

The Process of CAR-T Cell Therapy

Establishing the process¹

Novartis is the first to develop CAR-T cell therapy in collaboration with an academic institution. Novartis partnered with the University of Pennsylvania to pioneer the commercial CAR-T cell therapy manufacturing process.

The CAR-T cell therapy process²

The patient is at the center of the process for CAR-T cell therapy. The process begins with the patient at autologous T-cell collection and ends with the patient at infusion.

1. **Collection:** Patients' autologous T cells are isolated in a process called leukapheresis and then frozen
2. **Reprogramming:** CAR-coding viral DNA is incorporated into these cells at the manufacturing facility, transforming them into CAR-T cells
3. **Infusion:** Patients are treated with a short course of preparatory chemotherapy and then reinfused with their modified T cells

Watch the video below for more detailed information about the CAR-T manufacturing process.

Leukapheresis

Cell collection can be challenging, as patients often have underlying disease or prior treatment that may lower white blood cell counts and affect the properties of their lymphocytes.^{3,4} Previous chemotherapy may have a negative impact on T cell expansion, with poorer expansion linked to the total number of cycles administered.⁵

The timing of cell collection may matter for CAR-T cell production. Collecting cells as early as possible after relapsed or refractory diagnosis can help ensure the quality of the sample.⁶ In preparation for stem cell transplant in other haematologic malignancies, early cell collection is also recommended to help ensure the healthiest possible samples.⁴ Such early collection allows for flexibility in the timing of CAR-T cell therapy administration.

Cryopreservation⁶

Cryopreserved samples collected shortly after diagnosis may be better able to fight cancer than samples freshly collected after prior treatment. Therefore, some physicians are collecting and cryopreserving cells earlier in the patient's treatment journey with the goal of increasing CAR-T cell efficacy should the cells be needed at a later date.

Novartis utilises cryopreserved apheresis, which may allow for more flexibility in the CAR-T cell therapy process.⁷

Scheduling of cell collection can occur once a patient is identified⁸

Patients' autologous T cells can be stored for up to 30 months before CAR-T cell manufacturing⁸

As a provision against any possible shipping delays, the cryopreservation containers called dewars can keep samples frozen an extra 10 days⁹

Outpatient administration²

Some CAR-T cell therapies can be conveniently administered in an outpatient or inpatient setting, an advantage over some standard of care treatment options. Patients receive their reprogrammed CAR-T cells during a single infusion that usually takes less than 30 minutes. Some CAR-T cell therapies have the flexibility to be administered in an outpatient setting.

Outpatient administration has the following benefits for patients, caregivers, and clinicians:

Minimises time spent in the clinic, reducing the associated cost and burden on patients and care teams¹⁰

Decreases the possibility that patients will develop a hospital-acquired infection

As a result, may improve patient quality of life

Global reach and manufacturing

Initially investigated in multiple global, phase 2 trials, Novartis CAR-T cell therapy research will continue to expand its international reach.² This treatment is currently approved in Australia, Canada, the EU, Israel, Japan, Switzerland, Hong Kong, and the US.^{1,11-16} Novartis will continue to add new treatment centre locations, collaborating with an increasing number of hospitals to administer CAR-T cell therapy around the world.¹¹

Novartis is also investing in new CAR-T cell therapy manufacturing facilities around the world to reduce the time from patient identification to infusion. Novartis currently has manufacturing facilities in the following locations:

- Morris Plains, New Jersey, USA¹
- Stein, Switzerland¹⁷
- Les Ulis, France (formerly known as CELLforCURE)¹

In addition to the above, Novartis has third-party agreements with manufacturers in Germany, Japan, and China to produce CAR-T cell therapies.^{1,15,18,19} Novartis is constantly exploring potential partnerships to support and enhance its manufacturing process.¹

Next: The Landscape

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