

Chimeric Antigen Receptor (CAR) T-cell therapy

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Learning about CAR T-cell therapy can be like learning a new language. It takes time and practice. Please keep this document handy so you can refer back to it as often as you need to. **It will become easier to understand the more you read it.**

Overview

CAR T-cell therapy is a type of immunotherapy that enhances your immune system so it can recognise, and destroy cancerous lymphoma cells more effectively. It uses your own immune **T-cell lymphocytes**, which are collected in a procedure called apheresis. The T-cells are then bound to a CAR – (chimeric antigen receptor), which is specifically designed to attach to antigens on your lymphoma cells. The CAR- T cells are then returned to you, better able to fight your lymphoma.

Because CAR T-cell therapy uses your own **T-cell** lymphocytes to improve your immune system's ability to fight cancer, it is also called **cellular** therapy.

T-cells and your immune system

Our immune system monitors everything in our body and can recognise when something like a germ, or damaged or diseased cells do not belong. These germs, damaged or diseased cells are

found by our immune system because they grow specific proteins called "antigens" on them. When our immune system sees an antigen, it destroys the cell with the antigen and removes it from our bodies. However, some cancerous cells are able to hide from our immune system by putting up barriers that make it look like a normal cell. So our immune system leaves it alone, and the cancerous cells continue to grow and create more cancerous cells.

T-cell lymphocytes are important cells in our immune system that recognise and fight cancerous cells. They also help B-cell lymphocytes make antibodies to fight cancer and other illnesses. Additionally, our lymphocytes have a memory, so when they find an antigen, it remembers how to destroy it in the quickest and most efficient way possible in the future. This makes T-cells the perfect target to fight lymphoma more effectively.

CAR T-cell therapy aims to enhance the way your T-cells recognise, bind to and destroy lymphoma cells. It does this by

bypassing any barriers the lymphoma cells have put up, and attaching the T-cells directly to the antigens on the lymphoma cells.

Collecting your T-cells

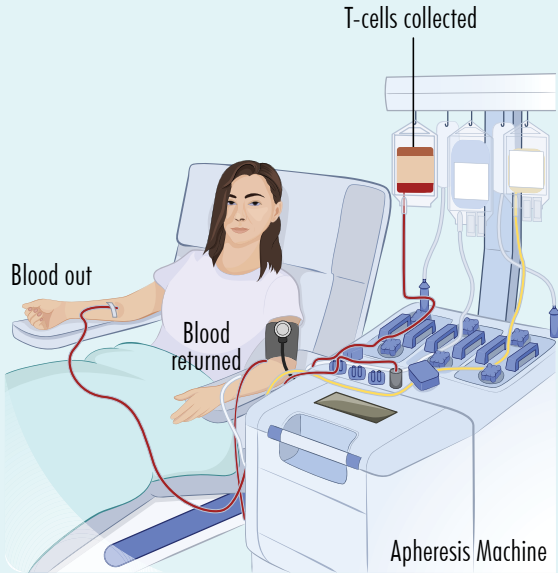
You will need to have an apheresis procedure to collect your T-cells before your CAR T-cell therapy. Apheresis is a procedure that separates certain cells from your blood. You will have a double central venous access device or two cannulas. Your blood will be removed from your body through one and returned through the other.

Before your blood is returned to you, it is processed in the apheresis machine, and your white blood cells (also called leukocytes) – including your T-cell lymphocytes are collected in a special blood bag. The rest of your blood is returned to you.

The procedure to remove your white blood cells is called a “white cell collection” or “leukapheresis”. It usually takes between two and five hours and may be done in one or two days, depending on how many T-cells are collected.

What are Chimeric Antigen Receptors (CARs)?

A chimeric antigen receptor (CAR) is a special molecule created in a laboratory, designed to attach to very specific antigens, unique to your cancer cells. Each



APHERESIS

T-cells collected

Blood out

Blood returned

Apheresis Machine

Step 1: Blood is removed from your IV line in your arm, or from your central line.

Step 2: Blood is processed in the apheresis machine and the T-cell lymphocytes are separated and removed from your blood.

Step 3: Your blood is then returned to you, minus the T-cells.

person will have slightly different antigens on their lymphoma cells, so CARs are tailored specifically to the antigens on your individual lymphoma cells.

The CAR is then bound to your T-cells in the laboratory, by using a lentiviral vector. Because the CAR is attached to your natural T-cells it is called chimeric.

Chimeric means the cell is now made from two different sources, one being your T-cell and the other, the man-made CAR. Once the CAR is bound to the T-cell, the cell is called a CAR T-cell.

CAR T-cells

The CAR T-cell is then multiplied in the laboratory until there are millions of identical cells. When these CAR T-cells are returned to you, they seek out your lymphoma cells, and the chimeric antigen receptor (CAR), attaches to the antigen on your lymphoma cell. By doing this, the T-cells are delivered directly to your lymphoma so they can begin to fight and destroy the lymphoma cells.

