

CAR-T cell therapy

This treatment fact sheet provides information about the new myeloma treatment, Chimeric Antigen Receptor T cell therapy (CAR-T cell therapy).

CAR-T cell therapy has not yet been approved by the Medical Services Advisory Committee (MSAC), the government advisory committee in Australia which assesses which new medical services, such as this therapy, should be publicly funded or subsidised by the Government.

At the moment, CAR-T cell therapy is available in Australia through clinical trials, where it is used to treat people with relapsed or refractory myeloma who have received a certain number of previous treatments.

When you need a new treatment for myeloma, ask your doctor if a CAR-T cell clinical trial, or a clinical trial with another new treatment, may be an option for you

What is CAR-T cell therapy?

CAR-T cell therapy is a completely new way to treat multiple myeloma. It is a type of treatment known as an immunotherapy. This means that the treatment works with your own immune system to detect and destroy cancerous cells.

Unlike cancer therapies that are continuous or require repeat courses, CAR-T cell therapy is a one-off procedure involving extracting, reprogramming, and reinfusing the person's own immune cells to fight the myeloma.

In clinical trials, CAR-T cell therapy has been able to achieve deep remission for some with no maintenance therapy required. However, the length of this remission varies between individuals and further treatment may be required at some stage.

How does CAR-T cell therapy work?

CAR-T cell therapy involves reprogramming the person's own T cells so they are better able to destroy the myeloma cells.

T cells are a type of white blood cell and are part of our first-line immune defense. T cells circulate in our body detecting abnormal cells or antigens such as bacteria and viruses and help to destroy them.

Unfortunately, T cells are unable to detect cancer.

CAR-T cell therapy involves collecting an individual's T cells and adding genetic information so that the T cells are then able to recognise, bind to, and destroy cancerous cells.

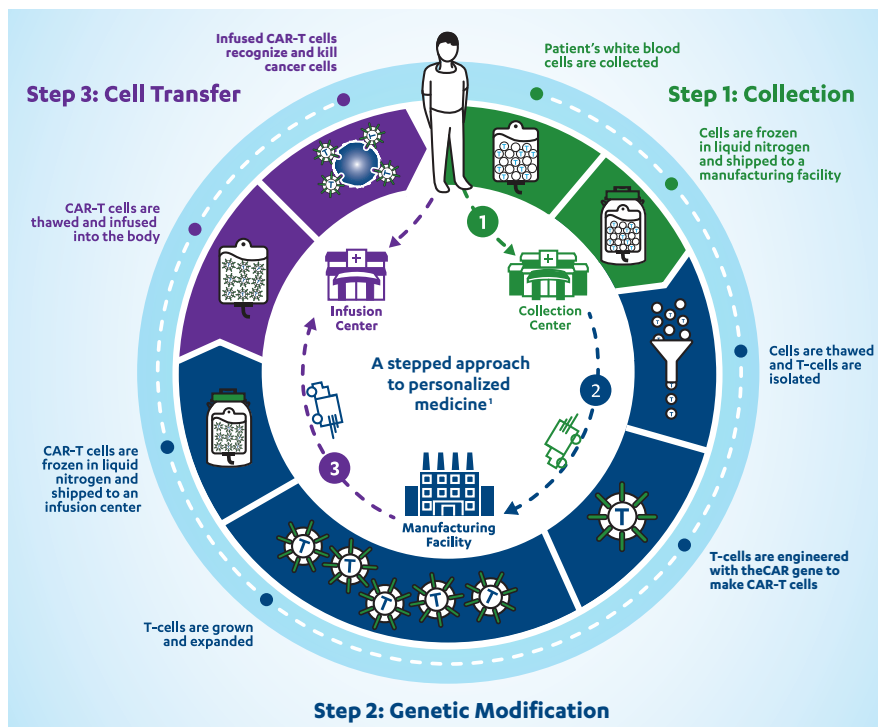
The genetic information added to the T cell targets a specific antigen expressed on the surface of the cancer cell. In myeloma, the most common target is B-cell maturation antigen (BCMA) but further targets are also being investigated.

