GILEAD | Medical Information

Trodelvy® (sacituzumab govitecan-hziy) Monotherapy: Reports of ILD/Pneumonitis

This document is in response to your request for information regarding Trodelvy® (sacituzumab govitecan-hziy [SG]) and interstitial lung disease (ILD)/pneumonitis. Information summarized in this document includes data for SG monotherapy (10 mg/kg IV on Days 1 and 8 of a 21-day treatment cycles) from Phase 2 and 3 clinical studies that constitute the largest pooled safety population of SG.

Gilead continually assesses safety data from all sources for unidentified drug reactions and updates the product label information accordingly to reflect the safety profile of Trodelvy®. Because case reports of potential adverse reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish causal relationship to drug exposure. For this reason, Gilead does not provide information from post-marketing spontaneous reports. Due to the limitations in the interpretation of case reports, single case reports found in the literature are not included in this summary.

Some data may be outside of the US FDA-approved Prescribing Information. In providing this data, Gilead Sciences, Inc. is not making any representation as to its clinical relevance or to the use of any Gilead product(s). For information about the approved conditions of use of any Gilead drug product, please consult the FDA approved prescribing information.

The full indication, important safety information, and boxed warnings for neutropenia and diarrhea are available at:
https://www.gilead.com/-/media/files/pdfs/medicines/oncology/trodelvy/trodelvy_pi.pdf

Summary

Relevant Product Labeling[1]

ILD/pneumonitis are not listed as adverse reactions in the SG US FDA-approved Prescribing Information.

Periodic Safety Update Report[2]

As of 21 October 2024, approximately 4249 patients have received SG in clinical trials and in post authorization exposure, cumulative patient exposure to SG is estimated to be 54,075 patients. To date, our cumulative data do not support a causal role of SG in the development of ILD or pneumonitis. ILD is not listed as a Warning in the SG US FDA-approved Prescribing Information and there are no specific recommendations for monitoring for ILD.

Reports of ILD/Pneumonitis With SG Monotherapy

A pooled safety analysis examined exposure to SG 10 mg/kg IV as monotherapy in 1063 patients from 4 studies of multiple solid tumors (IMMU-132-01,[3] ASCENT,[4] TROPiCS-02,[5] and TROPHY-U-01[6,7]). These studies included patients with metastatic triple negative breast cancer (mTNBC), hormone receptor-positive/human epidermal growth factor receptor 2-negative metastatic breast cancer (HR+/HER2- mBC), and metastatic urothelial

cancer (mUC).[8] The median treatment duration of SG in this population was 4.1 (range: 0–63) months[1]; ILD and pneumonitis were not reported.[8]

In the Phase 3 TROPiCS-02 study in HR+/HER2- mBC (overall safety population [OSP], n=517), no ILD was reported in the SG arm.[5]

In the Phase 3 ASCENT study in mTNBC (OSP, n=482), 1 patient (0.4%) in the SG arm developed Grade 3 pneumonitis in the context of multiple confounding factors. The patient had a history of lung metastases and radiation-related fibrosis. The pneumonitis event occurred 14 days after the last dose of SG, and it resolved 7 weeks later.[9,10]

In the Phase 2 TROPHY-U-01 study in mUC, 1 patient in Cohort 1 (OSP, n=113) developed a Grade 2 treatment-related severe adverse event (SAE) of ILD that resolved after SG was discontinued.[2,6]

In the Phase 1/2 IMMU-132-01 study in metastatic epithelial cancers (OSP, n=495), 1 patient developed Grade 2 radiation pneumonitis that resolved with delay of the next SG dose and treatment with steroids.[3]

