GILEAD | Medical Information

Trodelvy® (sacituzumab govitecan-hziy) Ocular Toxicity

This document is in response to your request for information regarding (sacituzumab govitecan-hziy [SG]) and ocular toxicity.

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 SG. 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 a causal relationship to drug exposure. For this reason, Gilead does not provide information from post-marketing spontaneous reports.

Information summarized in this document includes data for SG monotherapy (10 mg/kg IV on Days 1 and 8 of a 21-day treatment cycle) from phase 2 and 3 clinical studies that constitute the largest pooled safety population of SG.

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: www.gilead.com/-/media/files/pdfs/medicines/oncology/trodelvy/trodelvy_pi.

Summary

Relevant Product Labeling[1]

Prior to each dose of SG, premedication for prevention of infusion reactions is recommended. Premedicate with antipyretics, histamine 1 and histamine 2 blockers prior to infusion, and corticosteroids may be used for patients who had prior infusion reactions.

Please refer to the US FDA-approved prescribing information for complete product information, including guidance on dose modifications for adverse reactions.

Edema (including edema and peripheral, localized, and periorbital edema) is noted in the US Prescribing Information as a general disorder and administration site condition that occurred in ≥10% of patients with metastatic triple negative breast cancer (mTNBC) during the phase 1/2 basket trial (IMMU-132-01).

Incidence of Ocular Toxicity in SG Clinical Studies

A pooled safety analysis examined exposure to SG 10 mg/kg IV as monotherapy in 1063 patients from four studies of multiple epithelial tumors (IMMU-132-01,[2] ASCENT,[3] TROPiCS-02,[4] and TROPHY-U-01[5-7]). These studies included patients with 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 (range) duration of SG treatment in this population was 4.1 (0–63) months.[1] Ocular toxicity

was not among the any-grade or Grade ≥3 treatment-emergent adverse events (TEAEs) reported within the pooled analysis.[8]

- During the phase 3 ASCENT study in patients with mTNBC, treatment-related ocular toxicity of any grade was observed in 5% (n=12) of patients in the SG arm. No treatment-related ocular toxicity Grade >1 in severity was reported with SG use. In the chemotherapy treatment of physician's choice (TPC) arm, ocular toxicity of any grade was observed in 3% of patients (n=6), and no events of Grade >2 were reported.[3]
- During the phase 3 TROPiCS-02 study in patients with HR+/ HER2- mBC, adverse events (AEs) of ocular toxicity were not reported.[4,9]
- During the phase 2 TROPHY-U-01 study in patients with mUC, treatment-related ocular disorders of any grade were experienced by 4% of patients in Cohort 1. All occurrences of ocular toxicity were assessed as severity Grade ≤2. No ocular toxicity events were reported in Cohort 2.[5,13,14]
- During the phase 1/2 IMMU-132-01 basket study in patients with metastatic epithelial cancers, there were no reports of Grade >2 treatment-related ocular toxicity.[2]

Incidence of Ocular Toxicity in SG Clinical Studies

Pooled Safety Analysis

A pooled safety analysis (Figure 1) examined exposure to SG 10 mg/kg IV as monotherapy in 1063 patients from four studies of multiple epithelial tumors (IMMU-132-01,[2] ASCENT,[3] TROPiCS-02,[4] and TROPHY-U-01[5-7]). These studies included patients with mTNBC, HR+/HER2- mBC, and mUC.[8] The median (range) duration of SG treatment in this population was 4.1 (0–63) months.[1] Ocular toxicity was not among the most common any-grade (frequency ≥15%) or Grade ≥3 TEAEs (frequency ≥5%) reported in the pooled analysis.[8]

Figure 1. Pooled Clinical Studies[8]

