leukaemia & blood cancer NEW ZEALAND

Vision to Cure. Mission to Care.

MALAGHAN INSTITUTE OF MEDICAL RESEARCH

IMMUNOTHERAPY AND CANCER

A fact sheet for patients, families and whānau in partnership with the Malaghan Institute

WHAT IS IMMUNOTHERAPY?

Immunotherapy is any medical treatment that uses the immune system to improve health or fight disease. Immunotherapy drugs can be used to stimulate (increase) or suppress (decrease) certain parts of the immune system and can help the immune system to recognise and attack cancer cells.

What is the immune system?

Your immune system is a network of specialised cells, tissues and structures throughout your body. These cells communicate with each other at special 'hubs' that are found in your lymph nodes, spleen and gut.

There are hundreds of different types of immune cells, each with its own function. Some cells seek out and kill faulty cells that might turn into cancer cells, some defend against bacteria or viruses, some tag bad cells so other immune cells can find and destroy them, and others keep a 'memory' of past challenges.

Examples of immune cells include:

- T-lymphocytes (T-cells)
- B-lymphocytes (B-cells)
- Neutrophils
- Macrophages.

Immunotherapy and cancer

When a cell gets damaged or stops behaving as it should – such as dividing uncontrollably – it gets marked and destroyed by your immune system. Most precancerous cells are removed in this way before we even notice them, but occasionally these cells can evade the immune defence system and go on to develop into cancer. By understanding how to turn certain parts of the immune system up or down, we can use immunotherapy to help the immune system to better recognise and destroy the cancer cells.

Immunotherapy drugs can be given alone (called monotherapy) or in combination with other treatments such as chemotherapy (called combination therapy).

How does immunotherapy work?

There are different types of immunotherapy that work in different ways:

- **Monoclonal antibody drugs** – help the immune system recognise and attack cancer cells.
- **Immunomodulator drugs** (immune system modulators) – can either boost the immune system (increase its activity) or suppress the immune system (reduce its activity).
- **Checkpoint inhibitors** – turn off signals that stop immune cells from responding to cancer cells, which sustains their ability to fight the cancer.
- **Chimeric antigen receptor (CAR) T-cell therapy** – alters a patient's own immune cells so they can better find and attack cancer cells.
- **Bispecific antibodies** – bind to immune cells and cancer cells at the same time, enabling the immune cells to better attack cancer cells.
- **Vaccines** – give the immune system advance warning of diseases.

Monoclonal antibody drugs

These types of drugs are made up of immune system proteins which are created in a lab and attach to specific parts of cancer cells. Some monoclonal antibody drugs are checkpoint inhibitors (see below). Others mark cancer cells so that they can be seen and destroyed by the immune cells.

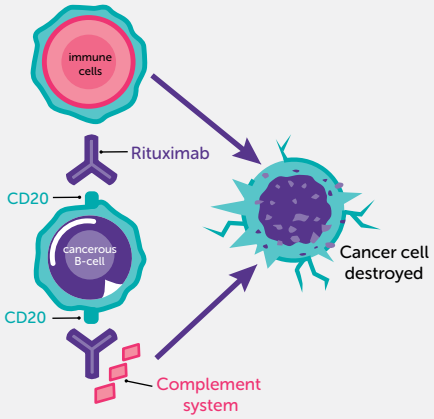
Some examples of monoclonal antibody therapies include:

- Rituximab (MabThera)
- Obinutuzumab (Gazyva).

These monoclonal antibodies target B-cells by binding to a cell marker called CD20. Figure 1 illustrates how Rituximab binds to CD20 to destroy a cancerous B-cell.

Figure 01

Mode of action of Rituximab monoclonal antibody



Immunomodulator drugs

An immunomodulator drug changes (modulates) the immune system to help your body respond to a disease or illness. Immunomodulator drugs either stimulate (increase) or suppress (decrease) the activity of the immune system.

Some examples of immunomodulator drugs that stimulate the immune system are:

- Thalidomide (Thalomid)
- Lenalidomide (Lenalidomide Viatris)
- Pomalidomide (Pomolide).

