GILEAD | Medical Information

# Trodelvy® (sacituzumab govitecan-hziy) Reports of Peripheral Neuropathy

This document is in response to your request for information regarding Trodelvy® (sacituzumab govitecan-hziy [SG]) and reports of peripheral neuropathy (PN).

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

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.**

## PN in SG Monotherapy Clinical Studies

### mBC Studies: ASCENT and TROPiCS-02

At study randomization in ASCENT and TROPiCS-02 (studies of patients with metastatic triple-negative breast cancer [mTNBC] treated in a second line or later setting and pretreated hormone receptor positive [HR+]/human epidermal growth factor receptor 2-negative [HER2-] metastatic breast cancer [mBC], respectively), patients must have recovered from any systemic anticancer therapy-related or radiation-related PN to Grade ≤2 prior to treatment initiation.[1,2] Patients with Grade 2 neuropathy were eligible for study entry but were not permitted to receive vinorelbine if randomized to chemotherapy treatment of physicians' choice (TPC).[2,3]

In these studies, SG-related Grade ≥3 neuropathy was reported at an overall low frequency (0–1%); 3 patients experienced Grade ≥3 neuropathy in the SG arm of TROPiCS-02. See Table 1 for details.[2-7]

**Table 1. Treatment Duration and Incidence of PN in mBC Studies[2-7]**

| | | ASCENT | | TROPiCS-02[a] | |
|---|---|---|---|---|---|
| | | SG (n=258) | TPC (n=224) | SG (n=268) | TPC (n=249) |
| **Treatment Duration** | | | | | |
| Median (range), mo | | 4.4 (0.03–22.9) | 1–1.6[b] | 4.1 (0.03–24.2) | 2.3 (0.03–22.3)[c] |
| **Neuropathy, n or n (%)** | | | | | |
| **TEAEs** | Any Grade | NR | NR | NR | NR |
| | Grade ≥3 | 0 | 5[d] | 7 | 9 |

| | | ASCENT | | TROPiCS-02[a] | |
|---|---|---|---|---|---|
| | | SG (n=258) | TPC (n=224) | SG (n=268) | TPC (n=249) |
| TRAEs | Any Grade | NR | NR | 24 (9) | 39 (16) |
| | Grade ≥3 | 0 | 4[e] | 3 (1) | 6 (2) |

Abbreviations: NR=not reported; TEAE=treatment-emergent adverse event; TRAE=treatment-related adverse event.
[a]Combined preferred terms of gait disturbance, hypoesthesia, muscular weakness, neuropathy peripheral, paraesthesia, and peripheral sensory neuropathy.
[b]1.6 mo (0.03–15.3) for eribulin, 1 mo (0.03–11.5) for vinorelbine, 1.4 mo (0.2–8.1) for gemcitabine and, 1.2 mo (0.3–10.6) for capecitabine [data were unavailable for 6 patients]).
[c]3.4 mo (0.03–18.3) for eribulin, 1.2 mo (0.03–8.1) for vinorelbine, 1.5 mo (0.03–22.3) for gemcitabine, and 4.5 mo (0.2–12.9) for capecitabine.
[d]Included Grade 3 PN (n=3) and Grade 3 peripheral sensory neuropathy (n=2).
[e]Included Grade 3 PN (n=2) and Grade 3 peripheral sensory neuropathy (n=2).

## ASCENT-03 Study in 1L PD-(L)1 Inhibitor-Ineligible mTNBC

ASCENT-03, an ongoing, global, open-label, randomized, phase 3 study, is comparing the efficacy and safety of SG vs TPC (gem + carbo, paclitaxel, or nab-paclitaxel), as 1L treatment in patients (N=558) with previously untreated, locally advanced, inoperable or mTNBC who are not candidates for PD-(L)1 inhibitor therapy.[8] The median (range) duration of SG treatment at the final PFS analysis was 8.3 (<0.1–28.7) mo.[8,9]

An exploratory analysis assessed exposure-adjusted incidence rates (EAIRs), defined as the number of patients with ≥1 specified TEAE divided by the total exposure time (patient years of exposure) in each treatment group. PN was reported in 12 patients (4%) with SG (EAIR, 0.06; 95% CI: 0.03–0.11) and in 35 patients (13%) with TPC (EAIR, 0.25; 95% CI: 0.17–0.34; EAIR difference, -0.18; 95% CI: -0.28 to -0.1).[10]

## TROPHY-U-01 Study in mUC

At study enrollment in Cohort 1 of TROPHY-U-01, patients with metastatic urothelial cancer (mUC; n=113) had to have recovered from neuropathy to Grade ≤2 prior to SG initiation.[10] Median follow-up in this cohort was 10.5 mo (range: 0.3–40.9). Treatment-related any grade PN was 5% overall, and 2%, 2%, and 29% in patients with wild-type (**1/*1* [n=45]), heterozygous (**1/*28* [n=47]), and homozygous (**28/*28* [n=14]) uridine diphosphate-glucuronosyl transferase 1A1, respectively.[11]

## IMMU-132-01 Study in Metastatic Epithelial Cancers

In IMMU-132-01, a phase 1/2 basket study in patients with various advanced epithelial cancers (including mTNBC and HR+/HER2- mBC) patients must have recovered from any systemic anticancer therapy-related or radiation-related PN to Grade ≤2 prior to treatment initiation.[12]

The median (range) treatment duration in the mTNBC cohort (n=108) was 5.1 (0.03–36.1) months. Any-grade neuropathy (ie, peripheral neuropathy, paresthesias, peripheral sensory neuropathy, and/or hypoesthesia) was reported in 20 patients (19%); no Grade 3 or 4 events were reported.[13]

In the HR+/HER2- mBC cohort (n=54), the median (range) treatment duration was 4.6 (0–29.4) months. PN was not among the any-grade TRAEs reported in ≥15% or Grade ≥3 AEs reported in ≥5% of patients.[14]

# PN in SG Combination Clinical Studies

## ASCENT-04 Study in 1L PD-L1+ mTNBC

ASCENT-04 is an ongoing, global, open-label, randomized, phase 3 study that is being conducted to investigate the efficacy and safety of SG + pembrolizumab (pembro) vs TPC + pembro as first-line (1L) treatment in patients with programmed death ligand-1 (PD-L1) and a combined positive score ≥10, with inoperable, locally advanced or mTNBC (N=443). Patients with unresolved Grade ≤2 neuropathy were permitted in the study. In the SG + pembro group, the median (range) duration of treatment was 8.9 (<0.1–27.1) mo for SG and 8.5 (<0.1–26.8) mo for pembro; in the TPC + pembro group, it was 6.2 (<0.1–26.3) mo for TPC and 6.4 (<0.1–25.6) mo for pembro.[15]

PN was one of the most common adverse events, with reports of any-grade PN in 15 patients (7%) with SG + pembro (EAIR, 0.09; 95% CI: 0.05–0.14) and 46 patients (21%) with TPC + pembro (EAIR, 0.35; 95% CI: 0.26–0.47; EAIR difference, -0.26; 95% CI: -0.39 to -0.15).[15,16] Grade ≥3 PN was reported in 1 patient (<1%) in the SG + pembro group and in 7 patients (3%) in the TPC + pembro group.[15]

# References


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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 Medical Information at:

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

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Gilead Pharmacovigilance and Epidemiology ☎ 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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