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Trodelvy® (sacituzumab govitecan-hziy) Use in Patients With Advanced, Recurrent, or Metastatic Endometrial Cancer

This document is in response to your request for information regarding Trodelvy® (sacituzumab govitecan-hziy [SG]) and its use in patients with advanced, recurrent, or metastatic 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 Advanced, Recurrent, or Metastatic 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 mo, the median PFS was 5 mo, and the median OS was 15 mo.[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 who progressed after PLT-based chemotherapy (N=50).[3,4]

- The ORR was 28% (n=14). The median PFS and OS was 5.52 mo and 17.5 mo, respectively. The median DOR was 9.3 mo, and 70.8% of patients had a reduction from baseline in the diameter of the target lesion.[4]
- In an analysis of efficacy according to Trop-2 expression, median PFS was not significantly different between subgroups according to H-score (*P*=0.81), and expression of Trop-2 did not significantly correlate with objective response (*P*=0.07).[4]
- The most common Grade 3 to 4 TEAEs included neutrophil count decreased (26 patients; 79 events), anemia (16 patients; 33 events), and fatigue (7 patients; 10 events).[4]

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.[5]

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

The ongoing phase 3 ASCENT-GYN-01 study is evaluating the efficacy and safety of SG vs TPC in patients with recurrent or persistent EC who have received up to three prior lines of systemic treatment, including PLT-based chemotherapy and PD-(L)1 inhibitor therapy. Eligible patients will receive SG or TPC (doxorubicin or paclitaxel). Dual primary endpoints will be PFS (BICR) and OS. Approximately 640 patients will be enrolled.[6]

Ongoing Clinical Studies of SG Use in Advanced, Recurrent, or Metastatic 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-d 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) mo.[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)

Key Demographics and Characteristics		Overall (N=41)
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)
	PD	8 (20)
	Not evaluable	1 (2)
	Not assessed[b]	4 (10)
CBR (confirmed CR + PR + SD ≥6 mo),[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-mo, % (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 BICR.
[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 Persistent/Recurrent EC

Study design and demographics

An open-label, non-randomized, single-center, phase 2 study is evaluating the safety and efficacy of SG in patients with persistent or recurrent EC who progressed after ≥1 line of PLT-based chemotherapy. Patients received SG 10 mg/kg IV on Days 1 and 8 of a 21-dtreatment cycle until disease progression or unacceptable toxicity. Trop-2 expression was evaluated per immunohistochemistry with an H-score.[3,4]

Fifty patients were screened during Stage 1, which included patients with Trop-2 expression of any staining intensity in ≥50% of tumor cells. Of these patients, 21 were evaluable for response.[3] During Stage 2 of the study (Trop-2 expression not required for eligibility), 34 patients were screened, and 29 were evaluable; thus, 50 patients were evaluated overall.[4]

Patients were a median (range) age of 68 (30–82) years; 18 patients (36%) were aged ≥65 years. The median (range) number of prior anticancer regimens was 2 (1–4); 50% of patients had not responded to treatment with pembrolizumab/dostarlimab. Histological/cytological diagnoses included serous (42%), endometrioid (22% [Grade 1, 4%; Grade 2, 4%; and Grade 3, 14%]), carcinosarcoma (22%), mixed serous (6%), and other (8%). Of the 46 patients with mismatch repair status available, 44 (96%) were proficient. The median (range) duration of follow-up was 10.3 (2–59.5) mo.[4]

Efficacy and safety[4]

The primary efficacy endpoint was met, as the ORR was >10%; additional efficacy outcomes are shown in Table 4.

Table 4. Recurrent/Persistent EC: Efficacy Outcomes[4]

Outcome		SG (N=50)
ORR (primary endpoint), n (%)		14 (28)
Best overall response, n (%)	CR	2 (4)
	PR	12 (24)
	SD	26 (52)
	PD	10 (20)
CBR, n (%)		26 (52)
DOR, median (95% CI), mo		9.3 (2–12.9)
PFS	Events, n (%)	42 (84)
	Median (95% CI), mo	5.52 (3.75–7.36)
	6-/12-month rate, % (95% CI)	44 (30–58)/26 (13–39)
OS	Deaths, n (%)	35 (70)
	Median (95% CI), mo	17.5 (10.4–22.2)
	6-/12-mo rate, % (95% CI)	82 (71–93)/58 (44–73)
Patients with reduction from baseline in diameter of target lesion, %		70.8

Efficacy analyses were performed according to Trop-2 expression; the median H-score was 240. The median PFS was not significantly different between subgroups by H-score: at or above median, 5.8 mo; below median, 3.8 mo (*P*=0.81). Additionally, there was a moderate negative correlation between the maximum change in tumor volume and baseline H-score (ρ=-0.45; *P*=0.003). Further, expression of Trop-2 varied among those who achieved PR, and some patients who had PD also had high levels of Trop-2 expression; overall, expression of Trop-2 did not significantly correlate with objective response (*P*=0.07).

Safety outcomes were consistent with the known safety profile of SG. Grade 3 to 4 TEAEs were reported in 40 patients (80%), with the most common being neutrophil count decreased (26 patients; 79 events), anemia (16 patients; 33 events), and fatigue (7 patients; 10 events); these TEAEs were managed with dose interruptions, dose reductions, and supportive care according to established guidelines.

