

CAR-T Patient Information

What is CAR-T?

CAR-T cells stand for chimeric antigen receptor T cells, which are genetically modified immune cells (T cells are a type of white blood cell). T cells fight foreign elements, such as bacteria and viruses, and remove diseased cells in the body. Our regular T cells are different, and they can learn to recognise many different things. The CAR-T cells, on the other hand, are reprogrammed and equipped with a selected receptor (antibody) that recognises one target in the cancer cells. In our case, they target a protein called CD19, which is usually found on the surface of another type of immune cell called B cells. In your case, it is the B cells that have developed into B-cell carcinoma which we call diffuse large B cell lymphoma (DLBCL). There are also CAR-T products that single out other targets.

The CAR-T cells are administered intravenously (similar to a blood transfusion) and will then seek out the cancer cells and attack them immediately. This triggers an immune response (inflammatory reaction) that causes the release of many inflammatory substances (cytokines), which among other things cause fever. This immune response can be much more powerful than, for example, infections. That is why you will be monitored closely after treatment for signs of immune-related side effects.

How is the treatment carried out?

Harvesting T cells ('leukapheresis')

Your body's T cells are used to make CAR-T cells. The T cells are harvested by a machine that filters your blood and extracts these cells. This is done at the Department of Cellular Therapy at the Norwegian Radium Hospital OUS. The process can take 3-6 hours. If you have been through high-dose treatment, the harvesting process is similar to stem cell harvesting. However, you do not need chemotherapy or growth factor injections in advance. You will be admitted to Bed Ward A8 at the Norwegian Radium Hospital the day before the procedure. Upon discharge, you will be given a plan for further follow-up.

Modification of T cells

Your T-cells are sent by courier from the Norwegian Radium Hospital to a factory in the Netherlands as soon as they are harvested. They are modified there in a specialised laboratory. It takes 3-4 weeks from when the cells are harvested until they are ready for use in Norway. Since the production time may vary slightly, the actual treatment date, when the CAR-T cells are returned to your body, will be provisional ('tentative') until a relatively short time before the planned treatment. Before admission for treatment, you will therefore receive a confirmation from our patient coordinator as to whether production is on schedule or if we have to postpone the admission for a few days.

Bridging Treatment

If there is a lot of cancer in the body, CAR-T treatment may be both less effective and cause more side effects. Some will therefore benefit from cancer treatment between harvesting the T cells and the CAR-T treatment itself. We call this bridging to CAR-T. This will be a type of immunotherapy, chemotherapy or radiation therapy. The time between harvesting the T cells and CAR-T treatment will therefore also be affected by this. You will receive a plan for bridging from the referring doctor or upon discharge after harvest. The treatment will be carried out at your local or regional hospital.

Go-ahead for CAR-T treatment

Prior to admission, you must attend an outpatient check-up at the hospital that referred you for treatment. You will be subject to CT scans, blood tests and health checks to make sure you are fit to carry out the treatment. If you have an ongoing infection, treatment must be delayed as there is an increased risk of serious side effects. It is also important that we have some control over the development of your cancer in order to have the best possible hope of an effect of the treatment and reduce the risk of serious side effects.

CAR-T Treatment

To increase the effect of the CAR-T cells, a pre-treatment with chemotherapy (fludarabine and cyclophosphamide) is given. This will remove other immune cells in the blood and make room for the CAR-T cells. This therapy is given over 3 days at Bed Ward A8, at the Norwegian Radium Hospital OUS. There should then be (at least) a break of two days until you get the CAR-T cells. You are admitted the day before the therapy starts, i.e. almost a week before you receive the actual CAR-T cells.

CAR-T cells are given intravenously, and there is only one treatment. The cells arrive frozen from the lab and are thawed at bedside in your hospital room. They are given as a normal blood transfusion, but with some medicines in advance to reduce the reaction to the freezing substance and with some monitoring (including pulse and blood pressure).

Side effects and complications

Pre-treatment with chemotherapy will result in a weakened immune system, so most people will need antibiotics. This differs little from the corresponding side effects of other chemotherapy. The special feature of CAR-T treatment is the strong immune response (inflammatory reaction) the treatment initiates in most patients. There are two conditions in particular that most people experience (to varying degrees): Cytokine release syndrome (CRS) and Immune effector Cell Associated-Neurotoxicity Syndrome (ICANS). CRS usually comes first, on days 2-3, while ICANS comes a few days later in most people. CRS starts with fever and you can get a drop in blood pressure and difficulty breathing, in addition to more non-specific symptoms such as malaise, lethargy, headache, nausea etc. Neurological side effects can typically be difficulty writing, finding words, disorientation, memory impairment and lethargy. Rarer complications include heart rhythm disturbances, heart failure, kidney failure, liver issues, clotting disorders of the blood (coagulation disorders), fluid in the lungs (pulmonary oedema), epileptic seizures, paralysis and swelling of the brain (cerebral oedema). Most patients develop mild to moderate symptoms that we manage well at the ward with simple measures, but some patients will have more severe or severe symptoms that require more extensive treatment and monitoring in the intensive care unit. Over time, a lot of experience has been gained in the treatment of these conditions. The treatment mainly consists of attenuating the immune response with agents that should not affect the effect of the CAR-T cells. Supportive treatment such as oxygen and fluids is also given intravenously. It is important to start treatment early, so you will be hospitalised at Bed Ward A8 after treatment. There will be frequent measurements taken (i.e. pulse, blood pressure, temperature and oxygen saturation) and we test language, writing, orientation and memory several times a day. Blood samples are taken daily. You will also be given some preventive medicines, including for seizures.

Discharge

Both CRS and ICANS will be over within 14 days and will not give lasting results. As a general rule, you will be hospitalised (at least) 14 days after the CAR-T cells have been

Avdeling for kreftbehandling

administered. Some might develop neurological side effects somewhat later, and it is therefore important to look for this also after discharge. You should therefore stay close to Oslo (max 2 hours of driving) until approx. 4 weeks after the CAR-T infusion, and there will be several check-ups at the outpatient clinic during that period. If you do not live within 2 hours of Oslo, we will of course cover the hotel costs. Persistently reduced levels of blood cells are common and may last several months. The immune system can also be affected in the longer term, especially low levels of antibodies. That is why some blood tests will be needed at a local hospital as well, and you should receive infection prevention therapy for at least 3 months and until your immune system (especially the lymphocytes) has recovered sufficiently. Some will also need antibody supplements. This is given intravenously as a repeating treatment every few weeks. Upon discharge, you will be provided with a patient alert card that includes safety information. You should carry this card with you and show it to the doctors and nurses you will meet in the time after treatment.

Before you are transferred to the referring hospital, we will take a CT scan or PET/CT to check for a response to treatment.

In total, you must be prepared for (at least) 3 weeks of hospitalisation and a total of 5 weeks stay in the Oslo region.

Long-term follow-up

There will be some check-ups in Oslo during the follow-up period going forward, otherwise the check-ups will mainly take place at your local/regional hospital. The first check-up in Oslo is 3 months after the CAR-T treatment. We will ask you if we can send anonymised data to the European Bone Marrow Registry for research purposes.