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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 and prevention of chemotherapy-induced nausea and vomiting 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. Premedicate with a two or three drug combination regimen (eg, dexamethasone with either a 5-hydroxytryptamine 3 receptor antagonist or a neurokinin-1 receptor antagonist, as well as other drugs as indicated).

Dose modifications for adverse reactions

Infusion-related reactions (IRRs)

Slow or interrupt the infusion rate of SG if the patient develops an IRR. Permanently discontinue SG for life-threatening IRRs.

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Dose modifications for adverse reactions

Withhold or discontinue SG to manage adverse reactions as described in Table 1. Do not re-escalate the SG dose after a dose reduction for adverse reactions has been made.

Table 1. Dose Modifications for Adverse Reactions[1]

Severe Non-Neutropenic Toxicity	Occurrence	Dose Modification
Grade 4 non-hematologic toxicity of any duration, OR Any Grade 3–4 nausea, vomiting, or diarrhea due to treatment that is not controlled with antiemetics and anti-diarrheal agents, OR Other Grade 3–4 non-hematologic toxicity persisting >48 hours despite optimal medical management, OR At time of scheduled treatment, Grade 3–4 non-neutropenic hematologic or non-hematologic toxicity, which delays dose by 2 or 3 weeks for recovery to ≤ Grade 1	First	25% dose reduction
	Second	50% dose reduction
	Third	Discontinue treatment
In the event of Grade 3–4 non-neutropenic hematologic or non-hematologic toxicity, which does not recover to ≤ Grade 1 within 3 weeks	First	Discontinue treatment

Warnings and Precautions

Hypersensitivity and infusion-related reactions

Serious hypersensitivity reactions including life-threatening anaphylactic reactions have occurred with SG treatment. Severe signs and symptoms included cardiac arrest, hypotension, wheezing, angioedema, swelling, pneumonitis, and skin reactions.

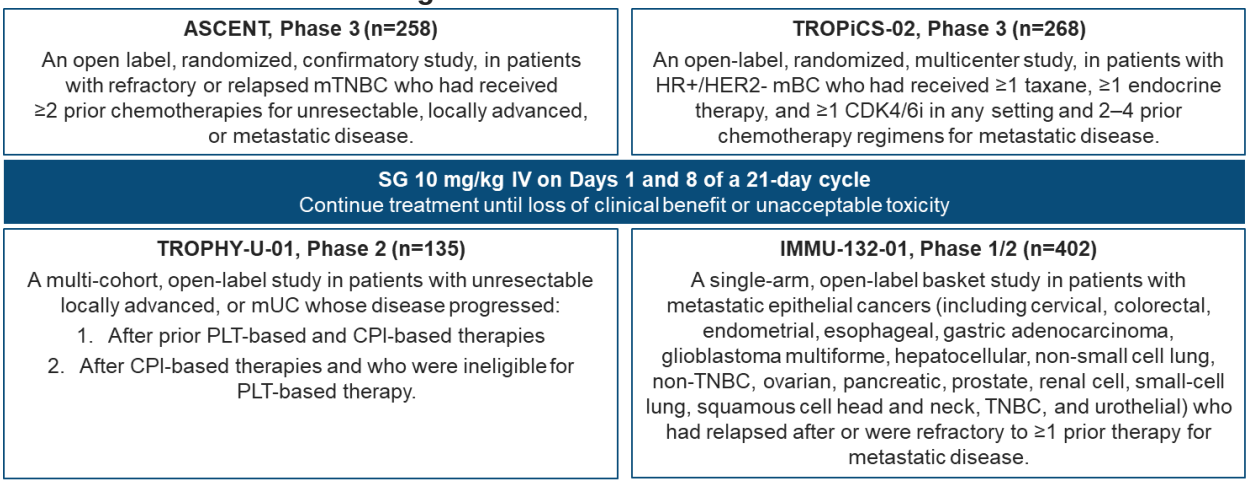
Incidence and Management of Rash in SG Clinical Studies

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 2. 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 3. Rash was not among the any-grade TRAEs with a reported incidence of ≥10%.[13]

Table 3. 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 4.[17,18] All adverse events associated with rash were Grade ≤2.[5]

Table 4. 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 5.

Table 5. 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

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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

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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