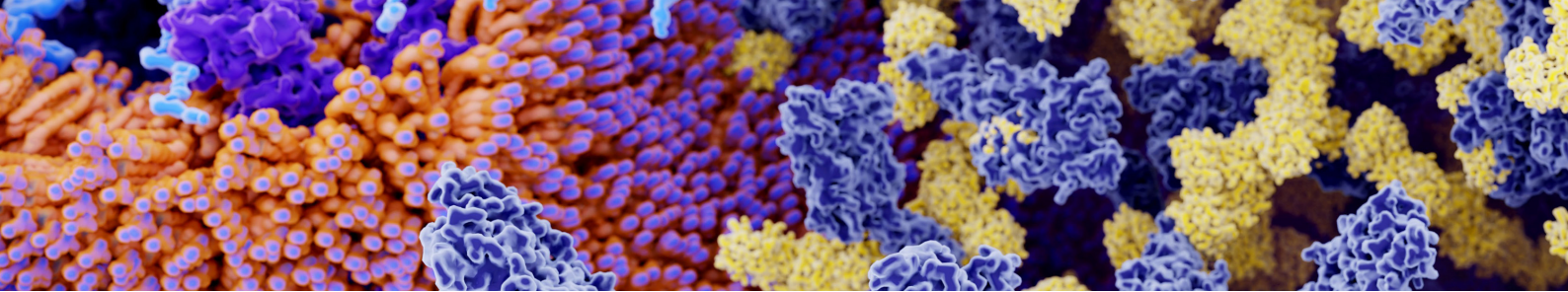
How is CAR-T cell therapy given?

Much like a stem cell transplant, CAR-T cell therapy is a one-off treatment. The process of collecting your T cells, engineering them to fight myeloma, and reinfusing back into your body is outlined below.

First, your T cells will be collected via a process called leukapheresis.

This involves being connected to an apheresis machine where blood is collected from your vein and the T cells are separated from the rest of the blood components. This process can take up-to four hours.





Depending on your veins, you may need a central line inserted to make this process easier.

Then, the T cells are sent to the laboratory where the genetic information is added to make CAR-T cells. The CAR-T cells then stay in the laboratory where they multiply and undergo quality and safety checks before being returned to the treating hospital for re-infusion (this process can take days to weeks).

Whilst waiting for the CAR-T cells to develop in the laboratory you may receive bridging chemotherapy.

The goal of bridging chemotherapy is to keep your myeloma under control so that you are well enough to receive the CAR-T cells. Whether you receive bridging chemotherapy will be decided by your treating team.

All people receiving CAR-T cell therapy receive lymphodepleting chemotherapy. The goal of lymphodepleting chemotherapy is to decrease the number of white blood cells in the body to make room for the CAR-T cells to grow, expand and multiply once they are re-infused.

Lymphodepleting chemotherapy is usually administered five days and then three days before the CAR-T cells are re-infused. The standard lymphodepleting chemotherapy regime for myeloma is a combination of fludarabine and cyclophosphamide but other agents may be used.

The CAR-T cells are then re-infused back into your veins through a central line as either a single infusion or as a series of infusions.

The CAR-T cells will then circulate around your body searching for the target expressed on the myeloma cells that they are programmed to recognise (such as BCMA). Once they recognise the myeloma, they will bind to this target and destroy the myeloma cells.

Some side effects associated with CAR-T cell therapy can be experienced up to a month after the infusion. Therefore, you will need to stay close to the hospital for four weeks for regular monitoring.

How will I know if CAR-T cell therapy has worked?

After the CAR-T cells have been infused and you have been discharged from hospital, you will continue to be monitored regularly by your doctor. They will order tests at certain timepoints to assess your response and review you for any signs or symptoms of myeloma returning or progressing. These tests vary from person to person, but generally include blood and/or urine tests and occasional scans or bone marrow biopsies.

Always contact your treating team if you experience a new symptom

What are the possible side effects of CAR-T cell therapy?

All treatments, including CAR-T cell therapy have possible side effects. These can vary a lot from person to person and may be mild or more serious.

Knowing about the possible side effects and talking openly about these with your treating team can help you to plan together and quickly get on top of any that you experience. Your team will explain more about the more common side effects, which include infusion-related reactions, cytokine release syndrome, neurotoxicity and low blood counts.

Infusion-related or allergic reactions

During the infusion of CAR-T cells an infusion-related or allergic reaction can occur. These reactions can range from mild to more serious.

Let your treating team know straight away if you notice any of these signs and symptoms while you are having the infusion:

- stuffy nose, cough or itchy throat
- chills or shaking
- fever
- feeling flushed
- diarrhoea, nausea or vomiting
- difficulty breathing or tightness in your throat
- feeling tired
- high blood pressure
- feeling like your heart is racing (palpitations).

What can help?

- Your treating team will watch you closely for any signs of an infusion-related reaction by performing your vital signs frequently.
- If you do have a reaction, your infusion may be slowed down or stopped until your symptoms have gone away. Your doctor may give you some medicine to help with the symptoms too.
- Usually, you will be able to slowly finish your infusion once your symptoms have gone.

