GILEAD | Medical Information

Trodelvy® (sacituzumab govitecan-hziy) Incidence of Treatment-Related Neutropenia and Growth Factor Support

This document is in response to your request for information about Trodelvy® (sacituzumab govitecan-hziy [SG]), and the incidence of treatment-related neutropenia and the use of growth factor support.

Gilead continually assesses safety data from all sources for unidentified drug reactions and updates the product label information accordingly to reflect the safety profile of Trodelvy®. Because case reports of potential adverse reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish causal relationship to drug exposure. For this reason, Gilead does not provide information from post-marketing spontaneous reports.

Information summarized in this document includes data for SG monotherapy (10 mg/kg IV on Days 1 and 8 of a 21-day treatment cycle) from Phase 2 and 3 clinical studies that constitute the largest pooled safety population of SG.

Some data may be outside of the US FDA-approved prescribing information. In providing this data, Gilead Sciences, Inc. is not making any representation as to its clinical relevance or to the use of any Gilead product(s). For information about the approved conditions of use of any Gilead drug product, please consult the FDA-approved prescribing information.

The full indication, important safety information, and boxed warnings for neutropenia and diarrhea are available at: www.gilead.com/-/media/files/pdfs/medicines/oncology/trodelvy/trodelvy_pi.

Summary

Relevant Product Labeling[1]

The pooled safety population reflect exposure to SG in 1063 patients, which included 366 patients with mTNBC and 322 patients with HR+/HER2- breast cancer from IMMU-132-01, ASCENT, and TROPiCS-02; and 375 patients with other tumor types. Among the 1063 patients treated with SG, the median duration of treatment was 4.1 mo (range: 0-63 mo). In this pooled safety population, decreased neutrophil count was reported in 75% of SG-treated patients.

- SG can cause severe, life-threatening, or fatal neutropenia as early as the first cycle of treatment.
- Neutropenia occurred in 64% of patients treated with SG. Grade 3-4 neutropenia occurred in 49% of patients. Febrile neutropenia occurred in 6% of patients. The median time to first onset of neutropenia (including febrile neutropenia) was 16 days (range: 1-435 days). Neutropenia occurred earlier in patients with reduced *UGT1A1* activity. Neutropenic colitis occurred in 1.4% of patients.

- Neutropenia was the most common reason for treatment interruptions and dose reductions of SG across studies. G-CSF was used in 44% of patients who received SG in the ASCENT study and in 54% of patients who received SG in the TROPiCS-02 study.
- The incidence of neutropenia was analyzed in 948 patients who received SG and had *UGT1A1* GT results. In patients homozygous for the *UGT1A1**28 allele (n=112), the incidence of Grade 3-4 neutropenia was 58%. In patients heterozygous for the *UGT1A1*28* allele (n=420), the incidence of Grade 3-4 neutropenia was 49%. In patients homozygous for the WT allele (n=416), the incidence of Grade 3 to 4 neutropenia was 43%.
- The median time to first neutropenia including febrile neutropenia was 9 days in patients homozygous for the *UGT1A1*28* allele, 15 days in patients heterozygous for the *UGT1A1*28* allele, and 20 days in patients homozygous for the WT allele.

Closely monitor patients with known reduced *UGT1A1* activity for adverse reactions. Withhold or permanently discontinue SG based on clinical assessment of the onset, duration, and severity of the observed adverse reactions in patients with evidence of acute early-onset or unusually severe adverse reactions, which may indicate reduced *UGT1A1* enzyme activity.

Primary prophylaxis with G-CSF is recommended starting in the first cycle of treatment in all patients at increased risk of febrile neutropenia, including older patients, patients with previous neutropenia, poor performance status, organ dysfunction, or multiple comorbidities. Initiate anti-infective treatment in patients with febrile neutropenia without delay.

Monitor ANC during treatment. Withhold SG for ANC <1500/mm^3 on Day 1 of any cycle or <1000/mm^3 on Day 8 of any cycle. Withhold SG for neutropenic fever. Dose modifications may be required due to neutropenia. Treat neutropenia with G-CSF and administer prophylaxis in subsequent cycles as clinically indicated or indicated in Table 2 of the Prescribing Information.

