



Patient Information Sheet CAR-T Cells

What are CAR-T cells?

CAR-T, or Chimeric Antigen Receptor T-cell therapy, is a type of treatment where your T-cells (a type of white blood cell that is part of your own immune system) are altered in a laboratory by adding a CAR gene. Adding this CAR gene can allow your own T-cells to home in on and target your cancer.

Who is eligible for CAR-T cell therapy?

In 2019 two CAR-T products were licensed, making them available for Scottish patients. One is called Yescarta (also referred to as Axicel, its full name is Axicabtagene cleoleucel), which has been licensed in Scotland for patients with relapsed or refractory high grade B cell lymphoma that has already been treated with two different types of chemotherapy, and one is called Kymriah (also called Tisagenlecleucel), which can be considered for high grade B cell lymphoma that has already been treated with two types of chemotherapy, and also to treat relapsed / refractory Acute Lymphoblastic Leukaemia in patients up to 25 years of age. There are more specific criteria regarding eligibility for these products and your Haematology Consultant will check these and discuss this with you. There are other indications for CAR-T cells being considered in clinical trials. These are not licensed but could be of benefit. If you are being considered for a CAR-T clinical trial, your Haematologist will discuss this with you and give you a specific information sheet about the relevant clinical trial.

What is the process for making CAR-T cells?

Since CAR-T cells are made from your own T-cells, it requires your Medical team to collect and separate your white blood cells. This collection process is called "leukapheresis". This process is done using a specialized machine and usually takes 3 to 4 hours. You will be counseled on this process separately by the Clinical Apheresis Unit (CAU) team. Following this procedure your collected cells are taken by a courier to the manufacturing lab to be engineered into CAR-T cells. This manufacturing process takes around 4 weeks (dependent on the product it is sometimes shorter or longer), the CAR-T cells will then be sent by a Courier back to the CAR-T centre where you will be treated. They are kept frozen until you are ready to have the CAR-T cells infused.

How are CAR-T cells given?

Before your CAR-T product is infused back to you, you have to undergo chemotherapy to prepare your body to accept the CAR-T cells. This is called "conditioning" chemotherapy and its needed to allow the CAR-T cells to expand in your body. Generally this starts five days before the CAR-T cells are infused, but varies with differing products. Your

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Haematologist will discuss your specific conditioning treatment with you. When the conditioning period is complete your CAR-T cells will be infused through a central line, this takes around 30 minutes. Your pulse, blood pressure and oxygen saturations will be closely monitored during this time and at regular intervals afterwards for the remainder of your admission.

What are the potential complications of CAR-T cell therapy?

You will be monitored closely as an in-patient for at least the first ten days after CAR-T therapy and required to stay within one hours drive from the treating centre (BMT Unit, Queen Elizabeth University Hospital) for the first 30 days after CAR-T cell therapy. The in-patient phase and the need to stay near the treating centre can be longer if you develop complications that take time to resolve and require longer specialized care. For the first 30 days that you require to stay within one of the Queen Elizabeth University Hospital (QEUH), you require a carer (a family member or friend) to be with you all the time. The journey time will be checked using your registered address by the BMT team. These requirements are in place to try and ensure any complications arising from CAR-T cell therapy are identified and treated very quickly. If you are an outpatient and develop complications of CAR-T cell therapy, you will be re-admitted to the QEUH for these complications to be treated. If you are unwell and present to another hospital other than the QEUH it is extremely important you or your carer tell the Doctor at this hospital that you have had a CAR-T product so they can contact the BMT Unit immediately. You will be issued with a patient alert card on discharge from the BMT unit for this purpose.

The main complications from CAR-T cells include Cytokine Release Syndrome (CRS), CAR-T Related Encephalopathy Syndrome (CRES) (also referred to in the literature as Immune effector Cell Associated Neurotoxicity Syndrome (ICANS)), low blood counts and the complications associated with this (e.g. the need for transfusions and an on-going risk of infection) and a rarer complication called Haemophagocytic Lymphohistiocytosis (HLH), which can be cause of fever, low blood counts and other blood test abnormalities after CAR-T cell infusion but is far less common than CRS or CRES.

CRS is caused by the rapid release of chemical messengers in the body (cytokines) that can be triggered by CAR-T cells finding the tumour cells in the recipient's body and expanding rapidly. To monitor for this happening you will have your observations done either continuously with a monitor or very regularly during your in-patient stay. This can be a mild problem which can sometimes just cause a fever and in this case does not necessarily require specific treatment unless the fever does not settle, or it can be a severe problem that leads to the need for oxygen therapy and blood pressure support. For some patients when CRS is severe they will require to be transferred from the BMT unit to the Critical Care unit in the QEUH. At this point and for cases that are not improving on the ward, specific treatments can be given to try and reverse this complication. This is generally a drug called tocilizumab that can help dampen these chemical messengers down, or in more serious cases steroids. There has been some worry in the past that use of these agents can stop the CAR-T cells from working against the underlying tumour, there is emerging data that this is not necessarily the case and the priority for patients in this situation is to keep them safe in the short term with steroids if needed.

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CRES is a neurological complication caused by CAR-T cells. To monitor for this happening the team at the BMT unit will ask you a series of questions to check you are not becoming confused by asking you a series of questions every 8 hours and to write a sentence every 8 hours or more frequently if there is a concern. This can be a mild problem or a severe problem. Mild CRES does not necessarily require any specific treatment, but more severe cases will also be transferred to Critical Care for closer monitoring and management. Again, if this occurs along with CRS tocilizumab can be used and / or steroids can be considered.

Although these complications can be serious and in some cases life-threatening, it is important to note that in the majority of cases in patients treated across the world to date, these complications have been reversible.

What is the process for follow-up after CAR-T cell therapy?

When you are discharged from your in-patient stay at the QEUEH, you will be seen at the BMT Clinic at the QEUEH twice a week (every Monday and Thursday) for the first 30 days after your CAR-T product. It is absolutely essential that during this time if you are unwell in any way, you or your carer must phone the BMT unit immediately. This includes the symptoms listed below but the key is to phone if you or your carer has any concerns at all, even if not listed below.

- Confusion
- Difficulty speaking or slurred speech
- Change in behavior
- Abnormal movement
- Fever
- Cough
- Shortness of breath
- Nausea and vomiting
- Diarrhoea

If you have recovered sufficiently by 30 days post your CAR-T infusion, your care can be transferred back to your referring hospital but you will still be required to have some visits back to the QEUEH as part of a shared care arrangement with your referring team. It would still be essential in at least the first 3 months after CAR-T infusion that if you are unwell you contact the BMT unit urgently.

What should I avoid after treatment with CAR-T cells?

You should not drive or operate heavy machinery or doing anything dangerous for at least 8 weeks after treatment with a CAR-T cell product. If you have had any Neurological complications this may be longer, please discuss this with your Haematologist when you are ready to be discharged from the BMT Unit back to your referring hospital (generally around 30 days after your CAR-T infusion).