Car T Cell Therapy: Types, Side Effects

July 10, 2026 • vajiramandravi.com

CAR T cell therapy is a promising new approach in cancer treatment that engineers a patient's T cells to attack their tumours. It involves **extracting T cells**, genetically modifying them to target **cancer antigens**, multiplying them and reinfusing the engineered CAR T cells back into the patient's body to provoke a potent immune response against cancer cells.

CAR T cell therapy has achieved remarkable outcomes in certain **blood cancers,** but limitations like **toxicity risks** and **high costs** remain. Understanding the mechanism, applications and future potential of this novel immunotherapy can provide insights into cutting-edge medical advances against cancer.

About CAR T Cell Therapy

CAR stands for **chimeric antigen receptor**. CAR T cell therapy involves collecting T cells from a patient's blood and genetically engineering them to produce **special receptors** called chimeric antigen receptors (CARs) on their surface.

- These engineered CAR T cells can recognise and bind to **specific protein targets (antigens) on cancer cells**. The binding of the CAR T cells to cancer cells signals the T cells to become activated and multiply, and

to kill the cancer cells.

- In contrast to general **immunotherapies** that boost the overall immune system, CAR T cell therapy involves engineering a patient's immune cells to specifically attack their cancer.
    - This makes the therapy a type of **personalised cell therapy.**
- CAR T cell therapy is being explored as a treatment option for different types of blood cancers including certain **lymphomas** and **leukemias.**
- The two CAR T cell therapies that are furthest along in development target the antigens **CD19** and **BCMA**, which are found in **B cells** and **plasma cells** respectively.

Development of CAR T Cell Therapy

The concept of CAR T cell therapy has been in development since the late 1980s, but early clinical trials showed limited efficacy and safety.

