TROPiCS-03, a Phase 2 Basket Study of Sacituzumab Govitecan (SG) in Patients (Pts) With Metastatic Solid Tumors: Early Analysis in Pts With Advanced/Metastatic Endometrial Cancer (EC)

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TROPiCS-03

Conclusions

The findings from the TROPiCS-03 phase 2 basket study showed encouraging efficacy of SG with a manageable toxicity profile in a heavily pretreated population with advanced/ metastatic endometrial cancer

- SG monotherapy showed an encouraging ORR of 22%
- Median DOR was 8.8 months and median PFS was 4.8 months, though these data will continue to mature with additional follow-up
- Overall, the types and frequency of AEs in this study are consistent with the known safety profile of SG, and no new safety signals were identified

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Supplemental materials

References: **1**. Post CCB, et al. *Gynecol Oncol*. 2022;165:223-229. **2.** Colombo N, et al. *Ann Oncol*. 2013;24:vi33-vi38. **3.** TRODELVY® (sacituzumab govitecan-hziy) [prescribing information]. Gilead Sciences, Inc., Foster City, CA; February 2023. **4.** Weiss J, et al. *Expert Rev Anticancer Ther*. 2019;19:673-679. **5.** Bardia A, et al. *Ann Oncol*. 2021;32:746-756. **6.** FDA approval. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-sacituzumab-govitecan-hziy-metastatic-triple-negative-breast-cancer. Accessed April 2023. **7.** FDA approval. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-sacituzumab-govitecan-advanced-urothelial-cancer. Accessed April 2023.

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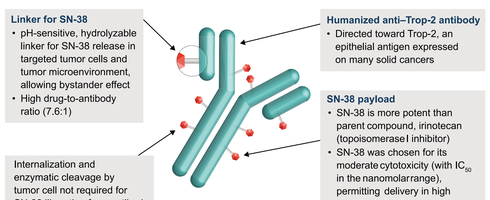
Background

- Endometrial cancer is the most common gynecological cancer in developed countries[1]
- Effective treatment options are lacking for patients with advanced disease and those progressing on platinum-based chemotherapy and immune checkpoint inhibitor therapy[1,2]
- Sacituzumab govitecan (SG) is a trophoblast cell surface antigen 2 (Trop-2)–directed antibody-drug conjugate[3-5]
  - Trop-2 is a transmembrane glycoprotein highly expressed in many epithelial cancers
  - SG is composed of a Trop-2–targeted monoclonal antibody, conjugated with SN-38, an active metabolite of irinotecan, a topoisomerase I inhibitor, via a hydrolysable linker (Figure 1)
  - The linker allows for intratumoral release of therapeutic concentrations of SN-38 as well as release extracellularly within the surrounding tumor microenvironment, providing a bystander effect (killing surrounding neighboring cells). Thus, cytotoxic chemotherapy is delivered selectively, while limiting exposure to normal tissues
- SG has been approved for the treatment of patients with unresectable, locally advanced or metastatic triple-negative breast cancer who have received ≥ 2 prior systemic therapies, at least 1 of them for metastatic disease; and metastatic hormone receptor-positive, human epidermal growth factor 2-negative breast cancer who have received endocrine-based therapy and at least 2 additional systemic therapies for metastatic disease. It is also approved for the treatment of patients with locally advanced or metastatic urothelial cancer who previously received a platinum-containing chemotherapy and either a programmed death (PD)-1 or a programmed death ligand (PD-L)1 inhibitor[3,6,7]
- In the open-label, phase 1/2 IMMU-132-01 basket study, SG monotherapy resulted in a 22% objective response rate (ORR) with a manageable safety profile in 18 patients with metastatic endometrial cancer who had relapsed after or were refractory to ≥ 1 prior standard therapeutic regimen[5]

Figure 1. Sacituzumab govitecan, antibody-drug conjugate[3-5]



IC_{50}, half maximal inhibitor concentration; Trop-2, trophoblast cell surface antigen 2.
Adapted from Rugo HS, et al. TROPiCS-02: a phase III study investigating sacituzumab govitecan in the treatment of HR+/HER2- metastatic breast cancer. *Future Oncol*. 2020;16:705-715. Complete licensing info can be found here: http://creativecommons.org/licenses/by-nc-nd/4.0/.

