Retrospective, Observational Analysis of Real-World Safety Outcomes in Sacituzumab Govitecan-Treated Patients With Locally Advanced/Metastatic Urothelial Cancer

Poster Bd# D6

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Conclusions

- This is the largest analysis to date of sacituzumab govitecan (SG) use in a real-world population with locally advanced or metastatic urothelial cancer (la/mUC), with a significant number of enfortumab vedotin (EV)-pretreated patients
- Observed adverse events (AEs) were consistent with the known safety profile of SG
  - Fatigue, diarrhea, nausea, and neutropenia occurred in > 20% of patients and were not associated with an earlier or later line of treatment
  - Discontinuation rate due to prespecified AEs was low (3%), indicating that these AEs were manageable and unlikely to result in treatment discontinuation
  - Primary prophylaxis with granulocyte colony stimulating factor (G-CSF) resulted in lower incidence of neutropenia (18%)
- Limitations of this study include observational real-world study design, missing data, and absence of information on AE grading and dose modifications

Plain Language Summary

- Sacituzumab govitecan is a drug being studied in patients with advanced bladder cancer. This study looked at the use of sacituzumab govitecan in real-world patients with advanced bladder cancer and the adverse events they experienced
- The study found that although diarrhea, neutropenia (low count of certain white blood cells), and nausea occurred frequently, these adverse events were manageable
- Most of the patients were able to continue sacituzumab govitecan treatment despite these adverse events
- Granulocyte colony stimulating factor is a growth factor that helps the bone marrow produce more white blood cells. In this study, this was used to prevent neutropenia, so not many patients experienced any neutropenia or severe neutropenia

References: **1.** Roviello G, et al. *Nat Rev Urol*. 2024;21:580-92. **2.** Tagawa S, et al. *J Clin Oncol*. 2021;39:2474-85. **3.** Gilead Press Release, October 2024. Available at: https://www.gilead.com/company/company-statements/2024/gilead-provides-update-on-us-indication-for-trodelvy-in-metastatic-urothelial-cancer. Accessed December 2024. **4.** Powles T, et al. Oral presented at ESMO-Asia Congress, December 6-8, 2024, Singapore. LBA9. **5.** Parikh M, et al. *J Clin Oncol*. 2024;42:608. **6.** Ma X, et al. *medRxiv*. 2023. https://doi.org/10.1101/2020.03.16.20037143. **7.** Bimbaum B, et al. *ArXiv*. 2020. https://doi.org/https://doi.org/10.48550/arXiv.2001.09765.

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Introduction

- Platinum-based chemotherapy for la/mUC results in poor survival rates, and not all patients are platinum-eligible[1]
- Immuno-oncology and other targeted therapies have gained prominence recently, and it is vital to understand the ways in which clinicians integrate available therapies into disease management[1]
- SG, a Trop-2–directed antibody drug conjugate, received accelerated approval in April 2021 for treatment of patients with la/mUC based on the TROPHY-U-01 study[2] and was administered to patients in clinical practice
  - The confirmatory TROPiCS-04 trial, however, did not meet the primary end point and SG approval was voluntarily withdrawn.[3,4] These data were presented at ESMO Asia 2024[4]
  - Safety data in TROPiCS-04 were consistent with the known toxicity profile of SG across tumor types, except for increased rates of neutropenic complications in this high-risk population (48% neutropenia and 12% febrile neutropenia reported with SG)[4]
- Real-world safety of SG in the United States was previously reported in a retrospective cohort study in 86 patients with la/mUC initiating SG from December 2019 to October 2022.[5] Here, we report results from the expansion cohort consisting of 220 patients and an additional year of follow-up

