



## Sansad TV Vishesh: CAR T-Cell Therapy

**For Prelims:** [CAR T-Cell Therapy](#), [Chimeric Antigen Receptor T-cell Therapy](#), [Leukaemias](#), [Lymphomas](#), [Living Drugs](#), [White Blood Cell](#), [NexCAR19](#), [Central Drugs Standard Control Organisation \(CDSCO\)](#), [Chemotherapy](#), [CRISPR-Cas9](#), [Platelets](#)

**For Mains:** Significance of CAR T-Cell Therapy in treatment of cancer patients.

### Why in News?

Recently, The **President of India** remarked indigenously developed [CAR-T Cell Therapy](#) for the treatment of cancer as a significant success in an event organized at the **Indian Institute of Technology (IIT) Bombay**.

### What is CAR T-Cell Therapy?

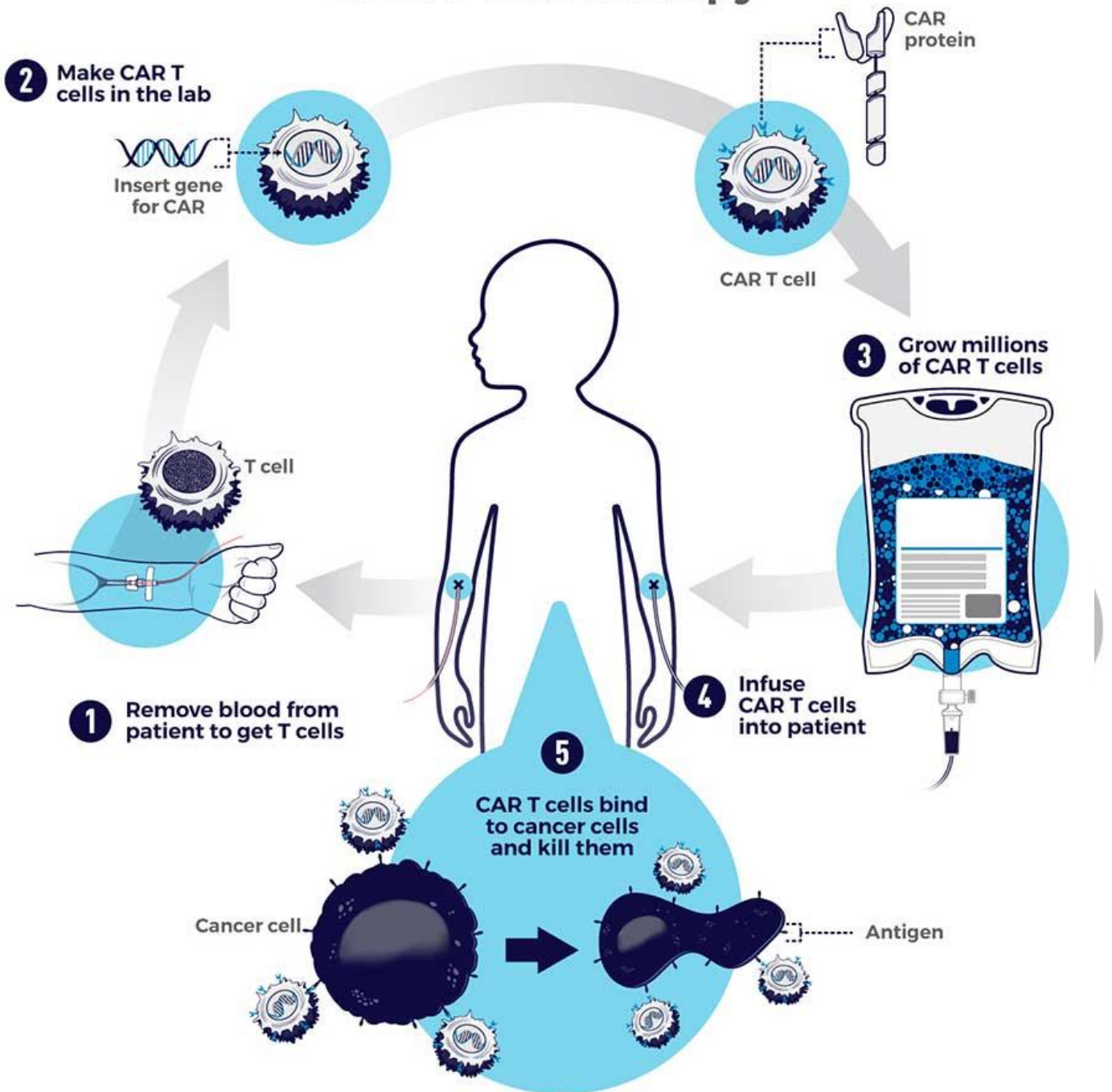
#### ▪ About:

- **CAR-T cell Therapy**, also known as [Chimeric Antigen Receptor T-cell Therapy](#), is a type of **immunotherapy** that uses a **patient's own immune system** to fight cancer.
- CAR T-cell therapy has been approved for [leukaemias](#) (cancers arising from the cells that produce [white blood cells](#) and [lymphomas](#) (arising from the lymphatic system).
- CAR-T cell therapies, often referred to as '[living drugs](#)'.
- Since **2017**, **six CAR T-cell therapies** have been approved by the **Food and Drug Administration (FDA)**.
- All are approved for the treatment of **blood cancers**, including **lymphomas**, some forms of **leukemia**, and, most recently, **multiple myeloma**.

