Efficacy and Safety of Sacituzumab Govitecan in Patients With Advanced/Metastatic Endometrial Cancer: Updated Results From TROPiCS-03

Bradley R Corr[1], Ecaterina E Dumbrava[2], Alexander Spira[3], Lyndsay Willmott[4], James Butrynski[5], Ka Yu Tse[6], Jilpa Patel[7], Sabeen Mekan[7], Simonetta Mocci[7], Tia Wu[7], Alessandro D Santin[8]

[1]University of Colorado Cancer Center, Aurora, CO, USA; [2]MD Anderson Cancer Center, Houston, TX, USA; [3]Virginia Cancer Specialists, Fairfax, VA, USA; [4]HonorHealth Virginia G. Piper Cancer Care Network Biltmore, Phoenix, AZ, USA; [5]Willamette Valley Cancer Institute and Research Center, Eugene, OR, USA; [6]Li Ka Shing Faculty of Medicine, University of Hong Kong, Hong Kong, China; [7]Gilead Sciences Inc., Foster City, CA, USA; [8]Yale School of Medicine, New Haven, CT, USA

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TROPiCS-03

Conclusions

- This is the first report of OS from TROPiCS-03 with longer follow-up (median, 19.4 months) in patients pretreated with platinum-based chemotherapy with or without immunotherapy for advanced/metastatic EC
- SG showed promising clinical activity with an ORR of 27%, durable responses (median duration of response, 9.0 months [95% CI, 2.8-NR]), and median OS of 15.0 months (95% CI, 5.9-NR)
- Safety of SG was manageable; the treatment discontinuation rate due to adverse events was low at 7%
- Safety findings were consistent with the known SG safety profile, and no new safety signals were identified with longer follow-up
- Based on the findings from this study, a larger, randomized phase 3 study has been initiated (ASCENT-GYN-01; NCT06486441)

Plain Language Summary

- Sacituzumab govitecan (SG) is a drug that is approved to treat breast and bladder cancers
- The TROPiCS-03 clinical trial tested SG in participants with endometrial cancer (EC) that is advanced or metastatic. All participants had previously received platinum-based chemotherapy and most had received immunotherapy to treat their cancer
- In this trial, SG showed encouraging results. Slightly over 1 in 4 participants responded to SG treatment; half of the participants lived for 5 months without their cancer worsening or the participant dying (progression-free survival); overall, 50% of participants lived for 15 months (overall survival)
- Side effects with SG were manageable, and the most common severe medical event was low white blood cell count

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Correspondence: bradley.corr@cuanschutz.edu

Introduction

- Patients with advanced endometrial cancer (EC) have limited treatment options and poor prognosis following progression on or after platinum-based chemotherapy (chemo) and immunotherapy (IO)[1]
- Sacituzumab govitecan (SG) is an antibody-drug conjugate composed of a humanized anti-trophoblast cell-surface antigen 2 (Trop-2) monoclonal antibody coupled to SN-38, the active metabolite of the topoisomerase inhibitor, irinotecan[2-5]
- SG is approved in multiple countries for unresectable, locally advanced, or metastatic triple-negative breast cancer (BC) and HR+/HER2– metastatic BC and for metastatic urothelial cancer in the United States[6,7]
- SG demonstrated encouraging efficacy (overall response rate [ORR] of 22% [95% CI, 11-38]) and manageable safety in an earlier analysis of the TROPiCS-03 study, with a median follow-up of 5.8 months in patients with advanced/metastatic EC[8]

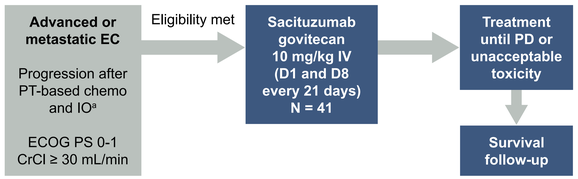
Objective

- To report updated results from the EC cohort of the TROPiCS-03 study

Methods

- TROPiCS-03 is a multicohort, open-label, phase 2 basket study in adult patients with metastatic solid tumors (NCT03964727) (Figure 1)

Figure 1. TROPiCS-03 EC Cohort Study Schema



[a]The requirement for progression with IO was added in a protocol amendment, hence the study originally enrolled patients who had or had not received IO.
CBR, clinical benefit rate; chemo, chemotherapy; CrCl, creatinine clearance; D, day; DOR, duration of response; EC, endometrial cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; IO, immunotherapy; IV, intravenous; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PT, platinum; RECIST v1.1, Response Evaluation Criteria in Solid Tumors, version 1.1.