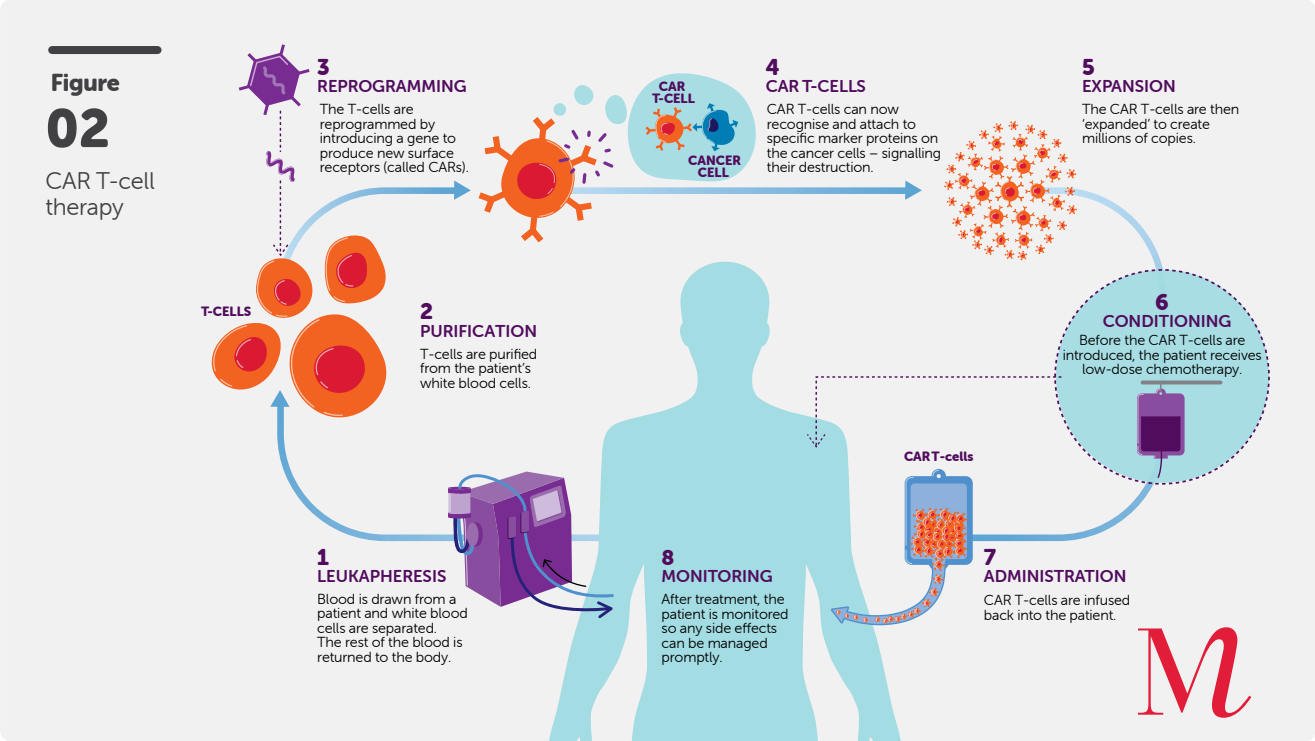
Immunomodulator drugs that suppress the immune system are used in stem cell transplants. Some examples include:

- Ciclosporin
- Tacrolimus
- Methotrexate.

Checkpoint inhibitors

Checkpoint inhibitors act on a type of white blood cell called T-cells. When T-cells are active, they can attack and destroy other cells, such as cancer cells. Cancer cells can switch off the T-cells by signalling to proteins on them called checkpoints. Checkpoint inhibitors block the checkpoints and stop the T-cells from being switched off, allowing the T-cells to kill the cancer cells.

Pembrolizumab (Keytruda) is a checkpoint inhibitor drug sometimes used in Hodgkin lymphoma, and in solid tumours such as melanoma, colon cancer and some lung cancers.



CAR T-cell therapy

CAR T-cell therapy works by changing a patient's own T-cells so they can recognise and attack cancer cells. T-cells are taken from the patient's blood using a process called leukapheresis. The T-cells removed from the blood are modified by giving them a new gene (a new instruction code) that tells them to destroy the cancer cells. The CAR T-cells are then given as an infusion back into the patient, a few days after receiving some chemotherapy. The new CAR T-cells can then recognise cancerous cells and destroy them. Usually CAR T-cell treatment is given as a single infusion. Some CAR T-cells can stay active in the body for months or even years after infusion, which can help prevent the cancer from returning.

Research and clinical trials investigating how CAR T-cells can be used to treat lymphoma, myeloma and other cancers are underway around the world, including in New Zealand. CAR T-cell therapies have been licensed for the treatment of certain blood cancers in Australia, the USA, and parts of Asia and Europe.

Bispecific antibodies

Bispecific antibodies work by bringing together the patient's own immune cells (T-cells) and the cancer cells. This enhances the ability of the T-cells to kill the cancer cells. Bispecific antibody therapies are showing promising effects and have been licensed for the treatment of certain lymphomas and of myeloma in Australia, the USA and parts of Europe. At the time of writing, there are no funded bispecific antibodies in New Zealand, but they may be available as part of a clinical trial or compassionate access treatment.

