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Trodelvy® (sacituzumab govitecan-hziy) Use in Patients With Endometrial Cancer

This document is in response to your request for information regarding Trodelvy® (sacituzumab govitecan-hziy [SG]) and its use in patients with endometrial cancer (EC).

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Trodelvy is not indicated for use in patients with EC. 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 Studies of SG Use in EC

The phase 2 TROPiCS-03 study is evaluating the efficacy and safety of SG in adult patients with metastatic solid tumors, including advanced/metastatic EC, who progressed after PLT-based chemotherapy and anti-PD-L1-directed therapy.[1,2]

- At the data cutoff, the ORR was 27%. The median DOR was 9 months, the median PFS was 5 months, and the median OS was 15 months.[2]
- Any-grade TEAEs were reported in all patients, and 85% reported Grade ≥3 TEAEs. The most common Grade ≥3 TEAEs were neutropenia (49%), diarrhea (22%), and anemia (20%).[2]
- Any-grade and Grade ≥3 TRAEs were reported in 95% and 76% of patients, respectively.[2]
- Deaths due to TEAEs occurred in 3 patients; 1 was deemed related to SG.[2]

An open-label, non-randomized, phase 2 study is evaluating the safety and efficacy of SG in patients with persistent or recurrent EC overexpressing Trop-2 who progressed after PLT-based chemotherapy.[3]

- In the preliminary analysis of 21 patients, 7 patients had an ORR, the median PFS was 5.7 months, the median OS was 22.2 months, and durable disease control (confirmed CR + PR + SD ≥6 months) was observed in 7/20 evaluable patients for this endpoint.
- The most common Grade ≥3 TRAEs observed in ≥10% of patients included neutropenia (43%), fatigue (19%), anemia (14%), diarrhea (14%), and febrile neutropenia (10%).

The phase 1/2 IMMU-132-01 study investigated the efficacy and safety of SG in patients with metastatic epithelial cancers, including EC, who had relapsed after or were refractory to ≥1 prior therapy for metastatic disease. The EC cohort consisted of 18 patients.[4]

- In the EC cohort, the ORR was 22.2%, the median PFS was 3.2 months, and the median OS was 11.9 months.

- Safety data specific to patients with EC were not reported. In the OSP (n=495), the most common TRAEs were nausea (62.6%), neutropenia (57.8%), diarrhea (56.2%), fatigue (48.3%), and alopecia (40.4%).

Ongoing Clinical Studies of SG Use in EC

Ongoing clinical studies are summarized below.

Clinical Studies of SG Use in EC

TROPiCS-03 Study in Metastatic Solid Tumors

Study design and demographics

TROPiCS-03 (NCT03964727) is a multicohort, open-label, phase 2 basket study evaluating the efficacy and safety of SG in adult patients with metastatic solid tumors, including advanced/metastatic EC, who progressed after PLT-based chemotherapy and anti-PD-L1-directed therapy. Patients received SG 10 mg/kg IV on Days 1 and 8 of a 21-day treatment cycle.[1]

As of the data cutoff, 41 patients were enrolled, with a median (range) follow-up of 19.4 (14.4–30.3) months.[2] Key baseline demographics for the EC cohort can be found in Table 1.

Table 1. TROPiCS-03 EC Cohort: Baseline Demographics and Disease Characteristics[2]

Key Demographics and Characteristics		Overall (N=41)
Age, median (range), years		68 (44–83)
Race, n (%)	White	21 (51)
	Asian	8 (20)
	Other/not reported	6 (15)/6 (15)
Eastern Cooperative Oncology Group Performance Status, n (%)	0/1	18 (44)/23 (56)
Microsatellite instability high, n (%)	Yes	8 (20)
Histological diagnosis, n (%)	Endometrioid	20 (49)
	Serous	17 (42)
	Other	4 (10)
Number of prior anticancer regimens, median (range)		3 (1–6)
Prior anticancer therapy type, n (%)	Chemotherapy	41 (100)
	Immunotherapy	35 (85)
	Targeted agents	26 (63)
	Hormonal therapy	5 (12)
	Other	1 (2)
Prior PLT-based chemotherapy + immunotherapy, n (%)		35 (85)

Efficacy[2]

Efficacy outcomes are shown in Table 2.

