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IN BRIEF

Afamitresgene Autoleucel *(Tecelra)* for Synovial Sarcoma

Afamitresgene autoleucel (*Tecelra* – Adaptimmune), a melanoma-associated antigen A4 (MAGE-A4)-directed genetically modified autologous T-cell immunotherapy, has received accelerated approval from the FDA for one-time treatment of adults with unresectable or metastatic synovial sarcoma who received prior chemotherapy and are HLA-A*02:01P, -A*02:02P, -A*02:03P, or -A*02:06P positive and whose tumor expresses the MAGE-A4 antigen. It is the first gene therapy to be approved in the US for treatment of synovial sarcoma. Accelerated approval of the immunotherapy was based on the overall response rate and duration of response.

Pronunciation Key
Afamitresgene autoleucel: af' am it ras jeen au toe loo' sel
***Tecelra*:** te cell' ra

Key Points: Afamitresgene Autoleucel *(Tecelra)*

- **Description:** A melanoma-associated antigen A4 (MAGE-A4)-directed genetically modified autologous T-cell immunotherapy.
- **Indication:** Treatment of adults with unresectable or metastatic synovial sarcoma who received prior chemotherapy and are HLA-A*02:01P, -A*02:02P, -A*02:03P, or -A*02:06P positive and whose tumor expresses the MAGE-A4 antigen.
- **Efficacy:** A single infusion of the immunotherapy produced an overall response rate of 39%.
- **Adverse Effects:** Cytokine release syndrome, immune effector cell-associated neurotoxicity, prolonged severe cytopenias, severe infection, and secondary malignancies can occur.
- **Dosage:** A single IV infusion of 2.68 x 10^9 to 10 x 10^9 MAGE-A4 TCR positive T cells.
- **Cost:** One dose costs $727,000.
- **Conclusion:** About 40% of patients with previously treated unresectable or metastatic synovial sarcoma who received a single infusion of *Tecelra* achieved a response.

THE PRODUCT — *Tecelra* is prepared from autologous peripheral blood mononuclear cells obtained by leukapheresis. The cells are sent to a commercial laboratory where they are enriched for T cells and then transduced with a replication-incompetent lentiviral vector containing the MAGE-A4 TCR transgene. *Tecelra* is formulated as a cell suspension containing 2.68 x 10^9 to 10 x 10^9 MAGE-A4 TCR positive T cells. *Tecelra* contains dimethyl sulfoxide (DMSO), which can cause serious hypersensitivity reactions.

MECHANISM OF ACTION — MAGE-A4 peptide is an intracellular cancer-testis antigen that is expressed in synovial sarcoma. The autologous T-cell immunotherapy recognizes an HLA-A*02 restricted MAGE-A4 peptide expressed on the cell surface. Activation of *Tecelra* results in T cell proliferation, cytokine secretion, and death of MAGE-A4/HLA-A*02-expressing synovial sarcoma cells.

CLINICAL STUDIES — FDA approval of afamitresgene autoleucel was based on the results of an open-label trial (SPEARHEAD-1) in 44 HLA-A*02:01-03 and 06 allele-positive patients with inoperable or metastatic synovial sarcoma who received prior systemic chemotherapy (doxorubicin and/or ifosfamide) and whose tumor expressed the MAGE-A4 antigen. All patients received a single infusion of afamitresgene autoleucel. After a median follow-up of 32.6 months, the overall response rate was 39%.[1]

ADVERSE EFFECTS — The *Tecelra* label includes a boxed warning about the risk of cytokine release syndrome (CRS), which can cause hypotension, pulmonary edema, coagulopathy, multiorgan failure, and death. Nausea, vomiting, fatigue, pyrexia, constipation, dyspnea, abdominal pain, decreased appetite, tachycardia, back pain, hypotension, diarrhea, and edema can occur. Immune effector cell-associated neurotoxicity syndrome (ICANS),

prolonged severe cytopenias, severe infection, and secondary malignancies have been reported. Patients should avoid driving or engaging in hazardous occupations or activities for at least 4 weeks after receiving *Tecelra*. The immunotherapy is contraindicated in patients who are heterozygous or homozygous for HLA-A*02:05P.

DOSAGE, ADMINISTRATION, AND COST — Patients should receive lymphodepleting chemotherapy (cyclophosphamide and fludarabine) starting the seventh day before the *Tecelra* infusion. Acetaminophen and an H_1-antihistamine should be given about 30-60 minutes before the *Tecelra* infusion. Administration of a granulocyte-colony stimulating factor (G-CSF) can be considered for patients with neutropenia. Patients should be monitored at the treatment facility for at least 7 days after receiving *Tecelra* and stay near the treatment facility for at least 4 weeks. One dose of *Tecelra* costs $727,000.[2] ■

1. SP D'Angelo et al. Afamitresgene autoleucel for advanced synovial sarcoma and myxoid round cell liposarcoma (SPEARHEAD-1): an international, open-label, phase 2 trial. Lancet 2024; 403:1460.
2. Approximate WAC. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. September 5, 2024. Reprinted with permission by First Databank, Inc. All rights reserved. ©2023. www.fdbhealth.com/policies/drug-pricing-policy.