (currently frozen).
- thaw your frozen CAR-T cells in a water bath (this is done once everything else is ready for the procedure).

Once your CAR-T cells have thawed, we will return these to you via your cannula. The infusion will take approximately 10 to 20 minutes. We will check your blood pressure, temperature, oxygen levels, pulse and respiration rate throughout the infusion. After the infusion is complete, we will flush the drip with saline (salt water solution).

Once they are returned to you, the CAR-T cells are designed to expand and multiply, attacking the cancer cells. That is why during the infusion, and for a period of time afterwards (approximately four to five hours), we will observe you very closely for side effects (see the 'What are the side effects?' section below for more information).

How long you will need to stay in hospital under observation for will depend on how well you tolerate the treatment and whether you experience any complications. Most people will need to stay in hospital for around two to five weeks.

Please note that the CAR-T cells have a preservative added to them so that the freezing process doesn't damage the cells. The preservative carries a smell similar to sweetcorn. You may not be able to detect the smell, but those around you may notice it for around 24 hours after the infusion.

What are the side effects?

Like most medical treatments, you may experience side effects after having CAR-T therapy. Each person who has CAR-T therapy will react differently to the treatment. Sometimes side effects can resolve on their own but in some cases, you may need treatment.

Although most side effects will happen in the first few days while you are in hospital, they can happen up to eight weeks after the infusion. It is important that you familiarise yourself, as well as your family and/or carers, with the potential side effects so that you can all recognise the signs when you return home.

Some people may experience serious side effects after having CAR-T therapy. We will monitor you closely in hospital and in the outpatient setting (if you are having ambulatory care) after your cell return and provide any necessary treatment.

It is important to raise any concerns or side effects to us as soon as you experience them.

Cytokine release syndrome (CRS)

CRS is one of the most common side effects of CAR-T therapy. It is an inflammatory response which happens when your body's immune cells are activated, releasing large amounts of chemicals called cytokines into the body. An increase in cytokines can cause you to experience a type of immune reaction (similar to having an infection) and can make you feel unwell.

Symptoms of CRS include:
- a fever (a temperature of 38°C or above)
- chills
- a rapid heart rate
- low blood pressure
- low oxygen levels
- a headache

Most people receiving CAR-T therapy will experience CRS. It usually occurs in the first 10 days after receiving your CAR-T cells. We will use a CRS monitoring tool regularly throughout your stay on C6L to monitor for this. If we notice any abnormalities, we will take immediate action.

Neurological toxicities
In some people, the same immune activation can affect the brain and neurological system temporarily. This is called 'immune effector cell-associated neurotoxicity syndrome' (ICANS).

Symptoms of ICANS can include:
- confusion
- speech problems
- difficulty with writing, talking and memory
- headaches and dizziness
- shaking or tremor
- movement difficulty
- drowsiness

The above symptoms are all reversible with the correct treatment.

We will use a neurological monitoring tool regularly throughout your stay in hospital to monitor for neurological toxicities. This involves us asking you questions or asking you to perform certain tasks, such as a handwriting test. If we notice any abnormalities, we will take immediate action.

Tumour lysis syndrome
When large numbers of cancer cells die, the contents of these cells are released into the bloodstream. This can result in a shift of fluids and salts in your body, which can potentially cause damage to your kidneys (this is known as 'acute kidney' or 'renal disorder'). If you notice you are passing less urine or have discomfort when going to the toilet, please let us know.

Low blood counts
Lymphodepletion chemotherapy and CAR-T cell therapy can lower your blood counts (for example, your level of red blood cells, white blood cells and platelets). We will test your blood regularly to check for this. We may give you a blood transfusion, if needed. If you experience any bruising or bleeding, let us know immediately.

Infection
Low levels of white blood cells in your bloodstream can increase your risk of developing an infection. We will monitor you for any potential signs of infection.

Gastrointestinal problems
This treatment can affect your bowel and stomach. While you are in hospital, we will give you anticipatory medications to help prevent these symptoms.

However, it is important that you let us know immediately if you experience:
- abdominal pain
- constipation (dry, hard stools that are difficult to pass)
- diarrhoea (loose, watery stools)
- nausea (feeling sick) and vomiting

Skin rash
You may experience a rash on your body which can vary from mild to severe. Let us know immediately if you notice any changes to your skin.

Please note that this is not a complete list of all the potential side effects. If you experience any unusual symptoms, contact us immediately for advice using the details at the end of this factsheet.

Stage 9: Going home

Once you have completed your treatment and your medical team have agreed that you are well enough, you will be allowed to go home.

Before you leave hospital, we will discuss your needs and concerns and answer any questions you may have. We will then agree with you a recovery and support plan.

You may experience delayed side effects up to 30 days after your infusion. For this reason, you must:
- stay close to the hospital (within an hour's travelling time)
- have someone to stay with you at all times for 30 days after your infusion

When should I seek medical advice?

Contact us immediately using the details at the end of this factsheet if you experience:
- a high temperature (38°C or above) or any other signs of infection
- any neurological abnormalities (examples of neurological abnormalities can be found in the 'Neurological toxicities' section on **page 6**)
- any other abnormalities or feel generally unwell

It is important that you contact us straight away for advice (including if you experience symptoms at nighttime or at the weekend).

What follow-up care will I receive?

We will arrange a number of follow-up appointments for you in our outpatient department, starting one month after your CAR-T cell infusion. At these appointments, we will monitor your disease and your body's response to the treatment.

These follow-up appointments will initially be weekly but will become less frequent over the next 12 months. After 12 months, we will then need to see you on a yearly basis. For more information about your follow-up appointments, please refer to your appointment letters.

Additional support

Macmillan Cancer Support
Telephone: **0808 808 0000**
Website: **www.macmillan.org.uk**

Bloodwise
Telephone: **0808 208 0888**
Website: **www.bloodwise.org.uk**

Cancer Research UK
Telephone: **0808 800 4040**
Website: **www.cancerresearchuk.org**

Notes

Contact us

If you have any further questions or concerns, please contact us.

CAR-T therapy clinical nurse specialist team (Monday to Friday, 9am to 5pm)
Telephone: **023 8120 8481**
Mobile: **07717 138754**

Outside of these working hours, if you feel unwell and need urgent assistance, call our 24-hour acute oncology service on **023 8120 1345**.

Useful links

www.bloodcancer.org.uk/understanding-blood-cancer/treatment/what-is-car-t-therapy

www.yescarta.com/receiving-yescarta

www.macmillan.org.uk/cancer-information-and-support/treatments-and-drugs/car-t-cell-therapy

www.health.novartis.co.uk/sites/health.novartis.co.uk/files/kymriah-patient-carer-educational-material.pdf

www.lymphoma-action.org.uk/about-lymphoma-treatment-lymphoma/car-t-cell-therapy

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For help preparing for your visit, arranging an interpreter or accessing the hospital, please visit **www.uhs.nhs.uk/additionalsupport**

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