Objective

- To report the efficacy and safety of SG in patients with advanced/metastatic disease from the endometrial cancer cohort of the TROPiCS-03 phase 2 study

Methods

- TROPiCS-03 (NCT03964727) is a multicohort, open-label, phase 2 basket study in patients with metastatic solid tumors
- Adult patients in the endometrial cancer cohort (n = 41) had progression after prior platinum-based chemotherapy and anti–PD-(L)1-directed therapy (requirement for PD-(L)1 progression added in protocol amendment), an Eastern Cooperative Oncology Group performance status of 0 to 1, and creatinine clearance ≥ 30 mL/min
- Patients received 10 mg/kg of SG on day 1 and day 8 of a 21-day cycle
- The primary end point was ORR by investigator's assessment per RECIST 1.1
- Secondary end points included duration of response (DOR), clinical benefit rate, and progression-free survival (PFS) per investigator's assessment, overall survival, and safety

Results

- As of the data extraction date April 18, 2023, 41 patients were enrolled (Table 1); 41 (100%) received ≥ 1 dose of SG; 29 (70.7%) patients discontinued treatment, majority (22 [53.7%]) due to disease progression; treatment is ongoing in 12 (29.3%) patients
- Median study follow-up was 5.6 months (range, 0.7-19.1 months)

Table 1. Demographics and clinical characteristics

	SG (n = 41)
Median age at study entry, y (range)	68 (44-83)
Race, n (%)	
White	21 (51.2)
Black or African-American	1 (2.4)
Asian	8 (19.5)
Other	5 (12.2)
Not reported	6 (14.6)
ECOG performance status, n (%)	
0	18 (43.9)
1	23 (56.1)
Microsatellite instability high, n (%)	
Yes	8 (19.5)
No	32 (78.0)
NA	1 (2.4)
Histological/cytological diagnosis, n (%)	
Serous	17 (41.5)
Endometrioid	20 (48.8)
Others	4 (9.8)
Number of prior anticancer regimen, n (%)	
1-3	32 (78.0)
> 3	9 (22.0)
Median prior anticancer regimens, n (range)	3 (1-6)
Prior anticancer therapy type, n (%)	
Chemotherapy	41 (100.0)
Hormonal therapy	5 (12.2)
Immunotherapy	35 (85.4)
Targeted agents	26 (63.4)
Other	1 (2.4)
Chemotherapy + IO, n (%)	35 (85.4)
Chemotherapy + IO + ≤ 3 LOT, n (%)	27 (65.9)

ECOG, Eastern Cooperative Oncology Group; IO, immunotherapy; LOT, line of therapy; NA, not available; SG, sacituzumab govitecan.

Efficacy analysis

- Best overall response and ORR are shown in Table 2. Best overall response is also shown in Figures 2 and 3
- Median DOR was 8.8 months (95% confidence interval [CI], 2.8 months-not reached; Figure 4)

Table 2. Objective response rate and clinical benefit rate

SG (n = 41)	n (%)	95% CI
Best overall response		
Confirmed CR	0 (0)	–
Confirmed PR	9 (22)	–
SD/SD ≥ 6 months	18 (44)/4 (10)	–
Progressive disease	8 (20)	–
Not evaluable	2 (5)	–
Not assessed[a]	4 (10)	–
ORR (confirmed CR + PR)[b]	9 (22)	10.6-37.6
CBR (confirmed CR + PR + SD ≥ 6 months)[b]	13 (32)	18.1-48.1

CBR, clinical benefit rate; CI, confidence interval; CR, complete response; ORR, objective response rate; PR, partial response; SD, stable disease; SG, sacituzumab govitecan.
[a]Patients discontinued study treatment before reaching the first post-baseline tumor assessment. [b]Calculated using exact method of binomial distribution.

