Immune cell therapy shows promising results for lymphoma patients

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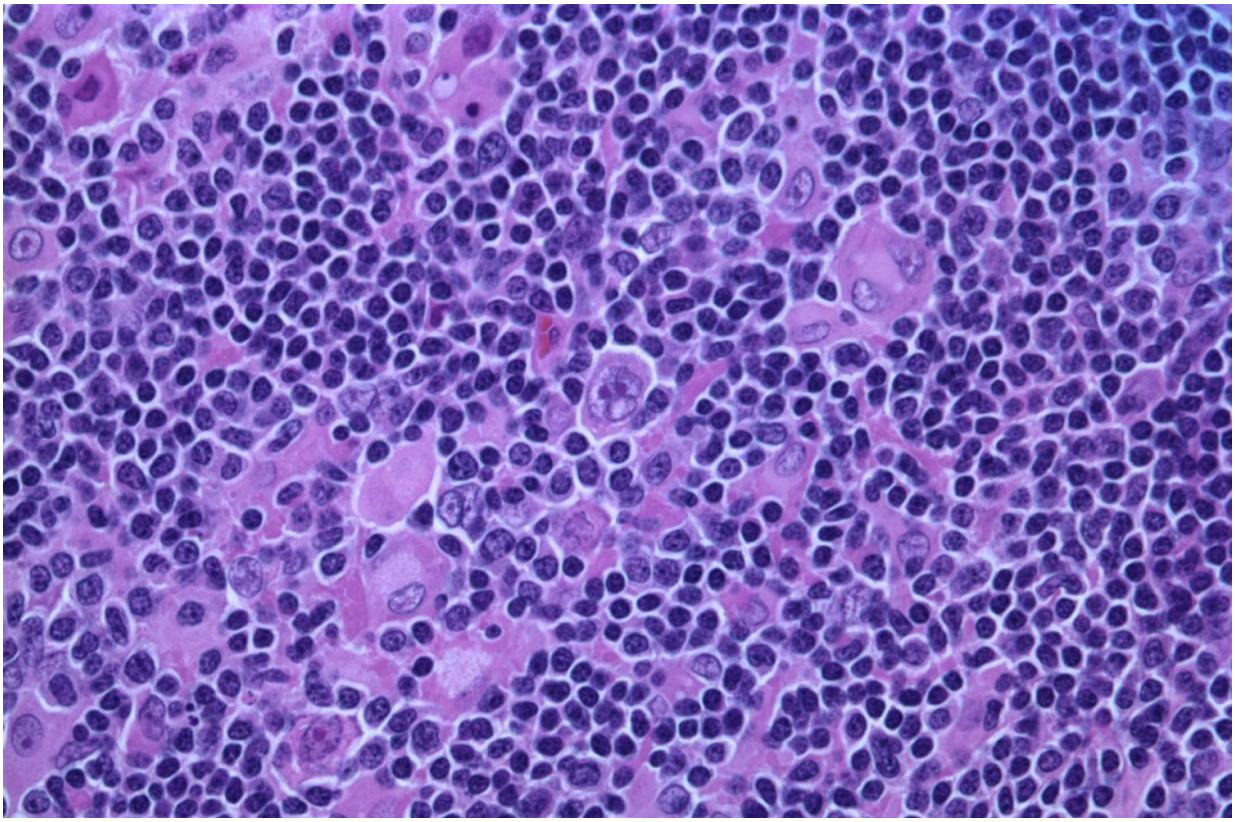

Hodgkin lymphoma, nodular lymphocyte predominant (high-power view) Credit: Gabriel Caponetti, MD./Wikipedia/CC BY-SA 3.0

Lymphoma is the most common blood cancer. The disease occurs when immune cells called lymphocytes multiply uncontrollably. Cancerous

lymphocytes can travel throughout the body and form lymph node tumors. The body has two types of lymphocytes that can develop into lymphoma - B cells and T cells. B-cell lymphomas account for 85 percent of all non-Hodgkin lymphomas and 30 percent of those patients are diagnosed with diffuse large B-cell lymphoma.

Diffuse large B-cell lymphoma is an aggressive B-cell cancer that can quickly spread throughout the body. This means it requires immediate treatment including drug therapy, radiation therapy and possibly a stem cell transplant. However, half of all diffuse large B-cell patients relapse after standard therapies and become unresponsive to chemotherapy treatments (refractory disease).

Moffitt Cancer Center physician investigators are working to bring immune cellular therapies to refractory diffuse large B-cell lymphoma patients. Promising results from the phase 1 portion of the ZUMA-1 study, which uses chimeric antigen receptor (CAR) modified T cells to treat b-cell lymphoma patients, were published in the January issue of *Molecular Therapy*, the official journal of the American Society of Gene and Cell Therapy.

Axicabtagene ciloleucel (KTE-C19), developed by Kite Pharma, is an autologous chimeric antigen receptor (CAR) T-cell therapy. In CAR-T therapy using axicabtagene ciloleucel (KTE-C19), T cells are isolated from a patient's blood and engineered in Kite Pharma's central manufacturing facility to target the CD19 protein that is found on lymphoma cells. The re-targeted T cells are then infused back into the same patient. Axicabtagene ciloleucel (KTE-C19) T cells are able to recognize cancerous lymphoma cells that express CD19 and target them for destruction.

The goal of the phase 1 portion of the ZUMA-1 study was to determine the safety of axicabtagene ciloleucel (KTE-C19) as assessed by the

frequency of dose-limiting toxicities in patients with diffuse large B-cell lymphoma who were refractory to prior therapy that included anti-CD20 therapy and an anthracycline-containing regimen. The study included patients who had highly refractory disease, with two to four prior treatments.

This is the first multicenter study of a CAR-T therapy that was produced manufactured at a centrally located facility. The Moffitt research team, led by Frederick L. Locke, M.D., reports that the manufacturing process for axicabtagene ciloleucel (KTE-C19) was successful for all of the patients and was completed within approximately two weeks.

After the successful manufacturing of axicabtagene ciloleucel (KTE-C19), cells were shipped back to Moffitt and the other participating sites where patients were treated with conditioning chemotherapy followed by infusion with axicabtagene ciloleucel (KTE-C19). Locke's team found that axicabtagene ciloleucel (KTE-C19) caused expected, but manageable, toxicity over a median follow-up period of nine months. Of the 7 patients treated with axicabtagene ciloleucel (KTE-C19), 1 patient experienced dose-limiting toxicity of cytokine release syndrome and neurotoxicity.

Axicabtagene ciloleucel (KTE-C19) resulted in promising clinical activity. The overall response rate was 71 percent (5 of 7 patients) and 4 patients developed a rapid complete response within 1 month of treatment. The treatment was also durable with 43 percent, or 3 patients remaining in complete remission after one year.

"The overall and complete response rate in this small group of patients is remarkable, as the expected complete response rate for such patients is 8 percent with conventional chemotherapies. This is truly an exciting time for the oncology community and our patients. Engineered immune cell therapies are one step closer to widespread availability." said Locke,

Director of Research for Moffitt's Immune Cell Therapy Clinical Trial Group.

The promising phase 1 results led to the initiation of the pivotal phase 2 portion of the ZUMA-1 study in aggressive non-Hodgkin lymphoma which includes diffuse large B-cell lymphoma, primary mediastinal B-cell lymphoma and transformed follicular lymphoma.

Provided by H. Lee Moffitt Cancer Center & Research Institute