GILEAD | Medical Information

Trodelvy® (sacituzumab govitecan-hziy) Incidence and Management of Rash

This document is provided in response to your request for information about Trodelvy® (sacituzumab govitecan-hziy [SG]) and the incidence and management of rash.

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.

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

Relevant Product Labeling[1]

Dosage and Administration

Recommended dosage

Premedication

Prior to each dose of SG, premedication for prevention of infusion reactions is recommended. Premedicate with antipyretics, H1 and H2 blockers prior to infusion, and corticosteroids may be used for patients who had prior infusion reactions.

Management of adverse reactions may require temporary interruption, dose reduction, or treatment discontinuation of SG as described in Tables 1 and 2. Do not re-escalate the SG dose after a dose reduction for adverse reactions has been made.

Table 1. Dosage Reduction Levels[1]

Dose Level	Dosage and Schedule
Recommended starting dose	10 mg/kg once weekly on Days 1 and 8 of 21-day treatment cycles
First dose reduction	Reduce to 7.5 mg/kg
Second dose reduction	Reduce to 5 mg/kg
Requirement for further dose reduction	Permanently discontinue SG

The recommended dosage modifications for adverse infusion-related reactions (IRRs) are provided in Table 2.

Table 2. Dose Modifications for IRRs[1]

Severity	Dose Modification
Grade 1-3 IRRs	Slow infusion rate or interrupt the infusion
Grade 4 IRRs	Discontinue SG

Warnings and Precautions

Hypersensitivity and IRRs

SG can cause serious hypersensitivity reactions including life-threatening anaphylactic reactions. Severe signs and symptoms included cardiac arrest, hypotension, wheezing, angioedema, swelling, pneumonitis, and skin reactions.

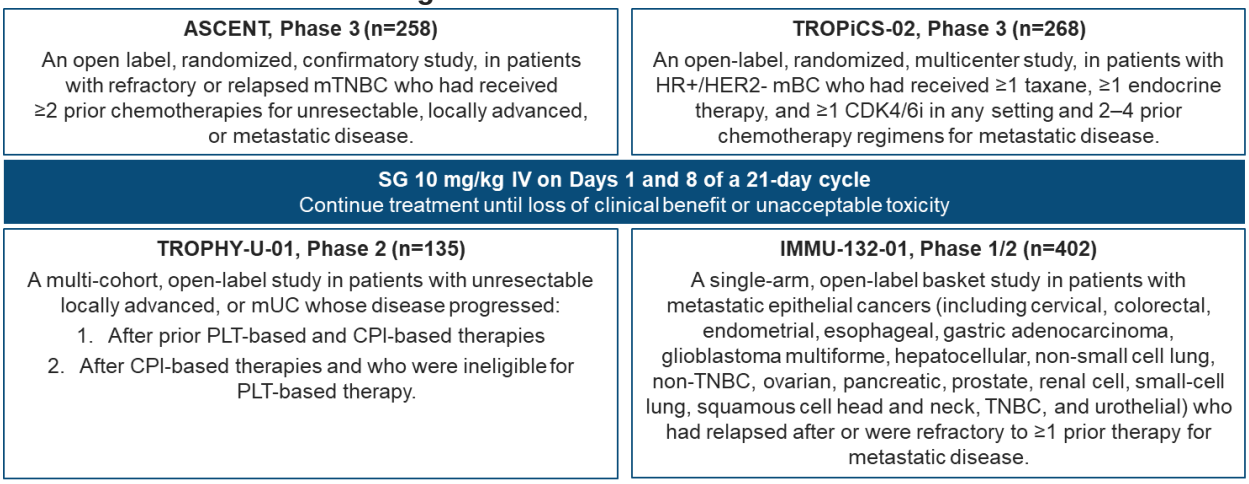
Incidence and Management of Rash in SG Clinical Studies

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 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) mo[1]; rash was not among the most common (≥15%) treatment-emergent adverse events (TEAEs) reported.[8]

