GILEAD | Medical Information

Trodelvy® (sacituzumab govitecan-hziy) Peripheral Neuropathy

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

Information summarized in this document includes data for SG monotherapy (10mg/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.

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.

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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

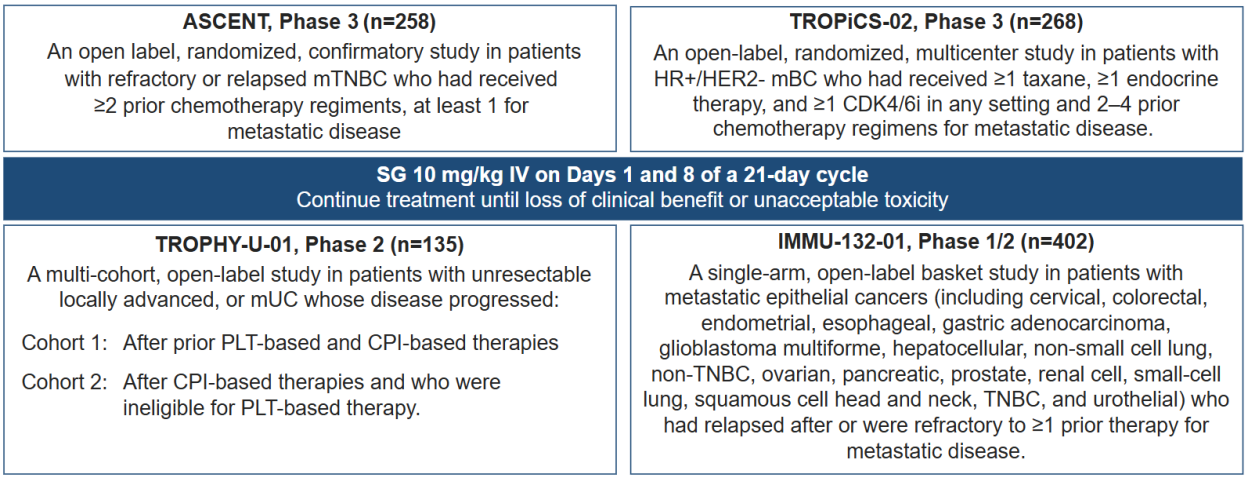
Peripheral Neuropathy in SG Clinical Studies

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,[1] ASCENT,[2] TROPiCS-02,[3] and TROPHY-U-01[4-6]). 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).[7]

The median treatment duration of SG in this population was 4.1 (range: 0–63) months[8]; PN was not among the most commonly reported (≥15%) any-grade treatment-emergent adverse events (TEAEs).[7]

Figure 1. Pooled Clinical Studies[7]



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

mBC Studies: ASCENT and TROPiCS-02

At study randomization in ASCENT and TROPiCS-02 (studies of patients with mTNBC and HR+/HER2- mBC, respectively), patients must have recovered from any systemic anticancer therapy-related or radiation-related PN to Grade ≤2 prior to treatment initiation.[9,10] 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).[10,11]

In these metastatic breast cancer (mBC) studies, SG-related Grade ≥3 neuropathy was reported with an overall low frequency of 0–1%; 3 patients experienced Grade ≥3 neuropathy in the SG arm of TROPiCS-02. See Table 1 for details.[2,3,10-13]

Table 1. Treatment Duration and Incidence of PN in mBC Studies[2,3,10-13]

		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
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]Includes Grade 3 PN (n=3) and Grade 3 peripheral sensory neuropathy (n=2).

[e]Includes Grade 3 PN (n=2) and Grade 3 peripheral sensory neuropathy (n=2).

mUC Study: TROPHY-U-01

At study enrollment in Cohort 1 of TROPHY-U-01, patients with mUC (n=113) had to have recovered from neuropathy to Grade ≤2 prior to SG initiation.[4] 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-glucuronosyltransferase 1A1 (*UGT1A1*), respectively.[6]

In Cohort 2 (n=38), patients with Grade ≥2 PN were ineligible for cisplatin-based therapy. Median follow-up in this cohort was 9.3 mo (range 0.5–30.6). The most common any-grade and Grade ≥3 TEAEs were reported at an incidence of ≥20% and ≥5% of patients, respectively; PN was not observed within these categories.[5]

Metastatic Epithelial Cancer Study: IMMU-132-01

In IMMU-132-01, a phase 1/2 basket study in patients with various advanced epithelial cancers (including mTNBC, HR+/HER2- mBC and mUC) patients must have recovered from any systemic anticancer therapy-related or radiation-related PN to Grade ≤2 prior to treatment initiation.[14]

Of the 495 patients in the overall safety population (OSP), 402 patients received SG 10 mg/kg. Median treatment duration was 3.7 mo (range: 0–55.2). There were no reports of treatment-related Grade >2 neuropathy in the OSP.[1]

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11. Rugo HS, Bardia A, Marme F, et al. Sacituzumab govitecan in hormone receptor-positive/human epidermal growth factor receptor 2-negative metastatic breast cancer [Supplementary Appendix]. *J Clin Oncol.* 2022;40(29):3365-3376.
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13. Rugo HS, Bardia A, Marmé F, et al. Overall survival with sacituzumab govitecan in hormone receptor-positive and human epidermal growth factor receptor 2-negative metastatic breast cancer (TROPiCS-02): a randomised, open-label, multicentre, phase 3 trial [Supplementary Appendix]. *The Lancet.* 2023;402(10411):1423-1433.
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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

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

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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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