Trodelvy® (sacituzumab govitecan-hziy) Use in Patients With Hepatic Impairment

This document is in response to your request for information regarding the use of Trodelvy® (sacituzumab govitecan-hziy [SG]) in patients with hepatic impairment, including patients with hepatic impairment due to liver metastases.

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.

Summary

Relevant Product Labeling[1]

Warnings and Precautions: Patients homozygous for *the uridine diphosphate-glucuronosyl transferase 1A1* (*UGT1A1) *28* allele are at increased risk for neutropenia, febrile neutropenia, and anemia; and may be at increased risk for other adverse reactions when treated with SG.

Closely monitor patients with known reduced UGT1A1 activity for adverse reactions. Withhold or permanently discontinue SG based on clinical assessment of the onset, duration, and severity of the observed adverse reactions in patients with evidence of acute early-onset or unusually severe adverse reactions, which may indicate reduced UGT1A1 enzyme activity.

Use in Specific Populations – Hepatic Impairment: The safety of SG in patients with moderate (total bilirubin >1.5 to 3 × upper limit of normal [ULN]) or severe (total bilirubin >3 × ULN) hepatic impairment has not been established. SG has not been evaluated in patients with AST or ALT >3 × ULN without liver metastases, or AST or ALT >5 × ULN with liver metastases.

PK – Patients With Hepatic Impairment: The exposure of SG for patients with mild hepatic impairment (total bilirubin ≤ULN with AST >ULN, or bilirubin >1 to ≤1.5 × ULN with any AST) is within range of that of patients with normal hepatic function (total bilirubin and AST <ULN).

SG and free SN-38 exposures are unknown in patients with moderate (total bilirubin >1.5 to 3 × ULN) or severe (total bilirubin >3 × ULN) hepatic impairment.

SG PK in Patients With Mild Hepatic Impairment

A population pharmacokinetic (PK) analysis assessed exposure to SG, the free active metabolite of irinotecan (SN-38), and total antibody (tAB) across 3 studies: ASCENT (in metastatic triple-negative breast cancer [mTNBC]), TROPiCS-02 (in hormone receptor-positive/human epidermal growth factor receptor 2-negative [HR+/HER2-] metastatic breast cancer [mBC]), and IMMU-132-01 (in metastatic epithelial cancer).[2]

Exposure to the 3 analytes in patients with mild hepatic impairment (bilirubin > upper limit of normal [ULN] –1.5 × ULN or AST >ULN [n=257]) relative to those with normal hepatic function (bilirubin and AST ≤ULN [n=525]) were evaluated. Results of the analyses showed that SG, SN-38, and tAB exposures were similar between patients with mild hepatic impairment and those with normal hepatic function. Predicted exposure (90% CI) in the first cycle in patients with mild hepatic impairment relative to normal hepatic function was the following[2]:

- 0.976 (0.958–0.994) and 0.983 (0.97–0.996) for the area under the curve (AUC) and maximum concentration (C_{max}) with SG, respectively.
- 0.915 (0.848–0.982) and 0.941 (0.887–0.996) for AUC and C_{max} with SN-38, respectively.
- 0.931 (0.901–0.962) and 0.961 (0.934–0.989) for AUC and C_{max} with tAB, respectively.

Study of SG in Patients With Moderate Hepatic Impairment

A phase 1, open-label, multicenter, dose-escalation study (NCT04617522) is being conducted to understand the safety and dosing of SG in patients with advanced or metastatic solid tumors and moderate hepatic impairment.[3]

Phase 3 Clinical Studies in SG Monotherapy: Inclusion of Patients With Adequate Hepatic Function

In five Gilead-sponsored, phase 3 studies of SG as monotherapy that have results available (ASCENT, ASCENT-03, EVOKE-01, TROPiCS-02, and TROPiCS-04), patients, including those with liver metastases, were required to have adequate hepatic function, as described in the summary below.[4-8]

SG PK in Patients With Mild Hepatic Impairment

SG PK in Patients With mTNBC, HR+/HER2- mBC, or Metastatic Epithelial Cancer and Mild Hepatic Impairment[2]

A population PK analysis using data from ASCENT (n=253), TROPiCS-02 (n=260), and IMMU-132-01 (n=276) evaluated the impact of clinical covariates on SG exposure. SG exposure was similar in patients with mild hepatic impairment compared to patients with normal hepatic function (Table 1 and Table 2).

