CAR T-cells for relapsed B-cell ALL in adults

Adults with relapsed B-cell acute lymphoblastic leukaemia (ALL) might achieve durable responses to chimeric antigen receptor (CAR) T-cell therapy, according to recent findings.

In a phase 1 trial by Jae Park (Memorial Sloan Kettering Cancer Center, New York, NY, USA) and colleagues, 53 adults with relapsed or refractory B-cell ALL received one infusion of 19-28z CAR T cells, which expressed a second-generation CD19-specific CAR. The primary endpoint was safety, and the secondary objective was to assess activity.

At a median follow-up of 29 months (range 1–65), 44 (83%; 95% CI 70–92) of 53 patients achieved complete remission. Median event-free survival was 6·1 months (95% CI 5·0–11·5) and median overall survival was 12·9 months (8·7–23·4). Patients with a low pretreatment disease burden (<5% bone marrow blasts) had especially good outcomes, with a median event-free survival of 10·6 months (95% CI 5·9–not reached) and overall survival of 20·1 months (8·7–not reached), compared with 5·3 months (95% CI 3·0–9·0; p=0·01) and 12·4 months (5·9–20·7; p=0·02), respectively, in patients with a high pretreatment disease burden.

14 (26%; 95% CI 15–40) patients had severe cytokine release syndrome, but the incidence was higher in patients with high pretreatment disease burden (41%; 95% CI 25–61) than in those with a low disease burden (5%; 0–25; p=0·004). Patients with higher pretreatment disease burden also had more neurotoxicities (59%; 95% CI 39–75 *vs* 14%; 3–38; p=0·002).

Park noted this was the longest follow-up study of ALL and CAR T-cell therapy, and the first time predictive biomarkers of survival could be reported. He said, "These results generate the question: should we be using CAR T-cells in earlier lines of ALL treatments before morphologic relapse? We may be able to reduce toxicities of CAR T cell therapy and spare prolonged…maintenance chemotherapy in these patients."

Hagop Kantarjian (MD Anderson Cancer Center, Houston, TX, USA) commented that CAR T-cells are a major breakthrough, but warned that the treatment value might be overestimated. "[In this study,] of 83 enrolled patients, only 53 were infused; of 78 who underwent leukapheresis, 44 experienced complete remissions, which is actually a 56% response rate. Long-term results for all 53 patients indicated that 2-year survival is 30%, and 2-year event-free survival is under 20%. Therefore, the treatment value needs to be improved."

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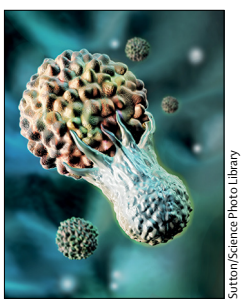

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For the **study by Park and colleagues** see *N Engl J Med* 2018; **378:** 449–59. https://dx.doi.org/10.1056/NEJMoa1709919