GILEAD | Medical Information

Trodelvy® (sacituzumab govitecan-hziy) 2L Monotherapy Use in Cisplatin- or Platinum-Ineligible mUC

This document is in response to your request for information regarding Trodelvy® (sacituzumab govitecan-hziy [SG]) and its use as monotherapy in the 2L setting in patients with locally advanced or metastatic urothelial cancer (mUC) who are ineligible for cisplatin (cis)- or platinum (PLT)-based therapy.

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.

Trodelvy is not indicated for use in patients with mUC. 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

Clinical Data on SG as 2L Monotherapy in Cis- or PLT-Ineligible Patients

TROPHY-U-01 is an ongoing, global, phase 2, multi-cohort, open-label study of SG in patients with unresectable locally advanced or mUC. Approximately 827 patients are anticipated to be enrolled.[1]

Cohort 2 of TROPHY-U-01 is evaluating the efficacy and safety of SG in patients with mUC who were ineligible for PLT-based chemotherapy and progressed after previous CPIs in the 1L metastatic setting. Data from 38 patients were included in the preliminary analysis.[2]

- Treatment with SG resulted in an ORR of 32% (12/38; 95% CI: 17.5–48.7), a median (range) PFS of 5.6 (4.1–8.3) months, a median (95% CI) OS of 13.5 (7.6–15.6) months, and a median DOR of 5.6 months (n=12; 95% CI: 2.8–13.3).
- A reduction in tumor size was observed in 22 of 32 patients.
- The most common all-grade TEAEs included diarrhea, nausea, fatigue, alopecia, and neutropenia.

The phase 1/2 basket study (IMMU-132-01) evaluated the use of SG in adult patients with various advanced epithelial cancers, including patients with mUC (n=49) that was refractory to or relapsed after ≥1 prior treatment.[3,4]

- Among patients with mUC who received SG 10 mg/kg (n=45), the ORR was 28.9% (95% CI: 16.4–44.3%), and the median PFS and OS were 6.8 and 16.8 months, respectively.[3]
- In an earlier analysis of patients in the mUC cohort who received SG 10 mg/kg (n=45), the most common (≥5% of patients) Grade ≥3 AEs included neutropenia/decreased neutrophil count, anemia, hypophosphatemia, diarrhea, fatigue, and febrile neutropenia.[4]

Clinical Data on SG as 2L Monotherapy in Cis- or PLT-Ineligible Patients

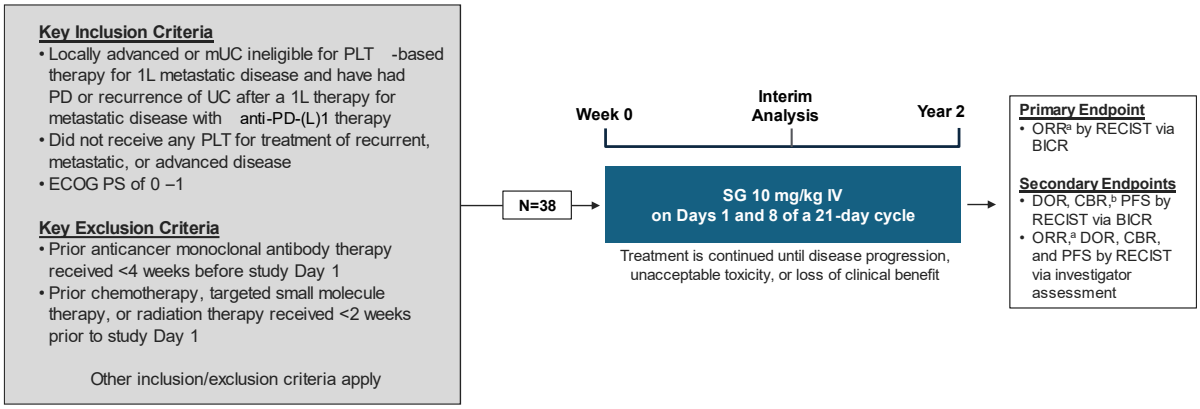
TROPHY-U-01 Cohort 2 in PLT-Ineligible Patients

Study design and demographics

TROPHY-U-01 (NCT03547973), a global, multicohort, open-label, phase 2 study, is investigating the efficacy and safety of SG in approximately 827 patients with unresectable locally advanced or mUC.[1] Results from Cohort 2 are summarized.

