Advances in Cellular Immunotherapy

The Evolution of CAR T-Cell Therapy

From Blood Cancers to Solid Tumors



Dr. Maurizio Chiriva Internati

Associate Professor, MD Anderson Cancer Center

h-index: 53

8,000+ Citations

170+ Publications

The CAR T-Cell Revolution in Blood Cancers

CAR T-cell therapy engineers a patient's own T cells to recognize and attack cancer cells by adding a chimeric antigen receptor (CAR) that targets specific proteins on tumor surfaces.

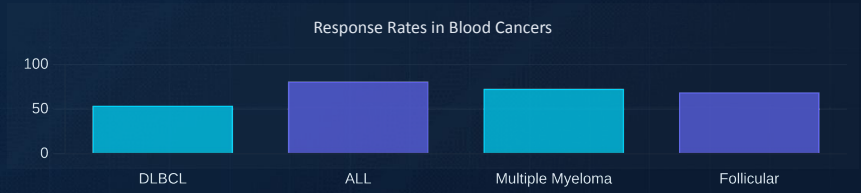
6 FDA-Approved Products	**40-50%** Complete Remission
2017 First FDA Approval	**8+** Cancer Types Treated

December 2025 Milestone

Breyanzi (liso-cel) approved as the first CAR T-cell therapy for relapsed/refractory **marginal zone lymphoma**, expanding treatment options for patients with limited alternatives.

FDA Approval Timeline

2017	**Kymriah (tisagenlecleucel)** Pediatric ALL, DLBCL
2017	**Yescarta (axicabtagene ciloleucel)** Large B-cell lymphoma
2021	**Abecma (idecabtagene vicleucel)** Multiple myeloma
2022	**Carvykti (ciltacabtagene autoleucel)** Multiple myeloma
2025	**Breyanzi (lisocabtagene maraleucel)** Marginal zone lymphoma



The Solid Tumor Challenge

> *"Understanding the Achilles heel of CAR T-cell therapy is essential for developing next-generation cellular immunotherapies capable of treating solid malignancies."*
>
> — Dr. Chiriva Internati & Grizzi, Frontiers in Immunology, 2025

Immunosuppressive TME

Tumor microenvironment actively suppresses T-cell function through regulatory cells and inhibitory signals

Antigen Heterogeneity

Solid tumors lack universal surface antigens, making targeting difficult without harming healthy tissue

Physical Barriers

Dense stroma and abnormal vasculature prevent CAR T-cells from infiltrating tumor masses effectively

T-Cell Exhaustion

Prolonged antigen exposure leads to functional exhaustion, reducing persistence and efficacy

Dr. Chiriva Internati's Research

His pioneering work on **cancer-testis antigens** offers promising targets for solid tumors—expressed in cancer cells but absent in normal adult tissues.

- SP17
- AKAP4
- SPEF1/SPEF2

Clinical Trial Landscape

500+	15+	50+
Active Trials	Tumor Types	Target Antigens

Innovations Overcoming Barriers (2025-2026)

Armored CAR T Cells

Next-generation T cells engineered to express their own cytokines, enabling proliferation and persistence in hostile tumor microenvironments.

IL-18 | IL-12 | IL-15 | IL-7

Logic-Gated Circuits

Synthetic biology approaches that program CAR T cells to recognize multiple antigens, reducing off-target effects and improving specificity.

AND Gates | NOT Gates | Kill Switches

Nanotechnology Delivery

Lipid nanoparticles and targeted delivery systems enhance CAR T manufacturing and enable in vivo T-cell engineering without extraction.

LNP Delivery | In Vivo CAR

AI-Driven Optimization

Machine learning accelerates **CAR construct design**, predicts patient response, and identifies optimal **antigen targets**. AI models now analyze tumor microenvironment data to personalize therapy selection.

Combination Approaches

- CAR T + Checkpoint Inhibitors
- CAR T + Oncolytic Viruses
- CAR T + Bispecific Antibodies
- CAR T + Radiation Therapy

The Future: Where Research Is Heading

Novel Targets

Cancer-Testis Antigens

Dr. Chiriva Internati's expertise in SP17, AKAP4, and SPEF antigens offers universal targets expressed only in tumors—not healthy tissue.

Expanding Indications

Hepatocellular carcinoma, ovarian cancer, and pancreatic cancer are key targets for next-generation therapies.

Technology

Off-the-Shelf CAR T

Allogeneic products from healthy donors eliminate manufacturing delays and reduce costs dramatically.

In Vivo Generation

Direct reprogramming of T cells inside the patient's body—no cell extraction or manufacturing required.

AI-Optimized Design

Machine learning accelerates CAR construct optimization and patient selection.

Next Generation

Training Scientists

Scholarships and mentorship programs are essential to build the workforce needed for immunotherapy breakthroughs.

STEM Pipeline

STEM jobs growing 10.4% through 2033—cancer research needs diverse, skilled talent.

Global Collaboration

International research networks accelerate discovery and expand access to life-saving therapies.

The Path Forward

With 70% five-year cancer survival rates achieved in 2026, continued investment in immunotherapy research and education will drive the next wave of breakthroughs—transforming CAR T-cell therapy from a treatment of last resort to a first-line cure.

Presented by

Dr. Maurizio Chiriva Internati