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Trodelvy® (sacituzumab govitecan-hziy) TROPHY-U-01 Cohort 3

This document is in response to your request for information regarding Trodelvy® (sacituzumab govitecan-hziy [SG]) and its use in patients with locally advanced or metastatic urothelial cancer (mUC).

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

TROPHY-U-01 Study on SG in mUC

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

Cohort 3 is evaluating the efficacy and safety of SG + PEMBRO in CPI-naïve patients with mUC that progressed after PLT-based chemotherapy. Data from 41 patients were included in the interim analysis.[2,3]

- Treatment with SG + PEMBRO resulted in an ORR per independent review of 41% (17/41; 95% CI: 26.3–57.9%), a CR of 20%, and a median PFS of 5.3 months (95% CI: 3.38–10.18); the median DOR was 11.1 months (4.76–NE; n=17).[3]
- A reduction in tumor size was observed in 72% of evaluable patients.[3]

The most common all-grade TRAEs included diarrhea (71%), nausea (56%), neutropenia (51%), and anemia (49%).[3]

TROPHY-U-01 Study on SG in mUC

TROPHY-U-01, a global, open-label, phase 2, multi-cohort study, is investigating the efficacy and safety of SG in patients with unresectable locally advanced/mUC.[1] Approximately 827 patients are anticipated to be enrolled, and interim results from Cohort 3 are summarized.

Cohort 3

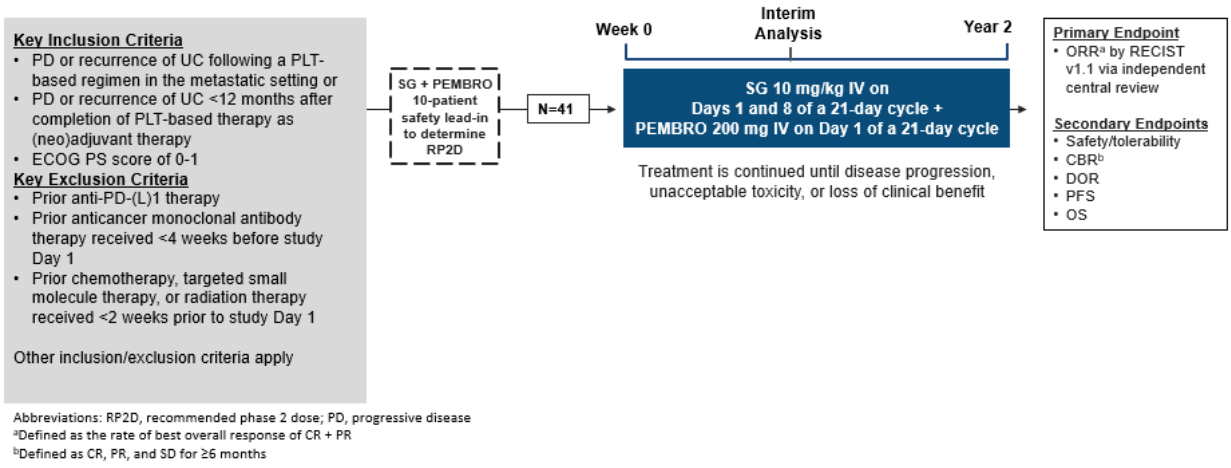
Study design and baseline demographics

Cohort 3 was a single-arm design investigating the role of SG + PEMBRO in CPI-naïve patients who had progression of urothelial cancer after PLT-based chemotherapy in the metastatic setting or ≤12 months after completion of PLT in the neoadjuvant setting. The primary endpoint was ORR (CR + PR) by independent central review per RECIST 1.1 criteria.[3]

A total of 55 patients were enrolled, and 41 patients were treated and included in the interim analysis. A 10-patient safety lead-in with SG + PEMBRO was performed to determine the recommended phase 2 dosing of SG.[3] SG 10 mg/kg IV was administered on Days 1 and 8 + PEMBRO 200 mg (standard approved dose) on Day 1 of a 21-day cycle (

Figure 1).[3] Please see Table 1 for patient baseline demographics and disease characteristics.

Figure 1. TROPHY-U-01 Cohort 3 Study Design[2,4]



Abbreviations: RP2D, recommended phase 2 dose; PD, progressive disease
[a]Defined as the rate of best overall response of CR + PR
[b]Defined as CR, PR, and SD for ≥6 months

Table 1. TROPHY-U-01 Cohort 3: Baseline Demographics and Disease Characteristics[2]

Key Demographics and Characteristics		Cohort 3 (N=41)
Age, median (range), y		67 (46–86)
Male, n (%)		34 (83)
Race, n (%)	White	22 (54)
	Other or not reported	19 (46)
ECOG PS 1, n (%)		25 (61)
Type of disease, n (%)	mUC	32 (78)
	Locally advanced unresectable	9 (22)
Visceral Metastases, n (%)		32 (78)
	Lung/pleura	22 (54)
	Liver	12 (29)
	Other	8 (20)
Time since initial diagnosis, median, mo (range)		13.5 (2.3–98.1)
Number of prior anticancer regimens, median (range)		1 (1–2)
Bellmunt risk factors, n (%)	0	10 (24)
	1	20 (49)
	2	11 (27)