Cytokine Release Syndrome (CRS)

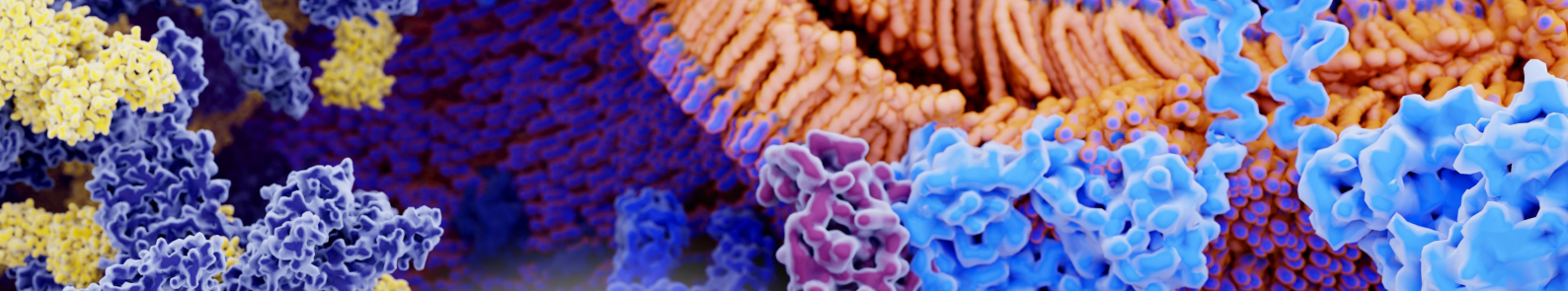
Many people treated with CAR-T cell therapy experience some degree of CRS. This occurs as a result of the CAR-T cells expanding and multiplying in the body and attacking the myeloma cells which causes an inflammatory response that is sometimes known as a 'cytokine storm'. Symptoms and severity vary in individuals. You may experience some of the following:

- Fever
- Headache
- Low blood pressure
- Rapid breathing
- Rapid heartbeat
- Low oxygen level
- Fatigue
- Muscle/joint pain
- Nausea and vomiting

CRS usually occurs in the days following the CAR-T cells being re-infused and symptoms usually resolve. Sometimes when symptoms persist that cannot be managed with standard interventions (such as high fevers that cannot be controlled with paracetamol) a medication called tocilizumab may be administered. Tocilizumab helps to reduce the severity of the CRS symptoms by reducing the inflammatory response caused by the cytokines without effecting the work of CAR-T cells. Tocilizumab is given as an infusion into the vein over one hour. Some individuals may only require one dose while others may require multiple. If you need more than one dose of tocilizumab you will likely be given a small dose of steroids like dexamethasone to help further reduce the cytokine levels.

While most individuals only experience mild to moderate CRS, in severe cases this syndrome can affect multiple organs including your heart, lungs, liver and kidneys and requires more intensive treatment.

It is very important to quickly let your treating team know about any side effects that you have while being treated with CAR-T.



What can help?

- You will be monitored closely by your treating team for any signs and symptoms of CRS through frequent checking of your vital signs.
- Remember to let your treating team know about any symptoms you experience as soon as you notice them.

Neurotoxicity

Immune-effector cell-associated neurotoxicity syndrome (ICANS) is a less common side effect in comparison to CRS and is also not as well understood as to why this occurs in individuals receiving CAR-T cell therapy. Symptoms and severity vary in individuals, and you may experience some of the following:

- Headaches
- Tremors
- Loss of balance
- Confusion
- Agitation
- Difficulty speaking or finding words

Neurotoxicity usually occurs later than CRS, one to two weeks after the CAR-T cells are reinfused but in some cases they can occur simultaneously. Neurotoxicity is treated with corticosteroids, usually dexamethasone and symptoms resolve over days.

What can help?

- You will be monitored closely by your treating team for any signs and symptoms of neurotoxicity using a tool that assesses your orientation, ability to name objects, ability to follow directions, concentrate and write clearly.
- Remember to let your treating team know about any symptoms you experience as soon as you notice them.

Low blood counts

CAR-T cell therapy can cause a decrease in the number of platelets, white blood cells and red blood cells in the blood from the lymphodepleting chemotherapy you receive. It is common for these low blood levels to last for a few months.

Low white blood cell count

White blood cells are part of your body's immune system that help to fight infections. A low white blood cell count increases the risk of developing an infection.

What can help?

- Take extra care to prevent infections, such as washing or sanitising your hands regularly and staying away from other people with coughs, colds or other infections.
- If your white cell count stays low, you may need to have an injection of granulocyte-colony stimulating factor (G-CSF) to increase your white blood cell count. Your doctor will also prescribe medicine to help prevent infections.
- If you do develop an infection, your doctor may prescribe antibiotics.

Having a temperature of 38°C or higher is a common sign of infection.

Always get urgent medical attention for a temperature of 38°C or more.

Low platelet count (thrombocytopenia)

Platelets, which are also called thrombocytes, help your blood to clot. Having a low platelet count can result in bruising and bleeding.

What can help?

- Your doctor will monitor your platelet count before, during and after treatment.
- If your platelets need help returning to normal, you may need a platelet transfusion.

