CAR T therapy shows long-lasting remissions in non-hodgkin lymphoma

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A significant number of non-Hodgkin lymphoma (NHL) patients in a Penn Medicine-initiated clinical trial continue to be in remission five years after receiving the chimeric antigen receptor (CAR) T cell therapy

Kymriah, researchers in Penn's Abramson Cancer Center reported today in the *New England Journal of Medicine*. The findings represent the longest follow-up published data to date for CAR T cell therapies approved by the U.S. Food and Drug Administration for the treatment of relapsed or refractory large B-cell lymphomas.

Among 24 patients with diffuse large B-cell lymphoma (DLBCL), the most common form of NHL, who received the therapy after their cancers had come back following standard treatments, 46 percent achieved complete remission and 31 percent achieved progression-free survival at five years. Among 14 patients with relapsed or refractory follicular lymphoma, the second most common form of the disease, 71 percent achieved complete remission and 43 percent achieved progression-free survival at five years.

"We found that most of the patients who achieve a remission lasting one year remain in remission five years after being infused with CAR T cells . This is really exciting and demonstrates the durability of this approach," said lead author Elise A. Chong, MD, an assistant professor of Medicine in the division of Hematology-Oncology in Penn's Perelman School of Medicine. "Patients who do not respond to chemotherapy have another option that may offer them long-lasting remissions."

Co-authors of this research include senior author Stephen J. Schuster, MD, the Robert and Margarita Louis-Dreyfus Professor in Chronic Lymphocytic Leukemia and Lymphoma Clinical Care and Research in Penn's Perelman School of Medicine and director of the Lymphoma Program at the Abramson Cancer Center, and Marco Ruella, MD,, an assistant professor in Hematology-Oncology at the Perelman School of Medicine and scientific director of the Lymphoma Program.

The team also studied the long-term persistence of CAR T cells, and found that 50 percent of the patients who experienced and remained in

remission after the first year did not have detectable levels of the CAR19 transgene after five years, while only one of the 18 patients who had a relapse of lymphoma within one year after infusion had loss of the transgene. The results suggest that loss of CAR T cell presence may not be a frequent mechanism of resistance to the therapy.

The study results are a follow up to a study from the same clinical trial published in *NEJM* in 2017 by Schuster, among other researchers, that included patient outcomes collected at 28 months. The results of a global CAR T cell therapy trial in lymphoma patients, sponsored by Novartis and led in part by Penn, were also published in *NEJM*, which led to the FDA approval for Kymriah for the treatment of relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including DLBCL, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma, in 2018. Kymriah is a registered trademark of Novartis.

Diffuse large B-cell lymphoma comprises approximately 30 percent of all NHLs, and there are an estimated 27,000 newly diagnosed patients with DLBCL in the U.S. each year. About 6,500 of those patients have relapsed or refractory disease after two or more therapies and may be eligible for approved CAR T cell therapies.

More information: Elise A. Chong et al. Five-Year Outcomes for Refractory B-Cell Lymphomas with CAR T-Cell Therapy, *New England Journal of Medicine* (2021). DOI: 10.1056/NEJMc2030164

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