

Treatment fact sheet

CAR T-CELL THERAPY

This treatment fact sheet provides information about the myeloma treatment, chimeric antigen receptor (CAR) T-cell therapy.

There are many different CAR T-cell therapies in development, but only one is publicly funded in Australia for treating myeloma. This CAR T-cell therapy is called cilta-cel (short for ciltacabtagene autoleucel) and is also called by the brand name Carvykti®.

Cilta-cel is available to people with relapsed or refractory myeloma whose myeloma has come back after receiving four different previous treatments for myeloma.

Other types of CAR T-cell therapies and the use of cilta-cel as an earlier line of therapy for myeloma are currently only available through clinical trials.

When you need a new treatment for myeloma, ask your doctor if cilta-cel, a different 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 type of treatment known as an immunotherapy. This means that the treatment works with your own immune system to detect and destroy cancer cells.

How does CAR T-cell therapy work?

T cells are a type of white blood cell and are part of our first-line immune defence. T cells circulate in our bodies, detecting and helping to destroy abnormal cells or antigens such as bacteria and viruses. However, T cells are unable to detect cancer by themselves.

CAR T-cell therapy involves collecting a small amount of a person's T cells and 'retraining' them by adding genetic information so that they are able to recognise, bind to, and destroy cancer cells.

The genetic information added to the T cell targets a specific antigen that is on the surface of cancer cells. In myeloma, the most common target is B-cell maturation antigen (BCMA). Other target antigens are also being researched.

What happens in each step of the CAR T-cell therapy process?

Much like an autologous stem cell transplant CAR T-cell therapy is a once-only treatment. It involves collecting some of your T cells, engineering them to fight myeloma, and then infusing them back into your body.

This is how the process works:

Step 1: Collecting your T cells

- A small amount of T cells are collected from your blood using a process that's called *leukapheresis* or *apheresis*. This is similar to a stem cell collection, but without the need for chemotherapy or GCSF injections before the collection.
- To do this, you will be connected to a machine where blood is taken from a vein and the T cells are separated from other parts of your blood.
- Once the T cells are collected, the rest of your blood is returned to your body through the same vein.
- Leukapheresis can take 3-6 hours and may need to be repeated.

Step 2: Engineering your T cells to fight myeloma

- Your T cells are then sent to a specialised laboratory where genetic information is added to make CAR T cells.
- The engineered cells stay in the laboratory where they are multiplied into hundreds of millions of cells.
- The cells undergo quality and safety checks before being returned to your treating hospital for infusion. This process can take days to weeks.

Step 3: Chemotherapy to prepare for CAR T-cell therapy

- To help prepare the body for CAR T-cell therapy, all patients are given a special type of chemotherapy called *lymphodepleting chemotherapy*.
- This type of chemotherapy is usually a combination of cyclophosphamide and fludarabine, given through a drip into a vein (intravenously) daily for 3 days.
- This is designed to decrease the number of white blood cells in your body, making room for the CAR T cells to grow, expand and multiply when they are infused.
- The CAR T infusion is usually given 5–7 days after you started the lymphodepleting chemotherapy.
- While waiting for the CAR T cells to be manufactured in the laboratory, some people may be given bridging chemotherapy to keep their myeloma under control and make sure they are well enough to receive the CAR T cells. Your treating team will let you know if you may need this additional type of chemotherapy.

Step 4: Infusion of CAR T cells

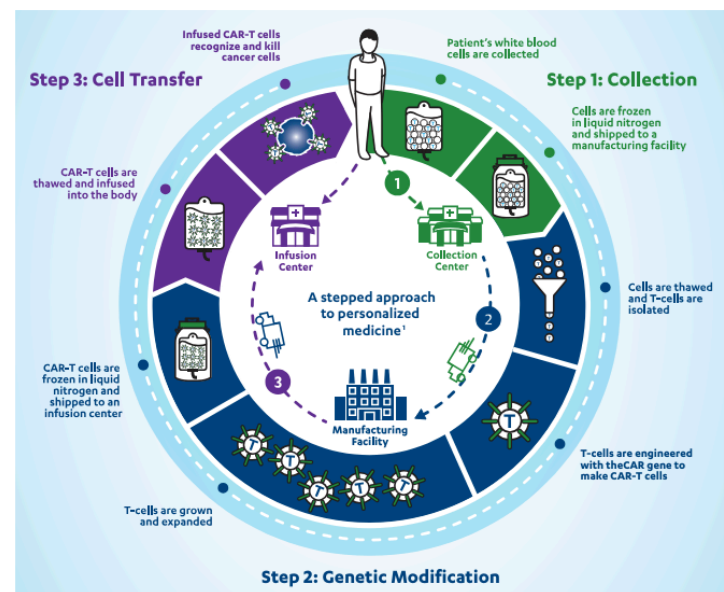
- To help reduce side effects, you will be given paracetamol and an antihistamine 30–60 minutes before your CAR T-cell infusion.
- The CAR T cells are then infused into your body through a vein. This takes about 30–60 minutes.
- The engineered cells circulate around your body, searching for the target expressed on the myeloma cells that they are programmed to recognise (such as BCMA). The CAR T cells bind to this target and destroy the myeloma cells.

