FDA Approves Second CAR-T Therapy for Multiple Myeloma

98% of people who received the customized immunotherapy responded to the one-time treatment.

March 1, 2022 By Liz Highleyman

On February 28, the Food and Drug Administration (FDA) approved Carvykti (ciltacabtagene autoleucel, or cilta-cel), a new CAR-T therapy for the treatment of adults with relapsed or refractory multiple myeloma who have tried at least four previous lines of therapy.

The "living drug" reprograms a patient's own T cells to fight cancer. In the CARTITUDE-1 trial, almost all heavily pretreated patients with recurrent multiple myeloma who received a single infusion of Carvykti experienced remission, including 78% with no signs of remaining cancer.

> Overall my impression is that this is a landmark approval. This CAR-T product was developed in China. @LegendBiotech
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> People were astounded by the 100% response rate when it was first reported in the US. The results held out on confirmatory studies. Now we have approval. Great.
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> — Vincent Rajkumar (@VincentRK) March 1, 2022

Multiple myeloma involves uncontrolled growth of plasma cells, which give rise to antibody-producing B-cells. These malignant cells multiply in the bone marrow, where they can crowd out

normal blood-producing cells and generate abnormal antibody fragments, leading to increased risk of infection, bone fractures and kidney damage.

Chimeric antigen receptor T-cell therapy—better known as CAR-T—involves removing a sample of a patient's white blood cells, genetically modifying the T cells to recognize and attack their cancer, manufacturing a large number of the modified cells and infusing them back into the body.

Carvykti T cells carry synthetic receptors that target B-cell maturation antigen (BCMA), a protein on plasma cells. Last April, the FDA approved Abecma (idecabtagene vicleucel, or ide-cel), the first CAR-T therapy for multiple myeloma, which also targets BCMA. Four other approved CAR-T therapies target the CD19 protein on B cells that grow out of control in people with leukemia and lymphoma.

Carvykti (formerly known as JNJ-4528 and LCAR-B38M) was initially developed by the Chinese company Legend Biotech and was licensed to Janssen; the companies will jointly market the new therapy in the United States. In November, the FDA requested more time to review Carvykti study data, ultimately deciding that it measured up.

The Phase Ib/II CARTITUDE-1 trial (NCT03548207) enrolled adults with relapsed or refractory multiple myeloma who had tried a median of six prior therapies. Multiple myeloma is treated with medications including immunomodulators, proteasome inhibitors and CD38-blocking monoclonal antibodies, typically in various combinations. These often lead to remission, but they can stop working, and relapse is common.

A total of 97 participants received a single infusion of Carvykti after undergoing conditioning chemotherapy to kill off their existing immune cells and make room for the new ones. This study did not have a control group to compare Carvykti to other therapies, but such trials are underway, enrolling people with less prior treatment or newly diagnosed disease.

Interim results from the ongoing trial were initially reported at the 2019 American Society of Hematology (ASH) Annual Meeting, with follow-up presented at last year's ASH conference. Measuring response to multiple myeloma treatment is complex and continues to evolve as new tests make it possible to detect an ever-smaller number of residual cancer cells.

In the latest analysis, 98% of participants responded to Carvykti, including 78% with a stringent complete response, meaning no remaining signs or symptoms of disease according to imaging and other tests. An addition 12% of patients achieved a very good partial response and 3% achieved a partial response. What's more, 92% of evaluable patients achieved minimal residual disease (MRD) negativity, another measure indicating no detectable remaining cancer cells.

The one-time treatment was durable, with a median duration of response of 21.8 months. And responses appeared to deepen over time, with 83% achieving a stringent complete response after a median 22 months of follow-up. The two-year progression-free survival rate was 61%, and the overall survival rate was 74%. Among the subset of people with MRD negativity, the respective survival rates were 91% and 100%.

“The responses in the CARTITUDE-1 study showed durability over time and resulted in the majority of heavily pretreated patients achieving deep responses after 18-month follow-up,” trial investigator Sundar Jagannath, MD, of the Tisch Cancer Institute at the Icahn School of Medicine at Mount Sinai said in a press release. “The approval of cilta-cel provides physicians an immunotherapy treatment option that offers patients an opportunity to be free from anti-myeloma therapies for a period of time.”

CAR-T therapy can cause serious side effects. Unleashing genetically modified T cells can trigger a potentially life-threatening immune reaction known as cytokine release syndrome (CRS), which can lead to fever and chills, falling blood pressure, organ failure and neurologic toxicity. While almost all trial participants patients experienced CRS, lasting a median of four days, few had severe cases; about 10% experienced severe neurotoxicity.

In addition to CRS, common adverse reactions in people treated with Carvykti include fever, chills, headache, fatigue, low blood pressure, muscle and bone pain, diarrhea, nausea and laboratory abnormalities. The treatment process depletes white blood cells (neutropenia), red blood cells (anemia) and platelets (thrombocytopenia), which can lead to infections, fatigue and easy bleeding. The Carvytki label includes warnings about CRS, neurologic toxicity, hypersensitivity reactions, Parkinsonism and Guillain-Barré syndrome, macrophage activation syndrome and prolonged low blood cell counts. It is available only through a restricted program under a Risk Evaluation and Mitigation Strategy.

Carvykti will be priced at $465,000 for the one-time treatment, Endpoints News reported. Janssen and Legend Biotech said that they will activate a limited network of certified treatment centers as they works to scale its production capacity and increase the availability of Carvykti throughout the United States in 2022 and beyond.

Click here for full prescribing information for Carvykti.
Click here to learn more about multiple myeloma.
Click here for more news about CAR-T therapy.
