

CAR-T cell treatments

Horizons Infosheet

Clinical trials and new treatments

This Horizons Infosheet contains information on CAR-T cell treatments, which are being investigated for use in myeloma.

The 'Horizons Infosheet' series provides information about new drugs and treatments that are 'on the horizon' – ones that are currently being investigated for use in myeloma. The series also aims to highlight the large amount of research currently taking place.

The treatments described in the Horizons Infosheets may not be licensed or approved for use in myeloma. You may however, be able to access them as part of a clinical trial.

What are CAR-T cell treatments?

CAR-T cell (chimeric antigen receptor T cell) treatments are a type of immunotherapy. These treatments use the body's own immune system to kill myeloma cells.

Some existing myeloma treatments use the immune system to kill myeloma cells including, lenalidomide (Revlimid®) and daratumumab (Darzalex®).

CAR-T cell treatments are different as they use a patient's own immune cells. These cells are collected and genetically modified in a laboratory to allow them to kill myeloma cells.

What is the immune system?

The immune system is made up of specialised cells, tissues and organs. These work together to protect the body from infection and disease caused by foreign organisms such as bacteria or viruses. The immune system also identifies and kills faulty or abnormal cells in the body.

White blood cells are an important part of the immune system. Different types of white blood cells, such as T cells, perform specific functions.

What are T cells?

T cells are white blood cells that travel around the body looking for abnormal or infected cells. T cells can directly kill and remove abnormal or infected cells. They can also release chemicals called cytokines which signal for more immune cells to kill the abnormal cell.

How do CAR-T cell treatments work?

Myeloma cells can avoid being recognised as abnormal by the immune system, meaning that a patient's own T cells are not able to kill the myeloma cells. CAR-T cell treatments boost the ability of a patient's T cells to recognise and kill myeloma cells.

There are several steps in the process of making and using CAR-T cells:

- The patient's blood is pumped through a machine that filters out the T cells and returns the blood to the body. This is called apheresis (shown in Figure 1 on page 3)
- The collected T cells are genetically modified in a laboratory so that they can recognise myeloma cells
- The modified T cells are called CAR-T cells. They have a receptor on their surface that recognises a specific protein on the surface of myeloma cells
- While the patient is waiting for the CAR-T cells to be made, they are given treatment to keep the myeloma under control. This is called 'bridging treatment'

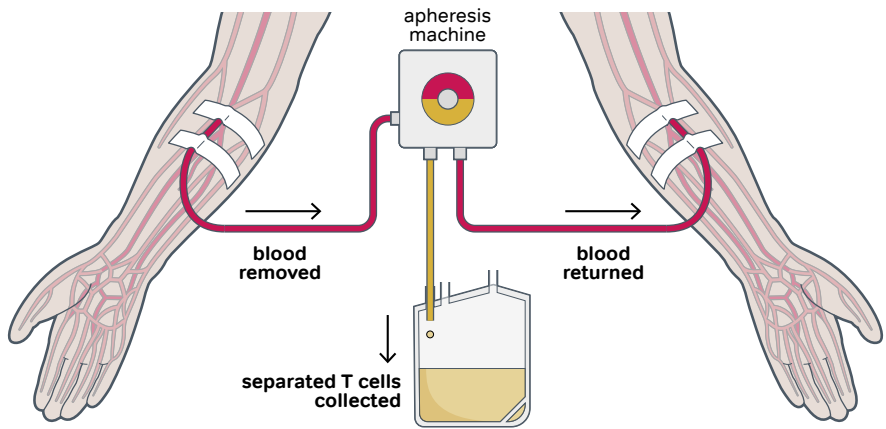


Figure 1. Apheresis process. Blood is removed and passes through a machine which separates out T cells. The blood is then returned to the body