ASCENT, Phase 3 (n=258) An open label, randomized, confirmatory study in patients with refractory or relapsed mTNBC who had received ≥2 prior chemotherapy regiments, at least 1 for metastatic disease	**TROPiCS-02, Phase 3 (n=268)** An open-label, randomized, multicenter study in patients with HR+/HER2- mBC who had received ≥1 taxane, ≥1 endocrine therapy, and ≥1 CDK4/6i in any setting and 2–4 prior chemotherapy regimens for metastatic disease.
SG 10 mg/kg IV on Days 1 and 8 of a 21-day cycle Continue treatment until loss of clinical benefit or unacceptable toxicity	
TROPHY-U-01, Phase 2 (n=135) A multi-cohort, open-label study in patients with unresectable locally advanced, or mUC whose disease progressed: 1. After prior PLT-based and CPI-based therapies 2. After CPI-based therapies and who were ineligible for PLT-based therapy.	**IMMU-132-01, Phase 1/2 (n=402)** A single-arm, open-label basket study in patients with metastatic epithelial cancers (including cervical, colorectal, endometrial, esophageal, gastric adenocarcinoma, glioblastoma multiforme, hepatocellular, non-small cell lung, non-TNBC, ovarian, pancreatic, prostate, renal cell, small-cell lung, squamous cell head and neck, TNBC, and urothelial) who had relapsed after or were refractory to ≥1 prior therapy for metastatic disease.

Abbreviations: CDK4/6i=cyclin-dependent 4/6 inhibitor; CPI=checkpoint inhibitor therapies; PLT=platinum; TNBC=triple-negative breast cancer.

ASCENT Study in mTNBC

Patients received a median of 7 treatment cycles of SG, for a median (range) treatment duration of 4.4 (0.03–22.9) months.[10]

In the safety population, which comprised all patients who received ≥1 dose of study treatment (SG, n=258; TPC, n=224), treatment-related ocular toxicity of any grade was observed in 5% of the patients (n=12) in the SG arm. No Grade >1 treatment-related ocular toxicity was reported with SG use. In the TPC arm, ocular toxicity of any grade was observed in 3% of patients (n=6), and no Grade >2 events were reported with TPC use.[3] Among patients aged ≥65 years who were treated with SG (n=49), treatment-related ocular toxicity of any grade was observed in 8% of patients. Data for patients ≥65 years of age in the TPC arm are currently not available.[11]

TROPiCS-02 Study in HR+/HER2- mBC

The overall safety population included 517 patients (SG, n=268; TPC, n=249) 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) treatment duration of 4.1 (0.03–24.2) months. The median (range) treatment duration in the TPC arm was 2.3 (0.03–22.3) months.[4] AEs of ocular toxicity were not reported in TROPiCS-02.[4,9]

TROPHY-U-01 Study in mUC

Current relevant data from Cohorts 1 and 2 of the study are provided below.

Cohort 1

The Cohort 1 primary analysis included 113 SG-treated patients who received SG for a median of 6 treatment cycles and a median (range) treatment duration of 3.7 (0–20) months. Treatment-related ocular disorders of any grade were experienced by 4% of patients in Cohort 1. All occurrences of ocular toxicity were assessed as severity Grade ≤2.[5]

Updated safety data for 113 patients (median [range] follow-up duration, 10.5 [0.3–40.9] months) did not provide any further information on the incidence or severity of AEs of ocular toxicity.[12]

Cohort 2

The Cohort 2 primary analysis included 38 SG-treated patients who received SG for a median (range) follow-up duration of 9.3 (0.5–30.6) months. AEs of ocular toxicity were not reported in the primary analysis.[13]

IMMU-132-01 Study in Metastatic Epithelial Cancer

In the overall safety population (n=495), patients received a median (range) of 6 (1–73) treatment cycles, with a median (range) treatment duration of 3.7 (0–55.2) months. There were no reports of Grade >2 treatment-related ocular toxicity. Ocular toxicity AEs were not described as occurring in association with any individual dose of SG.[13]

References

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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.
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Product Label

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

Follow-Up

For any additional questions, please contact Trodelvy Gilead 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
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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