Because T-cells have a memory, CAR T-cells may have a lasting effect against your lymphoma even if it returns (relapses) years later.

Who is eligible for CAR T-cell therapy?

In Australia CAR T-cell therapy is currently publicly funded for people who meet strict eligibility criteria. It is currently only approved for people with:

- Relapsed or refractory Diffuse Large B-cell Lymphoma (DLBCL) (Note: Relapsed DLBCL is when your disease has come back after a time remission. Refractory DLBCL means your DLBCL has not gotten better with your current treatment)

- Transformed Follicular Lymphoma
- Primary Mediastinal B-cell Lymphoma (PMBCL)
- B-cell acute lymphoblastic lymphoma (B-ALL) for people 25 years old or younger

Clinical trials

In some cases, you may be able to access CAR T-cell therapy by joining a clinical trial. Clinical trials involving CAR T-cell therapy are looking at:

- different types of lymphoma or CLL that may be treatable with CAR T-cells
- treating lymphoma at earlier stages with CAR T-cell therapy
- how to manufacture or deliver CAR T-cell therapy in a way that reduces the side-effects you experience
- using T-cells from a donor rather than your own T-cells
- different antigen targets.

Clinical trials may offer you the opportunity to access CAR T-cell therapy when you otherwise would not be eligible; however, there is no guarantee that the CAR T-cell therapy will work.

If you join a clinical trial your costs for your CAR T-cell therapy should be covered through the trial funds.

Where can I get CAR T-cell therapy?

All people in Australia who have an eligible subtype of lymphoma, and have been deemed well enough to undergo a CAR T-cell therapy procedure, and who meet other strict eligibility criteria are able to have the procedure. The procedure is publicly funded, so you should not have to pay anything.

However, CAR T-cell therapy is not available in all cancer centres. In some cases, you may need to travel to larger cities or even interstate to have your CAR T-cell therapy. This is because the cost of providing CAR T-cell therapy for health care providers is over \$500,000 per patient. It is also a very specialised area of medicine needing doctors and nurses with specialised training in CAR T-cell therapy.

If you have to travel interstate or to a bigger city to have treatment, the costs of your travel and accommodation will be covered under Medicare, or by the drug company who is manufacturing your CAR T-cells. This will include the costs for one carer to travel with you. If you think you may be eligible for CAR T-cell therapy, but it is not offered where you are receiving treatment, **ask your doctor about the patient access scheme for CAR T-cell therapy.**

You can also contact our Lymphoma Care Nurses on 1800 953 081 or email us at nurse@lymphoma.org.au

In Australia CAR T-cell therapy is currently offered at the following hospitals:

- Western Australia – Fiona Stanley Hospital
- New South Wales – Royal Prince Alfred Hospital
- New South Wales - Westmead Hospital
- Victoria – Peter MacCallum Cancer Centre
- Victoria - The Alfred Hospital
- Queensland - Royal Brisbane and women's Hospital
- South Australia – Not currently available but stay tuned.

Types of CAR T-cell therapy

There are two pharmaceutical companies that have been given approval to manufacture and supply a product for CAR T-cell therapy in Australia. These include:

- [Novartis – Kymriah™ \(tisagenlecleucel\)](#)
- [Gilead - Yescarta™ \(axicabtagene ciloleucel\).](#)

Both Kymriah™ and Yescarta™ CAR T-cells are publicly funded, so that means you should have no out-of-pocket expense. Whether you get Kymriah™ or Yescarta™ CAR T-cells will depend on what's available in the facility that you attend, or the product your doctor feels will be the best option given your individual circumstances.

How is CAR T-cell therapy given?

Car T-cell therapy is a multistep procedure. From the time you have your T-cells collected to the time you have the CAR T-cell therapy, there may be a 3 to 6 week waiting time. During this time you may have chemotherapy or other anticancer treatments to keep your lymphoma under control. This is because it takes time to make your individualised CARs and bind them to your T-cells. The process for getting your CAR T-cell cell therapy is:

- 1. T-cell collection** – before you have your T-cell therapy you will need to have your T-cells collected as described above. Once your T-cells are collected they will be sent to the laboratory for manufacturing and binding with the CAR.
- 2. Manufacture of CAR T-cells** – once the T-cells arrive at the laboratory they will be genetically modified to be bound with the chimeric antigen receptor (CAR) using a lentiviral vector. The resulting CAR T-cell will be multiplied millions of times while they're in the laboratory. They will then be frozen until you are ready to have them back. This part of the process can take several weeks.
- 3. Chemotherapy** – before your CAR T-cells are re-infused (given back to you), you will have chemotherapy to kill off some of your existing T cells to make room for the new CAR T-cells.