Table 2. TROPiCS-03 EC Cohort: Efficacy Outcomes[2]

Outcome		SG (N=41)
ORR (confirmed CR + PR; primary endpoint),[a] n (%) [95% CI]		11 (27) [14–43]
Best overall response, n (%)	Confirmed CR	1 (2)
	Confirmed PR	10 (24)
	SD	17 (42)
	Progressive disease	8 (20)
	Not evaluable	1 (2)
	Not assessed[b]	4 (10)
CBR (confirmed CR + PR + SD ≥6 months),[c] n (%) [95% CI]		17 (42) [26–58]
DOR (confirmed CR or PR),[c] median (95% CI), months		9 (2.8–NR)
PFS,[c] median (95% CI), months		5 (2.8–9.8)
PFS rate,[d] 6-/12-months, % (95% CI)		41 (25–56)/23 (11–38)
OS, median (95% CI), months		15 (5.9–NR)
OS rate,[d] 6-/12-months, % (95% CI)		65 (49–78)/50 (34–64)
Patients with target lesion reduction from baseline, n (%)		26 (63)

[a]Assessed by investigators per RECIST version 1.1.
[b]Patients without any post-baseline assessment were not assessed.
[c]Per investigator assessment and blinded independent central review.
[d]Assessed per Kaplan-Meier.

Safety[2]

Any-grade TEAEs were reported in all patients, and Grade ≥3 TEAEs were reported in 85% of patients. The most common Grade ≥3 TEAEs were neutropenia, diarrhea, and anemia (Table 3). Seven percent of patients discontinued due to TEAEs. Three patients died due to TEAEs (unknown cause, n=2; pneumonia, n=1); 1 death of unknown cause was deemed SG-related by the investigator. Any-grade TRAEs were reported in 39 patients (95%), and Grade ≥3 TRAEs were reported in 31 patients (76%).

Table 3. TROPiCS-03 EC Cohort: Most Common (>20% Any-Grade) TEAEs[2]

TEAE, n (%)	Any-Grade	Grade ≥3
Neutropenia	26 (63)	20 (49)
Diarrhea	23 (56)	9 (22)
Fatigue	23 (56)	3 (7)
Nausea	22 (54)	3 (7)
Anemia	20 (49)	8 (20)
Alopecia	17 (42)	0
Constipation	15 (37)	0
Hypomagnesemia	11 (27)	0
Vomiting	11 (27)	2 (5)
Hypokalemia	10 (24)	6 (15)

Study in EC Overexpressing Trop-2[3]

Study design and demographics

An open-label, non-randomized, phase 2 study (NCT04251416) is evaluating the safety and efficacy of SG in patients with persistent or recurrent EC overexpressing Trop-2 who progressed after PLT-based chemotherapy. Patients received SG 10 mg/kg IV on Days 1 and 8 of a 21-day treatment cycle until disease progression or unacceptable toxicity.

Fifty patients were screened during Stage 1, of which 92% were ≥1% Trop-2+, and 31 (62%) demonstrated any staining intensity in ≥50% of tumor cells. Of the 31 patients, 23 were enrolled in the study, and 21 were evaluable for response. Fifty patients will be enrolled in the study.

Patients were a median (range) age of 63 (47–77) years. The median (range) number of prior anticancer regimens was 3 (1–6); 52.4% of patients had 1 to 3, and 47.6% of patients had >3 prior anticancer regimens. Histological/cytological diagnoses include serous (47.6%), endometrioid (28.6%), carcinosarcoma (14.3%), and others (9.5%). The median (IQR) duration of follow up duration was 17 (7.6–35.2) months.

Efficacy and safety

In the preliminary analysis of 21 patients, 7 patients (33.3%) had an ORR (primary endpoint; confirmed CR + PR), the median PFS was 5.7 months, and the median OS was 22.2 months. Confirmed PR and CR were observed in 1 (4.8%) and 6 (28.5%) patients, respectively. Durable disease control (confirmed CR + PR + SD ≥6 months) was observed in 7/20 evaluable patients (35%) for this endpoint.

The most common Grade ≥3 TRAEs observed in ≥10% of patients included neutropenia (n=9; 43%), fatigue (n=4; 19%), anemia (n=3; 14%), diarrhea (n=3; 14%), and febrile neutropenia (n=2; 10%).

IMMU-132-01 Study in Metastatic Epithelial Cancer[4]

Study design

IMMU-132-01, a phase 1/2, single-arm, open-label basket study, investigated the efficacy and safety of SG in patients with metastatic epithelial cancers, including EC, who had relapsed after or were refractory to ≥1 prior therapy for metastatic disease. In the EC cohort (n=18), SG 10 mg/kg IV was administered on Days 1 and 8 of a 21-day treatment cycle until disease progression or unacceptable toxicity, death, or withdrawal of consent.