Key Demographics and Characteristics		Cohort 3 (N=41)
Prior PLT chemotherapy, n (%)	Cisplatin	29 (71)
	Carboplatin	12 (29)
Setting of last systemic therapy	Neoadjuvant, n (%)	17 (41)
	Metastatic, n (%)	24 (59)

Results[3]

Interim efficacy and safety results for 41 patients were included in this analysis, with a data cutoff of July 26, 2022, and a median follow-up of 14.8 (95% CI: 12.6-16.8) months. At data cutoff, 5 patients were continuing treatment, and 36 had permanently discontinued treatment.

Efficacy

The ORR by independent central review was 41% (95% CI: 26.3-57.9) with a median time to response of 1.4 months (Table 2).

Table 2. TROPHY-U-01 Cohort 3: Response and Survival Results[3]

Endpoints		Cohort 3 (N=41)
ORR per independent review, n (%); 95% CI		17 (41); 26.3–57.9
Best response per independent review, n (%)	CR	8 (20)
	PR	9 (22)
	SD	9 (22)
	Progressive disease	10 (24)
	Not assessed or evaluable	5 (12)
CBR, n (%); 95% CI		19 (46); 30.7–62.6
DOR, median (95% CI), mo, (n=17)		11.1 (4.76–NE)
PFS, median (95% CI), mo		5.3 (3.38–10.18)
OS, median (95% CI), mo		12.8 (10.74–NE)
Evaluable patients with target lesion reduction, %[a]		72

[a]The change was durable for most responders and some non-responders.

Safety

A total of 26/36 patients discontinued treatment due to disease progression. All 41 patients experienced at least 1 TRAE. Sixteen patients (39%) required a SG dose reduction, and 15% of patients discontinued SG due to a TRAE. The most common all-grade TRAEs are listed in Table 3. Grade 3 to 4 TRAEs occurred in 61% of patients. Five patients required steroids (ie, oral steroids in 4 patients and IV steroids in 1 patient) for PEMBRO-related AEs (diarrhea, n=3; pruritus, n=1; pneumonitis, n=1). A total of 9 patients (22%) received G-CSF for prophylactic use, and 8 patients (20%) received G-CSF for treatment of an AE. No treatment-related deaths were reported. At data cutoff, 20 patients had died, primarily due to disease progression (19 of 20).

Table 3. TROPHY-U-01 Cohort 3 TRAEs[3]

TRAEs	Cohort 3 (N=41)

	All-Grade TRAEs Reported by ≥15% of Patients, n (%)	Grade ≥3 TRAEs Reported by ≥5% of Patients, n (%)
Diarrhea	29 (71)	8 (20)
Nausea	23 (56)	3 (7)
Neutropenia	21 (51)	15 (37)
Anemia	20 (49)	7 (17)
Asthenia	17 (41)	3 (7)
Alopecia	16 (39)	0
Fatigue	13 (32)	3 (7)
Decreased appetite	12 (29)	2 (5)
Vomiting	12 (29)	0
Leukopenia	11 (27)	8 (20)
Pruritus	10 (24)	0
Stomatitis	7 (17)	0
Hypomagnesemia	7 (17)	0
Febrile neutropenia	4 (10)	4 (10)
Pneumonitis	2 (5)	2 (5)

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: 1 December 2025. Last Updated 15 April 2025.
2. 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.
3. Grivas P, Pouessel D, Park CH, et al. Sacituzumab Govitecan in Combination With Pembrolizumab for Patients With Metastatic Urothelial Cancer That Progressed After Platinum-Based Chemotherapy: TROPHY-U-01 Cohort 3. *J Clin Oncol.* 2024;42(12):1415-1425.
4. 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.

Abbreviations

AE=adverse event
CBR=clinical benefit rate
CPI=checkpoint inhibitor
CR=complete response
DOR=duration of response
ECOG=Eastern Cooperative Oncology Group
G-CSF=granulocyte colony-stimulating factor
mUC=metastatic urothelial cancer
NE=not estimable
NR=not reached
ORR=objective response rate
OS=overall survival
PD-1=anti-programmed cell death-1
PD-L1=programmed death ligand 1
PEMBRO=pembrolizumab
PFS=progression-free survival
PLT=platinum
PR=partial response
PS=performance status
RECIST=Response Evaluation Criteria In Solid Tumors
SD=stable disease
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: https://www.gilead.com/-/media/files/pdfs/medicines/oncology/trodelvy/trodelvy_pi.pdf.

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 🖱 https://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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