The chemotherapy most often used prior to CAR T-cell therapy is called fludarabine and cyclophosphamide. Your specialist Dr or lymphoma care nurse will be able to explain to you what chemotherapy protocol you will have, and any side-effects of that treatment.

- 4. CAR T-cell infusion** – after your chemotherapy your CAR T-cells will be infused. This process is similar to having a blood transfusion or stem cells reinfused.
- 5. After infusion** – once your CAR T-cells have been reinfused into your body they will continue to multiply very quickly, so that you will have millions and millions of specialised CAR T-cells to fight your lymphoma. Some CAR T-cells may remain for many years and may be able to continue to fight lymphoma if it relapses at a later time.

Recovery – you will be monitored very carefully during and after your CAR T-cell therapy infusion. It can take 2 to 3 months to recover from having CAR T-cell therapy. During this time your healthcare team will keep a close eye on you for any side-effects to the treatment. Once you are discharged from hospital you will need to stay close to the hospital (within a 20 minute drive) for at least 30 days. As mentioned earlier many of the costs relating to travel and accommodation for CAR T-cell therapy are covered for yourself as the patient and one carer.

Possible side-effects of CAR T-cell therapy

All treatments for cancer have the possibility of causing unwanted side-effects. CAR T-cell therapy is no different. Some side-effects happen more commonly in patients having CAR T-cell therapy. Some of these side-effects can be serious and potentially life-threatening. For this reason, CAR T-cell therapy can only be given in hospitals that are specially set up to care for patients receiving this treatment type.

Cytokine release syndrome (CRS)

Cytokine release syndrome (CRS) is the most common and potentially serious side effect associated with CAR T-cell therapy. It is not an unexpected side effect, because cytokines are naturally occurring chemicals in our bodies that help our T cells to work. When you have CAR T-cells you may produce more cytokines than usual, and this can result in mild flu like symptoms, or be more serious causing inflammation to all your body organs. Your healthcare team will monitor you closely for signs of CRS which can include:

- fever equal to or more than 38°, with or without chills and rigors (shaking or shivering)
- low blood pressure
- low oxygen levels
- nausea, vomiting or loss of appetite – not wanting to eat

- difficulty swallowing
- extreme tiredness or fatigue not improved with sleep and rest
- shortness of breath and/or coughing
- dizziness
- headaches
- confusion and/or hallucinations
- diarrhoea
- body aches and pains particularly in your muscles and joints
- rash
- swelling in your arms or legs.

CRS can be treated. If you experience any of the above symptoms after having CAR T-cell therapy, report them immediately to your doctor or specialist lymphoma nurse.

Neurotoxicity

Neurotoxicity is another side effect of CAR T-cell therapy, which results from inflammation to your central nervous system including your brain and spinal cord. Neurotoxicity associated with CAR T-cell therapy is often called “immune effector cell – associated neurotoxicity syndrome (ICANS)”.

Symptoms of neurotoxicity include:

- difficulty speaking or swallowing
- changes to your levels of consciousness and ability to concentrate

- tremors, or weakness of your body
- seizures caused by swelling of your brain
- changes to your vision
- headaches.

If you experience any of these side-effects, report them immediately to your healthcare team.

Other side-effects

Because you may have chemotherapy in the lead up to your CAR T-cell therapy re-infusion, you can also have side effects associated with that chemotherapy. This can include having low blood cell counts including low neutrophils which can increase your risk of infection, low red blood cells which may require a blood transfusion, or low platelets which may require a platelet transfusion.

You may also experience nausea and vomiting, a sore mouth, diarrhoea or constipation. Your lymphoma nurse will be able to talk to you about the side-effects of the chemotherapy that you have received, and how best to manage these.

Summary

- CAR T-cell therapy is both an immunotherapy and a cellular therapy, because it improves the way your immune system recognises and fights your lymphoma, by genetically changing your T-cell lymphocytes.
- Chimeric antigen receptors (CARs)

are attached to your T-cells in the laboratory using a lentiviral vector.

- The CARs help your T-cells to find your lymphoma cells and binds to unique receptors found only on your lymphoma cells. The T-cells can then begin to destroy the lymphoma.
- You may need to have chemotherapy while waiting for your CAR T-cells to be manufactured.
- Cytokine release syndrome and Immune effector cell-associated neurotoxicity are the main side effects of CAR T-cell therapy that can be mild or life threatening.
- You will need to stay close to the hospital for at least one month after you are discharged from the hospital in case you need medical attention.
- Patient access schemes from Novartis and Gilead as well as Medicare ensure you should have no out-of-pocket expenses, even if you need to travel to a big city or interstate for your treatment.

