FDA Approves First T-Cell Receptor Gene Therapy for Solid Tumors

Tecelra, for the treatment of synovial sarcoma, is the latest novel type of immunotherapy to win approval.

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On August 2, the Food and Drug Administration (FDA) granted accelerated approval of Tecelra (afamitresgene autoleucel, or afami-cel), the first T-cell receptor therapy for solid tumors, for people with inoperable or metastatic synovial sarcoma.

Synovial sarcoma is a rare type of cancer in which malignant cells form tumors in soft tissues, often in the extremities. It is most common among men in their thirties or younger. Treatment typically involves surgery to remove the tumor and may also include radiation or chemotherapy, especially if it spreads beyond its original location.

"Potentially life-threatening cancers such as synovial sarcoma continue to have a devastating impact on individuals, especially those for whom standard treatments have limited efficacy due to tumor growth and progression," Peter Marks, MD, PhD, director of the FDA's Center for Biologics Evaluation and Research, said in a news release. "The approval of this state-of-the-art immunotherapy technology provides a critical new option for a patient population in need and demonstrates the FDA's dedication to the advancement of beneficial cancer treatments."

Tecelra, from Adaptimmune, is a gene therapy created from patient's own T cells. A sample of cells is removed and genetically modified to express a natural T-cell receptor that targets MAGE-A4, an antigen expressed on synovial carcinoma cells. This approach is similar to CAR-T therapy, but existing CAR-Ts, which work well for blood cancers such as leukemia and lymphoma, have had less success against solid tumors. Tecelra is the first FDA-approved engineered T cell receptor therapy and the first new treatment for synovial sarcoma in more than a decade.

Tecelra is one of three new types of cancer immunotherapy approved this year. In February, the FDA approved Amtagvi (lifileucel), the first tumor-infiltrating lymphocyte therapy, for people with advanced melanoma. In April, the agency approved Anktiva (nogapendekin alfa inbakicept), a novel interleukin 15 receptor agonist that promotes the activity of natural killer cells and T cells, for patients with early bladder cancer.

Tecelra was approved for adults with unresectable or metastatic synovial sarcoma that expresses

MAGE-A4 who test positive for specific HLA antigens (A*02:01P, A*02:02P, A*02:03P or A*02:06P) and have previously received chemotherapy. Treatment involves strong conditioning chemotherapy to eliminate existing T cells followed by a single infusion of the modified cells.

The accelerated approval is supported by results from the Phase II SPEARHEAD-1 study (NCT04044768), an open label clinical trial that included 44 treated patients. As reported in The Lancet, the overall response rate was 43.2%, including 4.5% with complete responses. The median duration of response was six months, and among responders, 39% were still responding a year later.

Tecelra was generally safe but side effects were common. The most frequently reported adverse reactions include nausea, vomiting, decreased appetite, diarrhea, constipation, fatigue, fever, infections, shortness of breath, abdominal pain, back pain, non-cardiac chest pain, rapid heartbeat and swelling. The conditioning chemotherapy can cause blood cell deficiencies. T-cell therapies can cause cytokine release syndrome due to an aggressive immune response, with symptoms including excessive inflammation and organ failure. Other severe side effects may include neurological toxicity and hypersensitivity reactions.

Tecelra "is significantly different than the current standards of care for advanced synovial sarcoma," SPEARHEAD-1 principal investigator Sandra D'Angelo, MD, of Memorial Sloan Kettering Cancer Center, said in an Adaptimmune press release. "This approval represents a much-needed new option for people diagnosed with this sarcoma and an important milestone for the use of cell therapies in solid tumor cancers."

"For decades, therapeutic options for people diagnosed with synovial sarcoma have been limited. With a current five-year survival rate as low as 36%, and for those with metastatic disease at diagnosis, as low as 20%, it is long past time that synovial sarcoma patients have expanded treatment options," added Brandi Felser, chief executive officer of the Sarcoma Foundation of America. "Since one third of patients are diagnosed under age 30, improved outcomes can have a tremendous impact. Today, there is a renewed sense of hope for this patient community."

Tecelra is priced at $727,000 for the one-time treatment. Adaptimmune expects to have at least six to ten authorized treatment centers up and running this year and approximately 30 centers within the first two years. The SURPASS trial (NCT04044859) is evaluating the company's next-generation T-cell receptor therapy, ADP-A2M4CD8, for other solid tumors including endometrial, esophageal, ovarian and non-small cell lung cancers.

Therapies that receive FDA accelerated approval are expected to undergo further testing in larger trials to confirm that they offer clinical benefits—such as improved survival—and the agency can rescind approval if they fail to measure up.

Click here for full prescribing information for Tecelra.

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