A Retrospective Cohort Study to Monitor Real-World Safety in Patients With Locally Advanced or Metastatic Urothelial Carcinoma Treated With Sacituzumab Govitecan in the United States

Bd# G14

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Conclusions

- Compared with the TROPHY-U-01 phase 2 clinical study (which resulted in accelerated FDA approval of SG),[3] this real-world population was older, with poorer performance status, most were treated in a community setting, with SG 2L or later, and the majority received enfortumab vedotin (EV) in the prior line
- The most common AEs were consistent with the known safety profile of SG,[2,3] regardless of line or type of prior therapy, including EV
- Further safety and efficacy analyses are planned with a larger cohort

Plain Language Summary

This is the largest study of sacituzumab govitecan in patients with advanced bladder cancer treated in clinical practice

It provides insights into the side effects of this therapy and shows that the most common issues are neutropenia (low white blood cell count), diarrhea, and nausea/vomiting

These issues are consistent with what we know about this drug from clinical studies and can be managed by a doctor by following established guidelines

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Introduction

- Although patients with locally advanced or metastatic urothelial carcinoma (LA/mUC) experience poor outcomes, the treatment landscape is rapidly evolving[1-4]
- In April 2021, sacituzumab govitecan (SG, a Trop-2–directed antibody drug conjugate) received accelerated US Food and Drug Administration (FDA) approval for patients with LA/mUC who progressed after platinum-based chemotherapy (CT) and immune checkpoint inhibitor (CPI) therapy, based on the TROPHY-U-01 study (NCT03547973)[5,6]
- In TROPHY-U-01, 113 patients who received SG (10 mg/kg on days 1 and 8 of 21-day cycles) after progression on CT/CPI had an objective response rate of 27% (95% CI, 20%-37%) at a median follow-up of 9 months. Key grade ≥ 3 treatment-related adverse events (TRAEs) included neutropenia (35%), leukopenia (18%), anemia (14%), diarrhea (10%), and febrile neutropenia (10%). The safety profile was manageable, with 6% of patients discontinuing due to TRAEs[6]
- We sought to evaluate the emerging use of SG in a real-world database

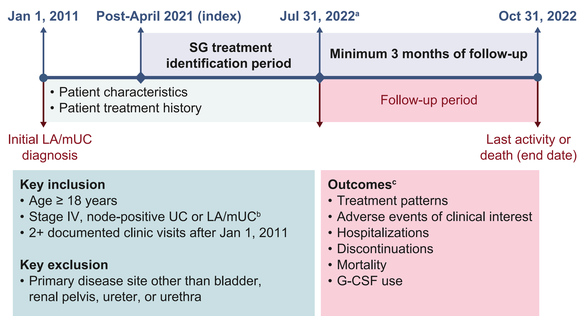
Objective

- To evaluate the safety of SG in patients with LA/mUC treated in a real-world setting in the United States, including patients who had previously received enfortumab vedotin (EV)

Methods

- A retrospective, observational cohort study of patients aged ≥ 18 years with LA/mUC treated with SG in the United States (**Figure 1**)
- Data were evaluated from Flatiron Health, a longitudinal database, comprising de-identified patient-level structured and unstructured data, curated via technology-enabled abstraction.[7,8] Data were accessed from Jan 1, 2011, to Oct 31, 2022. During the study period, data originated from ~280 cancer clinics in the United States (~800 sites of care), and patients were predominantly treated in community oncology settings
- Descriptive statistics were used for data analysis

Figure 1. Study Design



[a]Date chosen to ensure ≥ 3 months of follow-up after approval of SG in LA/mUC. [b]Based on International Classification of Diseases-9-CM UC codes. [c]Outcomes recorded post-approval.
G-CSF, granulocyte-colony stimulating factor; LA/mUC, locally advanced or metastatic urothelial carcinoma; SG, sacituzumab govitecan; UC, urothelial carcinoma.

Results

Participants and Treatment Patterns

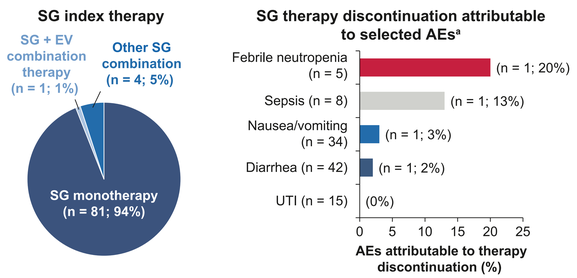
- This study included 86 SG-treated patients (**Table 1**). Most patients (n = 79; 92%) previously received platinum-based CT in a prior line, and 61 (71%) received EV in the line prior to SG. SG use was predominantly monotherapy (n = 81; 94%) (**Figure 2**). Most patients (n = 85; 99%) received SG as second-line (2L) or later; 1 (1%) as first-line, 10 (12%) as 2L, 31 (36%) as third-line, 25 (29%) as fourth-line, and 19 (22%) as fifth-line or later