Step 5: Follow-up monitoring

- It is likely you will be admitted to hospital for observation for 5 days after receiving your CAR T cells.
- If you are not an inpatient, you will need to visit your treating hospital every day for at least 14 days after your CAR T-cell infusion. This is so your treating team can check if the treatment is working and to manage side effects.

- If you develop side effects, you will need to be admitted to hospital until these are under control.
- You and your carer will need to stay within 1 hour of your treating hospital for at least 4 weeks after your infusion.

The CAR T-cell therapy process



How will I know if CAR T-cell therapy is working?

After treatment with CAR T-cell therapy, you may notice fewer symptoms caused by your myeloma and this may give you an improved quality of life.

Your doctor will monitor you closely and will order tests to see how you are responding to the treatment. The tests will vary from person to person, but generally include blood and/or urine tests and occasional scans or bone marrow biopsies.

How long does CAR T-cell therapy keep working?

CAR T cells can stay in your body for a long time and can also multiply to create new CAR T cells that continue to recognise and destroy myeloma cells.

This means that CAR T cells may have the potential to provide longer-term control of myeloma.

Over time, it appears that CAR T cells can get 'exhausted' and stop working. There is a lot of research being done to see how CAR T cells can be kept active in the body for longer.

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 cytokine release syndrome (CRS), neurological toxicities, risk of infections, and low blood counts.

It is very important to learn about the side effects that may need urgent medical attention and quickly let your treating team know about any side effects you have while receiving your infusion or after CAR T-cell therapy.

Cytokine release syndrome (CRS)

Nearly all people treated with cilta-cel experience some degree of cytokine release syndrome (CRS).

CRS happens when the active CAR T cells cause an inflammatory response and release large numbers of proteins, called cytokines. This is sometimes called a 'cytokine storm'.

If CRS does happen, it usually begins 3–7 days after your CAR T cells are infused.

The signs, symptoms and severity of CRS can vary between different people and may include:

- fever – which can also be a sign of infection
- chills
- rapid heartbeat
- difficulty breathing
- low blood pressure – which can make you feel dizzy or lightheaded
- low oxygen level
- increased liver enzymes.

In most people who experience CRS, the symptoms are mild to moderate and will settle with simple treatments, but it's important to know that CRS can be very severe and life-threatening.

Always let your treating team know if you experience any of the symptoms listed above.

What can help?

- You will be monitored closely by your treating team for any signs and symptoms of CRS by regularly checking your vital signs.
- Before you leave hospital, your treating team will provide you and your carer with information and tools to help you track any side effects.
- Your team will also provide you with contact numbers to call if there are any changes in your condition. Remember to urgently let them know about any symptoms as soon as you notice them.
- Symptoms of CRS usually get better with simple treatments, such as paracetamol to bring down fever.
- Severe symptoms are treated with a medicine called tocilizumab, which is given as an infusion. Tocilizumab reduces the inflammatory response caused by the cytokines without affecting how the CAR T cells work.

Neurological toxicities

Neurological toxicities are also a common side effect of CAR T-cell therapy, although they affect fewer people than CRS.

These toxicities include immune-effector cell-associated neurotoxicity syndrome (ICANS), toxicities that affect your movement and cognition similar to Parkinson's disease, Guillain-Barre syndrome, peripheral neuropathy, and problems with moving your eyes or double vision.

The symptoms and severity of neurotoxicity can vary between different people and may include:

- confusion
- feeling less alert, disoriented or anxious
- memory loss
- difficulty speaking or slurred speech
- coordination problems that affect your movement and balance
- difficulty reading, writing and understanding words
- personality changes – like being less talkative, uninterested in usual activities, and having less facial expression.

Neurological toxicity symptoms can occur at any time and may be delayed by weeks after your CAR T infusion. Symptoms may occur before CRS, at the same time as CRS, after CRS symptoms have resolved, or independently of CRS.

What can help?

- You will be monitored closely by your treating team for any signs and symptoms of neurological toxicities using a tool that checks your ability to name objects and follow directions, as well as your orientation, concentration and handwriting.
- Before you leave hospital, your treating team will provide you and your carer with information and tools to help you track any side effects.

- Your team will also provide you with contact numbers to call if there are any changes in your condition. Remember to urgently let them know about any symptoms as soon as you notice them.
- Your treating team will decide on the best way to manage these side effects, depending on the type and severity of your symptoms.

Increased risk of infections

Both lymphodepleting chemotherapy and CAR T-cell therapy itself can cause a decrease in white blood cells that form part of your body's immune system to help fight infections. A low white blood cell count increases the risk of developing infections.

