Management of Neutropenia and Effectiveness of Sacituzumab Govitecan in Patients With Metastatic Triple-Negative Breast Cancer Treated in Real-World Settings in the United States

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*At the time study was conducted.

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Conclusions

- In this real-world study, SG demonstrated effectiveness and a manageable safety profile in patients treated in 2L+ for mTNBC, consistent with results from the phase 3 ASCENT study and other real-world evidence studies
- Patients treated with SG had a median rwOS of 11.3 months
- Overall, 25% of the patients experienced grade 2 neutropenia during SG treatment, and 27% had grade 3/4 neutropenia; grade 2 neutropenia was lower in patients receiving any G-CSF prophylaxis (13%) than in those who had no G-CSF use (28%)
- The incidence of grade 2 and grade 3/4 neutropenia was low among patients receiving G-CSF prophylaxis, suggesting that SG-related neutropenia can be effectively managed with prophylactic G-CSF use

Plain Language Summary

- Sacituzumab govitecan (SG) is a drug that is approved in several countries to treat metastatic triple-negative breast cancer (mTNBC)
- This real-world study of adults with mTNBC receiving SG as the second or later treatment from April 2020 through June 2023 showed:
  - Survival outcomes consistent with those seen in a large clinical trial (ASCENT) and other real-world studies
  - The occurrence of neutropenia (low white blood cell count, which is common among people receiving cancer treatments), was infrequent among people who received a preventive growth factor, which is used to produce more white blood cells. This shows that SG-related neutropenia is manageable

References: **1.** Zhang X, et al. *Curr Breast Cancer Rep*. 2023;15:288-97. **2.** Zagami P, et al. *NPJ Breast Cancer*. 2022;8:95. **3.** Allison KH, et al. *J Clin Oncol*. 2020;38:1346-66. **4.** Wolff AC, et al. *J Clin Oncol*. 2023;41:3867-72. **5.** TRODELVY® (sacituzumab govitecan-hziy) [prescribing information]. Gilead Sciences, Inc., Foster City, CA: February 2023. **6.** TRODELVY® summary of product characteristics. October 2024. **7.** Bardia A, et al. *N Engl J Med*. 2021;384:1529-41. **8.** Ma X, et al. 2023. doi: https://doi.org/10.1101/2020.03.16.20037143. **9.** Birnbaum B, et al. 2020. https://arxiv.org/abs/2001.09765.

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Introduction

- Triple-negative breast cancer (TNBC) is an invasive breast cancer (BC) that is hormone receptor negative/human epidermal growth factor receptor 2 (HER2)-negative[1,2] (defined by the ASCO/CAP guidelines[3,4] as HER2 IHC 0, 1+, or 2+/ISH–; ER– and PR–)
- Sacituzumab govitecan (SG) is a Trop-2–directed antibody-drug conjugate approved for the treatment of patients with metastatic TNBC (mTNBC) who received 2 or more prior systemic therapies, at least 1 of them for metastatic disease, based on the results from the phase 3 ASCENT study (NCT02574455)[5-7]
- In ASCENT, 529 patients with relapsed/refractory mTNBC were randomized to receive SG (n = 267) or standard-of-care chemotherapy (n = 262). SG showed significant clinical benefit compared with chemotherapy[7]
  - The median progression-free survival (PFS) was 4.8 months with SG vs 1.7 months with chemotherapy; the median overall survival (OS) was 11.8 months with SG vs 6.9 months with chemotherapy
  - Over the course of the study, treatment discontinuation due to adverse events with SG was low at 5%
  - Any-grade neutropenia occurred in 64% (n = 165/258) of patients receiving SG and 44% (n = 98/224) of patients receiving chemotherapy; grade 3/4 events were reported in 52% (n = 134) and 34% (n = 76) of patients, respectively
- There is a need for physicians to understand the management of neutropenia and effectiveness of SG in the real world

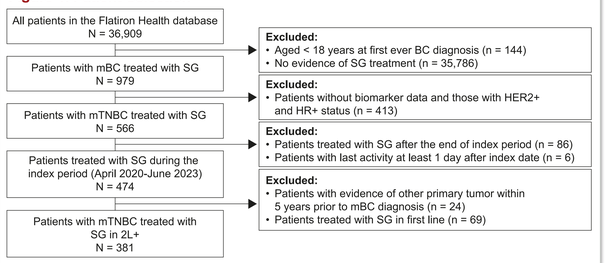
Objective

- This retrospective analysis of real-world data from the United States aims to describe the incidence and management of neutropenia and clinical outcomes of SG as second line or later (2L+) treatment for mTNBC

