FDA Approves New CAR-T Therapy for Adults With Acute Leukemia

About 40% of ALL patients who received Aucatzyl immunotherapy, made from their own T cells, experienced complete remission within three months.

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On November 8, the Food and Drug Administration (FDA) approved Aucatzyl (obecabtagene autoleucel, or obe-cel), a CAR-T therapy for previously treated adults with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (B-ALL). Thanks to its more tolerable safety profile, the FDA did not require a Risk Evaluation Mitigation Strategy (REMS).

The approval is supported by results from the FELIX study, which showed that about 40% patients treated with two infusions of modified T cells achieved a complete response within three months, and about 60% did so at some point during the trial.

“Adult ALL is an extremely aggressive cancer, and there is a high unmet medical need that exists in the treatment of patients with this disease once they relapse, where historically they suffer from poor outcomes,” U.S. lead investigator Elias Jabbour, MD, of the University of Texas MD Anderson Cancer Center, said in a news release. “This milestone approval, based on the demonstrated clinical benefit of Aucatzyl, brings new hope for adult patients with relapsed/refractory B-ALL.”

Aucatzyl, from Autolus Therapeutics, targets the CD19 protein on B cells that grow out of control in several types of leukemia and lymphoma. ALL is rapidly progressing blood cancer that originates in the bone marrow and leads to production of immature white blood cells. ALL is the most common type of cancer in children, but it can also occur in adults. Treatment typically involves chemotherapy and targeted therapy and may also include radiation or a stem cell transplant. Adults who do not respond or relapse after standard treatment have poor survival.

Aucatzyl is a type of immunotherapy that reprograms a patient’s own T cells to fight cancer. Chimeric antigen receptor T-cell therapy—better known as CAR-T—involves removing a sample of a patient’s white blood cells, genetically modifying T cells with a receptor that recognizes their cancer, manufacturing a large number of the engineered cells in a laboratory and infusing them back into the body. Aucatzyl was designed to minimize excessive activation of the reprogrammed T cells in an effort to reduce side effects.

The Phase Ib/II FELIX trial (NCT04404660) enrolled adults with relapsed or refractory CD19-positive B-cell ALL. They had relapsed after a remission lasting a year or less, relapsed or were nonresponsive following two or more prior lines of systemic therapy or relapsed three or more months after an allogeneic donor stem cell transplant. They first received strong chemotherapy to kill off malignant blood cells and then were treated with two infusions of modified T cells 10 days apart.

Among the 65 evaluable patients, 42% achieved complete remission within three months, with a median response duration of 14.1 months. Nearly two-thirds (63%) achieved overall complete remission at any time during the trial, including 12% who experienced complete remission with incomplete hematologic recovery.

Aucatzyl was generally safe, but side effects were common. The most frequently reported adverse reactions included infections, fever, muscle and bone pain, diarrhea, neutropenia (low white blood cell count), fatigue, headache and hemorrhage. Introducing engineered T cells can trigger a strong immune reaction known as cytokine release syndrome (CRS), which can lead to fever and chills, falling blood pressure and organ failure. Three quarters of patients experienced CRS, but just 3% had severe (Grade 3 or higher) symptoms. About two thirds developed neurologic toxicity, including 12% with severe cases.

Unlike previously approved CAR-T therapies, such as Gilead Sciences' Tecartus (brexucabtagene autoleucel), the FDA did not require a REMS for Aucatzyl, which will simplify treatment. Moreover, it was approved for adults of all ages, unlike Novartis' Kymriah (tisagenlecleucel), which is approved for ALL patients up to age 25.

"Based on the experience in the FELIX trial Aucatzyl is highly active and can be well managed, offering an attractive risk benefit profile for B-ALL patients," said study lead investigator Claire Roddie, MD, PhD, of University College London Cancer Institute. "In the FELIX trial, Aucatzyl has shown long term persistence and deep responses which we believe are critical for long term remissions in B-ALL."

Aucatzyl will be manufactured at Autolus' commercial manufacturing site in the United Kingdom and exported to patients in the United States. The company said it is working with existing treatment centers to make the treatment commercially available in the U.S. The initial delivery turnaround time is 16 days, and the list price will be $525,000, Fierce Pharma reported.

Click here for full prescribing information for Aucatzyl.
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