AMTAGVI (lifileucel) 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).

### Patient Selection Criteria
- Diagnosis of unresectable or metastatic melanoma
- Treated with a prior PD-1 blocking antibody, and if BRAF mutation positive, a BRAF +/-MEK inhibitor

### Additional Considerations for AMTAGVI*
- ECOG performance status of 0-1
- Slow to moderate speed of disease progression
- Overall physical fitness, including appropriateness to undergo lymphodepletion (LD) and IL-2, as part of a cell therapy regimen
- Study excluded patients with uncontrolled brain metastases

### 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

### Surgical Resection Considerations

#### Amount of Viable Tumor Tissue Needed
To generate lifileucel, at least one resectable lesion (or aggregate of lesions) with a minimum of 1.5 cm diameter up to 4 cm diameter is required. If the selected lesion is not at least 1.5 cm in diameter, other lesions can be added up to 4 cm in diameter total.\(^1\)

#### Tumor Site Selection
Lifileucel can be manufactured regardless of anatomic surgery site. Lesion origin of AMTAGVI products in the C-144-G1 trial were skin, lymph nodes, liver, lung, peritoneal, musculoskeletal, breast, and other anatomic sites including chest wall, abdominal wall, adrenal gland, abdominal-peritoneal, paraaortic, axillary, thoracic, back, supraclavicular, and soft tissue.\(^1\) When possible, nonvisceral lesions should be considered over visceral lesions. During surgery, consider selecting zones within the resected lesion that are more likely to be highly infiltrated with T cells.\(^2\)

#### Minimizing Contamination
Tumor tissue should be procured in an aseptic environment, targeting anatomic site(s) of low/minimum bioburden when possible.\(^3\) Every effort should be made to keep tumor tissue free from contamination.

#### Recommendations for Prosection
Transport media must be prepped in advance in an OR under a hood with aseptic conditions. Promptly transfer tumor tissue to a sterile surface in the OR/surgical suite for immediate processing. Trim the tumor tissue to remove extraneous non-tumor tissue; care should be taken to exclude hemorrhagic, fibrotic, and necrotic tissue.\(^4\)

Please refer to full prescribing information for additional information on AMTAGVI (lifileucel)

*Select eligibility criteria from C-144-G1 study\(^*\)

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Please see next page for additional Important Safety Information
Adverse Reactions

The most common (incidence of ≥ 20%) non-laboratory adverse reactions were chills, pyrexia, 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 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 vascular thrombosis, cardiomyopathy, QT-prolongation. Cardiac arrhythmia occurred in 1 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 acute 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 if severe acute respiratory failure is indicated, or if patient is deemed ineligible for IL-2 (aldesleukin) infusion.

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 3.6% 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. If the event of febrile neutropenia, evaluate for infection and manage with prophylactic antimicrobials and fever reducing agents. Infections occurred in 13.3% of patients who received AMTAGVI, 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. Withhold or discontinue AMTAGVI if severe acute respiratory failure is indicated, or if patient is deemed ineligible for IL-2 (aldesleukin) infusion.

Prolonged Severe Cytopenia

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 (9.9%), neutropenia (7.3%), leukopenia (14.7%) and pancytopenia (1.3%). Monitor blood counts after AMTAGVI infusion.

Severe Infection

for additional Important Safety Information. Please see accompanying Full Prescribing Information, including BOXED WARNINGS, or at www.fda.gov/medwatch. You may report side effects to Iovance at 1-833-400-4682, or to the FDA, at 1-800-FDA-1088.

References


Important Safety Information (continued)

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You may see accompanying Full Prescribing Information, including BOXED WARNINGS, for additional Important Safety Information.