Some examples of bispecific antibodies include:

- Epcoritamab (Epkinly) – binds to the CD20 marker on cancerous B-cell lymphoma cells and to the CD3 marker on T-cells.
- Glofitamab (Columvi) – binds to the CD20 marker on cancerous B-cell lymphoma cells and to the CD3 marker on T-cells.
- Elranatamab (Elrexfio) – binds to the BCMA marker on cancerous plasma cells (myeloma cells) and to the CD3 marker on T-cells.

Vaccines

Vaccines are one of the oldest forms of immunotherapy. They teach the immune system how to find and attack infections such as the flu, measles or COVID-19 by telling your immune system what to look for. This means your immune system is better prepared to fight and remove infections when you encounter the real thing. Scientists are researching ways that vaccines could be used to target cancer cells.

What are the side effects of immunotherapy drugs?

Immunotherapy can sometimes make the immune system overactive and cause it to attack healthy cells in the body. This can cause side effects known as immune-related adverse events (irAEs).

Side effects of immunotherapy usually occur within the first 12 weeks of treatment but can happen at any time, even after treatment has finished. For this reason, your health care team will monitor you closely during and after your treatment. See Table 1 below for some of the possible signs and symptoms. The health care team treating you will discuss side effects you may experience with the specific immunotherapy you are receiving. If you have had immunotherapy treatment, check yourself regularly and tell your health care team immediately if you notice any of them.

Table 1.

Body part	Signs and symptoms
Skin, mouth	• Rash or itch • Blistering or peeling skin • Yellowing of skin • Blueish or red skin (particularly in fingertips) • Mouth sores
Eyes	• Yellowing of the whites of the eyes • Changes in vision (blurry vision, double vision) or loss of vision
Bowels, stomach	• Diarrhoea • Abdominal pain • Bloody, dark or sticky stools (poo) • Nausea and vomiting
Bladder, kidneys	• Pink, red or dark urine (wee) • Blood clots in your urine • Changes to how often you pass urine, or the amount you pass • Pain in your back or bladder
Lungs	• A new cough • Shortness of breath • Wheezing • Chest pain
Legs, feet, arms, hands	• Swollen legs, feet or ankles • Weakness in your muscles, or in your arms or legs • Numbness and/or tingling
Other	• Headache • Changes in appetite • Fatigue (feeling tired) • Bleeding or bruising more easily than normal • Feeling more cold or hot than normal • Changes in your heart rate • Changes in weight • Changes in balance • Fever • Feeling dizzy or fainting • Confusion or having trouble concentrating • Infusion-related reactions

Important information

Certain immune therapies, for example CAR T-cell therapy and bispecific antibodies, can cause specific side effects such as cytokine release syndrome (CRS) and a neurological toxicity called immune effector cell-associated neurotoxicity syndrome (ICANS). These effects usually occur within the first two weeks following treatment but can occasionally occur later.

Cytokine release syndrome (CRS)

CRS occurs due to chemicals released by the immune cells which can lead to a significant inflammatory response in the body. Fever is usually the first symptom of CRS, and may be followed by other symptoms such as fatigue, muscle aches, lightheadedness due to low blood pressure, difficulty breathing, bruising and rashes, or changes to organ function (as detected by a blood test).

Neurotoxicity (also called ICANS)

This is a form of CRS that happens in the brain. It may cause confusion, agitation, reduced responsiveness, or a reduced ability to follow commands, write words or to use language. Close monitoring from a support person can be helpful to identify any changes in behaviour or personality that may indicate ICANS.

Always seek urgent medical attention if you have symptoms of CRS or ICANS, or if your support person suspects you have these symptoms.

How is immunotherapy given?

Immunotherapy can be given as oral tablets, subcutaneous (under the skin) injections, or via infusion into the veins (IV). How your immunotherapy is given, how often it is given, and how long the break between your doses is will depend on your specific blood cancer.

Oral tablets – can be given at home, in the day unit or in hospital. Examples of oral immunotherapy drugs include thalidomide, lenalidomide and pomalidomide.

Subcutaneous injections – are given by needle injection under the skin. They can be given in the day unit or in hospital. Epcoritamab (a bispecific antibody) and daratumumab (a monoclonal antibody) are examples of immunotherapy drugs that can be given via injection.

Intravenous (IV) infusions – can be given in the day unit or in hospital. The drug is usually infused via a pump which controls the amount and speed it is given at. The infusion can take a few minutes or several hours. The drug is given via a vein through one of the following:

- **Cannula** – a short, thin tube inserted into your arm or hand, used for short-term infusions.
- **Central line** – a tube that goes under the skin of your chest and into a large vein nearby; examples include a Hickman or Groshong line.
- **PICC line** – a long, thin tube that is inserted into a vein in your arm and goes up into a large vein in your chest.
- **Port (or portacath)** – a disc inserted under the skin in your chest or arm.

