CAR-T Therapies Show Promise for More Blood Cancers

Customized treatments demonstrate good response rates for mantle cell lymphoma and chronic lymphocytic leukemia.

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Experimental CAR-T therapies led to high overall response rates in people with mantle cell lymphoma and chronic lymphocytic leukemia, according to studies presented at the recent American Society of Hematology (ASH) Annual Meeting in Orlando.

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 the altered cells in a laboratory and infusing them back into the body.

Two CAR-T therapies are currently approved, Novartis's Kymriah (tisagenlecleucel) for children with acute lymphoblastic leukemia and both Kymriah and Gilead Sciences/Kite's Yescarta (axicabtagene ciloleucel) for adults with large B-cell lymphoma. Other experimental CAR-T therapies are being studied for additional blood cancers, including multiple myeloma, mantle cell lymphoma and chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL).

KTE-X19 for Mantel Cell Lymphoma

Michael Wang, MD, of MD Anderson Cancer Center in Houston, presented findings from a Phase II clinical trial of Gilead/Kite's KTE-X19 for mantle cell lymphoma, a rare form of non-Hodgkin lymphoma that involves overgrowth of abnormal B cells in lymph nodes. Like Yescarta, KTE-X19 targets the CD19 protein on B cells, but the manufacturing process includes T-cell selection and lymphocyte enrichment.

The ZUMA-2 study included 74 adults with relapsed or refractory (nonresponsive) mantle cell lymphoma who had previously tried up to five prior therapies. They had a sample of their T cells collected and modified, received strong conditioning chemotherapy to kill off some of their existing immune cells to make room for the new ones and received a single infusion of the genetically engineered cells. Five people ended up not receiving KTE-X19 because of manufacturing failures or death due to progressive disease.

Wang presented results for the first 60 treated participants. Most were men, and the median age was 65. More than 80% had Stage IV disease, and over half had bone marrow involvement.

The overall response rate, meaning complete or partial remission, was 93%, including 67% with complete responses. After about a year of follow-up, 57% had ongoing responses. Among the first 28 treated patients, who were followed for at least two years, 43% were remained in remission without further treatment. The estimated one-year progression-free survival rate was 61%, and the estimated overall survival rate was 83%.

The treatment was generally safe. The most common serious (Grade 3 or higher) adverse events were low blood cell counts due to the conditioning chemotherapy. Introducing engineered T cells can trigger a strong immune reaction known as cytokine release syndrome (CRS). In this study, 15% of participants experienced Grade 3 or higher CRS, with symptoms including low blood pressure, low oxygen levels and fever; 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) and led to no deaths.

“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,” Wang said in an MD Anderson press release.

Based on these results, Kite recently submitted a biologics license application to the Food and Drug Administration for KTE-X19 for mantle cell lymphoma. KTE-X19 is also being evaluated for acute lymphoblastic leukemia and chronic lymphocytic leukemia.

Liso-Cel for CLL

Tanya Siddiqi, MD, of City of Hope National Medical Center in Duarte, California, presented updated results from the Phase I/II TRANSCEND CLL 004 study, evaluating Bristol-Myers Squibb’s lisocabtagene maraleucel (liso-cel) in previously treated people with chronic lymphocytic leukemia or small lymphocytic lymphoma. Liso-cel, which also targets CD19, contains equal proportions of modified CD4 helper T cells and CD8 killer T cells.

At least year’s ASH meeting, Siddiqi reported early findings from the first group of 16 treated patients. The overall response rate was 81%, including 43% with complete responses. At 30 days after the CAR-T infusion, 75% showed complete or partial responses. Of those evaluated for minimal residual disease, 73% had no remaining evidence of cancer in their blood or bone marrow.

This year, she reported longer-term findings for 22 evaluable participants. Just over half were women, and the median age was 65. More that 80% had high-risk disease, and they had received a median of five prior therapies.

After a median 11 months of follow-up, the overall response rate was 82%, including 46% with complete responses. Among the nine patients who had progressed despite taking both Imbruvica (ibrutinib) and Venclexta (venetoclax), the overall response rate was 89% and the complete response rate was 67%. Responses deepened over time, with some partial responders going on to achieve complete response with longer follow-up.

Among 20 participants evaluated for minimal residual disease, 75% had undetectable cancer in their blood and 65% had no remaining cancer in their bone marrow. These figures were even higher (88% and 75%) in the subgroup of people who did not respond to Imbruvica and Venclexta.

Here too, the most common serious adverse events were blood cell deficiencies due to the conditioning chemotherapy. In this study, 9% of participants developed Grade 3 CRS and 22% had Grade 3 or higher neurological toxicity. Again, these side effects were manageable and resulted in no deaths.

Liso-cel is also being evaluated for relapsed or refractory large B-cell non-Hodgkin lymphoma. Other researchers at ASH reported high response rates and acceptable safety for this indication, including for people being treated as outpatients, suggesting this CAR-T therapy may not need to be administered in a hospital.

Click here to read the KTE-X19 study abstract.

Click here to read the liso-cel study abstract.

Click here to learn more about the different types of blood cancer.

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