

CAR T Cell Therapy Leads to 10-Year Remissions in B-Cell Lymphoma Patients

Long-term follow-up from one of the earliest CAR-T clinical trials shows potential cures in more than one third of patients treated at Penn Medicine.

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After a median follow-up of 10 years, more than one third of patients with large B-cell lymphoma and nearly half of patients with follicular lymphoma who received a single infusion of tisagenlecleucel—the CAR T cell therapy developed by [Carl June, MD](#) that would go on to become [the first such treatment approved by the FDA](#)—were still alive without a lymphoma relapse, according to long-term follow-up data published today in the [New England Journal of Medicine](#) by researchers from the Abramson Cancer Center and Perelman School of Medicine at the University of Pennsylvania.

In the analysis of 38 patients from a Phase II clinical trial (including 24 patients with large B-cell lymphoma and 14 with follicular lymphoma) conducted at Penn Medicine’s Abramson Cancer Center, no patients experienced a relapse after 5.4 years, and most relapses occurred within the first year after CAR T cell infusion, supporting the hypothesis that patients who experience a long-term response to CAR T cell therapy may be cured.

“As oncologists, we use the word ‘cure’ with great care, but I am increasingly confident that CAR T cell therapy has the potential to cure a meaningful number of patients with B-cell lymphomas,” said senior author [Stephen J. Schuster, MD](#), the Robert and Margarita Louis-Dreyfus Professor in Chronic Lymphocytic Leukemia and Lymphoma Clinical Care and Research and director of Penn’s Lymphoma Program. “At the same time, our work is far from done. This therapy does not yet work for everyone, and we are committed to understanding why so we can continue to improve the next generation of CAR Ts.”

Patients with a longer response appeared to have higher levels of CAR T cells in their blood over the first two years after treatment, a finding consistent with [reports of durable response to CAR T cell therapy](#) in other cancer types. The persistence of CAR T cells also seemed to be more important than the early peak expansion of CAR T cells.

Long-term safety makes a case for earlier CAR T therapy

The clinical trial enrolled patients with relapsed/refractory disease, meaning that their cancer had returned after and/or had stopped responding to other treatments. At study enrollment, patients had received a median of four previous therapies, including chemotherapy, and for some, autologous (self) stem cell transplant. Many of these therapies also carry their own long-term risks, and it's difficult to attribute the specific cause of long-term adverse events.

Two of the 38 patients had ongoing grade 2 or 3 neutropenia (low white blood cell counts) and there were no cases of ongoing anemia or thrombocytopenia. Importantly, more than half of all patients with a long-term response recovered normal B cells, an important part of the immune system, without recurrence of their B-cell lymphoma.

No patients in the study had a secondary case of CAR T cell-related lymphoma, as assessed by the investigator. Nine patients did develop a second primary cancer, including acute myeloid leukemia (in three patients, all with characteristic prior therapy-associated genetic mutations), prostate cancer (two patients), lung cancer (two patients, both with a smoking history), melanoma (one patient), and a form of T-cell lymphoma that affects the skin (one patient).

The overall 10-year incidence of a second, primary cancer was higher in the study population than in comparable US SEER data, though it is consistent with other reports from patients with lymphoma treated with chemotherapy and autologous transplant.

“We’re encouraged by the long-term remissions of these patients over the past decade,” said lead author [Marco Ruella, MD](#), an associate professor of Hematology-Oncology and scientific director of the Lymphoma Program. “Moving CAR T cell therapy into earlier lines of treatment—before patients experience the cumulative effects of chemotherapy—may be key to extending its curative potential.”

The research team currently has multiple projects in progress evaluating different strategies to improve the effectiveness of CAR T cell therapy, including evaluating whether the lymphodepleting chemotherapy that patients currently receive before CAR T cell therapy is necessary, as it is for stem cell (bone marrow) transplants.

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Note: The University of Pennsylvania has licensed technologies used in these studies to Novartis. Some of the scientists involved in these trials are inventors of these technologies. As a result of the licensing relationship with Novartis, the University of Pennsylvania receives significant financial benefit, and these inventors have benefited financially and/or may benefit financially in the future.

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