Experimental CAR-T Therapy Shows Promise for Mantle Cell Lymphoma

KTE-X19 led to durable remission in a majority of study participants.

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KTE-X19, an experimental CAR-T therapy, could boost the prospects of people with relapsed or refractory mantle cell lymphoma whose condition has worsened despite targeted therapy, according to a study in The New England Journal of Medicine.

“Our study demonstrated significant and durable clinical benefit for patients with relapsed or refractory mantle cell lymphoma for which there are no curative treatment options,” Michael Wang, MD, of MD Anderson Cancer Center in Houston, said when he presented the findings at last year’s American Society of Hematology Annual Meeting.

Mantle cell lymphoma (MCL) is a form of non-Hodgkin lymphoma. It represents up to 10% of all non-Hodgkin lymphomas, in the United States. Typically, at the time of its diagnosis, MCL has spread to the lymph nodes, bone marrow and other organs. In many people, the lymphoma is refractory (nonresponsive) or relapses following a period of remission. Existing treatment is usually not effective—or only briefly so—in people with refractory or relapsed MCL.

Chimeric antigen receptor T-cell therapy—better known as CAR-T—involves removing a sample of a patient’s white blood cells, reprogramming the T cells to attack their cancer, manufacturing a large number of these altered cells and infusing them back into the body. KTE-X19 targets the CD19 protein on malignant B cells. Before reinfusion, conditioning chemotherapy is used to kill cancerous B cells and make room for the new ones.

Enrollment in the Phase II ZUMA-2 trial included 74 participants with relapsed or refractory MCL. They had previously been treated with chemotherapy, an anti-CD20 monoclonal antibody drug and a BTK inhibitor, either Calquence (acalabrutinib) or Imbruvica (ibrutinib).

Customized KTE-X19 was manufactured for 71 people and administered to 68.

The overall response rate, meaning complete or partial remission, was 93%. Included were 67% with complete responses. On the heels of approximately a year of follow-up, 57% were still in remission. At 12 months, the estimated progression-free survival and overall survival rates were 61% and 83%, respectively.

Generally, treatment was safe. However, among the most common severe—at least Grade 3—adverse events were low blood cell counts stemming from the conditioning chemotherapy.

A strong immune reaction, cytokine release syndrome (CRS), can be triggered by introducing engineered T cells. In this study, 15% of participants experienced Grade 3 or higher CRS. Low blood pressure, low oxygen levels and fever were among the symptoms. Further, 31% developed Grade 3 or 4 neurological side effects, including encephalopathy, confusion and tremors. CRS and neurotoxicity were effectively managed with steroids or the immunosuppressive drug Actemra (tocilizumab). There were no deaths due to these side effects.

In a majority of patients with relapsed or refractory mantle cell lymphoma, KTE-X19 induced durable remission, the study authors concluded. However, in some cases, the treatment led to serious and life-threatening side effects consistent with those reported for other CAR-T therapies.

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