Figure 1. Pooled Clinical Studies[8]



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

Premedication and Management of SG-Related Toxicities

Premedication for the prevention of IRRs such as rash included antihistamines that were to be administered before each SG infusion. Corticosteroids (hydrocortisone 50 mg or equivalent [oral or IV]) could also be administered prior to subsequent infusions if the patient experienced an IRR with a previous infusion.[2,9-11]

SG-associated toxicities were assessed and managed in accordance with standard clinical/institutional practices and accepted treatment guidelines.[2,9-11]

Metastatic Breast Cancer Studies

Treatment durations and rash-related safety data for the ASCENT study in patients with mTNBC are shown in Table 3. No frequency data are available for pre-infusion medication use of corticosteroids or systemic antihistamines for the prevention of IRRs in either treatment group.[3]

Table 3. ASCENT: Treatment Duration and Rash-Related Safety Data in OSP[3,12]

	SG (n=258)	TPC (n=224)
Treatment duration, median (range), mo	4.4 (0.03–22.9)	1–1.6[a]
Any-grade TRAE of rash of any kind, n (%)	22 (9)	3 (1)
Grade 3 TRAE of rash, n	1	1
Any-grade TEAE of rash, n (%)	32 (12)	12 (5)

Abbreviations: OSP=overall safety population; TPC=treatment of physicians' choice; TRAE=treatment-related adverse event.

[a]Treatment durations for TPC agents: eribulin, 1.6 (0.03–15.3) mo; vinorelbine, 1 (0.03–11.5) mo; gemcitabine, 1.4 (0.2–8.1) mo; and capecitabine, 1.2 (0.3–10.6) mo. Data were unavailable for 6 patients who received capecitabine.

Within the TROPiCS-02 study in patients with HR+/HER2- mBC, IRRs were defined as symptoms, including rash, that occurred within the first 6 hours after SG administration and could occur at any cycle.[10] Treatment durations and pre-infusion use of medications are shown in Table 4. Rash was not among the any-grade TRAEs with a reported incidence of ≥10%.[13]

Table 4. TROPiCS-02: Treatment Duration and Pre-Infusion Medications[4,14-16]

		SG (n=268)	TPC (n=249)
Treatment duration, median (range), mo		4.1 (0.03–24.2)	2.3 (0.03–22.3)[a]
Pre-infusion/concomitant use of medication,[b] %	Corticosteroids	54	39
	Systemic antihistamines	72	21

[a]Treatment durations for TPC agents: eribulin, 3.4 (0.03–18.3) mo; vinorelbine, 1.2 (0.03–8.1) mo; gemcitabine, 1.5 (0.03–22.3) mo; and capecitabine, 4.5 (0.2–12.9) mo.

[b]Data are from the ITT population (N=543). Use of pre-infusion medication in the OSP was not reported.[13]

Metastatic Urothelial Cancer Study

Within the multi-cohort TROPHY-U-01 study in mUC, patients in Cohort 1 received a median of 6 SG cycles; treatment duration and rash-related TRAEs are shown in Table 5.[17,18] All adverse events associated with rash were Grade ≤2.[5]

Table 5. TROPHY-U-01 Cohort 1: Treatment Duration and Rash-Related TRAEs[5,17]

		SG (N=113)
Treatment duration, median (range), mo		3.7 (0–20)
Rash-related TRAEs, %	Maculopapular rash	7
	Skin rash	6

In Cohort 2, patients treated with SG had median (range) follow-up duration of 9.3 (0.5–30.6) mo; median treatment duration was not provided for this cohort. Rash was not among the reports of any-grade TRAEs with an incidence of >20%.[18]

IRRs were defined as symptoms, including rash, that occurred within the first 6 hours after SG administration and could occur at any cycle.[11] No frequency data are available for pre-infusion medication use for the prevention of IRRs in the SG arms within these two cohorts.[5,17,18]

Metastatic Epithelial Cancer Study

Within IMMU-132-01, in patients with various advanced epithelial cancers (including mTNBC, HR+/HER2- mBC, or mUC), 402 of the 495 patients in the OSP received SG 10 mg/kg.[2] Treatment duration, rash-related safety data, and pre-infusion medications are shown in Table 6.