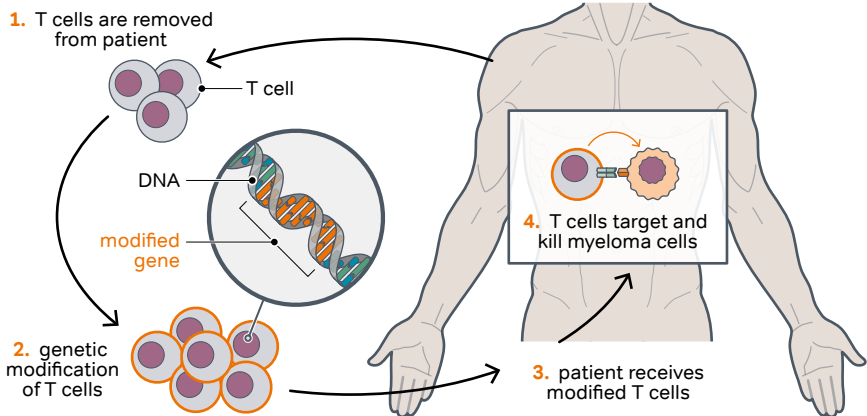


Figure 2. Steps in the process of making and using CAR-T cells

- The CAR-T cells are multiplied and infused back into the patient
- Once in the patient, the CAR-T cells continue to multiply, and they recognise and attack myeloma cells

The steps in this process are shown in Figure 2 on page 3.

Usually treatments have to be given multiple times or 'cycles' to achieve control of the myeloma. CAR-T cell treatment is designed as a one-time treatment. The cells can remain in the body for long periods of time and can continue to multiply in the body. This offers the opportunity for long term control of myeloma.

However, CAR-T cells can become 'exhausted' and stop working. The myeloma cells may also change over time so the CAR-T cells can no longer recognise and kill the myeloma cells. Further research is exploring ways to prevent these things happening for as long as possible.

What evidence exists to support the use of CAR-T cell treatments?

Several CAR-T cell treatments have been developed for use in myeloma.

Two of these are:

- Idecabtagene vicleucel (Abecma®, also called ide-cel)

- Ciltacabtagene autoleucel (Carvykti®, also called cilta-cel)

These two CAR-T cell treatments recognise a protein called BCMA on the surface of myeloma cells.

A clinical trial with ide-cel, called KarMMa-3, involved 386 patients with relapsed and/or refractory myeloma. 254 patients received ide-cel and 132 patients received a standard treatment. For those receiving treatment with ide-cel, it took an average of 13 months for their myeloma to become active again. For the patients receiving standard treatment, it took an average of 4 months for their myeloma to become active again.

A clinical trial with cilta-cel, called CARTITUDE-4, involved 419 patients with lenalidomide refractory myeloma. 208 patients received cilta-cel and 211 patients received a standard treatment. For those receiving cilta-cel, 7 in 10 of the patients found their myeloma had not returned after 12 months. For those receiving standard care, around 5 in 10 found their myeloma had not returned after 12 months.

The results of these clinical trials suggest that CAR-T cell treatments may be beneficial for patients who have had previous lines of treatment.

Other clinical trials are ongoing to investigate the use of CAR-T cells for other patient groups.

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

CAR-T cell treatments carry a risk of serious side effects that need expert care. Patients are frequently monitored for any side effects and quickly given treatment for these as needed. Possible side effects include:

Infusion reactions, also called cytokine release syndrome (CRS), causes symptoms such as fever, nausea and vomiting, fast heart rate, feeling short of breath and feeling dizzy. An infusion reaction can be serious, so other medicines are given alongside CAR-T treatment to reduce this risk.

Nervous system problems also called, Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) can occur when having CAR-T cell treatment. This causes symptoms including: feeling confused, feeling less alert, and difficulty writing or speaking.

Low blood cell levels including red blood cells, white blood cells and platelets. These can cause

symptoms including increased risk of infections, bleeding or bruising and anaemia.

Other side effects can occur after CAR-T cell treatment, including reduced levels of antibodies in the blood. Because CAR-T cell treatments for myeloma are new treatments, it is possible that other side effects will emerge.

Are CAR-T cell treatments currently available in any UK clinical trials?

For an up-to-date list of UK clinical trials involving CAR-T cell treatments, visit the Myeloma Trial Finder at trials.myeloma.org.uk

To be enrolled on a clinical trial, patients have to meet certain conditions known as eligibility criteria.

For more information about taking part in clinical trials, see the **Clinical trials and how treatments are developed Infoguide** from Myeloma UK

You should speak to your healthcare team if you are interested in taking part in a clinical trial. They will discuss the possible benefits and risks for you. They will give you the information you need to make an informed decision about whether to take part.

