Tecelra® (afamitresgene autoleucel) – New orphan drug approval

- On August 1, 2024, Adaptimmune Therapeutics announced the FDA approval of Tecelra (afamitresgene autoleucel), for the treatment of adults with unresectable or metastatic synovial sarcoma who have received prior chemotherapy, are HLA-A*02:01P, -A*02:02P, -A*02:03P, or -A*02:06P positive and whose tumor expresses the melanoma-associated antigen A4 (MAGE-A4) antigen as determined by FDA-approved or cleared companion diagnostic devices.
    - This indication is approved under accelerated approval based on overall response rate (ORR) and durability of response (DOR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.
- Synovial sarcoma is a rare form of cancer in which malignant cells develop and form a tumor in soft tissues of the body. Each year, synovial sarcoma impacts about 1,000 people in the U.S. and most often occurs in adult males in their 30s or younger.
    - Treatment typically involves surgery to remove the tumor and may also include radiotherapy and/or chemotherapy if the tumor is larger, returns after being removed or has spread beyond its original location.
- Tecelra is a T cell receptor (TCR) gene therapy. The product is an autologous T cell immunotherapy composed of a patient's own T cells. T cells in Tecelra are modified to express a TCR that targets MAGE-A4, an antigen (substance that normally triggers your immune system) expressed by cancer cells in synovial sarcoma.
    - The product is administered as a single intravenous (IV) dose.
- The efficacy of Tecelra was established in a single-arm, open-label study in patients with HLA-A*02:01P, HLA-A*02:02P, HLA-A*02:03P, and HLA-A*02:06P allele positive with inoperable or metastatic synovial sarcoma who had received prior systemic therapy and whose tumor expressed the MAGE-A4 tumor antigen. There were 44 patients who received a single infusion of Tecelra. The major outcome measure was ORR. DOR was an additional outcome measure.
    - The ORR was 43.2% (95% CI: 28.4, 59.0).
    - The median DOR was 6.0 months (95% CI: 4.6, not reached).
- Tecelra carries a boxed warning for cytokine release syndrome (CRS).
- Tecelra is contraindicated in patients who are heterozygous or homozygous for HLAA*02:05P.
- Additional warnings and precautions for Tecelra include immune effector cell-associated neurotoxicity syndrome; prolonged severe cytopenia; infections; secondary malignancies; hypersensitivity reactions; and potential for HIV nucleic acid test false-positive results.
- The most common adverse reactions (≥ 20%) with Tecelra use were CRS, nausea, vomiting, fatigue, infections, pyrexia, constipation, dyspnea, abdominal pain, non-cardiac chest pain, decreased appetite, tachycardia, back pain, hypotension, diarrhea, and edema. Grade 3 or 4 laboratory abnormalities (≥ 20%) were decreased lymphocyte count, decreased neutrophil count, decreased white cell blood count, decreased red blood cell, and decreased platelet count.

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- The recommended dose of Tecelra is between 2.68 x 10^9 to 10 x 10^9 MAGE-A4 TCR positive T cells administered as a single IV infusion.
    - Refer to the Tecelra drug label for complete dosing and administration recommendations.
- Adaptimmune Therapeutics' launch plans for Tecelra are pending.