The first and only FDA-approved T cell therapy for advanced melanoma

AMTAGVI is a tumor-derived autologous T cell immunotherapy indicated for the treatment of adult patients with unresectable or metastatic melanoma previously treated with a PD-1 blocking antibody, and if BRAF V600 mutation positive, a BRAF inhibitor with or without a MEK inhibitor.

This indication is approved under accelerated approval based on objective response rate (ORR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

WARNING: TREATMENT-RELATED MORTALITY, PROLONGED SEVERE CYTOPENIA, SEVERE INFECTION, CARDIOPULMONARY and RENAL IMPAIRMENT

- Monitor patients for prolonged severe cytopenia and monitor for internal organ hemorrhage
- Administer filgrastim or a biosimilar product to patients beginning Day 1 after AMTAGVI and continuing daily until the absolute neutrophil count (ANC) is greater than 1000 per mm^3 for 3 consecutive days, or per institutional standard
- Treat severe infections
- Monitor cardiopulmonary and renal functions throughout the treatment course

Administer in an inpatient hospital setting. An intensive care facility and specialists skilled in cardiopulmonary or intensive care medicine must be available.
medicine must be available.

Please see pages throughout and accompanying Full Prescribing Information, including BOXED WARNINGS, for additional Important Safety Information.

AMTAGVI™
(lifileucel) Suspension for IV infusion

Clinical Trial Experience

AMTAGVI (lifileucel) was evaluated in Study C-144-01, a global, multicenter, multicohort, open-label, single-arm clinical trial. Cohort 4 of Study C-144-01 enrolled patients with advanced melanoma who have previously been treated with at least one systemic therapy, including a PD-1 blocking antibody, and if BRAF V600 mutation positive, a BRAF inhibitor or BRAF inhibitor with MEK inhibitor.

The primary endpoint was IRC-assessed ORR by RECIST v1.1. Seventy-three patients received AMTAGVI (lifileucel), which was manufactured at an approved facility at the recommended dose. Supportive Pooled Data (n=153) includes Cohort 4 plus Cohort 2 in the C-144-01 study, which enrolled patients who met the same primary eligibility criteria.[1]

Cohort 4 Pivotal (n=73)	
ORR by IRC	31.5% (95% CI: 21.1, 43.4)[1]
mDOR	Not Reached* (range 1.4+, 26.3+)[1] Median follow up of 18.6 months

Supportive Pooled Data (n=153)	
ORR by IRC	31.4% (95% CI: 24.1, 39.4)[1]
mDOR	NR (range 1.4+, 45.0+)[1] Median follow up of 21.5 months

4-Year Pooled Analysis: mDOR Not Reached at 48.1 months (95% CI: 8.3, NR)[2]

The AMTAGVI (lifileucel) patient journey includes the following steps:

Step 1	Step 2	Step 3	Step 4
Tumor Tissue Procurement by Surgery	**Lymphodepletion†**	**AMTAGVI (lifileucel) Administration ‡**	**Short Course of High-Dose IL-2 Administration**

Note: Refer to full Prescribing Information for detailed information on dosing and administration of the treatment regimen. AMTAGVI (lifileucel) is a cell suspension for intravenous infusion. A single dose of AMTAGVI (lifileucel) contains 7.5 x 10^9 to 72.0 x 10^9 viable cells viable cells suspended in 1 to 4 patient-specific infusion bags.

Treatment-Related Mortality

AMTAGVI is associated with treatment-related mortality. In the clinical trial, the treatment-related mortality rate was 7.5% (N=160), including 2 deaths during the lymphodepleting period, 6 deaths within 30 days, and 4 deaths 38 to 150 days following AMTAGVI administration. Adverse reactions associated with these deaths included severe infections (sepsis, pneumonia and encephalitis), internal organ hemorrhage (abdominal hemorrhage and intracranial hemorrhage), acute renal failure, acute respiratory failure, cardiac arrythmia, extensive ascites and liver injury and bone marrow failure. Because clinical trials are conducted under widely varying conditions, treatment-related mortality rates observed in the clinical trials of a drug may not reflect the rates observed in practice.