Low red blood cell count

Red blood cells contain haemoglobin, which contain iron and transport oxygen in your body. A low red blood cell count may cause anaemia, tiredness, and make you short of breath.

What can help?

- If you become anaemic, you may need a blood transfusion.

Nausea

Nausea can occur with CAR-T cell therapy secondary to the lymphodepleting chemotherapy you receive.

What can help?

- Let your treating team know if you do develop nausea. They may give you some anti-nausea medicine to help.
- If your nausea worsens with meals try eating smaller portions more frequently throughout the day rather than large meals.

Diarrhoea

Diarrhoea can occur with CAR-T cell therapy.

What can help?

- If diarrhoea becomes a problem, ask your treating team for simple treatments that can help.
- Make sure you are drinking two litres (about eight glasses) of fluids a day to help prevent dehydration. Fluids can include water, ice chips or ice blocks, rehydration drinks and other clear drinks.

Fatigue

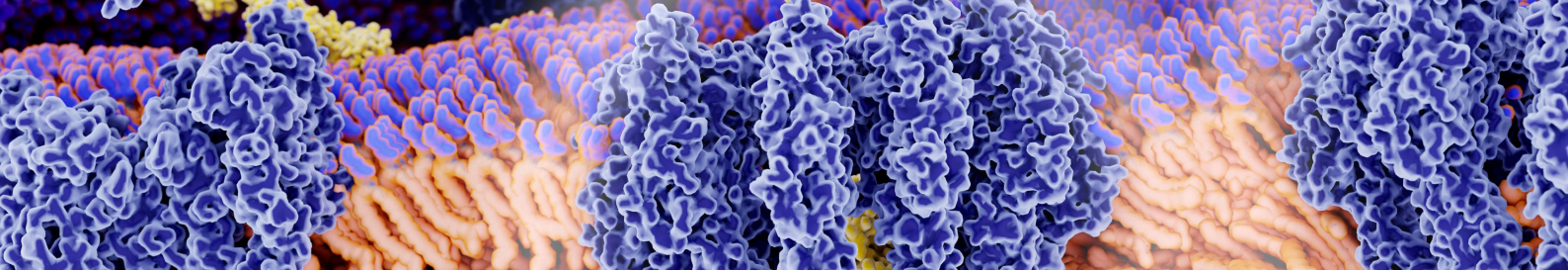
Many people receiving CAR-T cell therapy will experience fatigue.

It can be difficult to tell the difference between fatigue caused by a treatment or by the myeloma itself.

What can help?

- You may be able to help reduce fatigue by:
 - Eating a healthy diet
 - Keeping up your fluids
 - Enjoying gentle, regular exercise
 - Having a regular sleep schedule where you go to bed and get up at the same time each day.
- Talk to your treating team about any fatigue you are feeling. Your team will keep an eye on your red blood cell count, talk to you about other medicines or issues that may be adding to your fatigue, and may prescribe medicine to help reduce fatigue.

Myeloma Australia's *Fatigue and myeloma* information sheet includes more practical tips to help you manage cancer-related fatigue.



Effects on fertility, pregnancy and breastfeeding

There are no long-term studies on the effects of CAR-T cells regarding fertility and risk to an unborn child therefore it is recommended to practice safe sex using a barrier method (such as a condom) for a minimum of 12 months after receiving your CAR-T cells. The lymphodepleting chemotherapy you receive as part of this treatment can have effects on both male and female fertility. You may not be able to breastfeed for a period after receiving treatment. It is advised that you speak with your treating team about fertility and breastfeeding prior to commencing treatment.

The information in this fact sheet is not intended to replace medical care or the advice of your treating team.

Please talk to your doctor if you have any questions about your diagnosis or treatment. Your doctor can answer your questions, talk with you about your treatment goals, and provide you with extra support.

Questions to ask my treating team

Here are some suggested questions you might like to ask your treating team to help you understand more about what to expect with your CAR-T cell therapy treatment.

We have included some space for you to write down answers, as well as space to write down any extra questions of your own. Remember, there is no such thing as a silly question!

- How long will I be in hospital or need to stay close to my treating hospital for?
- How will I know if the treatment is working?
- Can you tell me more about cytokine release syndrome and neurotoxicity?
- Can you tell me more about leukapheresis?
- How often will I need to have blood tests during CAR-T cell therapy?
- Will I need bridging chemotherapy while I am waiting for my CAR-T cells?
- How long will the CAR-T cells live in my body?
- What should I do if I have a new or worsening side effect or symptom while on treatment?
- What should I do if I am already taking or need to start taking any other medicines?

For a list of references used to develop this treatment fact sheet, please email: nurses@myeloma.org.au

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For further information please contact our Myeloma Support Nurses on our toll free Support Line:

1800 MYELOMA (1800 693 566)
or visit our website: www.myeloma.org.au