#### ▪ Procedure:

- It is a complex and personalized treatment process that involves:
  - **Collecting T cells:** T cells, a type of **white blood cell** that helps fight infection, are extracted from the patient's blood through a process known as **Apheresis**.
  - **Genetic Engineering:** In the laboratory, the T cells are **genetically modified** to express a special protein called a **Chimeric Antigen Receptor (CAR)** on their surface.
    - This CAR is designed to recognise and bind to a specific antigen (marker) found on cancer cells.
  - **Expansion:** The engineered T cells are multiplied in large numbers in the lab.
  - **Infusion:** The expanded CAR-T cells are then infused back into the patient's bloodstream, where they can identify and attack cancer cells that express the targeted antigen.

# CAR T-Cell Therapy



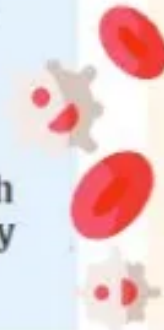
## Development in India:

- **NexCAR19**, India's first indigenous **CAR-T cell therapy** for cancer, was developed collaboratively by **ImmunoACT, Indian Institute of Technology Bombay (IIT-B), and Tata Memorial Hospital**.
- The commercial use of this therapy to treat certain blood cancers was approved by the **Central Drugs Standard Control Organisation (CDSCO)** in October 2023.
- **NexCAR19** is the first CAR-T cell therapy to get **CDSCO approval**.

# TREATMENT FOR SPECIFIC B-CELL CANCERS

NexCAR19 is a prescription drug for B-cell lymphomas, lymphoblastic leukaemias when other treatments have been unsuccessful

**PATIENT'S WHITE** blood cells are extracted by a machine through a process called leukapheresis and genetically modified, equipping them with the tools to identify and destroy the cancer cells.



**NEXCAR19 IS** manufactured to an optimal dose for the patient, and typically administered as a single intravenous infusion. Prior to this, the patient is put through chemotherapy to prime the body for the therapy.

## HOW NEXCAR19 WORKS



**T-cells** are naturally made by the body as an advanced defence against viruses and cancer cells.

As T-cells mature, they develop specific connectors (receptors) to target key signals on cancer cells.



**However, cancers** can limit the inbuilt extent and efficiency with which T-cells are able to seek and fight them. This results in an increase in cancer burden.



**Scientists have** identified certain proteins that are abnormally expressed on the surfaces of specific types of cancer cells. Specially designed receptors can find and bind to these cells.



**A safe shell** of a virus is used to genetically engineer T-cells so they express Chimeric Antigen Receptors – connectors that target a protein called CD19 on B-cell cancer.

### ▪ Potential Benefits of CAR-T Therapy:

- **High Remission Rates:** For some patients with advanced cancers who have not responded to other treatments, **CAR-T therapy** can lead to high rates of complete remission.
- **Targeted Treatment:** CAR T-cell therapy is highly targeted, as it specifically recognizes and attacks cancer cells expressing the **target antigen** while sparing healthy cells. This precision can lead to more effective treatment with fewer side effects compared to traditional chemotherapy and radiation therapy.
- **High Efficacy:** CAR T-cell therapy has shown remarkable efficacy, particularly in patients with certain types of blood cancers such as **Acute Lymphoblastic Leukemia (ALL)**, **Chronic Lymphocytic Leukemia (CLL)**, and **Non-Hodgkin Lymphoma (NHL)**. It has achieved high rates of complete remission in some patients who have not responded to other treatments.
- **Single Treatment:** In many cases, CAR T-cell therapy involves a **single infusion of**



**genetically engineered T cells**, which can provide long-lasting therapeutic effects. This contrasts with other treatments, such as **chemotherapy**, which may require multiple cycles of treatment over an extended period.

- **Personalized Medicine:** CAR T-cell therapy can be tailored to each individual patient by engineering T cells to target specific antigens present on their cancer cells. This personalized approach holds promise for treating a wide range of cancers and overcoming **tumor heterogeneity**.

## What is Cancer?

- Cancer is a broad term used to describe a **group of diseases** characterized by the **uncontrolled growth and spread of abnormal cells in the body**.
- These abnormal cells, known as cancer cells, can invade nearby tissues and organs, disrupting their normal function.
- Additionally, cancer cells can metastasize, or spread to other parts of the body through the bloodstream or lymphatic system, forming new tumors in distant locations.