Table 1. PK Analysis: Categorical Covariate Relationship to SG Exposure in the First Cycle Relative to Reference[2]

Covariate (Reference)	Covariate	Predicted SG Exposure (90% CI)	
		AUC	C_{max}
Hepatic impairment relative to normal (bilirubin and AST ≤ULN; n=525)	Mild hepatic impairment (bilirubin >ULN–1.5 × ULN or AST >ULN; n=257)	0.976 (0.958–0.994)	0.983 (0.97–0.996)

Table 2. PK Analysis: Continuous Covariate Relationships to SG Exposure in First Cycle Relative to Reference[2]

Covariate (Reference)	Percentile	Predicted SG Exposure (90% CI)	
		AUC	C_{max}
AST (27.5 IU/L)	95th (124 IU/L)	0.951 (0.925–0.977)	0.984 (0.965–1)
	5th (14 IU/L)	1.01 (0.994–1.02)	1 (0.993–1.01)
ALT (21.6 IU/L)	95th (88.3 IU/L)	0.985 (0.963–1.01)	0.996 (0.981–1.01)
	5th (8.84 IU/L)	1 (0.99–1.02)	1 (0.991–1.01)
Albumin (39 g/L)	95th (45 g/L)	1.06 (1.04–1.08)	1 (0.988–1.01)
	5th (30 g/L)	0.912 (0.892–0.932)	0.998 (0.983–1.01)
ALP (95 IU/L)	95th (339 IU/L)	0.959 (0.939–0.979)	0.986 (0.971–1)
	5th (51.4 IU/L)	1.01 (0.995–1.02)	1 (0.994–1.01)
Bilirubin (0.4 mg/dL)	95th (1 mg/dL)	0.986 (0.965–1.01)	1 (0.984–1.02)
	5th (0.2 mg/dL)	1 (0.989–1.02)	1 (0.989–1.01)

Abbreviation: ALP=alkaline phosphatase.

A bootstrap analysis confirmed final model estimates for SG, free SN-38, and tAB. The correlation between mild hepatic impairment and exposures to free SN-38 and tAB are presented in Table 3, Table 4, and Table 5.

Table 3. PK Analysis: Categorical Covariate Relationship to Free SN-38 and tAB Exposure in the First Cycle Relative to Reference[2]

	Covariate (Reference)	Covariate	Predicted Exposure (90% CI)	
			AUC	C_{max}
SN-38	Hepatic impairment relative to normal (bilirubin and AST ≤ULN; n=514)	Mild hepatic impairment (bilirubin >ULN–1.5 × ULN or AST >ULN; n=253)	0.915 (0.848–0.982)	0.941 (0.887–0.996)
tAB	Hepatic impairment relative to normal (bilirubin and AST ≤ULN; n=524)	Mild hepatic impairment (bilirubin >ULN–1.5 × ULN or AST >ULN; n=256)	0.931 (0.901–0.962)	0.961 (0.934–0.989)

Table 4. PK Analysis: Continuous Covariate Relationships to Free SN-38 Exposure in First Cycle Relative to Reference[2]

Covariate (Reference)	Percentile	Predicted SG Exposure (90% CI)	
		AUC	C_{max}
AST (27.8 IU/L)	95th (124 IU/L)	0.895 (0.797–0.992)	0.938 (0.858–1.02)
	5th (14 IU/L)	1.02 (0.966–1.06)	1.01 (0.969–1.05)
ALT (22 IU/L)	95th (88.9 IU/L)	0.994 (0.909–1.08)	1 (0.934–1.07)
	5th (8.46 IU/L)	1 (0.952–1.05)	0.999 (0.959–1.04)
Albumin (39 g/L)	95th (45 g/L)	1.05 (0.98–1.12)	1.01 (0.955–1.07)
	5th (30 g/L)	0.927 (0.848–1.01)	0.983 (0.919–1.05)
ALP (95 IU/L)	95th (338 IU/L)	0.917 (0.84–0.995)	0.948 (0.885–1.01)
	5th (51.6 IU/L)	1.01 (0.967–1.06)	1.01 (0.971–1.05)
Bilirubin (0.4 mg/dL)	95th (1 mg/dL)	0.978 (0.896–1.06)	0.999 (0.933–1.07)
	5th (0.2 mg/dL)	1.01 (0.95–1.06)	1 (0.954–1.05)

Table 5. PK Analysis: Continuous Covariate Relationships to tAB Exposure in First Cycle Relative to Reference[2]

Covariate (Reference)	Percentile	Predicted SG Exposure (90% CI)	
		AUC	C_{max}
AST (27.5 IU/L)	95th (123 IU/L)	0.885 (0.84–0.929)	0.935 (0.896–0.974)
	5th (14 IU/L)	1.02 (0.994–1.04)	1.01 (0.99–1.03)