Cohort 2 is investigating the role of SG in PLT-ineligible patients with mUC who have progressed after CPI-only therapy (Figure 1).[2]

Figure 1. TROPHY-U-01 Cohort 2 in 2L+ mUC: Study Design[2,5]



Abbreviations: 2L+=second line and later; PD-(L)1=programmed death (ligand)-1; RECIST=Response Evaluation Criteria in Solid Tumors; UC=urothelial cancer.
[a]Defined as the rate of the best overall response of CR + PR.
[b]Defined as CR, PR, and SD for ≥6 months.

Preliminary efficacy and safety data for 38 patients were included in this analysis (data cutoff: July 26, 2022). At the time of data cutoff, 36 patients (95%) had discontinued treatment. Of these, 20 patients (53%) discontinued due to PD. See Table 1 for key baseline demographics and disease characteristics.[2]

Table 1. TROPHY-U-01 Cohort 2: Baseline Demographics and Disease Characteristics[2]

Key Demographics and Characteristics		Cohort 2 (N=38)
Age, median (range), y		73 (41–87)
Male, n (%)		23 (61)
Race, n (%)	White	31 (82)
	Black	1 (3)
	Not provided	6 (16)
ECOG PS 1, n (%)		19 (50)
Site of disease at baseline, n (%)	Visceral metastasis	25 (66)
	Lung/pleura	16 (42)
	Liver	11 (29)
	Bone	3 (8)
	Other	6 (16)

Key Demographics and Characteristics		Cohort 2 (N=38)
Tumor stage at screening, n (%)	mUC	25 (66)
	Locoregional only	13 (34)
Bellmunt risk factors,[a] n (%)	0	11 (29)
	1	19 (50)
	2	8 (21)
Prior anticancer regimens, median (range), n		2 (1–5)
≤2 prior anticancer regimens, n (%)		28 (74)
Type of prior anticancer regimens, n (%)	CPI	38 (100)
	PLT-based therapy in (neo)adjuvant setting	19 (50)
	Enfortumab vedotin/enfortumab	6 (16)/1 (3)
	Erdafitinib	1 (3)

[a]Risk factors included an ECOG PS >0, liver metastases, and an Hgb level <10 g/dL.

Preliminary efficacy results[2]

The median (range) follow-up duration was 9.3 (0.5–30.6) months, with a median time to response of 1.4 months and an ORR of 32% (Table 2). In an analysis of prespecified subgroups, ORRs were similar across subgroups, which included those who had >2 previous anticancer therapies (29%; 2/7) vs those who had ≤2 (32%; 10/31). In patients with visceral metastases and those with liver metastases, the ORRs were 20% and 18%, respectively. A reduction in tumor size was observed in 22 of 32 patients per BICR, and an ongoing response was present in 2 patients at the time of data cutoff.

Table 2. TROPHY-U-01 Cohort 2: Response Assessment[2]

Endpoints		Cohort 2 (N=38)
ORR, n (%); 95% CI		12 (32); 17.5–48.7
Best response, n (%)	CR	0
	PR	12 (32)
	SD	13 (34)
	SD for ≥6 mo[a]	4 (11)
	PD	4 (11)
	Not assessed[b]	5 (13)
	Not evaluable[c]	4 (11)
CBR,[d] n (%); 95% CI		16 (42); 26.3–59.2
DOR, median (range),[e] mo		5.6 (2.8–13.3)
PFS, median (95% CI), mo		5.6 (4.1–8.3)
OS, median (95% CI), mo		13.5 (7.6–15.6)

[a]Nine patients had SD and were followed for <6 mo.
[b]Patients who did not have a postbaseline assessment.
[c]Patients who had one postbaseline imaging assessment but were assigned a best overall response of "not evaluable" per BICR assessment due to imaging quality issue or other reasons not currently provided in the BICR datasets.
[d]CBR was defined as CR + PR + SD for ≥6 mo.
[e]n=12.

Preliminary safety results[2]

The most commonly reported TEAEs and key Grade ≥3 TEAEs are listed in Table 3; 87% of patients experienced Grade ≥3 TEAEs. Two cases (5%) of Grade 3 and 1 case (3%) of Grade 4 febrile neutropenia occurred. TEAEs led to SG dose interruption in 61%, dose reduction in 37%, and discontinuation in 21% of patients (diarrhea, n=2; asthenia, colitis, febrile neutropenia, maculopapular rash, nausea, pneumonia, pyrexia, and sepsis, n=1 each). Thirty-six patients (95%) experienced ≥1 TRAE, and Grade ≥3 TRAEs included

diarrhea (n=4), colitis (n=3), febrile neutropenia (n=2), and sepsis (n=2; 1 patient had neutropenia). For the patients with a Grade ≥3 TRAE of colitis, the mean duration of time from CPI cessation to SG initiation was 4.2 months; all events were deemed related to SG treatment. No treatment-related deaths occurred. Seventeen patients were receiving granulocyte colony-stimulating factor, 7 (18%) for primary prophylaxis and 10 (26%) for secondary prophylaxis.