Availability of CAR-T cell treatments in the UK

Before any new treatment can be widely used on the National Health Service (NHS) in the UK, it goes through two processes:

- **Licensing** – the new treatment is licensed as safe and effective, and can be prescribed by doctors. Licensing is based on the results of clinical trials and other information about the treatment. The main licensing body in the UK is the Medicines and Healthcare products Regulatory Agency (MHRA)
- **Approval** – the licensed treatment is approved for general use on the NHS. Approval is based on clinical effectiveness and cost-effectiveness. Two of the approval bodies in the UK, that approve treatments for use on the NHS, are the National Institute for Health and Care Excellence (NICE) and the Scottish Medicines Consortium (SMC)

For more information see the **Clinical trials and how treatments are developed Infoguide** from Myeloma UK



CAR-T cell treatments for myeloma are not currently available on the NHS. Some of these treatments are accessible to patients as part of a clinical trial.

Future directions

CAR-T cell treatments for myeloma are an active focus of research. These are some of the areas of research:

Using CAR-T cell treatments at different stages in the treatment pathway

Initial clinical trials of CAR-T cell treatments were in patients with relapsed and/or refractory myeloma. Trials are now using CAR-T treatments in newly diagnosed patients who are not eligible for stem cell transplant, or in patients who relapse quickly after their first treatment.

Why CAR-T cell treatments eventually stop working, and how to keep them working as long as possible

CAR-T cell treatments do eventually stop working. The CAR-T cells may become 'exhausted' and less active. The myeloma cells may also reduce the amount of the target protein on their surface. The myeloma cells can then avoid the CAR-T

cells attaching to them. Research is exploring how to help CAR-T cell treatments work for longer.

CAR-T cell treatments that recognise different proteins on myeloma cells

Ide-cel and cilta-cel recognise a protein called BCMA on the surface of myeloma cells. Researchers are developing CAR-T cell treatments that target other proteins on the myeloma cells. They are also developing treatments that can recognise 2 different target proteins at the same time. Other trials are exploring giving 2 different CAR-T cell treatments, one after the other.

It is hoped this research could help CAR-T cell treatments work for longer and reduce the chance of myeloma cells avoiding the treatments.

Safety of CAR-T cell treatments

Research is exploring the long term impact of these treatments and their side effects. It is also helping healthcare professionals manage the serious side effects that can occur with CAR-T cell treatments.

Universal CAR-T cell treatments

Clinical trials using Universal CAR-T cell treatments are ongoing. These treatments modify the T cells of a healthy donor instead of using a patient's individual T cells. These treatments also avoid the delay while CAR-T cells are manufactured for an individual patient. This means that the patient does not need 'bridging therapy' while waiting for their CAR-T cells to be ready.

Key points

- CAR-T cell treatments are a new type of myeloma treatment that uses the body's own immune system to kill myeloma cells
- Some of the patient's own blood cells, called T cells, are taken out of the blood and modified in a laboratory
- The modified cells, called CAR-T cells, can recognise a protein on the surface of myeloma cells. The CAR-T cells are infused back into the patient
- Once in the patient, the CAR-T cells recognise and attack myeloma cells
- Results of trials with CAR-T cell treatments in myeloma have shown they may be an effective treatment for myeloma, and larger-scale trials are now underway
- Side effects of CAR-T cell treatments can be severe and can include infusion reactions, effects on the nervous system and low blood cell levels (causing anaemia, increased risk of infections, or bleeding and bruising)
- CAR-T cell treatments for myeloma are not currently available on the NHS. However, patients may be treated with them as part of a clinical trial

About this Horizons Infosheet

The information in this Infosheet is not meant to replace the advice of your healthcare team. They are the people to ask if you have questions about your individual situation.

For a list of references used to develop our resources, visit myeloma.org.uk/references

We value your feedback about our patient information. For a short online survey go to myeloma.org.uk/pifedback or email comments to patientinfo@myeloma.org.uk

Other information available from Myeloma UK

Myeloma UK has a range of information booklets available covering all aspects of myeloma and related conditions. Download or order them from myeloma.org.uk/publications

To talk to one of our Myeloma Information Specialists about any aspect of myeloma, call our Myeloma Infoline on **0800 980 3332** or **1800 937 773** from Ireland.

The Infoline is open from Monday to Friday, 9am to 5pm, and is free to phone from anywhere in the UK and Ireland.

Information and support about myeloma is also available around the clock at myeloma.org.uk

Notes

Notes



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We're here for everything
a diagnosis of myeloma brings

Get in touch to find out more about how we can support you

Call the Myeloma Infoline on

 **0800 980 3332**

Email Ask the Nurse at

 **AskTheNurse@myeloma.org.uk**

Visit our website at

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