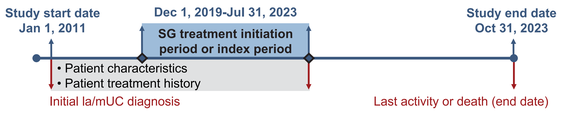
Objective

- 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 EV

Methods

- Data were evaluated from nationwide, longitudinal Flatiron Health electronic health record–derived deidentified database, comprising patient-level data, originating from ~ 280 cancer clinics (~ 800 sites of care; primarily community oncology settings) and curated via technology-enabled abstraction[6,7] (**Figure 1**)
- Additional information on the specified AEs in scope (listed in **Figure 1**) had abstracted elements like hospitalizations and treatment discontinuations extracted. Discontinuation rates were also measured based on general toxicity, covering events outside the scope of the abstracted AEs of interest, but no additional details were available for these events

Figure 1. Study Design



Key inclusion
- Aged ≥ 18 years
- Stage IV, node-positive UC or la/mUC[a]
- 2+ documented clinic visits after Jan 1, 2011

Key exclusion
- Primary disease site other than bladder, renal pelvis, ureter, or urethra
- Treatment with a clinical study drug anytime before the data cutoff

Outcomes[b]
- Treatment patterns
- Abstracted AEs of interest (anemia, neutropenia, febrile neutropenia, infections secondary to neutropenia, sepsis, UTI, stomatitis, nausea, vomiting, diarrhea, infusion-related reactions, fatigue)[c]
- Treatment discontinuations
- Hospitalizations
- Neutropenia incidence by G-CSF use

[a]Based on *International Classification of Diseases (ICD)-9 and 10-CM* UC codes. [b]Outcomes recorded post-approval. [c]AEs chosen a priori based on what was observed in clinical studies. AE, adverse event; G-CSF, granulocyte-colony stimulating factor; la/mUC, locally advanced or metastatic urothelial carcinoma; SG, sacituzumab govitecan; UTI, urinary tract infection.

Results

Baseline Characteristics and SG Treatment Patterns

- This study included 220 SG-treated patients (**Table 1**). Most patients received the first SG-containing therapy in the second-line (2L) or above setting (49% and 46% in 2L/third line [3L], and fourth line or later [4L+], respectively)
- SG use was predominantly as a monotherapy (n = 208, 95%) at the index line (2L+)
- Prior to the index line, which includes treatments administered in nonadvanced settings, 63% of patients received EV monotherapy (**Table 2**)

Results

Table 1. Key Demographic and Clinical Characteristics

Characteristic	All Patients (N = 220)
Male, n (%)	161 (73)
Median (IQR) age at index, years	71 (65-76)
Provider type, n (%)	
Academic	53 (24)
Community	147 (67)
Both	20 (9)
ECOG PS, n (%)	
0-1	134 (61)
2-3	63 (29)
Unknown	23 (10)
Stage at initial la/mUC diagnosis, n (%)	
Stage 0-II	35 (16)
Stage III-IV	87 (40)
Unknown/not documented	98 (45)
Primary site, n (%)	
Bladder	161 (73)
Renal pelvis	36 (16)
Ureter	22 (10)
Urethra	1 (< 1)

ECOG PS, Eastern Cooperative Oncology Group performance score; la/mUC, locally advanced/metastatic urothelial cancer.

Table 2. Treatment Immediately Prior to SG in All Patients and by SG-Containing Line

Treatment, n (%)	All Patients (N = 220)	2L/3L (n = 108)	4L+ (n = 102)
EV monotherapy	133 (63)	72 (67)	61 (60)
EV combination therapy	10 (5)	4 (4)	6 (6)
PD-L1 monotherapy	24 (11)	17 (16)	7 (7)
PD-L1 plus chemotherapy	7 (3)	4 (4)	3 (3)
Platinum-based chemotherapy	12 (6)	8 (7)	4 (4)
Other	24 (11)	3 (3)	21 (21)

2L, second line; 3L, third line; 4L+, fourth line and later; EV, enfortumab vedotin; PD-L1, programmed death-ligand 1; SG, sacituzumab govitecan.