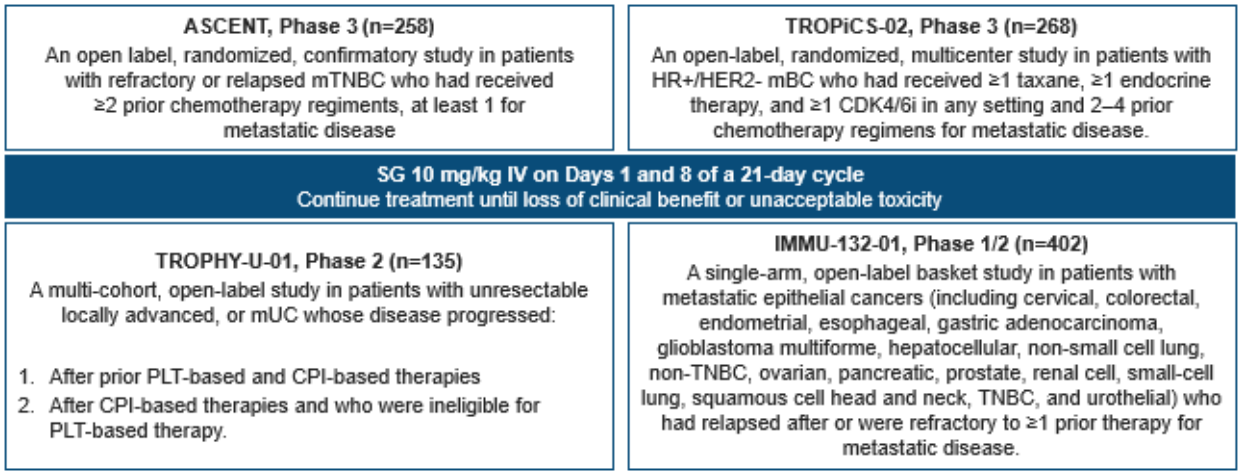
Reports of ILD/Pneumonitis With SG Monotherapy

Although ILD/pneumonitis are not listed as adverse reactions in the SG US FDA-approved Prescribing Information some treatment-emergent adverse events have been reported in the literature and are summarized below.

Pooled Safety Analysis

A pooled safety analysis (Figure 1) examined exposure to SG 10 mg/kg IV as monotherapy in 1063 patients from 4 studies of multiple solid tumors (IMMU-132-01,[3] ASCENT,[4] TROPiCS-02,[5] and TROPHY-U-01[6,7]). These studies included patients with mTNBC, HR+/HER2- mBC, and mUC.[8] The median treatment duration with SG in this population was 4.1 (range: 0–63) months[1]; ILD and pneumonitis were not reported.[8]

Figure 1. Pooled Clinical Studies[8]



Abbreviations: CKD4/6i, cyclin-dependent 4/6 inhibitor; CPI, checkpoint inhibitor; PLT=platinum; TNBC, triple-negative breast cancer.

TROPiCS-02 Study in HR+/HER- mBC[5]

The OSP included 517 patients (SG: 268; [treatment of physician's choice [TPC]: 249; [median age, 56 years]; 95% with visceral metastases) who received ≥1 dose of study treatment. Patients in the SG arm received a mean (range) of 8.2 (1–35) treatment cycles over a median (range) of 4.1 (0.03–24.2) months.

No ILD was reported in the SG arm.

ASCENT Study in mTNBC

The OSP included 482 patients (SG: 258; TPC: 224; [median age, 54 years]) who received ≥1 dose of study treatment. Patients in the SG treatment arm received a median (range) of 7 (1–33) treatment cycles over a median (range) of 4.4 (0.03–22.9) months.[9,10]

One patient (0.4%) in the SG arm developed Grade 3 pneumonitis.[2] The patient was a 52-year-old female with a past medical history of mTNBC with lung metastases, pneumothorax, left bronchial stenosis secondary to prior radiation, tumor-related left lung collapse, radiation-related fibrosis of the lung, and morbid obesity. Grade 3 pneumonitis occurred 14 days after her last dose of SG, approximately 7 months after the start of the study. CT scan findings included increased size of the known right upper lobe mass and new upper and lower lobe patchy ground glass opacities (probable infectious/inflammatory in the upper lung and hypo-ventilatory in the lower lung). The event was considered possibly related to SG by investigator assessment. SG was permanently discontinued; the patient was treated with antibiotics and IV steroids. Pneumonitis resolved 7 weeks after onset without sequelae.[9,10]