Table 3. TROPHY-U-01 Cohort 2: Most Commonly Reported (>20%) Any-Grade and Grade ≥3 TEAEs[2]

TEAE, n (%)	All Grades	Grade 3	Grade 4
Diarrhea	25 (66)	5 (13)	1 (3)
Nausea	20 (53)	1 (3)	0
Fatigue	19 (50)	7 (18)	0
Alopecia	19 (50)	0	0
Neutropenia	17 (45)	6 (16)	7 (18)
Anemia	15 (40)	9 (24)	0
Constipation	15 (40)	0	0
Leukopenia	13 (34)	3 (8)	4 (11)
Decreased appetite	12 (32)	0	0
Urinary tract infection	11 (29)	2 (5)	0
Vomiting	11 (29)	1 (3)	0
Abdominal pain	10 (26)	1 (3)	0
Hypomagnesemia	10 (26)	0	0
Hyponatremia	9 (24)	1 (3)	0
Pruritus	8 (21)	0	0

IMMU-132-01 Study in Metastatic Epithelial Cancer

Study design and demographics

The safety and efficacy of SG were evaluated in a multicenter, single-arm, phase 1/2 basket study that enrolled 495 adult patients with metastatic epithelial cancers who had relapsed after or were refractory to ≥1 prior standard therapeutic regimen. The median (range) follow-up duration for the OSP at data cutoff was 8.97 (0.26–55.72) months.[3] Overall, patients received SG IV on Days 1 and 8 of 21-day cycles and were treated with SG until disease progression or unacceptable toxicity, death, or withdrawal of consent.[3,6,7]

A total of 45 patients with mUC received SG 10 mg/kg, 3 received SG 8 mg/kg, and 1 received SG 12 mg/kg.[8] Baseline demographics for patients with mUC who received SG 10 mg/kg are listed in Table 4.

Table 4. IMMU-132-01: Baseline Demographics and Disease Characteristics in the mUC Cohort Who Received SG 10 mg/kg[4]

Key Demographics and Characteristics	mUC Cohort (n=45)
Age, median (range), y	67 (49–90)
Male, n	41
ECOG PS, 0/1, %	31/69
Prior treatment lines, median (range), n	2 (1–6)
PLT based, %	95
CPI based, %	38
Visceral metastases, n	33
Lung/liver/other, n	27/15/5

Efficacy in patients with mUC who received SG 10 mg/kg

In patients in the mUC cohort who received SG 10 mg/kg, the ORR was 28.9%. See Table 5 for details of further response rates in this cohort.[3]

Table 5. IMMU-132-01: Efficacy Data in the mUC Cohort That Received SG 10 mg/kg[3]

ORR, % (95% CI)	CR/PR/SD, n (%)	DOR, Median (95% CI), mo	OS, Median (95% CI), mo	PFS, Median (95% CI), mo	CBR, n (%) [95% CI]
28.9 (16.4–44.3)	2 (4.4)/11 (24.4)/ 16 (35.6)	12.9 (3.8–22.5)	16.8 (9–21.9)	6.8 (3.6–9.7)	20 (44.4) [29.6–60]

Preliminary efficacy results showed that, among the 33 patients who had visceral involvement, the ORR was 27% (n=9); among CPI-treated patients, the ORR was 23% (4/17).[4]

Safety

Results from the mUC cohort[4]

The most common (≥5% of patients) Grade ≥3 AEs included the following: neutropenia/decreased neutrophil count (38%), anemia (11%), hypophosphatemia (11%), diarrhea (9%), fatigue (9%), and febrile neutropenia (7%).

Results from the OSP[3]

All patients in the OSP received ≥1 dose of SG at 8, 10, 12, or 18 mg/kg. Nearly all patients (n/N=494/495) experienced ≥1 AE during the study; of these, 97.6% experienced TRAEs (Table 6). Nausea, neutropenia, diarrhea, fatigue, and alopecia were the most commonly reported (≥20%) TRAEs.