* *Cohort 4 mDOR 95% CI: (4.1, NR)*
† *Administer a lymphodepleting chemotherapy regimen of cyclophosphamide 60 mg/kg intravenously with mesna daily for 2 days followed by fludarabine 25 mg/m^2 intravenously daily for 5 days before infusion of AMTAGVI.*
‡ *AMTAGVI should be administered in an inpatient hospital setting under the supervision of a physician experienced in the use of anticancer agents. An intensive care facility and specialists skilled in cardiopulmonary or intensive care medicine must be available. Beginning Day 1 after AMTAGVI administer filgrastim daily until the absolute neutrophil count (ANC) is greater than 1000 per mm^3 for 3 consecutive days, or per institutional standard. Administer prophylactic antimicrobials according to institutional guidelines.*

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About AMTAGVI (lifileucel)

AMTAGVI (lifileucel) is administered as part of a one time treatment regimen comprised of multiple steps (or components). A specimen of tumor is resected, then prosected (trimmed and fragmented), and shipped fresh to a centralized GMP facility. Iovance's manufacturing process grows T cells into the billions.[§] After manufacturing, AMTAGVI (lifileucel) is shipped to an Authorized Treatment Center (ATC) for administration to the patient. AMTAGVI (lifileucel) is infused as part of a treatment regimen that includes lymphodepletion, a one-time infusion of AMTAGVI (lifileucel) and a short course of high-dose IL-2. AMTAGVI (lifileucel) should be administered in an inpatient hospital setting under the supervision of a physician experienced in the use of anticancer agents. An intensive care facility and specialists skilled in cardiopulmonary or intensive care medicine must be available. Administer prophylactic antimicrobials according to institutional guidelines. For more information on dosing and administration, refer to the full prescribing information.

About the lymphodepletion prior to infusion of AMTAGVI (lifileucel)

A lymphodepletion regimen consisting of cyclophosphamide (60 mg/kg) once daily with mesna for 2 days followed by fludarabine (25 mg/m^2) once daily for 5 days is initiated prior to AMTAGVI (lifileucel) infusion.

About the administration of a short course of high-dose IL-2 after the infusion of AMTAGVI (lifileucel)

Within 3 to 24 hours of completing infusion of AMTAGVI (lifileucel), a short course of high-dose IL-2 is administered every 8 to 12 hours for up to 6 doses to support cell expansion *in vivo*. Administer in an inpatient hospital setting under the supervision of a physician experienced in the use of anticancer agents. An intensive care facility and specialists skilled in cardiopulmonary or intensive care medicine must be available.

Please be aware that dosing of IL-2, when administered after lifileucel, is different from the dosing as described in the aldesleukin (IL-2) U.S. Prescribing Information for its approved uses. For more information regarding IL-2 dosing and administration in the context of this regimen, please refer to the AMTAGVI (lifileucel) Prescribing Information.

Tumor Tissue Procurement Supplies (TTPS) Kit

Authorized Treatment Centers (ATCs) will receive an AMTAGVI (lifileucel) tumor tissue procurement supplies (TTPS) kit with reagents required for tumor procurement. The tumor tissue procurement supplies kit will be sent to the ATC prior to tumor procurement. The kit's components include the following reagants and cooler:

- Amphotericin B (antifungal)
- Gentamicin (antibiotic)
- HypoThermosol® transport bottle (preservation media)
- CredoCube™

IOVANCE Cares[1]

Reimbursement Support Information

IovanceCares™ offers reimbursement support including benefit investigation, prior authorization assistance, and denials appeal assistance upon approval to assist with timely access to AMTAGVI (lifileucel).

- Benefits Verification: assistance in obtaining patient benefits information from the primary and secondary payer
- Prior Authorization Support: assistance with Prior Authorization form and other communication with the payers
- Appeals: assistance with the appeals process with the payer(s), should the Prior Authorization be denied

For more information or support, contact IovanceCares at 1-833-400-4682

Prolonged Severe Cytopenia

Patients treated with AMTAGVI may exhibit Grade 3 or higher cytopenia for weeks or longer. Based on adverse event reporting, Grade ≥ 3 cytopenia or pancytopenia which did not resolve to ≤ Grade 2 or lasted beyond 30 days post AMTAGVI infusion occurred in 45.5% of melanoma patients who received AMTAGVI. Prolonged cytopenia included thrombocytopenia (30.1%), lymphopenia (19.9%), neutropenia (17.3%), leukopenia (14.7%) and pancytopenia (1.3%). Monitor blood counts after AMTAGVI infusion.