Methods

- This retrospective, observational cohort study used the nationwide longitudinal Flatiron Health electronic health record–derived, deidentified database, comprising patient-level data originating from ~280 US cancer clinics (~800 sites of care) and curated via technology-enabled abstraction[8,9]
- Patients (aged ≥ 18 years) with mTNBC and treated with SG in the 2L+ setting from April 2020 through June 2023 were included. Data cutoff was December 31, 2023
  - Patients with evidence of other primary tumor (excluding nonmetastatic, nonmelanoma skin cancers) within 5 years prior to metastatic BC diagnosis were excluded
- SG use patterns, relative dose intensity (RDI), neutropenia incidence, and concomitant granulocyte colony-stimulating factor (G-CSF) use were summarized using descriptive statistics
  - Administration of G-CSF on or after index date and before first neutropenia onset/end of treatment was defined as primary prophylaxis, after neutropenia resolution and before end of treatment was defined as secondary prophylaxis, and on or after neutropenia onset and before resolution or end of SG treatment was defined as therapeutic use
- Real-world OS (rwOS) and time to next treatment or death (TTNTD; used as a proxy for PFS) were assessed using the Kaplan-Meier method

Figure 1. Patient Selection



2L+, second line or later; BC, breast cancer; HR, hormone receptor; HER2, human epidermal growth factor receptor 2; mBC, metastatic breast cancer; mTNBC, metastatic triple-negative breast cancer; SG, sacituzumab govitecan.

Results

- Of the 36,909 patients with metastatic BC in the Flatiron database, 381 patients with mTNBC were treated with SG in 2L+ during the index period and were included in the analysis (**Figure 1**)
- Patients had a median (IQR) age of 61 (52-69) years; 18% were Black, and 17% had an Eastern Cooperative Oncology Group performance status ≥ 2 (**Table 1**). Patients received a median (IQR) of 2 (1-3) prior lines of treatment in the metastatic setting

Table 1. Baseline Demographics and Clinical Characteristics

Characteristics	All Patients (N = 381)	Patients Receiving SG in 2L (n = 118)	Patients Receiving SG in 3L+ (n = 263)
Female, n (%)	379 (99)	118 (100)	261 (99)
Median age (IQR), years	61 (52-69)	60 (52-68)	61 (52-70)
Race, n (%)			
White	234 (61)	68 (58)	166 (63)
Black or African American	70 (18)	28 (24)	42 (16)
Other/Unknown	77 (20)	22 (19)	55 (21)
Treatment provider type[a] - community, n (%)	298 (78)	97 (82)	201 (76)
ECOG PS at index,[b] n (%)			
0-1	247 (65)	82 (69)	165 (63)
≥ 2	66 (17)	16 (14)	50 (19)
Unknown	68 (18)	20 (17)	48 (18)
De novo mBC, n (%)	97 (25)	14 (12)	83 (32)
Recurrent disease, n (%)	251 (66)	92 (78)	159 (60)
Time from eBC diagnosis to mBC diagnosis, n (%)	n = 251	n = 92	n = 159
Median (IQR), months	30 (17-55)	22 (13-41)	38 (21-65)
< 18 months	66 (26)	35 (38)	31 (20)
18-36 months	77 (31)	31 (34)	46 (29)
≥ 36 months	108 (43)	26 (28)	82 (52)
Brain metastasis,[c] n/N (%)	68/291 (23)	17/86 (20)	51/205 (25)
HER2-negative expression status,[d] n (%)	n = 298	n = 91	n = 207
HER2– (IHC 0)	190 (64)	60 (66)	130 (63)
HER2-low (IHC 1+ or IHC 2+/ISH–)	108 (36)	31 (34)	77 (37)
Prior use of taxanes,[e] n (%)	236 (62)	N/A	N/A
Prior use of PD-(L)1 inhibitors,[f] n (%)	167 (44)	N/A	N/A
Prior use of PARP inhibitors,[g] n (%)	25 (7)	N/A	N/A

[a]n (%) for patients receiving care from academic setting: 69 (18), 19 (16), and 50 (19); both community and academic settings: 14 (4), 2 (2), and 12 (5), respectively. [b]Records available from 30 days before initial diagnosis and until 7 days post index day were considered; if multiple records were available, the results closest to the index date were prioritized. [c]Metastasis sites were defined using *10th revision of the International Classification of Diseases* codes. Percentages reported among total number of patients in the cohort with ≥ 1 metastasis site recorded. Window to identify metastasis sites was 1 month before mBC diagnosis until 2 months after index date. [d]Records during the 30 days before the initial diagnosis and up to 90 days after the index date were used; if multiple records were available, the one closest to the index date was prioritized. [e]Taxanes include paclitaxel, paclitaxel protein bound, and docetaxel. [f]PD-(L)1 inhibitors include atezolizumab, pembrolizumab, and nivolumab. [g]PARP inhibitors include olaparib, talazoparib, and niraparib.
2L, second line; 3L+, third line or later; eBC, early breast cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; mBC, metastatic breast cancer; N/A, not applicable; PARP, poly (ADP-ribose) polymerase; PD-(L)1, programmed cell death (ligand) 1; SG, sacituzumab govitecan.