Results

- The study enrolled 41 patients and at data cutoff (March 8, 2024); median follow-up was 19.4 months (range, 14.4-30.3). Median number of prior anticancer regimens was 3 (range, 1-6) (Table 1)
- ORR was 27%; 1 patient had a confirmed complete response, and 10 patients had a confirmed partial response (Table 2)

Results

Table 1. Demographics and Baseline Clinical Characteristics

	SG (N = 41)
Median age (range), years	68 (44-83)
Race, n (%)	
White	21 (51)
Asian	8 (20)
Other	6 (15)
Not reported	6 (15)
ECOG PS, n (%)	
0	18 (44)
1	23 (56)
MSI-H, n (%)	8 (20)
Histological diagnosis, n (%)	
Endometrioid	20 (49)
Serous	17 (42)
Other	4 (10)
Prior anticancer therapy type, n (%)	
Chemotherapy	41 (100)
Immunotherapy	35 (85)
Targeted agents	26 (63)
Hormonal therapy	5 (12)
Other	1 (2)
Median prior anticancer regimens, n (range)	3 (1-6)
Prior platinum-based chemotherapy and immunotherapy, n (%)	35 (85)

ECOG PS, Eastern Cooperative Oncology Group performance score; MSI-H, microsatellite instability high; SG, sacituzumab govitecan.

Table 2. Summary of Efficacy End Points

	SG (N = 41)
ORR (confirmed CR + PR), 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[a]	4 (10)
Clinical benefit rate (confirmed CR + PR + SD duration ≥ 6 months[b]), n (%) [95% CI]	17 (42) [26-58]
Median DOR[c] [95% CI], months	9.0 [2.8-NR]

[a]Patients without any post-baseline assessments are counted as not assessed. [b]Duration ≥ 6 months for SD only. [c]Based on patients who achieved a confirmed CR or PR.
CR, complete response; DOR, duration of response; NR, not reached; ORR, overall response rate; PR, partial response; SD, stable disease; SG, sacituzumab govitecan.

- 26 (63%) patients had any reduction in target lesion diameters from baseline (Figure 2)
- Median progression-free survival (PFS) and overall survival (OS) are shown in Figures 3 and 4, respectively
- Patients who previously received both platinum-based chemo and IO (85%, n = 35) had similar outcomes as the overall population

Figure 2. Best Percent Change From Baseline in Total Sum of Target Lesion Diameters per Investigator Assessment

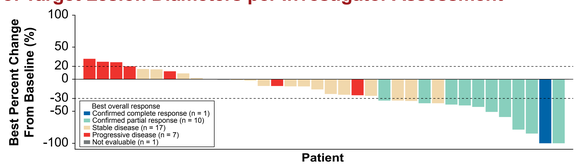
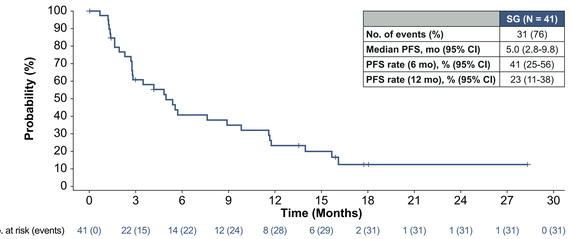
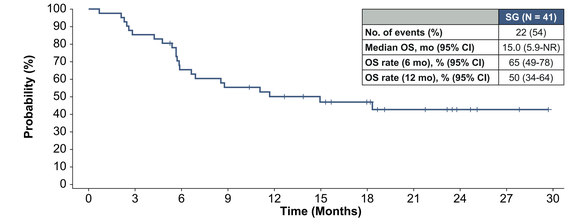


Figure 3. Kaplan-Meier Plot for Progression-Free Survival per Investigator Assessment



PFS, progression-free survival; SG, sacituzumab govitecan.

Figure 4. Kaplan-Meier Plot for Overall Survival



NR, not reached; OS, overall survival; SG, sacituzumab govitecan.

- Any-grade treatment-emergent adverse events (TEAEs) were reported in 41 (100%) patients. The most common TEAEs are listed in Table 3
- Grade ≥ 3 TEAEs occurred in 85% of patients, most commonly neutropenia (49%), diarrhea (22%), and anemia (20%)
- Any-grade treatment-related AEs (TRAEs) were reported in 39 (95%) patients; grade ≥ 3 TRAEs occurred in 31 (76%) patients
- Discontinuation rate due to TEAEs was 7%; 3 patients had TEAEs leading to death (1 due to pneumonia and 2 due to unknown cause, 1 of which was deemed related to SG by the investigator)

Table 3. Most Common TEAEs by Preferred Term (N = 41)

TEAE	Any Grade (Occurring in > 20% of Patients), n (%)	Grade ≥ 3, n (%)
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)	-
Constipation	15 (37)	-
Hypomagnesemia	11 (27)	-
Vomiting	11 (27)	2 (5)
Hypokalemia	10 (24)	6 (15)

TEAE, treatment-emergent adverse event.