Incident Adverse Events of Interest

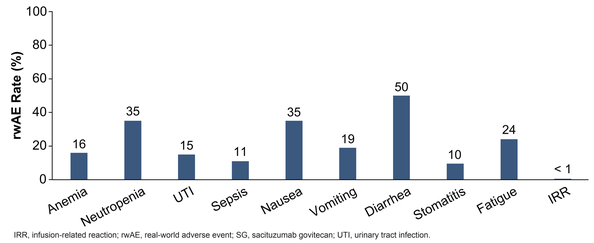
- The most common AEs of interest were diarrhea (110 [50%]), neutropenia (77 [35%]), and nausea (76 [35%]) (**Table 3**)
- Febrile neutropenia and infections secondary to neutropenia occurred in 18 (8%) and 9 (4%) patients, respectively (**Table 3**)
- Incident AEs are shown in **Figure 2**
- Of the 220 patients, 62 (28%) were hospitalized due to AEs, 141 (64%) had a documented reason for SG discontinuation; 106 (75%) patients discontinued due to disease progression
- Overall discontinuation rate due to AEs/toxicities was 13% (n = 19)
  - Among the 19 patients, 3 (16%) discontinued due to neutropenia and 3 (16%) due to fatigue
- For the prespecified AEs of interest occurring during therapy, the discontinuation rate was 3% (n = 7)

Table 3. Incident Adverse Events of Interest Overall and by SG-Containing Line

AE, n (%)	All Patients (N = 220)	1L (n = 10)	2L/3L (n = 109)[a]	4L+ (n = 107)[a]
Anemia	36 (16)	1 (10)	26 (24)	9 (8)
Neutropenia	77 (35)	3 (30)	32 (29)	42 (39)
Febrile neutropenia[b]	18 (8)	1 (10)	6 (6)	11 (10)
Infections secondary to neutropenia[b,c]	9 (4)	0	4 (4)	5 (5)
Sepsis	25 (11)	0	14 (13)	12 (11)
Urinary tract infection	34 (15)	2 (20)	14 (13)	18 (17)
Diarrhea	110 (50)	5 (50)	61 (56)	45 (42)
Nausea	76 (35)	7 (70)	37 (34)	32 (30)
Vomiting	41 (19)	4 (40)	19 (17)	18 (17)
Stomatitis	21 (10)	0	15 (14)	6 (6)
Fatigue	52 (24)	4 (40)	22 (20)	26 (24)
Infusion-related reaction	1 (< 1)	0	0	1 (< 1)

[a]Patients may have received SG in multiple lines. [b]Febrile neutropenia and infections are secondary to neutropenia and are prevalent AEs, as baseline status was not abstracted for them. [c]Any infections that occurred within the SG-containing lines. 1L, first line; 2L, second line; 3L, third line, 4L+, fourth line and later; AE, adverse event; SG, sacituzumab govitecan.

Figure 2. Incident rwAE Rates on All SG-Containing Lines



IRR, infusion-related reaction; rwAE, real-world adverse event; SG, sacituzumab govitecan; UTI, urinary tract infection.

G-CSF Use by Neutropenia Incidence

- With primary G-CSF prophylaxis, 35% of the patients did not experience neutropenia and 18% experienced any neutropenia (**Table 4**)
  - Of the patients who experienced any neutropenia, more patients experienced non-severe (30%) than severe (16%) neutropenia, although the small number of patients with non-severe neutropenia limits definitive conclusions (**Table 4**)

Table 4. G-CSF Use on Index Line by Neutropenia Occurrence and Severity

n (%)	Overall		By Severity	
	No Neutropenia (n = 141)	Any Neutropenia (n = 79)	Severe Neutropenia (n = 69)	Non-severe Neutropenia (n = 10)
Primary prophylaxis[a]	50 (35)	14 (18)	11 (16)	3 (30)
Secondary prophylaxis[b]	0	29 (37)	28 (41)	1 (10)
Therapeutic indication[c]	0	36 (46)	30 (43)	6 (60)

Neutropenia severity assessed using proxy, ie, occurrence of febrile neutropenia, infections secondary to neutropenia, death in patients experiencing neutropenia (cause of death unknown), sepsis, hospitalization, therapy discontinuation, therapy hold, or therapy dose/schedule change. [a]G-CSF administered prior to neutropenia onset and within 7 days of the index date. [b]G-CSF administered prior to the end of index treatment and after neutropenia resolution date. [c]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.

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