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IMMUNOTHERAPY

CAR T cells ready to go mainstream

Promising results have been obtained using T cells expressing CD19-specific chimeric antigen receptors (CARs) to treat patients with different B-cell malignancies. Diffuse large B-cell lymphoma (DLBCL), however, is one of the most aggressive haematological malignancies and remains a clinical challenge. In the 2016 ASCO Annual Meeting, James Kochenderfer and Steven Rosenberg presented the results of a study in which a new dosing strategy led to disease remission in a high proportion of patients treated.

CAR-T-cell transfer requires the prior administration of lymphodepleting cyclophosphamide-based chemotherapy. The investigators reasoned that a cyclophosphamide dose reduction would reduce toxicity and thus would result in improved patient outcomes. Importantly, the number of CAR T cells was also reduced to 2 x 10^5 cells per kg. This regimen was used to treat 19 patients with relapsed and/or refractory DLBCL, some of whom had disease progression after receiving an allogeneic haematological stem-cell transplant. Eight complete and five partial responses were observed; at the time of reporting, the complete responses were ongoing (for at least 7–20 months). Around half of the patients treated had neurological adverse effects, although these were mild and manageable.

Rosenberg explains: "we have found that reductions in cyclophosphamide dosing and CAR-T-cell numbers are effective for the treatment of DLBCL. The use of lower CAR-T-cell numbers means that it only takes 6–9 days to generate those cells."

> "this is likely … the first adoptive cellular therapy that would reach mainstream oncology"

Kite Pharma, a company that has collaborated with Rosenberg, is now conducting a larger multi-institutional study. To put these new results in perspective, Rosenberg adds: "we published the first report using anti-CD19 CAR T cells in 2010 to treat a patient with lymphoma who remains progression-free at present. The current results indicate that, because of the lower dose of lymphodepleting chemotherapy and CAR T cells used, this is likely to become the first adoptive cellular therapy that would reach mainstream oncology."

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ORIGINAL ARTICLE Kochenderfer, J. *et al.* Anti-CD19 chimeric antigen receptor T cells preceded by low-dose chemotherapy to induce remissions of advanced lymphoma [abstract]. *J. Clin. Oncol.* **34**, aLBA3010 (2016).
FURTHER READING Kochenderfer, J. *et al.* Eradication of B-lineage cells and regression of lymphoma in a patient treated with autologous T cells genetically engineered to recognize CD19. *Blood* **116**, 4099–4102 (2010)