Examples of immunotherapy drugs that are given via IV infusion include rituximab, obinutuzumab, and pembrolizumab.

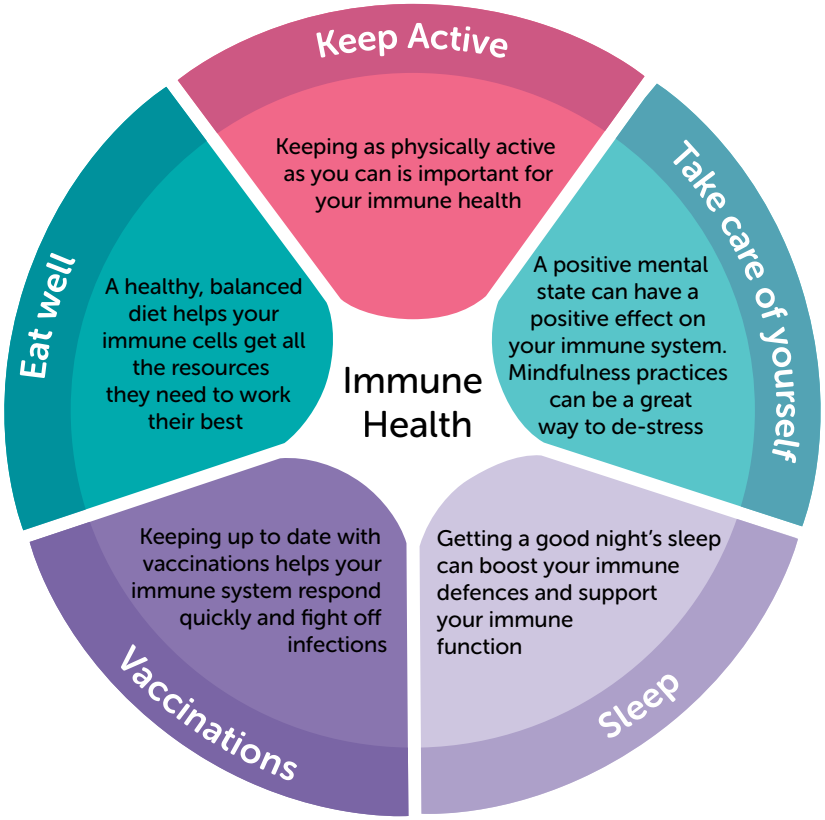
The future of immunotherapy

As scientists and doctors discover more about our immune system and how it works, there are new opportunities for prevention and treatment of disease. The hope is that future immunotherapy treatment will be:

- **Gentle and powerful** – immunotherapy can be very effective at fighting disease and can have fewer unpleasant side effects compared to conventional anticancer therapies such as surgery, radiotherapy, chemotherapy or other drugs.
- **Precise** – immunotherapies can find and target the exact cells that need treatment.
- **Individualised** – future immunotherapies may be made using a person's own genetic information and immune cells, which means a more personalised and effective overall treatment.
- **Available to everyone** – as immunotherapy becomes more common and affordable, more people will be able to access these treatments.

How can I support my immune system?

Looking after your immune system helps it to look after you. Below are some suggestions for how you can support your immune function. You don't have to do everything – even small, consistent changes can make a positive difference over time.



Questions to ask your doctor

- What immunotherapy options are available for my condition?
- Are these given alone or alongside any other treatments?
- How and where will my immunotherapy be given?
- How will my treatment and disease be monitored?
- What side effects can I expect?
- Are there any specific monitoring recommendations following the treatment?
- Will my treatment plan affect my fertility? What fertility-preserving options are available to me?

More information available online

For more information and to download other fact sheets, see our website **www.leukaemia.org.nz**

MALAGHAN INSTITUTE OF MEDICAL RESEARCH

This fact sheet has been developed in partnership with the Malaghan Institute of Medical Research. The Malaghan Institute is New Zealand's world-class independent biomedical research charity with a focus on breakthrough discoveries and translation in immunology and immunotherapy. To find out more visit **www.malaghan.org.nz**

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If you would like to get in touch:
Call: 0800 15 10 15
Email: info@leukaemia.org.nz
Visit: www.leukaemia.org.nz
Mail: PO Box 99182, Newmarket, Auckland 1149
Or visit one of our Support Services offices in Auckland, Hamilton, Wellington, Christchurch or Dunedin.