Post hoc analyses showed that treatment-related neutropenia of any grade had a median onset of 19 days and a median duration of 8.5 days, as assessed in post hoc analyses. Treatment-related diarrhea of any grade had a median onset of 14 days and a median duration of 8 days.

Table 6. IMMU-132-01: Select TRAEs of Interest in ≥20% of Patients in the OSP[3]

Event, n (%)		All Grades	Grade 3	Grade 4
Any TRAE		483 (97.6)	284 (57.4)	73 (14.7)
Gastrointestinal	Nausea	310 (62.6)	18 (3.6)	0
	Diarrhea	278 (56.2)	39 (7.9)	0
	Vomiting	191 (38.6)	14 (2.8)	0
Hematologic	Neutropenia	286 (57.8)	143 (28.9)	67 (13.5)
	Anemia	173 (34.9)	51 (10.3)	0
	Febrile neutropenia[a]	27 (5.5)	21 (4.2)	5 (1)
Systemic/other	Fatigue	239 (48.3)	31 (6.3)	0
	Alopecia	200 (40.4)	0	0

[a]No Grade 5 febrile neutropenia events were reported. For 1 patient, febrile neutropenia was entered as Grade 2 per investigator assessment; however, it was Grade ≥3 febrile neutropenia by definition.

Overall, 38.8% of study patients in the OSP had an SAE, and 15.2% of the SAEs were considered to be related to treatment. The most common treatment-related SAEs were febrile neutropenia (4%), diarrhea (2.8%), vomiting (1.4%), nausea (1.4%), and neutropenia

(1.2%). Dose reductions were required in 32.3% of patients, and 8.3% of patients permanently discontinued treatment due to AEs.

References

1. ClinicalTrials.gov. Phase II Open Label Study of IMMU-132 in Metastatic Urothelial Cancer. ClinicalTrials.gov Identifier: NCT03547973. Available at: https://www.clinicaltrials.gov/ct2/show/NCT03547973. Accessed: 13 February 2026. Last Updated 15 April 2025.
2. Petrylak DP, Tagawa ST, Jain RK, et al. TROPHY-U-01 cohort 2: a phase II study of sacituzumab govitecan in cisplatin-ineligible patients with metastatic urothelial cancer progressing after previous checkpoint inhibitor therapy. *J Clin Oncol.* 2024;42(29):3410-3420.
3. 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.
4. Tagawa ST, Faltas BM, Lam ET, et al. Sacituzumab govitecan (IMMU-132) in patients with previously treated metastatic urothelial cancer (mUC): Results from a phase I/II study [Abstract]. *American Society of Clinical Oncology.* 2019;37(7):354-354.
5. Petrylak DP, Tagawa ST, Jain RK, et al. TROPHY-U-01 cohort 2: a phase II study of sacituzumab govitecan in cisplatin-ineligible patients with metastatic urothelial cancer progressing after previous checkpoint inhibitor therapy [Protocol]. *J Clin Oncol.* 2024;42(29):3410-3420.
6. Ocean AJ, Starodub AN, Bardia A, et al. Sacituzumab govitecan (IMMU-132), an anti-Trop-2-SN-38 antibody-drug conjugate for the treatment of diverse epithelial cancers: Safety and pharmacokinetics. *Cancer.* 2017;123(19):3843-3854.
7. Starodub AN, Ocean AJ, Shah MA, et al. First-in-Human Trial of a Novel Anti-Trop-2 Antibody-SN-38 Conjugate, Sacituzumab Govitecan, for the Treatment of Diverse Metastatic Solid Tumors. *Clin Cancer Res.* 2015;21(17):3870-3878.
8. 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.

Abbreviations

1L=first line
2L=second line
AE=adverse event
BICR=blinded independent central review
CBR=clinical benefit rate
cis=cisplatin
CPI=checkpoint inhibitor
CR=complete response
DOR=duration of response
ECOG PS=Eastern Cooperative Oncology Group Performance Status
mUC=metastatic urothelial cancer
ORR=objective response rate
OS=overall survival
OSP=overall safety population
PD=progressive disease
PFS=progression-free survival
PLT=platinum
PR=partial response
SAE=serious adverse event
SD=stable disease
SG=sacituzumab govitecan-hziy
TEAE=treatment-emergent adverse event
TRAE=treatment-related adverse event

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 gilead.privacy@gilead.com.