## What is Gene Therapy?

- **About:**
  - **Gene therapy** is a medical approach aimed at treating or preventing diseases by modifying the **genetic material** of a **patient's cells**.
  - This technique involves **introducing genetic material** into a person's cells to either replace a **faulty gene** causing a disease or to provide a new function to the cells.
  - Gene therapy holds promise for treating a wide range of genetic disorders, such as **cystic fibrosis, muscular dystrophy**, and certain types of **cancer**.
- **Types of Gene Therapy:**
  - **Gene Replacement Therapy:** This involves inserting a healthy copy of a gene into the cells to replace a defective or missing gene.
  - **Gene Editing:** Techniques like **CRISPR-Cas9** enable precise editing of genes, allowing for corrections of mutations or modifications of gene expression.
  - **Gene Addition:** In some cases, genes may be added to cells to help them function more effectively or to produce a beneficial protein.
  - **Gene Silencing:** This approach involves inhibiting the expression of certain genes that may be causing disease by introducing molecules such as **small interfering RNA (siRNA) or antisense oligonucleotides**.

## What is Vector?

- **About:** In **gene therapy**, a vector is typically a **virus** or a **plasmid** that has been modified to carry and deliver therapeutic genes into target cells.
  - **Viral Vectors:** Viral vectors are derived from viruses that have been genetically engineered to remove their ability to cause disease while retaining their capacity to infect cells and deliver genetic material.
    - Examples of viral vectors used in gene therapy include **Lentiviruses, Adenoviruses, and Adeno-Associated Viruses (AAVs)**.
  - **Plasmid Vectors:** Plasmid vectors are **small, circular DNA molecules** that can replicate independently within a host cell.
    - They are commonly used in laboratory settings and experimental gene therapy approaches.
    - Plasmid vectors can be introduced into target cells through methods such as electroporation or direct injection.

## What are the Challenges Regarding CAR T-Cell Therapy?

- **Cytokine Release Syndrome (CRS):** CRS is a systemic inflammatory response triggered by the activation and proliferation of **CAR-T cells** in the body.
  - Symptoms can range from mild, flu-like symptoms to severe manifestations such as high fever, low blood pressure, and organ dysfunction. In severe cases, CRS can be life-threatening if not promptly managed.
- **Cytopenias:** Treatment with CAR T-cell therapy can lead to **cytopenias**, including **low levels of red blood cells (anemia)**, [white blood cells \(neutropenia\)](#), and [platelets \(thrombocytopenia\)](#).
  - These conditions can increase the risk of **infections, bleeding**, and other complications.
- **Immune Effector Cell-Associated Syndrome (ICANS):** ICANS encompasses a range of neurological symptoms associated with CAR T-cell therapy, including **confusion, aphasia, and seizures**. ICANS can occur concurrently with CRS or independently and may require close monitoring and intervention.
- **Tumor Lysis Syndrome (TLS):** In some cases, rapid destruction of cancer cells following CAR T-cell therapy can lead to the release of intracellular contents into the bloodstream, causing metabolic abnormalities such as **hyperkalemia, hyperuricemia, and acute kidney injury**.

## Way Forward

- **Cost Reduction:**
  - Explore strategies to reduce the high cost of CAR T-cell therapy, such as negotiating pricing agreements with manufacturers, implementing value-based pricing models, and investing in research and development to optimize manufacturing processes and increase efficiency.
- **Management of Cytokine Release Syndrome (CRS):**
  - Develop standardized protocols for the early detection and management of CRS, including the use of immunosuppressive medications (such as tocilizumab) to dampen the inflammatory response.
  - Enhance healthcare provider education and training on recognizing and managing CRS, including the importance of close monitoring and timely intervention.
- **Management of Cytopenias:**
  - Implement strategies to mitigate the risk of cytopenias associated with CAR T-cell therapy, such as supportive care measures (e.g., blood transfusions, growth factors) and dose optimization to minimize hematologic toxicity while maintaining therapeutic efficacy.
- **Management of Immune Effector Cell-Associated Syndrome (ICANS):**
  - Develop standardized approaches for the assessment and management of ICANS, including neurological monitoring and interventions (e.g., corticosteroids) for symptomatic relief.
  - Invest in research to better understand the underlying mechanisms of ICANS and identify predictive biomarkers to guide risk stratification and early intervention.
- **Prevention and Management of Tumor Lysis Syndrome (TLS):**
  - Implement protocols for the prevention and early detection of TLS, including hydration strategies and the use of urate-lowering agents.
  - Monitor patients closely for signs of TLS during CAR T-cell therapy and provide prompt intervention to mitigate metabolic abnormalities and prevent renal complications.

## UPSC Civil Services Examination, Previous Year Questions (PYQs)

### Prelims

**Q. Which one of the following statements best describes the role of B cells and T cells in the human body? (2022)**

- (a) They protect the environmental allergens. body
- (b) They alleviate the body's pain and inflammation.
- (c) They act as immunosuppressants in the body.
- (d) They protect the body from diseases caused by pathogens.

**Ans: (d)**

## **Mains**

**Q.** What are the research and developmental achievements in applied biotechnology? How will these achievements help to uplift the poorer sections of the society? **(2021)**

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