Figure 2. Waterfall plot of target lesion diameters by best overall response category

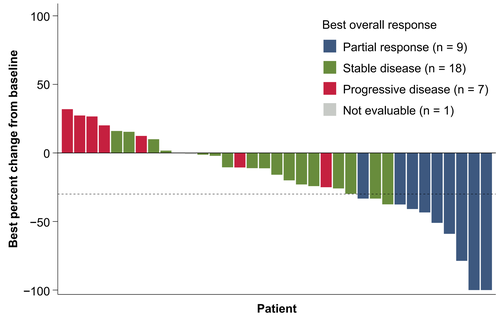


Figure 3. Spider plot of tumor response

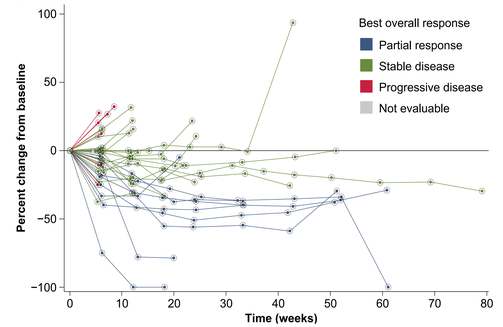
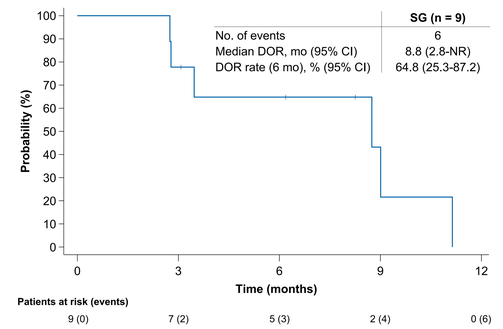


Figure 4. Kaplan-Meier plot for duration of response

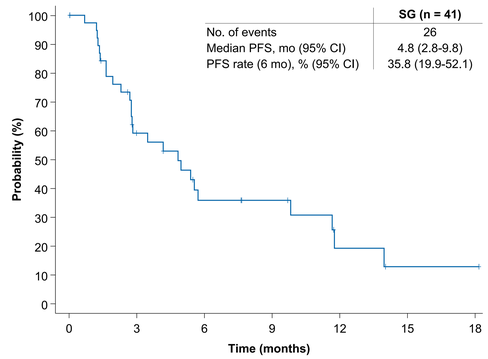


CI, confidence interval; DOR, duration of response; NR, not reached; SG, sacituzumab govitecan.

Progression-free survival

- The median PFS was 4.8 months (95% CI, 2.8-9.8 months) (Figure 5)

Figure 5. Kaplan-Meier plot for progression-free survival



CI, confidence interval; PFS, progression-free survival; SG, sacituzumab govitecan.

Safety

- Any-grade treatment-emergent adverse events (TEAEs) were reported in 40 (97.6%) of all patients; 33 (80.5%) reported grade ≥ 3 TEAEs
  - Any-grade treatment-related AEs (TRAEs) were reported in 38 (92.7%) of all patients; grade ≥ 3 TRAEs occurred in 30 (73.2%) of all patients
- TEAEs led to dose reduction in 9 (22.0%) and discontinuation in 2 (4.9%) of all patients; 2 (4.9%) patients died during treatment (1 due to pneumonia and 1 unknown cause); neither death was deemed as related to SG treatment by the investigator
- Most common TEAEs were diarrhea in 23 (56.1%), nausea in 22 (53.7%), and fatigue in 21 (51.2%) patients (Table 3)

Table 3. Most common TEAEs by preferred term (n = 41)

TEAE, n (%)	Any grade (occurring in > 20% of patients)	Grade ≥ 3
Diarrhea	23 (56.1)	8 (19.5)
Nausea	22 (53.7)	1 (2.4)
Fatigue	21 (51.2)	1 (2.4)
Alopecia	17 (41.5)	N/A
Anemia	16 (39.0)	6 (14.6)
Neutropenia[a]	16 (39.0)	13 (31.7)
Constipation	15 (36.6)	0
Hypomagnesemia	11 (26.8)	0
Vomiting	11 (26.8)	2 (4.9)
Hypokalemia	9 (22.0)	6 (14.6)

N/A, not applicable; TEAE, treatment-emergent adverse event.
[a]The following preferred terms were also reported but not included in the table: neutrophil count decreased (7 [17.1%] any grade and 5 [12.2%] grade ≥ 3); febrile neutropenia (7 [17.1%] any grade and 7 [17.1%] grade ≥ 3).
TEAE is defined as an AE with start date on or after the date of first dose of study treatment and up to 30 days after date of last dose of study treatment.