TROPHY-U-01 Study in mUC

An ongoing, global, open-label, multi-cohort, phase 2 study (NCT03547973) of SG in patients with unresectable locally advanced, or mUC.[6]

Cohort 1

The OSP included 113 patients with mUC that progressed on PLT-based chemotherapy and CPIs who were treated with SG 10 mg/kg IV on Days 1 and 8 of a 21-day cycle. The median age was 66 years, and 66% of patients had visceral disease. Patients received a median of 6 treatment cycles, over a median (range) of 3.7 (0–20) months.[6]

One patient developed Grade 2 ILD 19 days after enrollment.[2,6] The patient was a 76-year-old female with a past medical history of ischemic cardiomyopathy.[6] She discontinued avelumab 2 months prior to participation in the study.[2,6] The ILD was considered to be a treatment-related SAE that resulted in an interruption of SG therapy. SG was discontinued after Cycle 1 Day 8 due to progressive disease. The ILD resolved on Day 26.[2]

IMMU-132-01 Study in Metastatic Epithelial Cancers

During the dose-escalation phase of this study, SG was administered on Days 1 and 8 of 21-day cycle at doses of 8 (n=81), 10 (n=402), 12 (n=9), or 18 (n=3) mg/kg.[3]

The OSP included 495 patients (median age, 61 years) who received ≥1 dose of SG. Patients received a median (range) of 6 (1–73) SG treatment cycles, over a median (range) of 3.7 (0–55.2) months.[3]

One patient who was receiving 8 mg/kg of SG developed Grade 2 radiation pneumonitis.[2,3] The patient's medical history included mTNBC treated with palliative radiation therapy. The next dose of SG was delayed, the patient was hospitalized, and steroids were administered. The pneumonitis resolved, and the patient subsequently resumed treatment with SG.[3]

References

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3. Bardia A, Messersmith WA, Kio EA, et al. Sacituzumab govitecan, a Trop-2-directed antibody-drug conjugate, for patients with epithelial cancer: final safety and efficacy results from the phase I/II IMMU-132-01 basket trial. *Ann Oncol.* 2021;32(6):746-756.
4. Bardia A, Hurvitz SA, Tolaney SM, et al. Sacituzumab govitecan in metastatic triple-negative breast cancer. *N Engl J Med.* 2021;384(16):1529-1541.
5. Rugo HS, Bardia A, Marme F, et al. Sacituzumab govitecan in hormone receptor-positive/human epidermal growth factor receptor 2-negative metastatic breast cancer. *J Clin Oncol.* 2022;40(29):3365-3376.
6. Tagawa ST, Balar AV, Petrylak DP, et al. TROPHY-U-01: A phase II open-label study of sacituzumab govitecan in patients with metastatic urothelial carcinoma progressing after platinum-based chemotherapy and checkpoint inhibitors. *J Clin Oncol.* 2021;39(22):2474-2485.
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9. Rugo HS, Tolaney SM, Loirat D, et al. Safety analyses from the phase 3 ASCENT trial of sacituzumab govitecan in metastatic triple-negative breast cancer. *NPJ Breast Cancer.* 2022;98(8).
10. Bardia A, Hurvitz SA, Tolaney SM, et al. Sacituzumab govitecan in metastatic triple-negative breast cancer [Supplementary Appendix]. *N Engl J Med.* 2021;384(16):1529-1541.

Product Label

For the full indication, important safety information, and Boxed Warning(s), please refer to the Trodelvy US Prescribing Information available at: https://www.gilead.com/-/media/files/pdfs/medicines/oncology/trodelvy/trodelvy_pi.pdf.

Follow Up

For any additional questions, please contact Trodelvy Medical Information at:

☎1-888-983-4668 or www.askgileadmedical.com

Adverse Event Reporting

Please report all adverse events to:

Gilead Global Patient Safety ☎ 1-800-445-3235, option 3 or
https://www.gilead.com/utility/contact/report-an-adverse-event

FDA MedWatch Program by ☎ 1-800-FDA-1088 or ✉MedWatch, FDA, 5600 Fishers Ln, Rockville, MD 20852 or www.accessdata.fda.gov/scripts/medwatch

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