Efficacy

Efficacy data for the EC cohort are presented in Table 4.

Table 4. IMMU-132-01: Response Rates in Patients With EC (n=18)[4]

ORR,[a,b] % (95% CI)	CR,[b] n (%)	PR,[b] n (%)	SD, n (%)	DOR, Median (95% CI), mo	OS,[c] Median (95% CI), mo	PFS, Median (95% CI), mo	CBR,[d] n (%) [95% CI]
22.2 (6.4–47.6)	0	4 (22.2)	6 (33.3)	NR (9.1–NR)	11.9 (4.7–NR)	3.2 (1.9–9.4)	8 (44.4) [21.5–69.2]

[a]Primary endpoint; defined as PR + CR.
[b]Confirmed by investigator's assessment per RECIST version 1.1.
[c]Assessed per Kaplan-Meier.
[d]Defined as CR + PR + SD ≥6 months.

Safety

Safety data specific to patients with EC were not reported.

In the OSP (n=495), 41 patients (8.3%) permanently discontinued treatment due to adverse events. The most common TRAEs were nausea (62.6%), neutropenia (57.8%), diarrhea

(56.2%), fatigue (48.3%), and alopecia (40.4%). Grade ≥3 neutropenia and febrile neutropenia occurred in 42.4% and 5.3% of patients, respectively.

Ongoing Clinical Studies on SG Use in EC

ASCENT-GYN-01, a randomized, open-label, phase 3 study (NCT06486441) is evaluating the efficacy and safety of SG vs treatment of physician's choice, in patients with EC who have received prior treatment with PLT-based chemotherapy and immunotherapy.

An open-label, non-randomized, single-arm, phase 2 study (NCT04251416) is evaluating the efficacy and safety of SG in patients with persistent or recurrent endometrial carcinoma of epithelial origin that has progressed after or is refractory to PLT-based chemotherapy.

An open-label, non-randomized, single-arm, phase 2, pilot study (NCT06865677) is evaluating the efficacy and safety of SG in patients with relapsed ovarian, endometrial, and cervical carcinomas (three separate cohorts). Eligible patients must have recurrent epithelial (ie, endometrioid or serous) EC that is refractory to standard treatment.

An open-label, phase 1 study (NCT06040970) is evaluating the efficacy and safety of SG + cisplatin, in PLT-sensitive, recurrent ovarian cancer and EC (two separate groups); the primary objective is to determine the optimal dose of SG + cisplatin for treatment of epithelial ovarian cancer and EC.

References

1. Santin D, Corr B, Spira A, et al. Efficacy and safety of sacituzumab govitecan in patients with advanced solid tumors (TROPiCS-03): analysis in patients with advanced endometrial cancer. *J Clin Oncol.* 2024;42(29):3421-3429.
2. Corr B, Dumbrava E, Spira A, et al. Efficacy and safety of sacituzumab govitecan in patients with advanced/metastatic endometrial cancer: updated results from TROPiCS-03 (Poster #733P). Presented at: European Society for Medical Oncology (ESMO); September 13-17, 2024; Barcelona, Spain.
3. Santin AD, McNamara B, Siegel ER, et al. Preliminary results of a Phase II trial with sacituzumab govitecan (SG) in patients with recurrent endometrial carcinoma overexpressing Trop-2. [Poster 294]. Presented at: American Society of Clinical Oncology (ASCO) 2023; June 2-6, 2023; Chicago, IL & Online.
4. Bardia A, Hurvitz SA, Rugo HS, et al. A plain language summary of the ASCENT study: sacituzumab govitecan for metastatic triple-negative breast cancer. *Future Oncol.* 2021;17(30):3911-3924.

Abbreviations

CBR=clinical benefit rate
CR=complete response
DOR=duration of response
EC=endometrial cancer
NR=not reached or not calculable
ORR=objective response rate
OS=overall survival
OSP=overall safety population
PD-L1=programmed death-ligand 1
PFS=progression-free survival
PLT=platinum
PR=partial response
RECIST=Response Evaluation Criteria in Solid Tumors
SD=stable disease
SG=sacituzumab govitecan-hziy
TEAE=treatment-emergent adverse event
TRAE=treatment-related adverse event
Trop-2=trophoblast cell surface antigen 2

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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