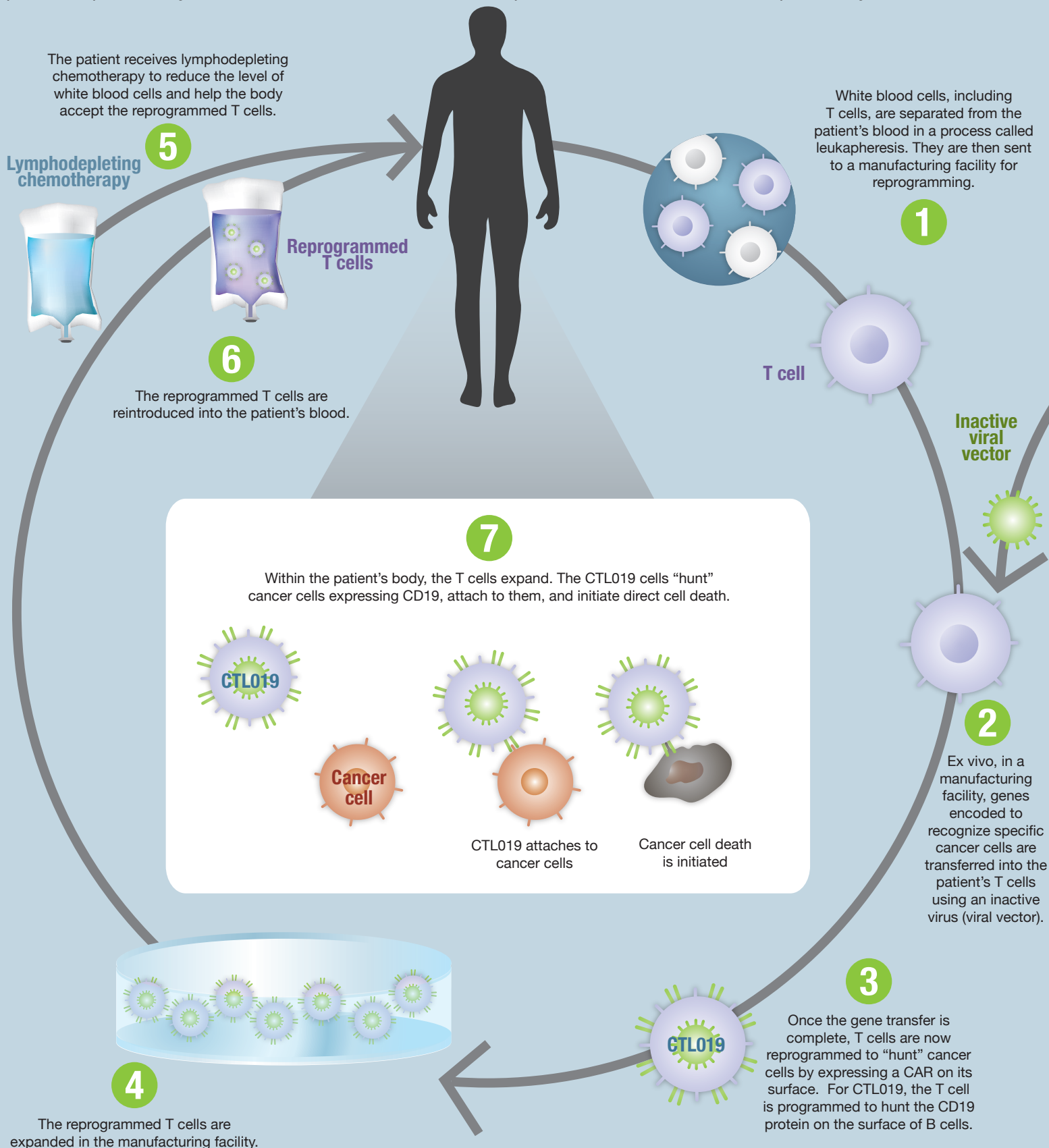


Chimeric antigen receptor (CAR) technology

Reprogramming a patient's T cells to "hunt" and destroy cancer cells

Individualized CAR T cell therapy uses the patient's own immune system to kill cancer. Outside of a patient's body, the patient's own T cells are reprogrammed to express receptors on their surface that allow them to recognize a specific protein expressed by tumor cells. Once re-infused into the patient, these cells "hunt" and potentially kill tumor cells.



MOA data is based on *in vitro/in vivo* data. Clinical benefit is unknown.

CTL019 is an investigational compound. Efficacy and safety have not been established. There is no guarantee that CTL019 will become commercially available.

Chimeric antigen receptor (CAR) technology

Modifying a patient's T cells to "hunt" and destroy cancer cells

Using the body's immune system to combat cancer is not a new approach; however, it has taken decades of research to increase our understanding of immune cells (T cells) and the signals they use to attack targets.

With CAR technology, in contrast to other approaches to personalized cell therapies for the potential treatment of cancer, T cells are drawn from a patient's blood and modified in the laboratory to create "chimeric" T cells genetically coded to "hunt" and potentially kill tumor cells. When these T cells are infused back into the patient, they become a new part of the patient's immune system specifically designed to target the patient's cancer.

CAR Technology – Step by Step

- 1 Leukapheresis:** White blood cells, including T cells, are separated from the patient's blood, in a process called leukapheresis. They are then sent to a manufacturing facility for reprogramming.
- 2 Reprogrammed genes:** Ex vivo, in a manufacturing facility, genes encoded to recognize specific cancer cells are transferred into the patient's T cells using an inactive virus (viral vector).
- 3 "Hunt" cancer cells:** Once the gene transfer is complete, the T cell is now reprogrammed to "hunt" cancer cells by expressing a CAR on its surface. For CTL019, the T cell is programmed to hunt the CD19 protein on the surface of B cells.
- 4 CTL019:** The reprogrammed T cells are then expanded in the manufacturing facility.
- 5 Lymphodepleting chemotherapy:** The patient receives lymphodepleting chemotherapy to reduce the level of white blood cells and help the body accept the reprogrammed T cells.
- 6 Reprogrammed T cells:** The reprogrammed T cells are reintroduced into the patient's blood.
- 7 Cancer cell death:** Within the patient's body, the T cells expand. The CTL019 cells "hunt" cancer cells expressing CD19, attach to them, and initiate direct cell death.

About CTL019

CTL019 is an investigational, personalized T cell therapy which was pioneered by Dr. Carl June and his team at the University of Pennsylvania (Penn). CTL019 Phase I/II trials advances Novartis' understanding of the novel CAR personalized cell therapy. Early stage CAR research conducted by Penn and the Children's Hospital of Philadelphia (CHOP) continues to be promising as we explore this innovative technology and investigational CTL019 therapy for the treatment of appropriate pediatric and adult patients.

MOA data is based on *in vitro/in vivo* data. Clinical benefit is unknown.



CTL019 is an investigational compound. Efficacy and safety have not been established. There is no guarantee that CTL019 will become commercially available.