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HAEMATOLOGICAL CANCER

After ibrutinib, CAR T cells induce responses

The therapeutic landscape for chronic lymphocytic leukaemia (CLL) changed with the approval of the targeted agents ibrutinib and venetoclax; however, patients with progressive CLL after treatment with these agents have poor outcomes. Now, Cameron Turtle and collaborators have demonstrated promising antitumour activity of CD19-specific chimeric antigen receptor (CAR) T cells in patients with progressive CLL after ibrutinib.

The 24 patients involved in this phase I/II study had high-risk disease that was refractory, or had relapsed after treatment with a regimen containing fludarabine and rituximab and, subsequently, ibrutinib. All patients received $CD4^+$ and $CD8^+$ CD19-specific CAR T cells following lymphodepletion using fludarabine and/or cyclophosphamide. Of 19 patients who underwent disease restaging after receiving fludarabine and cyclophosphamide (the preferred lymphodepletion regimen) and CAR T cells, 14 had a lymph-node response, four had a complete response and ten had a partial response, according to IWCLL criteria.

Bone-marrow disease was detected before treatment in 20 of the 24 patients; 4 weeks after CAR-T-cell infusion, flow cytometry revealed an absence of bone-marrow disease in 17 of 21 patients evaluated. Bone-marrow clearance was confirmed by the absence of malignant *IGH* sequences in seven patients, for whom the median progression-free survival duration was not reached, whereas for seven patients with *IGH*-positive disease it was 8.5 months.

A total of 20 of 24 patients developed cytokine-release syndrome, which was of grade 1–2 in 18 patients, grade 4 in one patient, and grade 5 in another. Eight patients had neurotoxicity, two of grade 1–2, five of grade 3, and one of grade 5.

The antitumour activity of CD19-specific CAR T cells in patients with ibrutinib-resistant CLL need to be confirmed in studies with large cohorts because the toxicities associated with this treatment required careful management.

Diana Romero

ORIGINAL ARTICLE Turtle, C. J. *et al.* Durable molecular remissions in chronic lymphocytic leukemia treated with CD19-specific chimeric antigen receptor-modified T cells after failure of ibrutinib. *J. Clin. Oncol.* http://dx.doi.org/10.1200/JCO.2017.72.8519 (2017)

FURTHER READING Younes, A. *et al.* The landscape of new drugs in lymphoma. *Nat. Rev. Clin. Oncol.* **14**, 335–346 (2017)