§ *A single dose of AMTAGVI (lifileucel) contains 7.5 x10^9 to 72.0 x10^9 viable cells suspended in 1 to 4 patient-specific infusion bags. For more information, see the full AMTAGVI (lifileucel) U.S. prescribing information.*

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References

1. AMTAGVI [package insert]. Iovance Biotherapeutics Inc., 2024.

2. Medina T, Chesney JA, Whitman E, et al. Long-term efficacy and safety of lifileucel tumor-infiltrating lymphocyte (TIL) cell therapy in patients with advanced melanoma: a 4-year analysis of the C-144-01 study. Poster presented at: Society for Immunotherapy of Cancer (SITC) Meeting; November 3-5, 2023; San Diego, CA

Acronyms

ORR, Objective Response Rate; IRC, Independent Review Committee; mDOR, Median Duration of Response; OS, Overall Survival; RECIST, Response Evaluation Criteria in Solid Tumors; CI, Confidence Interval; NR, Not Reached; IL-2, Interleukin-2; ATC, Authorized Treatment Center; TTPS, Tumor Tissue Procurement Supplies; FDA, U.S. Food & Drug Administration

Important Safety Information (ISI)

Internal Organ Hemorrhage

Patients treated with AMTAGVI may exhibit internal organ hemorrhage. Intraabdominal and intracranial hemorrhage can be life-threatening and have been associated with at least two deaths in patients who received AMTAGVI. Withhold or discontinue AMTAGVI infusion if internal organ hemorrhage is indicated, or if patient is deemed ineligible for IL-2 (aldesleukin) infusion. Patients with persistent or repeated thrombocytopenia after receiving AMTAGVI should not use anticoagulant(s) or must be under close monitoring if the patient must take an anticoagulant.

Severe Infection

Severe, life-threatening, or fatal infections occurred in patients after AMTAGVI infusion. Treatment-related infections (any severity) occurred in 26.9% of melanoma patients. Grade 3 or higher infections occurred in 13.5% of patients, including 10.9% of patients with infections of an unspecified pathogen and 3.8% of patients with infections of a specified pathogen.

Do not administer AMTAGVI to patients with clinically significant systemic infections. Monitor patients for signs and symptoms of infection before and after AMTAGVI infusion and treat appropriately. Administer prophylactic antimicrobials according to institutional guidelines.

Febrile neutropenia was observed in 46.8% of melanoma patients after AMTAGVI infusion. In the event of febrile neutropenia, evaluate for infection and manage with broad-spectrum antibiotics, fluids, and other supportive care as medically indicated.

Cardiac Disorder

Patients treated with AMTAGVI may exhibit cardiac disorder. Grade ≥ 3 cardiac disorders related to the AMTAGVI regimen occurred in 9.0% (14/156) of patients who received AMTAGVI including tachycardia, atrial fibrillation, arrhythmia, acute myocardial infarction, cardiac ventricular thrombosis, cardiomyopathy, QT-prolongation. Cardiac arrhythmia resulted in one death among melanoma patients who received AMTAGVI.

Monitor patients with signs and symptoms of cardiac disorder before and after AMTAGVI infusion. Withhold or discontinue AMTAGVI if severe cardiac disorder is indicated, or if patient is deemed ineligible for IL-2 (aldesleukin) infusion.

Respiratory Failure

Patients treated with AMTAGVI may develop worsened respiratory function which has been associated with deaths. Monitor patients with signs and symptoms of respiratory failure before and after AMTAGVI infusion. Withhold or discontinue AMTAGVI infusion if severe acute respiratory failure is indicated, or if patient is deemed ineligible for IL-2 (aldesleukin) infusion.

Acute Renal Failure

Patients treated with AMTAGVI may develop worsened renal function which has been associated with deaths. Monitor patients with signs and symptoms of acute renal failure before and after AMTAGVI infusion. Withhold or discontinue AMTAGVI if severe acute renal injury is indicated, or if patient is deemed ineligible for IL-2 (aldesleukin) infusion.

Hypersensitivity Reactions

Allergic reactions, including serious hypersensitivity (e.g. anaphylaxis), may occur with the infusion of AMTAGVI. Acute infusion reactions (within 1 day of infusion) may include fever, rigors or chills, tachycardia, rash, hypotension, dyspnea, cough, chest tightness, and wheezing. These events generally resolve on the same day of infusion. Monitor patients during and after infusion for signs and symptoms of a severe reaction and treat promptly.

Adverse Reactions

The most common (incidence of ≥ 20%) non-laboratory adverse reactions were chills, pyrexia, fatigue, tachycardia, diarrhea, febrile neutropenia, edema, rash, hypotension, alopecia, infection, hypoxia, and dyspnea. The most common Grade 3 or 4 laboratory abnormalities (incidence of at least 10%) were thrombocytopenia, neutropenia, anemia, leukopenia, lymphopenia, and hypophosphatemia.

Other adverse reactions that occurred in < 10% of patients included eye disorders, immune system disorders (infusion-related reactions, anaphylactic reaction, cytokine release syndrome), and vitiligo.

You may report side effects to Iovance at 1-833-400-4682, or to the FDA, at 1-800-FDA-1088 or at www.fda.gov/medwatch.

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