Table 6. IMMU-132-01 (OSP): Treatment Duration, Treatment-Related Rash, and Pre-Infusion Medications[2,19]

		SG (n=492)
Treatment duration, median (range), mo		3.7 (0–55.2)
TRAE of rash, n (%)		49 (12)
Pre-infusion medications, %	Systemic corticosteroids	54.7
	Antihistamines	29.3

References

1. TRODELVY® Gilead Sciences Inc. Trodelvy (sacituzumab govitecan-hziy) for injection, for intravenous use. U.S. Prescribing Information. Foster City, CA.

2. 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.
3. 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.
4. 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.
5. 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.
6. Petrylak DP, Tagawa ST, Jain RK, et al. Early results of TROPHY-U-01 cohort 2: sacituzumab govitecan in platinum-ineligible patients with metastatic urothelial cancer who progressed after prior checkpoint inhibitor therapy [Poster]. Presented at: American Society of Clinical Oncology (ASCO) Meeting; 29 May-2 June, 2020; Chicago, IL.
7. Loriot Y, Petrylak DP, Kalebasty AR, 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: updated safety and efficacy outcomes. *Ann Oncol.* 2024;35(4):392-401.
8. Rugo HS, Tolaney SM, Bardia A, et al. Pooled safety analysis of sacituzumab govitecan in multiple solid tumor types [Poster 3029]. Presented at: American Society of Clinical Oncology (ASCO); May 31-June 4, 2024; Chicago, IL.
9. Bardia A, Hurvitz SA, Tolaney SM, et al. Sacituzumab govitecan in metastatic triple-negative breast cancer [Protocol]. *N Engl J Med.* 2021;384(16):1529-1541.
10. Rugo HS, Bardia A, Marme F, et al. Sacituzumab govitecan in hormone receptor-positive/human epidermal growth factor receptor 2-negative metastatic breast cancer [Protocol]. *J Clin Oncol.* 2022;40(29):3365-3376.
11. 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 [Protocol]. *J Clin Oncol.* 2021;39(22):2474-2485.
12. 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.
13. 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.
14. 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. *The Lancet.* 2023;402(10411):1423-1433.
15. 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.
16. 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.
17. 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.
18. Petrylak DP, Tagawa ST, Jain RK, et al. Primary analysis of TROPHY-U-01 cohort 2, a phase 2 study of sacituzumab govitecan in platinum-ineligible patients with metastatic urothelial cancer

who progressed after prior checkpoint inhibitor therapy [Presentation]. Paper presented at: American Society of Clinical Oncology (ASCO) Genitourinary Cancers Symposium; 16-18 February, 2023; San Francisco, CA.
19. 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 [Supplementary Appendix]. *Ann Oncol.* 2021;32(6):746-756.

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 🖱 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

Data Privacy

The Medical Information service at Gilead Sciences may collect, store, and use your personal information to provide a response to your medical request. We may share your information with other Gilead Sciences colleagues to ensure that your request is addressed appropriately. If you report an adverse event or concern about the quality of a Gilead or Kite product, we will need to use the information you have given us in order to meet our regulatory requirements in relation to the safety of our medicines.

It may be necessary for us to share your information with Gilead's affiliates, business partners, service providers, and regulatory authorities located in countries other than your own. Gilead Sciences has implemented measures to protect the personal information you provide. Please see the Gilead Privacy Statement (www.gilead.com/privacy-statements) for more information about how Gilead handles your personal information and your rights. If you have any further questions about the use of your personal information, please contact privacy@gilead.com.