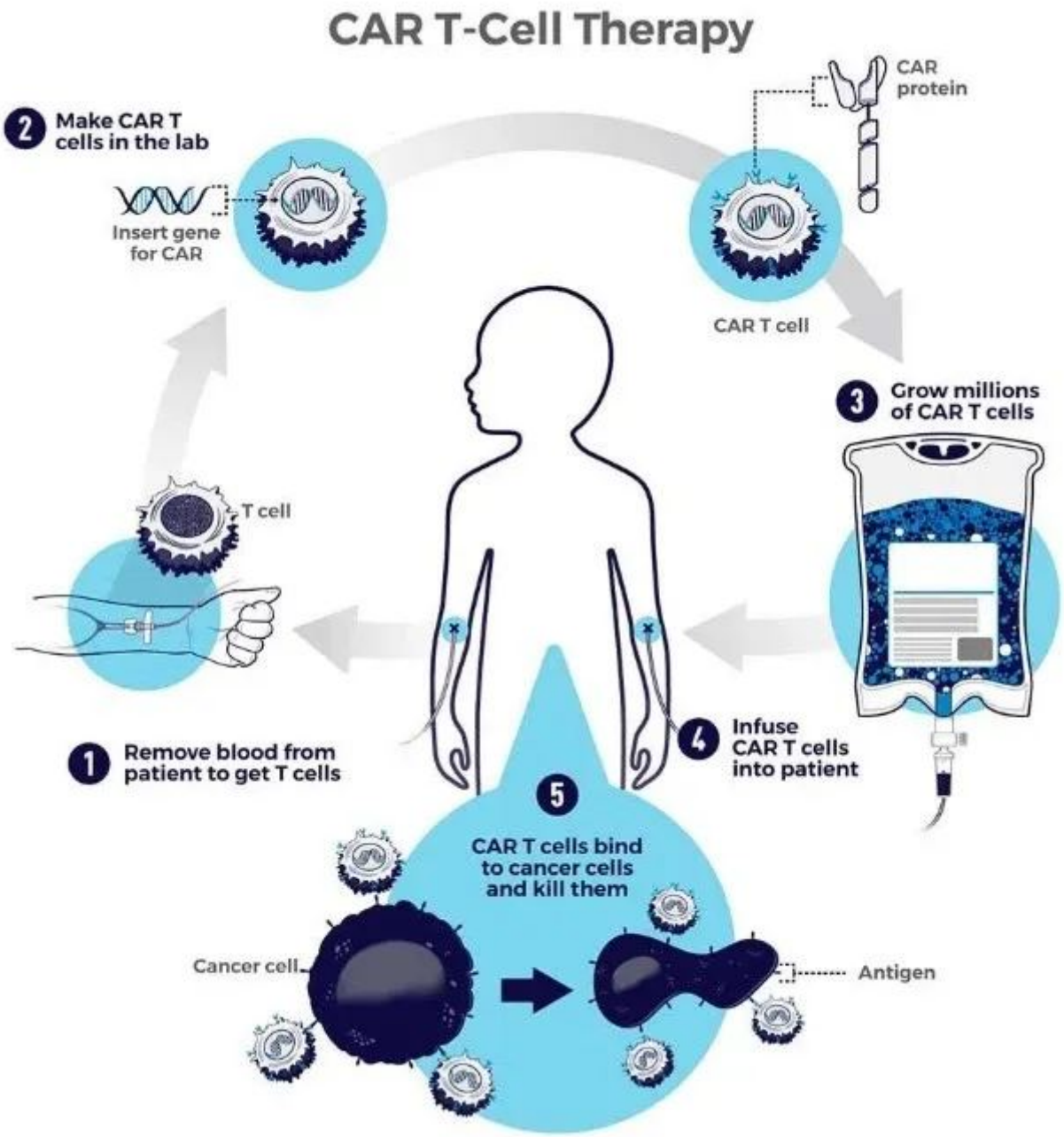
- Advances over the last decade have significantly improved the design of CAR T cells and the clinical protocols, leading to improved safety and efficacy.
- **U.S.A:** Two CAR T cell therapies have now been approved by the **US FDA - Kymriah** in **2017** for **B-cell acute lymphoblastic leukaemia**, and **Yescarta** in 2017 for diffuse large **B-cell lymphoma.**
- **India:** The Central Drugs Standard Control Organisation (**CDSCO**), a drug regulatory body, approved **NexCAR19** for commercial use in October 2023.
    - Developed by **ImmunoACT with Tata Memorial Hospital and IIT Bombay,** it's the first domestically made CAR-T therapy targeting B-cell cancers like leukaemia and lymphoma. It treats individuals **above 15** with **B-cell cancers.**
    - The therapy showcased its effectiveness with the remarkable recovery of the first patient. Accessible at a **fraction of the cost** compared to international alternatives, it emphasizes its affordability and potential to significantly impact patients' lives.
- Many other CAR T cell therapies are currently in clinical trials for a range of cancers. Research is also exploring CAR T cell therapies for solid tumours, as well as **"off-the-shelf"** CAR T cell therapies using T cells from donors instead of the patient.

How CAR T Cell Therapy Works?

CAR T cell therapy is a type of immunotherapy that uses genetically modified immune cells to target and kill cancer cells. It is a personalised treatment that involves the following steps:

- **T cell collection**: Patient's T cells are isolated from their blood using **apheresis**, a process similar to blood donation.
- **T cell engineering:** The collected T cells are genetically engineered to express the chimeric antigen receptor (CAR), using viruses as **vectors**. This gives the T cells specificity to target the cancer antigen.
- **T cell expansion:** The engineered CAR T cells are grown in the lab to expand their numbers to hundreds of millions. This process takes **2-3 weeks**.
- **Infusion into the patient:** The expanded CAR T cells are infused back into the patient as an **intravenous injection**. The patient is usually pretreated with **chemotherapy** beforehand to deplete existing T cells.

- **CAR T cells multiply and kill cancer cells:** In the patient's body, the infused CAR T cells bind to and kill cancer cells displaying the antigen on their surface. The CAR T cells proliferate and persist in the body, providing an ongoing cancer-killing ability.

