GILEAD | Medical Information

Trodelvy® (sacituzumab govitecan-hziy)

Reports of Ocular Toxicity

This document is in response to your request for information regarding sacituzumab govitecan-hziy (SG) and ocular toxicity. Information summarized in this document includes data from phase 2 and 3 clinical studies of SG monotherapy (10 mg/kg IV on Days 1 and 8 of a 21-day treatment cycle) and reported cases of 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.

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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

Reports of Ocular Toxicity With SG Monotherapy: Clinical Studies

During the phase 3 ASCENT study in patients with mTNBC treated in a second-line and later (2L+) setting, treatment-related ocular toxicity of any grade was observed in 5% of patients (n=12) 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.[1]

During the phase 2 TROPHY-U-01 study in patients with metastatic urothelial cancer (mUC), treatment-related ocular disorders of any grade were experienced by 4% of patients in Cohort 1.[2,3] All occurrences of ocular toxicity were assessed as severity Grade ≤2.[3]

Reports of Ocular Toxicity: Real-World Data

A real-world pharmacovigilance analysis using data from FDA Adverse Event Reporting System (FAERS) from 2011–2023 evaluated ocular adverse events (AEs) associated with seven antibody-drug conjugates (ADCs). Eighteen ocular AE reports (0.72% of all SG-associated AEs) were identified, and all patients who reported ocular AEs were female. Overall, SG was associated with the lowest frequency of ocular AE reports, positive signals, and signal clusters compared with other ADCs. Ocular AEs with SG occurred earlier than with other ADCs, with a median onset of 21 days.[4]

Reports of Ocular Toxicity With SG Monotherapy: Clinical Studies

ASCENT Study in 2L+ mTNBC

ASCENT was an open-label, randomized, confirmatory phase 3 study in patients with refractory or relapsed mTNBC who had received ≥2 prior chemotherapy regimens, including ≥1 for metastatic disease. Patients received SG 10 mg/kg IV on Days 1 and 8 of a 21-day cycle and continued treatment until loss of clinical benefit or unacceptable toxicity.[1] Patients received a median of 7 treatment cycles of SG, for a median (range) treatment duration of 4.4 (0.03–22.9) months.[5]

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.[1] 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.[6]

TROPHY-U-01 Study in mUC

TROPHY-U-01 is an ongoing, global, open-label, multi-cohort, phase 2 study of SG in patients with unresectable locally advanced mUC whose disease progressed after prior platinum (PLT)-based and checkpoint inhibitor (CPI)-based therapies in Cohort 1.[2]

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.[3]

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.[2]

Reports of Ocular Toxicity: Real-World Data

FAERS Analysis[4]

A real-world, pharmacovigilance analysis using data from FAERS from 2011 to 2023 evaluated ocular AEs associated with seven ADCs, including belantamab mafodotin, brentuximab vedotin, enfortumab vedotin, mirvetuximab soravtansine, SG, trastuzumab deruxtecan, and trastuzumab emtansine.

Eighteen ocular AE reports (0.72% of all SG-associated AEs) were identified, and all patients who reported ocular AEs were female. Eleven cases had patient ages reported: 10 were aged 18 to 64 years, and 1 was aged 65 to 85 years. Of the cases with reported

outcomes, the following outcomes were noted: other serious important medical events, n=13; initial or prolonged hospitalization, n=4; death, n=3; unknown, n=5. Seven ocular toxicity reports originated from France, 6 were from other countries, 2 were from Spain, and 1 each were from the US, Germany, and Italy.

Overall, SG was associated with the lowest frequency of ocular AE reports, with a reporting odds ratio of 0.22 (95% CI, 0.15–0.32) and a proportional reporting ratio of 0.22 (chi-square=75.65). A total of 212 positive signals were identified at the preferred term level; SG had the fewest positive signals (n=3) compared with other ADCs (range: 9–111). After utilizing the high-level group term, AEs identified at the preferred term level were clustered into groups corresponding to ocular disorders, with SG showing the fewest signal clusters (n=2) compared with other ADCs (range: 5–12). Compared with other ADCs, ocular AEs occurred earlier with SG, with a median (IQR) onset of 21 (6–22) days.

References

1. 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.
2. 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.
3. Tagawa ST, Balar AV, Petrylak DP, et al. Updated outcomes in TROPHY-U-01 cohort 1, a phase 2 study of sacituzumab govitecan in patients with metastatic urothelial cancer who progressed after platinum-based chemotherapy and a checkpoint inhibitor [Poster 526]. Paper presented at: American Society of Clinical Oncology (ASCO) Genitourinary Cancers Symposium; 16-18 February, 2023; San Francisco, CA.
4. Mao K, Chen P, Sun H, Zhong S, Zheng H, L X. Ocular adverse events associated with antibody-drug conjugates in oncology: a pharmacovigilance study based on FDA adverse event reporting system (FAERS). *Front Pharmacol.* 2024;15:1425617.
5. 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.
6. 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).

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 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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