

 IMMUNOTHERAPY

# DLBCL remissions driven by CARs

The typical survival duration of patients with diffuse large-B-cell lymphoma (DLBCL) who have disease progression after chemotherapy or autologous stem-cell transplantation is 9 months. Now, promising new data indicate that immunotherapy with anti-CD19 chimeric antigen receptor (CAR-19) T cells offers the hope of achieving longer-term survival.

The efficacy of CAR-19 T cells against B-cell acute lymphoblastic leukaemia is well publicized, but less data are available for B-cell lymphomas, of which DLBCL is the most common form. In 2010, James Kochenderfer reported on the first patient to obtain a remission with CAR-19 T cells — a patient, incidentally, with lymphoma. In the current study, Kochenderfer *et al.* treated 22 patients with advanced-stage lymphoma, predominantly DLBCL, using CAR-19 T cells following low-dose chemotherapy (which depletes host lymphocytes and enhances the antitumour activity of the adoptively transferred T cells).

Kochenderfer summarizes: “in a larger group of patients than we previously reported, and with lower doses of chemotherapy than we previously used, we showed that CAR-19 T cells are an effective therapy for lymphoma; the overall response rate was 73%, with a 55% complete remission rate. Another important finding was the durability of the complete remissions: 11 of 12 are ongoing, with durations of 7–24 months.” A potential biomarker for early assessment of response was identified: responders had higher peak serum levels of IL-15, which promotes T-cell proliferation, and also higher peak numbers of circulating CAR-19 T cells than nonresponders.

The use of low-dose chemotherapy curbed the haematological toxicities typically seen with high-dose chemotherapy. However, most patients experienced grade 3–4 adverse events, including neurological events that are common with CAR-19 T cells.

Kochenderfer predicts that “CAR-19 T cells will become a standard treatment for lymphoma in the near future.” He concludes, “this work has encouraged us to investigate the approach in other types of lymphomas; I am leading a new clinical trial of anti-CD30 CAR T cells, mainly in patients with Hodgkin or T-cell lymphoma.”

David Killock

**ORIGINAL ARTICLE** Kochenderfer, J. N. *et al.* Lymphoma remissions caused by anti-CD19 chimeric antigen receptor T cells are associated with high serum interleukin-15 levels. *J. Clin. Oncol.* <http://dx.doi.org/10.1200/JCO.2016.71.3024> (2017)