Covariate (Reference)	Percentile	Predicted SG Exposure (90% CI)	
		AUC	C_{max}
ALT (21.6 IU/L)	95th (87.8 IU/L)	0.973 (0.934–1.01)	0.991 (0.957–1.02)
	5th (8.84 IU/L)	1.01 (0.983–1.03)	1 (0.982–1.02)
Albumin (39 g/L)	95th (45 g/L)	1.08 (1.05–1.11)	1.05 (1.02–1.07)
	5th (30 g/L)	0.881 (0.846–0.915)	0.928 (0.897–0.959)
ALP (95 IU/L)	95th (334 IU/L)	0.91 (0.876–0.944)	0.934 (0.904–0.964)
	5th (51.3 IU/L)	1.02 (0.995–1.04)	1.01 (0.993–1.03)
Bilirubin (0.4 mg/dL)	95th (1 mg/dL)	0.967 (0.929–1)	0.969 (0.936–1)
	5th (0.2 mg/dL)	1.01 (0.985–1.04)	1.01 (0.987–1.03)

Study of SG in Patients With Moderate Hepatic Impairment[3]

IMMU-132-15 an ongoing, phase 1, open-label, multicenter, dose-escalation study (NCT04617522) being conducted to understand the safety and dosing of SG in patients (estimated enrollment, N=30) with advanced or metastatic solid tumors and moderate hepatic impairment. Moderate hepatic impairment is defined as a bilirubin level >1.5 to <3 × ULN and any AST level. SG will be administered on Days 1 and 8 at escalating doses of 5, 7.5, and 10 mg/kg, if determined by the study investigator to be tolerable. The primary outcomes of this study include the percentage of patients who have treatment-emergent adverse events, have clinically significant laboratory abnormalities, and develop positive anti-SG antibodies. PK parameters will also be analyzed. Patients who had a treatment benefit were eligible to continue SG in a rollover study, IMMU-132-14.

Study results have not yet been reported.

Phase 3 Clinical Studies in SG Monotherapy: Inclusion of Patients With Adequate Hepatic Function

In the five Gilead-sponsored, phase 3 studies of SG as monotherapy that have results available (ASCENT, ASCENT-03, EVOKE-01, TROPiCS-02, and TROPiCS-04), patients, including those with liver metastases, were required to have adequate hepatic function. Inclusion criteria regarding hepatic function are summarized in Table 6.[4-8]

Table 6. SG Studies: Definitions of Adequate Hepatic Function[4-8]

Hepatic Function Test	Value
Bilirubin	≤1.5 × ULN[a]
AST and ALT	≤2.5 × ULN
AST and ALT in patients with known liver metastases	≤5 × ULN
Serum albumin	≥3 g/dL[b]
ALP[c]	≤5 × ULN

[a]In TROPiCS-02, patients with documented Gilbert's syndrome were required to have a bilirubin level ≤3 × ULN.
[b]In EVOKE-01, serum albumin was required to be >3 g/dL.
[c]Only required in TROPiCS-02 study. If a patient had known bone metastases, liver-specific ALP levels were separated from the total ALP level and were used to assess liver function instead of total ALP.

References

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2. Sathe AG, Jones AK, Diderichsen PM, et al. Sacituzumab govitecan population pharmacokinetics: updated analyses using HR+/HER2− metastatic breast cancer data from the phase 3 TROPiCS-02 trial. *Clinical and Translational Science.* 2025;18(7):e70291.
3. ClinicalTrials.gov. Study of Sacituzumab Govitecan in Participants With Advanced or Metastatic Solid Tumor and Moderate Liver Impairment. ClinicalTrials.gov Identifier: NCT04617522. Available at: https://clinicaltrials.gov/ct2/show/NCT04617522. Accessed: 28 September 2023. Last Updated: 15 September 2023. 2021.
4. 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.
5. Cortés J, Punie K, Barrios C, et al. Sacituzumab govitecan in untreated, advanced triple-negative breast cancer [Supplementary Appendix]. *N Engl J Med.* 2025. https://doi.org/10.1056/NEJMoa2511734.
6. Paz-Ares L, Juan-Vidal O, Mountzios GS, et al. Sacituzumab govitecan versus docetaxel for previously treated advanced or metastatic non–small cell lung cancer: the randomized, open-label phase III EVOKE-01 study [Data supplement]. *J Clin Oncol.* 2024:1-13.
7. 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.
8. Powles T, Tagawa S, Vulsteke C, et al. Sacituzumab govitecan in advanced urothelial carcinoma: TROPiCS-04, a phase III randomized trial [Supplementary Appendix]. *Annals of Oncology.* 2025;36(5):561-571.

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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