IMMU-132-01 Study in Metastatic Epithelial Cancer[5]

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-d treatment cycle until disease progression or unacceptable toxicity, death, or withdrawal of consent.

Efficacy

Efficacy data for the EC cohort are presented in Table 5.

Table 5. IMMU-132-01: Response Rates in Patients With EC (n=18)[5]

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 mo..

Safety

Safety data specific to patients with EC were not reported.

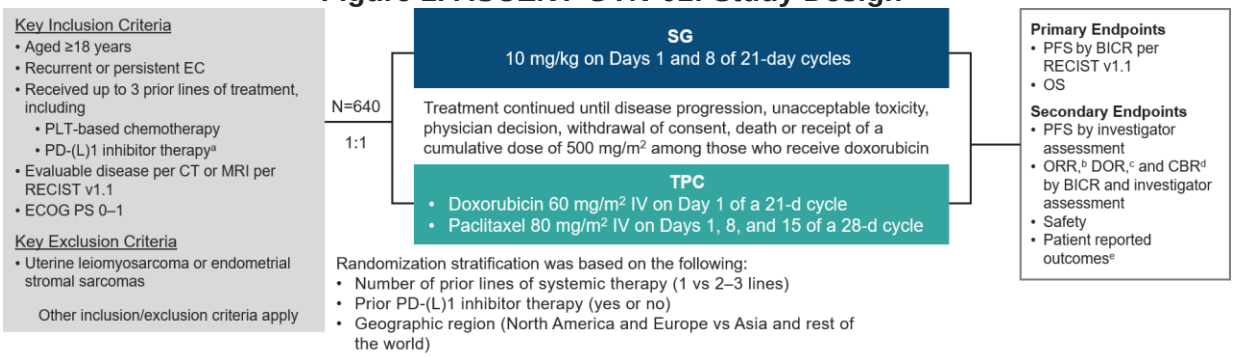
In the OSP (n=495), 41 patients (8.3%) permanently discontinued treatment due to adverse events. The most common TRAEs were nausea (62.6%), neutropenia (57.8%), diarrhea (56.2%), fatigue (48.3%), and alopecia (40.4%). Grade ≥3 neutropenia and febrile neutropenia occurred in 42.4% and 5.3% of patients, respectively.

ASCENT-GYN-01[6]

An ongoing, randomized, open-label, phase 3 study (NCT06486441) is evaluating the efficacy and safety of SG vs TPC in patients with recurrent or persistent EC who have received up to three prior lines of systemic treatment, including PLT-based chemotherapy and PD-(L)1 inhibitor therapy (Figure 1). Eligible patients will be randomly assigned (1:1) to receive SG 10 mg/kg IV on Days 1 and 8 of a 21-d cycle or either doxorubicin (60 mg/m^2 IV on Day 1 of a 21-d cycle) or paclitaxel (80 mg/m^2 IV on Days 1, 8, and 15 of a 28-d cycle). The dual primary endpoints are PFS (by BICR per RECIST v1.1) and OS.

No results have been reported.

Figure 1. ASCENT-GYN-01: Study Design[6]



Abbreviation: EORTC QLQ-C30=European Organisation for the Research and Treatment of Cancer Quality of Life Questionnare-Core 30.
[a]Patients with comorbidities that prevented treatment with PD-(L)1 inhibitor therapy or for whom it was not available as standard of care per local standards were eligible for inclusion (enrollment cap, 10%).
[b]Confirmed CR or PR.
[c]Time from confirmed CR or PR to PD or death from any cause.
[d]Confirmed CR or PR ≥4 wk or SD for ≥6 mo.
[e]Change from baseline to Week 16 in the physical functioning and Global Health Score/Quality of Life domains of the EORTC QLQ-C30.

Ongoing Clinical Studies on SG Use in EC

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, 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 the 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. *Journal of Clinical Oncology.* 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); June 2-6, 2023; Chicago, IL & Online.
4. Santin AD, Roque DM, Siegel E, et al. A phase II evaluation of the efficacy and safety of sacituzumab govitecan in patients with recurrent uterine cancer [Oral Presentation]. Presented at: International Society of Gynecological Cancer (IGCS) Annual Global Meeting; November 5-7, 2025; Cape Town, South Africa.
5. 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.

6. Eskander RN, Corr B, Cibula D, et al. A randomized, phase III study of sacituzumab govitecan versus treatment of the physician's choice in patients with endometrial cancer after platinum-based chemotherapy and immunotherapy: the ASCENT-GYN-01 study (GOG-3104/ENGOT-en26/APGOT-EN2). *Int J Gynecol Cancer.* 2025;36(6):102654.

Abbreviations

BICR=blinded independent central review
CBR=clinical benefit rate
CR=complete response
DOR=duration of response
EC=endometrial cancer
H-score=histochemical score
NR=not reached or not calculable
ORR=objective response rate
OS=overall survival
OSP=overall safety population
PD=progressive disease
PD-(L)1=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
TPC=treatment of physician's choice
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.

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