CAR T-cell therapy can also cause a decrease in normal antibody levels, which further reduces your body's ability to fight infections.

As a result, infections are a common side effect with CAR T-cell therapy. These include upper respiratory tract infections (colds) and coughs, as well as serious infections.

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.
- Let your treating team know straight away if you develop any signs or symptoms of an infection.
- Your doctor will prescribe medicines to help protect against infections.
- Vaccines can also help protect against infections. Talk to your doctor about which vaccines are recommended for you. It's important to note that 'live' vaccines are not recommended for people with myeloma; only 'inactive' vaccines are safe to use.
- If your white cell count stays low, you may need to have daily injections of granulocyte-colony stimulating factor (G-CSF) to increase your white blood cell count.
- If you do develop an infection, your doctor may prescribe antibiotics.

- If you are experiencing recurrent infections, your doctor may recommend immunoglobulin replacement therapy, given either as an infusion into a vein (intravenously) or as an injection into the skin (subcutaneously).

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, or if you have any signs or symptoms of an infection.

CAR T-cell therapy can also cause both increased and lower levels of other substances in your blood. Your treating team will keep a close eye on these through regular blood tests. The therapy may cause some commercial HIV tests to incorrectly give you a HIV-positive result, even if you are HIV-negative.

Muscle and joint pain and headaches

Muscle and joint pain (often called musculoskeletal pain) and headaches are common side effects with CAR T-cell therapy.

What can help?

- Let your treating team know about any new pain you are experiencing. Your team can recommend pain relief medicine that's suitable for you, as well as helpful lifestyle tips – like exercise, relaxation and positioning – that can help you to manage pain.
- Managing fatigue and getting enough sleep can also help you to manage pain.

Myeloma Australia's Managing myeloma pain information sheet includes many practical tips to help manage pain.

Low blood counts

As well as low white blood cell counts, both lymphodepleting chemotherapy and CAR T-cell therapy can cause a decrease in red blood cells and platelets in the blood.

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.

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.

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 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.

Digestive (gastrointestinal) symptoms

Digestive symptoms such as diarrhoea, nausea and decreased appetite are quite common in people receiving CAR T-cell therapy.

What can help?

- If any digestive symptoms become a problem, ask your treating team about preventative medicines, dietary changes and treatments that can help.
- Make sure you are drinking 2 litres (about 8 glasses) of fluids a day to help prevent dehydration. This is especially important if you have diarrhoea or vomiting. Fluids can include water, ice chips or ice blocks, rehydration drinks and other clear drinks.

Myeloma Australia's Nutrition and myeloma information sheet includes practical tips to help make eating easier when your appetite is low.

Other important things to know before and after CAR T-cell therapy

Vaccinations

People with myeloma are not able to receive live vaccines due to the risk of developing an active infection. It is particularly important that you do not have any live vaccines in the 6 weeks before lymphodepleting chemotherapy, during CAR T-cell therapy, and after treatment, while your immune system is still recovering.

Always talk to your treating team about any vaccinations you are considering.

Steroids

Tell your treating team if you are taking steroids or other medicines that weaken your immune system, as they can interfere with the effectiveness of CAR T-cell therapy.

Driving or using machinery

Do not drive, use tools or machinery for at least 8 weeks after having CAR T-cell therapy, or if any symptoms like fatigue, dizziness, loss of balance or coordination come back after this time.

Effects on fertility, pregnancy and breastfeeding

There are no long-term studies on the effects of CAR T-cells on fertility, their risk to an unborn baby, presence in breastmilk, or effect on a breastfed child.

The lymphodepleting chemotherapy you receive as part of this treatment can have effects on both female and male fertility, and may result in being unable to have children. The chemotherapy treatments pass into breastmilk where they may affect a breastfed child.

Before starting CAR T-cell therapy, women of childbearing potential need to have a pregnancy test, which needs to show they are not pregnant.

If you are planning a pregnancy or to breastfeed, please talk to your treating team before starting CAR T-cell therapy. Your doctor can advise on fertility preservation options if you are planning to have children in the future.

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.

We have included some space for you to write down any extra questions of your own.

Remember, there is no such thing as a silly question!

- Can you tell me more about leukapheresis?
- How long will I be in hospital or need to stay close to my treating hospital?
- How will I know if the treatment is working?
- Can you tell me more about cytokine release syndrome (CRS) and neurological toxicities?
- How often will I need to have blood tests during and after 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 during or after treatment?
- What should I do if I am already taking or need to start taking any other medicines?

My Questions

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.

For more information and support, please contact our Myeloma Australia Nurses on our free Telephone Support Line:

call 1800 MYELOMA (1800 693 566), Monday-Friday, 9am-5pm AEST/AEDT

email: nurses@myeloma.org.au at any time.

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