CAR T-cell cocktail therapy for B-cell malignancies

The sequential infusion of CAR19 and CAR20 T cells could be a promising treatment strategy for patients with relapsed or refractory B-cell haematological malignancies, reducing the rate of antigen escape relapse—a major challenge to long-term disease control following CD19-directed therapies— according to new research.

In a pilot trial, Na Wang (Huazhong University of Science and Technology, Wuhan, China) and colleagues enrolled 89 eligible patients with relapsed or refractory B-cell malignancies. Patients were given fludarabine 25 mg and cyclophosphamide 300 mg for 3 days (days –4 to –2) as lymphodepletion chemotherapy, before the CAR19 and CAR20 T-cell infusion, separately on successive days from day 0. Outcomes included responses, progression-free survival, and overall survival.

In patients with B-cell acute lymphoblastic leukaemia, a minimal residual disease-negative complete response was achieved by 48 (96·0%) of 51 patients (95% CI 86·3–99·5). At a median follow-up of 16·7 months (range 1·3–33·3), median progression-free survival was 13·6 months (95% CI 6·5–not reached [NR]) and median overall survival was 31·0 months (10·6–NR). In patients with B-cell non-Hodgkin lymphoma, 26 (72·2%; 95% CI 54·8–85·8) of 36 evaluable patients achieved an overall response, including 18 (50·0%; 95% CI 32·9–67·1) complete responses. At a median follow-up of 14·4 months (range 0·4–27·4), median progression-free survival was 9·9 months (95% CI 3·3–NR) and median overall survival was 18·0 months (6·1–NR). One patient experienced antigen loss during follow-up. In total, 85 (95·5%) of 89 patients experienced cytokine release syndrome, mostly low-grade (grade 1–2).

"[These] findings demonstrate that sequential infusion of CAR19 and CAR22 T cells is a highly active and welltolerated solution to reduce the rate of antigen escape relapse after CD19/CD22-directed therapies", explained coauthor Jianfeng Zhou (Huazhong University of Science and Technology).

"Tumour relapse due to CD19 loss is frequent after CD19 CAR T-cell treatment of B-cell lymphoma or leukaemia", commented Hinrich Abken (University of Regensburg, Regensburg, Germany). "Wang and colleagues increased the therapeutic pressure by sequentially applying CD19 and CD22 CAR T cells with superior potency in avoiding antigen loss and with moderate side-effects. Consequently, one CAR with CD19–CD22 dual-targeting capacities will be key for further developments."

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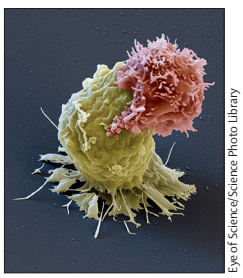

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For the **study by Wang and colleagues** see *Blood* 2019; published online Oct 29. DOI:10.1182/blood.2019000017