Pooled Safety Data: SG 10 mg/kg as Monotherapy

The pooled safety profile reflects exposure to SG 10 mg/kg in 1063 patients from four studies of multiple epithelial tumors (IMMU-132-01 [n=402], ASCENT [n=258], TROPiCS-02 [n=268], and TROPHY-U-01 [n=135]). These studies included patients with mTNBC, HR+/HER2- mBC and mUC.[2]

The median treatment duration of SG was 4.1 (range: 0–63) mo.[1] Incidence of all-grade neutropenia, febrile neutropenia and neutropenic colitis was 64%, 6% and 1.4%, respectively. Neutropenia was the most common Grade ≥3 TEAE in 46% of patients, and one of the most common reasons for dose interruptions, reductions and discontinuations with SG across studies.[1,2]

Of the 948 patients with available GTs, those homozygous for the *UGT1A1*28* allele were at increased risk for neutropenia and febrile neutropenia.[2]

An exploratory analysis of G-CSF use during SG clinical trials showed decreased neutropenia rates and longer time to onset of Grade ≥3 neutropenia after primary or secondary prophylaxis vs those without prophylaxis.[2]

Data on onset and duration of neutropenia from the pooled safety analysis are provided below.

Incidence of Treatment-Related Neutropenia and Growth Factor Use in SG Clinical Studies

Across the four studies evaluated in the pooled analysis, the total use of growth factor support in the OSP of SG-treated patients was 30 to 54%, and incidence of Grade ≥3 neutropenia and febrile neutropenia was 34 to 51% and 5 to 10% of SG-treated patients, respectively.[3-6]

Fatal infections secondary to neutropenia with SG were reported in 1 patient in both TROPiCS-02 (n=272, ITT) and the TROPHY-U-01 Cohort 1 Study in mUC (n=113, ITT). In the ASCENT study (n=267, ITT), fatal infections secondary to neutropenia with SG were not reported.[3,7-11]

TROPiCS-04 Study in mUC

TROPiCS-04 is an open-label, global, multicenter, randomized, phase 3 study evaluating the efficacy and safety of SG vs TPC in patients with locally advanced unresectable or mUC who progressed after prior PLT-based and CPI therapies.[12]

- In the overall study population, 32 fatal TEAEs (25/349 [7%] in the SG group and 7/337 [2%] in the TPC group) were observed.[12]
- Sixteen out of 25 fatal AEs in the SG group were fatal infections secondary to neutropenia, 14 of which occurred within the first month of treatment. In the TPC group, 4 TEAEs leading to death were infections with neutropenia (1%) and 3 were unrelated to an infection.[12]
- Any-grade and Grade ≥3 neutropenia occurred in 166 (48%) and 122 (35%) patients in the SG group, and in 51 (15%) and 35 (10%) patients in the TPC group, respectively.[12]
- Primary prophylaxis with G-CSF was 21% and 22% with SG and TPC, respectively, and incidence of Grade ≥3 neutropenia with or without primary prophylaxis with G-CSF was 32% and 48%, respectively.[12]

PRIMED Study in mTNBC and HR+/HER2- mBC

PRIMED (N=50) evaluated the impact of primary prophylactic G-CSF as management of neutropenia. The primary safety analysis (median follow-up 4.3 mo), after 2 cycles of SG, reported incidences of any-grade, Grade 3, and 4 neutropenia as 28% (n=14), 12% (n=6), and 4% (n=2), respectively.[13] The extended safety analysis (median follow-up 9 mo) reported incidences of any-grade, Grade 3, and 4 neutropenia as 42% (n=21), 18% (n=9) and 6% (n=3), respectively.[14]

Clinical Guidelines for Neutropenia Management

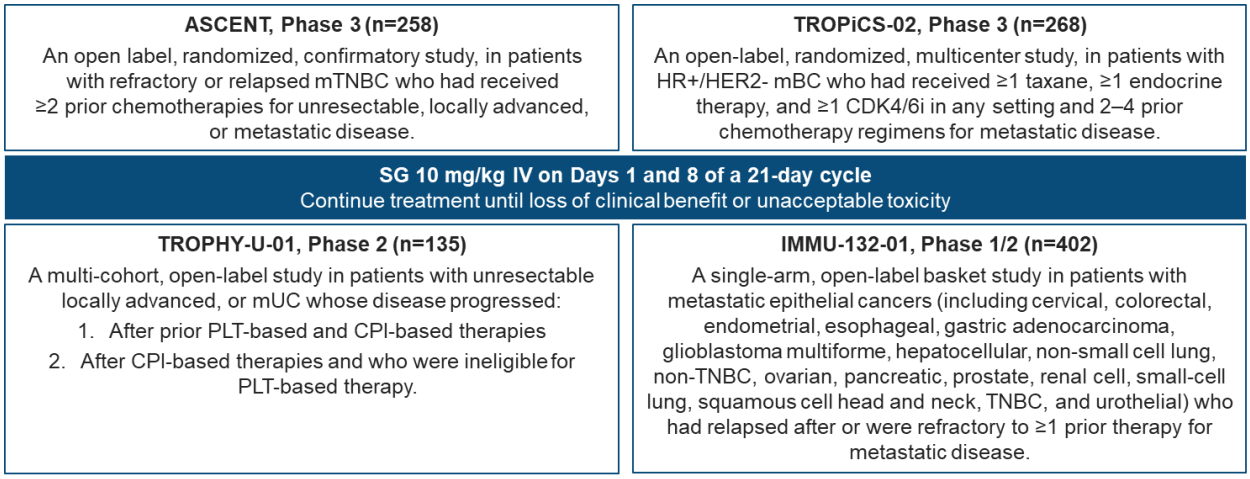
For guidance on the management of neutropenia please refer to National Comprehensive Cancer Network (NCCN)[15], American Society of Clinical Oncology (ASCO)[16] and European Society for Medical Oncology (ESMO)[17] Guidelines.

