

Bispecific CAR T-Cell Therapy Shows Promise for B-cell Lymphoma

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Bispecific anti-CD19/CD20 chimeric antigen receptor (CAR) T-cell therapy was well tolerated and showed signs of clinical efficacy in patients with relapsed/refractory B-cell lymphoma, according to Phase I clinical trial data presented during Week 1 of the virtual AACR Annual Meeting 2021, held April 10-15.

“Patients with relapsed/refractory B-cell lymphoma tend to have a more aggressive disease trajectory and limited treatment options,” said presenting author Sanaz Ghafouri, MD, a fellow of hematology and oncology at University of California Los Angeles Medical Center. “Anti-CD19 CAR T-cell therapy has revolutionized the management of this disease in recent years, but it still has several limitations,” she noted, explaining that approximately half of patients relapse within six months of starting the treatment due to a lack of CAR T-cell persistence and/or downregulation of the target antigen, CD19, on the tumor. “The prognosis of patients who relapse after CAR T-cell therapy is dismal,” Ghafouri added.

Bispecific CAR T cells target two tumor antigens at once and have been explored as a strategy to reduce the risk of relapse. In this study, Ghafouri and colleagues evaluated the safety and efficacy of anti-CD19/CD20 bispecific CAR T-cells using naïve memory cells. “This is the first bispecific CAR T-cell therapy developed with naïve memory T cells to be tested in patients,” she said. “We hypothesized that this approach might increase CAR T-cell persistence and expansion in the patient, while limiting relapses due to loss of the tumor antigen.”

The presented analysis included five patients with B-cell malignancies that were positive for both CD19 and CD20 tumor antigen expression. Patients had received a median of four prior lines of therapy, and four patients had received bridging therapy. Naïve memory T cells were extracted from each patient, engineered to express an anti-CD19/CD20 CAR, expanded, and infused back into the patient at one of two different doses (either 5×10^7 cells or 2×10^8 cells).

After a median follow-up of 13 months, four of the five patients had ongoing complete remission. The patient whose cancer did not respond to treatment had early disease progression with CD19/CD20- negative disease by day 14 after infusion. Median progression-free and overall survival were not reached at the time of follow-up, and all responding patients continued to have

CAR T-cell persistence at the time of data cutoff.

No dose-limiting toxicities or immune effector cell-associated neurotoxicity were observed in any of the patients. All patients had grade 1 cytokine release syndrome, and all responding patients had ongoing B- cell aplasia at the time of data cutoff.

“Although long-term follow-up and analysis of additional patients are needed, our results indicate that bispecific anti-CD19/CD20 CAR in naïve memory T cells may be safe and effective in patients with relapsed or refractory B-cell lymphomas,” Ghafouri said. “Our findings raise the possibility of a lasting long-term remission with bispecific CAR T-cell therapy in patients with this aggressive disease.” Ghafouri and colleagues plan to expand their patient cohort and are also interested in evaluating the therapy in additional B-cell lymphoma subtypes.

Limitations of the study include the small sample size and lack of long-term follow-up.

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