

The Process of CAR-T Cell Therapy ^[1]

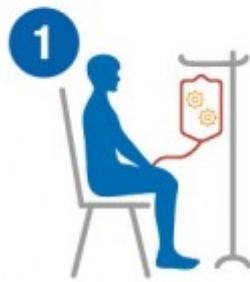


Establishing the process¹

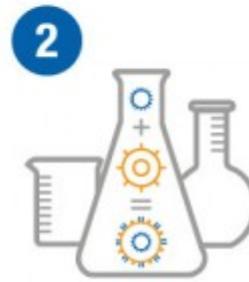
Novartis is the first to develop CAR-T cell therapy in collaboration with an academic institution. Novartis partnered with the University of Pennsylvania to pioneer the commercial CAR-T cell therapy manufacturing process.

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.



Collection



Reprogramming



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.

[Video of Manufacturing CAR-T Cell Therapies: The Novartis Approach](#)



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 identified ⁸
	Patients' autologous T cells can be stored for up to 30 months before CAR-T cell manufacturing ⁸
	As a provision against any possible shipping delays, the cryopreservation containers called dewars can keep samples frozen an extra 10 days ⁹

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 [2])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 ? [3]

Disclaimer:

References:

1. Novartis receives European Commission approval of its CAR-T cell therapy, Kymriah® (tisagenlecleucel) [press release]. Basel, Switzerland. Novartis Pharma AG; August 27, 2018.
2. Kymriah Summary of Product Characteristics. Novartis Pharma AG; 2018.
3. Allen ES, Stroncek DF, Ren J, et al. Autologous lymphapheresis for the production of chimeric antigen receptor (CAR) T cells. *Transfusion*. 2017;57(5):1133-1141.
4. Fesnak A, Lin CY, Siegel DL, Maus MV. CAR-T cell therapies from the transfusion medicine perspective. *Transfus Med Rev*. 2016;30(3):139-145.
5. Das RK, Vernau L, Grupp SA, Barrett DM. Naïve T cell deficits at diagnosis and after chemotherapy impair cell therapy potential in pediatric cancers. *Am Assoc for Cancer Res*. <http://cancerdiscovery.aacrjournals.org/content/9/4/492> [4]. Doi:10.1158/2159-8290. Accessed April 22, 2019.
6. Künkele A, Brown C, Beebe A, et al. Manufacture of chimeric antigen receptor T cells from mobilized cryopreserved peripheral blood stem cell units depends on monocyte depletion. *Biol Blood Marrow Transplant*. 2019;25(2):223-232.
7. Novartis receives positive CHMP opinion for Kymriah® for treating two aggressive blood cancers, marking important medical advance for patients in Europe [press release]. Novartis Pharma AG; June 29, 2018.
8. Data on file. Novartis CTL019 leukapheresis reference manual: leukapheresis collection. Novartis Pharma AG; May 2018.
9. Data on file. PVR5135-7A Shipping Validation Report: CTL019 pALL. Novartis Pharma AG; October 2016.
10. Broder MS, Quock TP, Chang, E, et al. The cost of hematopoietic stem-cell transplantation in the United States. *Am Health & Drug Benefits*. 2017;10(7):366-379.
11. Novartis. Novartis Annual Review. Novartis Pharma AG. Accessed April 22, 2019. <https://www.novartis.com/sites/www.novartis.com/files/novartis-annualreview-2018-en.pdf> [5].
12. Kymriah® (tisagenlecleucel), CAR-T therapy from Novartis, receives TGA approval for

treating two aggressive blood cancers [press release]. Sydney, Australia: Novartis Pharma AG; December 17, 2018.

13. Novartis receives Health Canada approval of its CAR-T cell therapy, Kymriah™ (tisagenlecleucel) [press release]. Dorval, Quebec, Canada. Novartis Pharmaceuticals Canada Inc; September 6, 2018.
14. Expanding the healthcare basket for 2019. Israeli Ministry of Health. January 2019.
15. Oxford Biomedica notes the Japanese approval of Kymriah® (tisagenlecleucel), the first CAR-T cell therapy authorised in Asia [press release]. Oxford, UK. Oxford Biomedica plc; March 26, 2019.
16. Novartis leukaemia drug approved in Switzerland [press release]. Swissinfo.ch; October 22, 2018.
17. Novartis. Novartis in Switzerland. Novartis Pharma AG; 2019.
18. Fraunhofer Institute website. <https://www.fraunhofer.de/en/institutes.html> [6]. Accessed April 22, 2019.
19. Cellular Biomedicine Group enters into strategic licensing and collaboration agreement with a global leader in CAR-T cell therapy for patients in China [press release]. Shanghai, China and Cupertino, CA: Cellular Biomedicine Group Inc; September 27, 2018.

Source URL: <https://www.novartis.com/our-focus/cell-and-gene-therapy/car-t/car-t-healthcare-professionals/process-car-t-cell-therapy>

Links

- [1] <https://www.novartis.com/our-focus/cell-and-gene-therapy/car-t/car-t-healthcare-professionals/process-car-t-cell-therapy>
- [2] <https://www.cellforcure.com/>
- [3] <https://www.novartis.com/our-focus/cell-and-gene-therapy/car-t/car-t-healthcare-professionals/treatment-landscape-haematologic-malignancies>
- [4] <http://cancerdiscovery.aacrjournals.org/content/9/4/492>
- [5] <https://www.novartis.com/sites/www.novartis.com/files/novartis-annual-review-2018-en.pdf>
- [6] <https://www.fraunhofer.de/en/institutes.html>