CAR T-Cell Therapy Leads to Durable Remissions in Multiple Myeloma

BY MARK L. FUERST

CHICAGO—Chimeric antigen receptor (CAR) T-cell therapy appears to be an innovative and highly effective treatment for multiple myeloma. In an early clinical trial, virtually all patients showed clinical remission of multiple myeloma upon receiving immunotherapy with CAR T cells targeting B-cell maturation protein (BCMA), and with only mild side effects in most patients.

Although recent advances in chemotherapy have prolonged life expectancy in multiple myeloma, “this cancer remains incurable. It appears that with this novel immunotherapy there may be a chance for cure in multiple myeloma,” said study co-author Wanhong Zhao, MD, PhD, Associate Director of Hematology at The Second Affiliated Hospital of Xi’an Jiaotong University in Xi’an, China. He noted that patients will need to be followed longer for confirmation of the treatment’s effects.

Zhao presented the results of the study in a press briefing at the 2017 ASCO Annual Meeting, held June 2-6 (Abstract LBA3001).

Multiple myeloma is a serious cancer of the bone marrow that is still considered incurable because current therapies eventually lead to disease resistance or relapse. “Precision therapy like CAR T cells holds great promise for treating blood cancers, including multiple myeloma,” Zhao noted.

CAR T-Cell Therapy

A new type of CAR T-cell therapy was recently created that targets the cancer’s cell surface. The therapy is custom-made for each patient, with the patient’s own T cells collected, genetically reprogrammed in a laboratory, and injected back into the patient. The reprogramming involves inserting an artificially designed gene into the T-cell genome, which helps the genetically reprogrammed cells find and destroy cancer cells throughout the body.

In an early clinical trial, the CAR T-cell therapy led to quick and durable remission of relapsed or refractory multiple myeloma in the majority of patients, said Zhao. “This autologous cell therapy is a proprietary CAR design that is enabled to catch cancer cells with high avidity. It is a professional killer that never missed the target.”

CAR T-cell therapy targeting the B-cell biomarker CD19 is a novel immunotherapeutic approach for cancer treatment and has been clinically validated in the treatment of acute lymphoblastic leukemia and some types of lymphoma. Until now, there has been little success with CAR T-cell therapies targeting other biomarkers in other types of cancer. This is one of the first clinical trials of CAR T cells targeting BCMA, which was discovered to play a role in progression of multiple myeloma in 2004.

In a single-arm, ongoing phase I clinical trial, Zhao reported the results of the first 35 patients with relapsed or treatment-resistant multiple myeloma. The first signs of treatment efficacy appeared as early as 10 days after initial injection of CAR T cells. Patients received three split doses of cells over a week.

The objective response rate was 100 percent, and 33 (94%) patients had clinical remission of myeloma within 2 months of receiving CAR T cells. Of the 19 patients who have been followed for more than 4 months, 14 have reached stringent complete response (sCR) criteria, one patient has reached partial response, and four patients have achieved very good partial response (VGPR).

There has been only a single case of disease progression from VGPR, with an extramedullary lesion reappearing 3 months. There has not been a single case of relapse among patients who reached sCR criteria. The five patients who have been followed for 12-14 months all remain in sCR and are free of minimal residual disease as well, Zhao reported.

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This CAR T-cell technology “exerts quick and reproducible therapeutic effects in refractory and relapsed multiple myeloma patients. More than 12 months follow-up of early patients shows durable and sCR, which raises hopes of cure,” Zhao explained.

Safety Profile

Cytokine release syndrome (CRS), a common and potentially dangerous side effect of CAR T-cell therapy, occurred in 85 percent of patients, but was only transient. The majority of the patients experienced mild or manageable CRS, and six patients were even free of diagnosable CRS.

CRS is associated with symptoms such as fever, low blood pressure, difficulty breathing, and problems with multiple organs. Only two patients experienced severe grade 3 CRS and recovered upon receiving tocilizumab. No patients experienced neurologic side effects, another common and serious complication from CAR T-cell therapy.

“The technology not only demonstrated outstanding efficacy, but also suggests a great safety profile,” said Zhao.

Ongoing Research

The researchers plan to enroll 100 patients in this clinical trial at four participating hospitals in China. “In early 2018, we also plan to launch a similar clinical trial in the U.S. Looking ahead, we would also like to explore whether BCMA CAR T-cell therapy benefits patients who are newly diagnosed with multiple myeloma,” said Zhao.

While it’s still early, these data are a strong sign that CAR T-cell therapy can send multiple myeloma into remission. It’s rare to see such high response rates, especially for a hard-to-treat cancer,” ASCO Expert Michael S. Sabel, MD, Chief, Division of Surgical Oncology at the University of Michigan Health Systems in Ann Arbor, concluded.

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Mark L. Fuerst is a contributing writer.