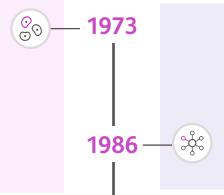


#### KEY MILESTONES IN THE DEVELOPMENT OF CAR T CELL THERAPY



#### First bone marrow stem cell transplants used to treat cancer

In what is considered by many to be one of the first successful immunotherapies, scientists take stem cells from the bone marrow of a donor and transplant them into a cancer patient. The immune cells in the donor's bone marrow kill cancer cells in the recipient and the healthy donor cells repopulate the patient's bone marrow.



#### Tumor infiltrating lymphocytes (TILs) first used to treat cancer

TILs are immune cells that are removed from a tumor, grown in a lab, and then given back to the patient to fight their cancer. Early studies showed a few patients with advanced cancers were cured, indicating that a person's own immune cells can kill cancer cells.

#### Scientists experiment with enhancing T cells to fight cancer

Scientists take T cells from patients and modify them in the lab to be stronger cancer fighters. They use genetic engineering to make these modifications.

# First-generation chimeric antigen receptors (CARs) created CAR T cells are developed by adding CARs to the surface of T cells. These early

CAR T cells are developed by adding CARs to the surface of T cells. These early CARs do not work in the body but are an important innovation in immunotherapy.

#### CAR T cell therapy is first used in cancer patient

Throughout the 1990's and early 2000's, research and technology advances enhance the effectiveness of CAR T cell therapy. In 2010, a newer generation of CAR T cell therapy is first used in a human patient ushering in a new era of personalized medicine.

## First pediatric patient with cancer treated with CAR T cell therapy

At age 7, Emily Whitehead is the first pediatric patient in the world treated with CAR T cell therapy for acute lymphoblastic leukemia (ALL). Emily experienced serious side effects which helped doctors better understand the side effect profile of CAR T cell therapy and how to manage some of those side effects. Just 22 days after treatment with CAR T cell therapy, Emily's doctor determined that she was cancer-free.

#### First CAR T cell therapy study results published and "Cancer Immunotherapy" named Breakthrough of the Year

Results from a clinical study of CAR T cell therapy in adults with ALL are published.

This is the first published study of CAR T cell therapy in people.

Science magazine votes "Cancer Immunotherapy" the Breakthrough of the Year. CAR T cell therapy is one of several cellular therapies mentioned in the article.



2010

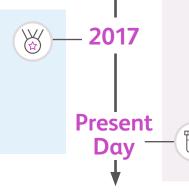
2012

## US Food & Drug Administration (FDA) designates CARs a "breakthrough" therapy

In an important regulatory step, the FDA grants CART cell therapy "breakthrough" designation. This helps speed up the development of this therapy for serious conditions.

### CAR T cell therapy gains first FDA approval

44 years after early research on using the immune system to target cancer, the FDA approved the first CAR T cell therapy for children and young adults with ALL.



#### Multiple CAR T products approved in the US for use in several blood cancers

Today, there are several FDA-approved CAR T cell therapy products. CAR T cell therapy is currently approved for use in patients with certain blood cancers. The number of products and uses is expected to continue to grow with ongoing research in other diseases.