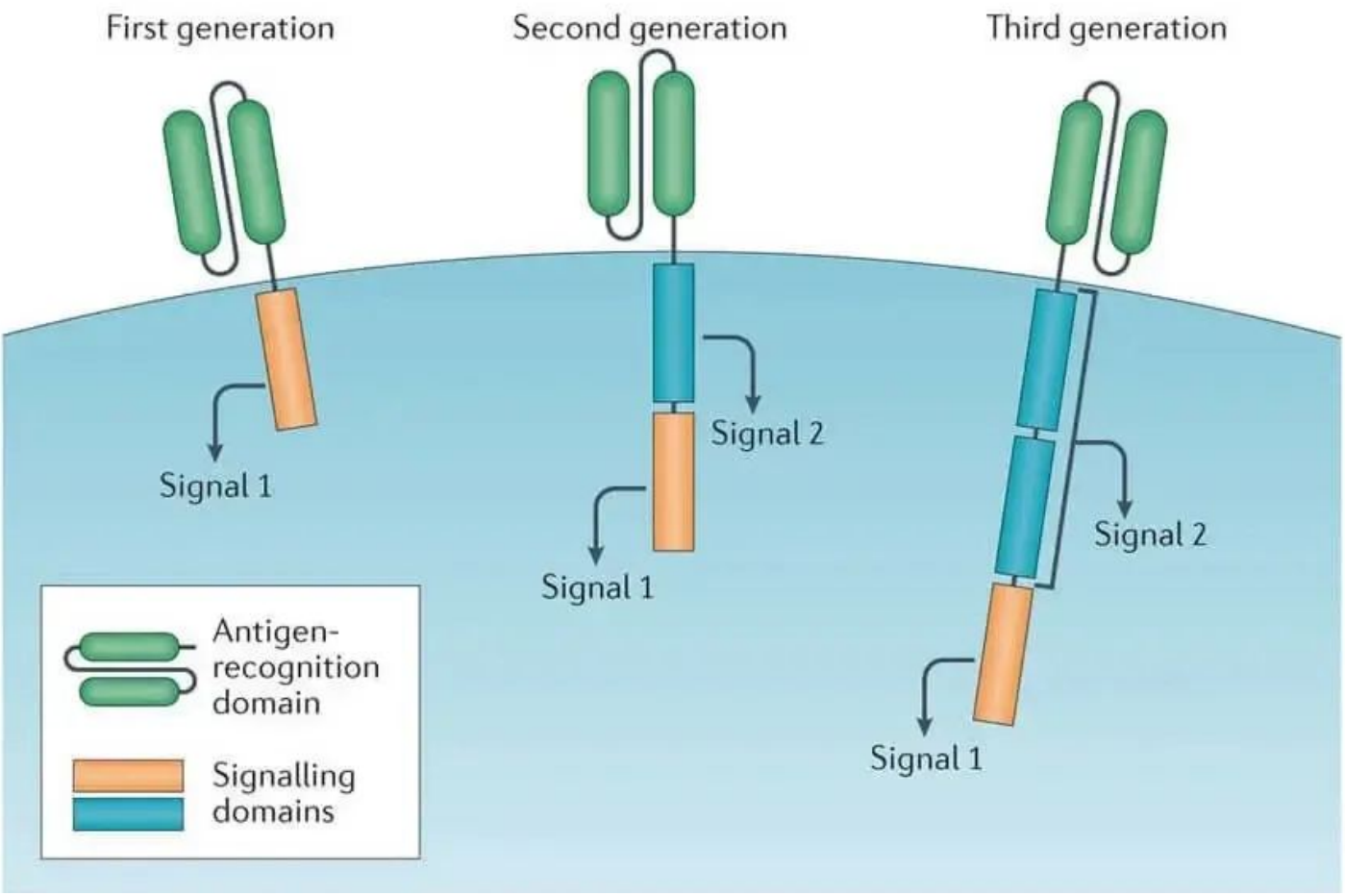


Mechanism of Action

- The engineered CAR receptor on the T cells binds to the target antigen on cancer cells. This activates the T cell to proliferate and release cytotoxic proteins like **perforin** and **granzymes**, which enter the cancer cell and trigger cell death.
- CAR T cells also secrete **cytokines** like **IL-2** and **IFN-gamma** that recruit and activate other immune cells to amplify the immune response against cancer cells across the body.
- CAR T cells can persist in the patient for years after **infusion**, providing durable anti-cancer activity. However, some patients relapse if their cancer stops expressing the target antigen.

