CAR T-cell therapy for relapsed or refractory multiple myeloma

The results of a new study suggest that bb2121, a CAR T-cell therapy that targets B-cell maturation antigen (BCMA), has potential for the treatment of relapsed or refractory multiple myeloma.

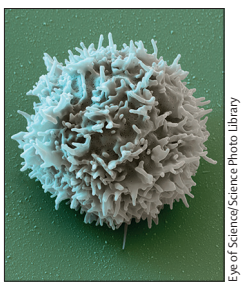
In the open-label, phase 1 trial, Noopur Raje (Massachusetts General Hospital Cancer Center, Boston, MA, USA) and colleagues enrolled 33 patients with multiple myeloma who had either received at least three previous therapies, including a proteasome inhibitor and an immunomodulatory agent, or were refractory to both drug classes. The 21 patients in the dose-escalation cohort received bb2121 as a single infusion at doses of 50×10^6, 150×10^6, 450×10^6, or 800×10^6 CAR T cells, and the 12 patients in the dose-expansion cohort received 150×10^6 to 450×10^6 CAR T cells. The primary endpoint was safety, and the secondary endpoints were the proportion of patients achieving an objective response and duration of response.

At data cutoff (6·2 months after the last infusion date), the most common adverse events were grade 3 or worse haematological toxic effects, including neutropenia in 28 (85%) of 33 patients, leukopenia in 19 (58%), anaemia in 15 (45%), and thrombocytopenia in 15 (45%). 25 (76%) patients had cytokine release syndrome, and any-grade neurological toxicities were recorded in 14 (42%) patients. 28 (85%) of 33 patients achieved an objective response, with a complete response in 15 (45%). Median duration of response was 10·9 months (range 7·2 to not estimable). In 16 responders evaluable for minimal residual disease (MRD) status, all were MRD negative.

Co-author James Kochenderfer (National Institutes of Health, Bethesda, MD, USA) said, "We hope to continue to develop this therapy and to move it earlier in the line-up of multiple myeloma therapies. We are also working on a phase 1 trial of a new anti-BCMA CAR T-cell product, and we are opening a new trial of CAR T cells targeting SLAMF7 soon."

Hartmut Goldschmidt (Heidelberg University, Heidelberg, Germany) said: "This type of therapy seems to be a very active therapy in heavily pretreated patients. In my opinion, it's very interesting that the duration of response is limited." He added, "The rate of MRD negativity is impressive, although the number of patients with MRD data is not high. Phase 3 trials need to be performed and different CAR T-cell constructs should be tested."

Robert Stirrups



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For the **study by Raje and colleagues** see *N Engl J Med* 2019; **380:** 1726–37