Resources and support

Lymphoma Australia offers a wide range of resources and support for people living with lymphoma or CLL, and their carers.

How to access our resources:

- **Visit** our website www.lymphoma.org.au for more information.
- **Phone** our Lymphoma Care Nurse Hotline on 1800 953 081.

- **Email** our Lymphoma Care Nurses nurse@lymphoma.org.au
- **Booklet:** Understanding Non-Hodgkin Lymphoma (NHL)
- **Downloadable information:** Visit our [website](#), or give us a call if you would like some more information on a variety topics related to lymphoma
- **Join** our Facebook page [Lymphoma Down Under](#) (make sure you complete all the membership questions when you join).

Cancer Council offers a range of services, including free counselling, to support people affected by cancer, including patients, families and friends. Services may be different depending on where you live. You can contact them at www.cancer.org.au or by phone on 13 11 20.

Medicare Australia: Check with your GP if you are eligible for a Mental Health Treatment Plan (MHTP). This plan is funded by Medicare and can provide you with up to 10 sessions with a registered psychologist. More information can be found [here](#).

WeCan is an Australian supportive care website to help find the information, resources and support services you may need following a diagnosis of cancer. You can visit their website at www.wecan.org.au.

Canteen provides support for young people aged 12-25 years who have cancer, or, who have a parent with cancer. Find out more at their website here www.canteen.org.au.

Health Translations: A collection of health related information collected by the Victorian Government with resources in different languages. You can visit their website at www.healthtranslations.vic.gov.au.

Useful links

To watch a video on CAR T-cell therapy by the Lymphoma Coalition and Acute Leukemia Advocates Network please click [here](#) or scan the below QR code.

Video: CAR-T cell therapies and what it means for Patients



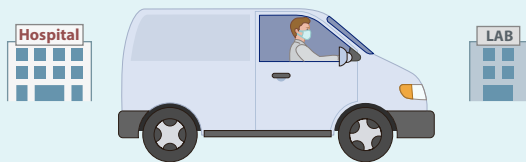
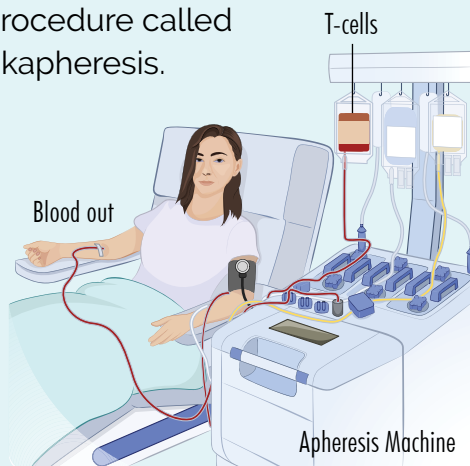
Additional information can also be found on the NSW Government webpage [here](#), or scan the QR code below.

Video: An introduction to CAR T-cell therapy

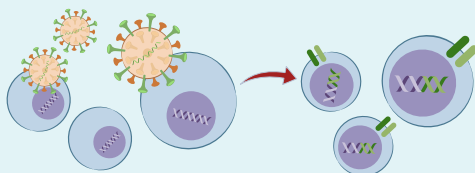


CAR T CELL IMMUNOTHERAPY

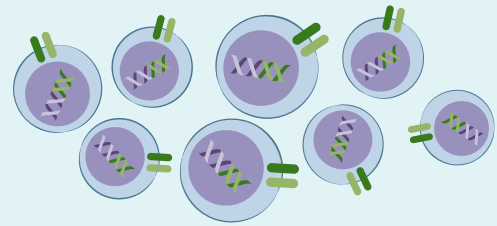
Step 1: Your T-cells are collected during a procedure called leukapheresis.



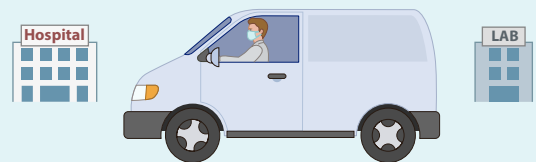
Step 2: Your T-cells are taken to the laboratory so they can be genetically changed to have Chimeric antigen receptors (CARs) attached to them.



Step 3: CARs that have been made to precisely match the antigens on your lymphoma cells are attached to your T-cells using a lentiviral vector.



Step 4: The CAR T-cells are multiplied millions of times.



Step 5: Your CAR T-cells will then be transported back to the hospital.

Step 6: Your CAR T-cells will then be given to you (re-infused).



Step 7: Once your T-cells are reinfused, they will continue to multiply and destroy your lymphoma cells.

Disclaimer: Lymphoma Australia has taken every precaution to make sure the information in this document is accurate and up-to-date. However, this information is intended for educational purposes only and does not substitute for medical advice. If you have any concerns about your health or wellbeing, please contact your treating team.