CAR T Cell Generations

- **First-generation:** CARs only had the **CD3-zeta signalling domain**, providing suboptimal activation of T cells.
- **Second-generation:** CARs added a **costimulatory domain (e.g. CD28, 4-1BB),** improving T cell activation and persistence.
- **Third-generation:** CARs contain two costimulatory domains for greater T cell activity but increased toxicity risk.
- **Fourth-generation:** CARs additionally express **cytokines** or other enhancements to improve efficacy and safety.



Types of CAR T Cell Therapies

While most approved CAR T cells target CD19 in B cell leukaemias and lymphomas, new targets are expanding applications:

- **CD19 CAR T Cells: CD19 is a cell surface marker on B cells and B cell cancers.**
  - These cells have induced **high remission rates** in refractory B cell **acute lymphoblastic leukaemia (ALL)** and certain lymphomas.
- **BCMA CAR T Cells: B cell maturation antigen (BCMA)** is expressed on **multiple myeloma cells**.
  - These cells have achieved robust response rates in **relapsed/refractory myeloma.**

- **Other CAR Types:** CARs targeting antigens like **CD20, CD22** and **CD30** are also being evaluated for **hematologic malignancies**.
    - CAR T cells targeting **solid tumour antigens(e.g. MUC1)** are in early-phase trials.

Toxicities and Side Effects

CAR T cell therapy has achieved remarkable outcomes in certain blood cancers, but toxicity risks and Side effects remain as follows:

- **Cytokine release syndrome (CRS):** Caused by high levels of inflammatory cytokines released by activated CAR T cells. Symptoms may include **fever, low blood pressure, difficulty breathing** and **organ toxicities**. CRS can be severe or life-threatening in some cases.
- **Neurological toxicity:** Some patients experience neurological issues like **delirium, seizures** or **cerebral oedema,** likely also related to cytokine elevations. These are usually reversible.
- **On-target off-tumor toxicity:** If the target antigen is also expressed on some normal cells, the CAR T cells may cause toxicity to those tissues.
    - For example, **CD19 CAR T** cells can **deplete normal B cell**s.
- Other side effects can include **infections, anaemia, neutropenia and hypogammaglobulinemia**. Supportive care measures are given to manage toxicities.
- Risk mitigation strategies for CAR T cell toxicity include dose adjustment, incorporating safety switches, and **cytokine blockade.**

Current Challenges and Limitations

Some challenges and limitations need to be overcome before CAR T-cell therapy can be widely applied to solid tumours and haematological malignancies.

- **Relapses** can occur in some patients due to antigen escape when cancer cells stop expressing the CAR's target antigen. Combination treatments or CAR T cells targeting multiple antigens may help prevent relapse.
- **Efficiency:** CAR T cell therapies have mostly been successful against **blood cancers**, with limited efficacy seen so far against solid tumours. Additional bioengineering strategies are being explored to improve solid tumour treatments.
- **Toxicity:** Severe toxicities like **cytokine release syndrome** and neurological issues can occur in some patients after CAR T cell infusion, although usually manageable.
- Complex, personalised manufacturing is logistically challenging. **Allogeneic off-the-shelf** CAR T cell products from donors aim to simplify manufacturing and administration.
- **High costs and reimbursement** difficulties make CAR T cell therapies inaccessible for many patients. Health systems need funding models to improve access.

Way Forward

CAR T cell therapy is currently very expensive with treatment costing several hundred thousand dollars per patient. The future outlook remains promising - CAR T cell research is surging ahead to:

- CAR T cell therapy is poised to become a major advancement in cancer treatment alongside **surgery, chemotherapy** and **radiation.**
- Ongoing innovation is expanding the range of cancer targets and working to **improve efficacy, safety** and **accessibility.**
- It may eventually be an **off-the-shelf treatment** used earlier in cancer therapy, rather than later.
- **Combination regimens** with checkpoint inhibitors, bispecific antibodies or systemic immunomodulators may further enhance **CAR T cell potency**.
- **Next-generation enhancements** like **TRUCKs, ARM T cells** and the use of **iPSC-derived NK or T cells** may also help overcome current limitations.
- CAR T cell therapy is on the leading edge of **personalised cell therapies** and **cancer immunotherapy advances.**

It is thus spearheading innovation at the confluence of cell engineering, gene therapy and synthetic biology. The decades ahead will see continuous refinements potentiate CAR T cells into a **transformative anti-cancer platform technology.**
