IMMUNOTHERAPY

CAR-modified T cells targeting CD19—curing the incurable

Relapsed or refractory acute lymphoblastic leukaemia (ALL) is associated with an extremely poor prognosis and poses a considerable therapeutic challenge, especially for patients who do not achieve a second complete remission or who relapse after stem-cell transplantation. Engineered T-cell therapy is a new strategy for the treatment of this disease that has already demonstrated durable complete remissions in a small number of patients. One T-cell therapy approach uses chimeric antigen receptors (CAR). By infusing autologous T cells transduced with a CD19-targeting CAR (CTL019) lentiviral vector in 25 children and five adults with relapsed or refractory ALL, Stephan Grupp and coauthors reported a staggering 90% complete remission rate in 27 of these patients. Responses were seen in two patients who were refractory to the agent blinatumomab, an antibody that targets the CD19 antigen present on B cells.

Sustained remission was noted with an impressive 6-month event-free survival

rate of 67% and an overall survival rate of 78% at 2 years. Of the 27 patients with complete remission, 19 remained in remission until study completion, and 15 received no further therapy. These results are considerably better than achieved with the most-recently approved chemotherapy drugs for relapsed ALL, which produce complete remission rates <25%, and median response durations of 4–9 weeks.

Severe cytokine-release syndrome—a systemic inflammatory response caused by elevated levels of cytokines—was the main adverse effect. All patients had at least mild-to-moderate cytokine-release syndrome that required hospitalization, while eight patients developed severe cytokine-release syndrome requiring intensive care and some degree of respiratory support; these responses were managed effectively with the IL-6 blocking agent tocilizumab.

“A short term remission rate of 90% is far better than we could have expected when we started this study. We are particularly excited about the fact that we have survivors 1–2 years out who remain in remission without further therapy, such as bone marrow transplant,” concludes Grupp.

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