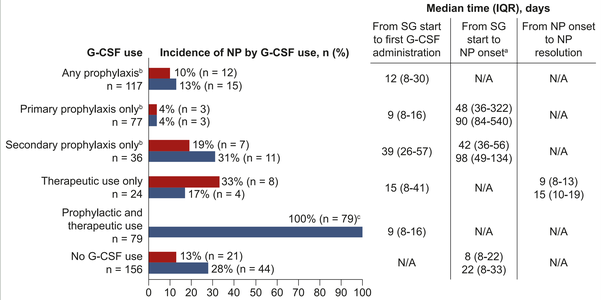
SG Use Patterns

- Overall, 31% (n = 118) of patients received SG in the 2L setting, and 69% (n = 263) received SG in the third-line or later (3L+) setting
- Patients received a median (IQR) of 12 (5-21) total SG doses; the maximum number of doses administered during the study period was 74. Median (IQR) SG treatment duration was 4.0 (1.9-7.6) months. Among patients receiving SG in 2L and 3L+, the duration of SG treatment was 4.2 (1.6-8.1) and 4.0 (2.1-7.4) months, respectively
- Median (IQR) RDI was 90% (71-102); 76% of patients had RDI > 70%, and 24% had RDI < 70%
- During the study period, 55% (n = 211) of patients received a subsequent line of therapy (after SG); the median number of lines of therapy (IQR) administered after SG was 2 (1-2). At the end of the study period, 13% (n = 51) of patients were still receiving SG treatment
- Among 308 patients with available dosing data, 44% (n = 137) had SG dose reduction. The reason for dose reduction or treatment discontinuation was not recorded in the database

Neutropenia Incidence and G-CSF Use

- Overall, 25% (n = 94) of patients experienced grade 2 neutropenia during SG treatment; 27% (n = 101) had grade 3/4 neutropenia
- Concomitant G-CSF use (any) was observed in 59% (n = 225) of patients
- Grade 2 neutropenia was seen in 13% of patients who had received any G-CSF prophylaxis and in 28% of patients who had no G-CSF use (**Figure 2**)
- Grade 3/4 neutropenia occurred in 10% of patients after any G-CSF prophylaxis, in 4% receiving primary prophylaxis, in 33% receiving G-CSF as treatment, and in 13% receiving no G-CSF (**Figure 2**)

Figure 2. Concomitant G-CSF Use With SG and Management of Neutropenia

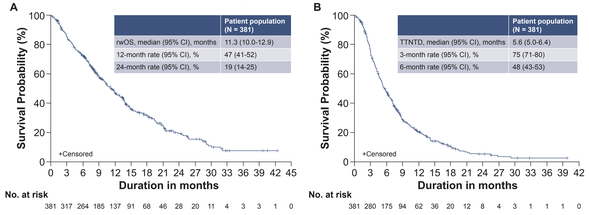


Five patients received G-CSF during SG treatment, but usage was not categorized as prophylactic or therapeutic. Four patients received both primary and secondary prophylaxis. Neutropenic events were defined using *International Classification of Diseases* (ICD) *10/9* diagnostic codes (D70, 288) and/or laboratory data (absolute neutrophil count < 1500 mm³). [a]For patients receiving primary or secondary prophylaxis, onset date refers to NP subsequent to G-CSF use. [b]NP subsequent to G-CSF use. [c]Refers to grade ≥ 2 NP.
G-CSF, granulocyte colony-stimulating factor; N/A, not applicable; NP, neutropenia; SG, sacituzumab govitecan.

Effectiveness

- Median (IQR) study follow-up was 8.7 (4.5-14.6) months
- Median (95% CI) rwOS was 11.3 (10.0-12.9) months; the 24-month rwOS rate was 19% (**Figure 3A**)
- Median (95% CI) TTNTD was 5.6 (5.0-6.4) months (**Figure 3B**)

Figure 3. Kaplan-Meier Analysis of Real-World Overall Survival (A) and TTNTD (B) for Patients With mTNBC Receiving SG in 2L or Later



2L, second line; mTNBC, metastatic triple-negative breast cancer; rwOS, real-world overall survival; SG, sacituzumab govitecan; TTNTD, time to next treatment or death.