

# Secondary cancers following CAR T cell therapy are rare, analysis shows

January 25 2024

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The development of any type of second cancer following CAR T cell therapy is a rare occurrence, as found in an analysis of more than 400 patients treated at Penn Medicine. Researchers from the Perelman

School of Medicine at the University of Pennsylvania report their findings in [Nature Medicine](#).

The team also described a single case of an incidental T cell lymphoma that did not express the CAR gene and was found in the lymph node of a patient who developed a secondary lung tumor following CAR T cell therapy.

CAR T cell therapy, a personalized form of immunotherapy in which each patient's T cells are modified to target and kill their [cancer cells](#), was pioneered at Penn. More than 30,000 patients with blood cancers in the United States—many of whom had few, if any, remaining treatment options available—have been treated with CAR T cell therapy since the first such therapy was approved in 2017.

Some of the earliest patients treated in [clinical trials](#) have gone on to experience [long-lasting remissions](#) of a decade or more.

Secondary cancers, including T cell lymphomas, are a known, rare risk of several types of cancer treatment, including chemotherapy, radiation, and [stem cell transplant](#). CAR T cell therapy is currently only approved to treat blood cancers that have relapsed or stopped responding to treatment, so patients who receive CAR T cell therapies have already received multiple other types of treatment and are facing dire prognoses.

In November 2023, the [FDA announced](#) an investigation into several reported cases of secondary T cell malignancies, including CAR-positive lymphoma, in patients who previously received CAR T cell therapy products.

In January 2024, the [FDA began requiring](#) drugmakers to add a safety label warning to CAR T cell products. While the FDA review is still ongoing, it remains unclear whether the secondary T cell malignancies

were caused by CAR T cell therapy.

As a leader in CAR T cell therapy, Penn has longstanding, clearly established protocols to monitor each patient both during and after treatment—including follow-up for 15 years after infusion—and participates in national reporting requirements and databases that track outcomes data from all cell therapy and bone marrow transplants.

"When this case was identified, we did a detailed analysis and concluded the T cell lymphoma was not related to the CAR T cell therapy. As the news of other cases came to light, we knew we should go deeper, to comb through our own data to better understand and help define the risk of any type of secondary cancer in patients who have received CAR T cell products," said senior author Marco Ruella, MD, an assistant professor of Hematology-Oncology and Scientific Director of the Lymphoma Program.

"What we found was very encouraging and reinforces the overall safety profile for this type of personalized cell therapy."

Of 449 patients treated with commercially available CAR T cell therapies at Penn Medicine between January 2018 and November 2023, only 16 were diagnosed with a second cancer after receiving CAR T cell therapy. Most of the secondary cancers (12 of the 16) were solid tumors, including skin cancer, prostate cancer, and lung cancer.

In one patient who developed a secondary lung tumor following CAR T cell therapy, an incidental T cell lymphoma was also identified in a lymph node removed during surgery for the lung tumor.

Molecular analyses demonstrated that the T cell lymphoma did not harbor the CAR transgene, which means it was not a CAR-positive lymphoma and there is not a clear connection to the CAR T cell therapy.

These studies were possible thanks to the Penn Medicine Cellular Therapy and Transplant BioBank, which facilitates the preservation of routinely collected medical data and specimens for research purposes.

"It's important to have long-term follow-up and reporting systems in place for any new [cancer](#) treatment to understand the risks and benefits over time, so that we can—together with patients and their families—evaluate the best possible [treatment options](#) for each individual," said David Porter, MD, the Jodi Fisher Horowitz professor in Leukemia Care Excellence and director of Cell Therapy and Transplantation at the Abramson Cancer Center.

"Just as Penn Medicine researchers and scientists are continually working on finding new ways to make CAR T cell therapy more effective for more patients, our team also has robust systems in place to study future cases like this so that we can contribute to a comprehensive understanding of secondary cancers in this patient population."

**More information:** Guido Ghilardi et al, T-cell Lymphoma and Secondary Primary Malignancy Risk After Commercial CAR T-cell Therapy, *Nature Medicine* (2024). [DOI: 10.1038/s41591-024-02826-w](https://doi.org/10.1038/s41591-024-02826-w)

Provided by Perelman School of Medicine at the University of Pennsylvania

Citation: Secondary cancers following CAR T cell therapy are rare, analysis shows (2024, January 25) retrieved 27 April 2024 from <https://medicalxpress.com/news/2024-01-secondary-cancers-car-cell-therapy.html>

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