Table 1. Demographic and Baseline Characteristics

Characteristic	All Patients (N = 86)
Male, n (%)	60 (70)
Age (years) at SG start date, median (range)	
1L	85[a]
2L	72 (25-81)
3L	70 (46-85)
4L	69 (57-85)
5L+	71 (53-79)
Provider type – academic, n (%)	14 (16)
Provider type – community, n (%)	72 (84)
ECOG PS, n (%)[b]	
0	14 (16)
1	41 (48)
2	19 (22)
3	4 (5)
Treatment immediately prior to SG start date, n (%)	
EV monotherapy	56 (65)
EV combination therapy	5 (6)
CPI monotherapy	7 (8)
CPI combination therapy	3 (3)
Platinum-based chemotherapy	6 (7)
Other/not applicable	9 (10)

[a]1 patient received 1L treatment so range not estimable. [b]Excludes missing data (n = 8).
1L, first-line; 2L, second-line; 3L, third-line; 4L, fourth-line; 5L+, fifth-line or later; CPI, checkpoint inhibitor; ECOG PS, Eastern Cooperative Oncology Group performance status; EV, enfortumab vedotin; SG, sacituzumab govitecan.

Figure 2. SG Treatment Patterns



[a]Patients could discontinue for ≥ 1 reason. Only the selected AEs and their association with therapy discontinuation were examined.
AE, adverse event; EV, enfortumab vedotin; SG, sacituzumab govitecan; UTI, urinary tract infection.

SG Dose

- The median (IQR) starting SG dose was 10.0 (10.0-10.1) mg/kg, and the median (IQR) final SG dose was 10.0 (7.8-10.0) mg/kg. There was no dose change in 46 (53%) patients
- Median (IQR) duration of treatment was 61 (36-113) days

AEs of Interest

- The most common AEs of interest (any grade, overall) were neutropenia (n = 34; 40%), diarrhea (n = 30; 35%), and nausea/vomiting (n = 18; 21%) (**Table 2**)

Table 2. Summary of AEs

AE,[a] n (%)	All (N = 86)	1/2L (n = 11)	3L (n = 31)	4L (n = 25)	5L+ (n = 19)
Neutropenia	34 (40)	4 (36)	9 (29)	10 (40)	11 (58)
Grade 2	13 (15)	3 (27)	3 (10)	5 (20)	2 (11)
Grade 3	9 (10)	0 (0)	5 (16)	1 (4)	3 (16)
Grade 4	7 (8)	1 (9)	0 (0)	2 (8)	4 (21)
Diarrhea	30 (35)	3 (27)	14 (45)	5 (20)	8 (42)
Nausea or vomiting	18 (21)	1 (9)	9 (29)	4 (16)	4 (21)
Urinary tract infections	9 (10)	1 (9)	2 (6)	2 (8)	4 (21)
Sepsis	8 (9)	0 (0)	4 (13)	1 (4)	3 (16)
Febrile neutropenia	5 (6)	0 (0)	2 (6)	1 (4)	2 (11)

[a]Only incidence AEs that were not presented at baseline were counted here.
1/2L, first- and second-line; 3L, third-line; 4L, fourth-line; 5L+, fifth-line or later; AE, adverse event.

Hospitalizations, Discontinuations, and Mortality

- Overall, 14 (16%) patients were hospitalized due to AEs (7 had multiple reasons for hospitalizations; **Table 3**)
- 49 (57%) patients discontinued, including 34 (40%) due to progression and 8 (9%) due to toxicity or AEs; 24 patients were still on SG treatment at data cut-off
- Three (3%) patients died during or within 7 days after the line of treatment (reasons unknown)

G-CSF Use

- During SG treatment, 45 (52%) patients used G-CSF (**Table 4**). Only 1 (4.5%) patient who had primary G-CSF prophylaxis developed grade ≥ 3 neutropenia

Table 3. Hospitalizations

AE, n (%)	All (N = 86)
Sepsis	7 (8)
Diarrhea	5 (6)
Urinary tract infection	5 (6)
Febrile neutropenia	4 (5)
Nausea/vomiting	2 (2)

AE, adverse event.

Table 4. G-CSF Use

n (%)	All (N = 86)
Any G-CSF use[a]	66 (77)
Any G-CSF use during SG treatment	45 (52)
Primary prophylaxis[b]	22 (26)
Secondary prophylaxis[c]	16 (19)
Therapeutic use[d]	23 (27)

[a]Includes G-CSF use outside of treatment line (eg, prior to SG use). [b]G-CSF administered prior to neutropenia onset and within 7 days of the index date. [c]G-CSF administered prior to the end of index treatment and after neutropenia resolution date. [d]G-CSF administered on or after neutropenia onset and prior to the resolution date (if applicable) or the end of index treatment.
G-CSF, granulocyte-colony stimulating factor; SG, sacituzumab govitecan.

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