Pooled Safety Data

A pooled safety analysis examined exposure to SG 10 mg/kg IV as monotherapy in 1063 patients from four studies of multiple epithelial tumors (IMMU-132-01[4], ASCENT[3], TROPiCS-02[9], and TROPHY-U-01[5,11,18]). These studies included patients with mTNBC, HR+/HER2- mBC and mUC (Figure 1).[2]

The median treatment duration of SG in this pooled population was 4.1 (range: 0–63) mo.[1] See Table 1 for incidence of neutropenia in the pooled safety analysis.

Figure 1. Pooled Clinical Studies[2]



Abbreviations: CKD4/6i, cyclin-dependent 4/6 inhibitor; CPI, checkpoint inhibitor therapies; PLT=platinum; TNBC, triple-negative breast cancer.

Table 1. Pooled Safety Analysis: Neutropenia[1,2]

	Pooled Safety Population
Incidence of all-grade neutropenia	64%
Incidence of Grade ≥3 neutropenia	46%
Incidence of febrile neutropenia	6%
Incidence of neutropenic colitis	1.4%

Neutropenia was the most common Grade ≥3 TEAE, and one of the most common reasons for dose interruptions and reductions with SG across studies.[1] Treatment discontinuation occurred in 1% of patients due to TEAEs of neutropenia.[2]

Of the 948 patients with available GTs, those homozygous for the *UGT1A1*28* allele were at increased risk for neutropenia and febrile neutropenia. Grade ≥3 neutropenia was 43%, 49%, and 58% for those with a UGT1A1 status of *1/*1, *1/*28, and *28/*28, respectively. Grade ≥3 febrile neutropenia was 6%, 5%, and 14% for those with a UGT1A1 status of *1/*1, *1/*28, and *28/*28, respectively.[2]

Any-grade and Grade ≥3 neutropenia developed within a median (range) of 2.3 (0.1-62.1) and 2.3 (0.3-86.1) weeks and resolved within a median (range) of 1.1 (0.1-89.1) and 1.1 (0.1-89.1) weeks, respectively. Any-grade and Grade ≥3 febrile neutropenia developed within a median (range) of 2.1 (1.0-67.3) and 2.1 (1.0-67.3) weeks and resolved within a median (range) of 0.9 (0.1-3.3) and 0.9 (1.0-2.3) weeks, respectively.[2]

An exploratory analysis of G-CSF use during SG clinical trials on or after the first dose date of SG up to 30 days after the last dose date, excluding incomplete G-CSF administration dates, demonstrated that fewer patients experienced neutropenia, and had a longer time to onset of Grade ≥3 neutropenia after receiving either primary or secondary prophylaxis compared with those who did not receive prophylaxis (Table 2). Of the patients who received G-CSF treatment for the first time, 9% also required a dose reduction due to the neutropenia being treated.[2]

Table 2. Pooled Safety Analysis: Treatment of Neutropenia[2]

Patients, n (%)	Primary Prophylaxis[a]	Secondary Prophylaxis[b]

	Received Primary Prophylaxis (n=54)	Did Not Receive Primary Prophylaxis (n=1009)	Received Secondary Prophylaxis (n=116)	Did Not Receive Secondary Prophylaxis (n=893)
Any-grade neutropenia[c]	17 (31)	658 (65)	48 (41)	542 (61)
Grade ≥3 neutropenia[c]	14 (26)	504 (50)	29 (25)	408 (46)
Median time to onset of first Grade ≥3 neutropenia, days	29	14	78	14

[a]Defined as G-CSF use on or after cycle 1 day 1 and prior to onset of first occurrence of neutropenia, regardless of grade, or G-CSF use when there is no event of neutropenia.
[b]Defined as G-CSF use after resolution of Grade ≥2 neutropenia (to Grade ≤1) or occurrence of Grade ≥ 1 neutropenia, and prior to onset of any subsequent Grade ≥2 neutropenia or no occurrence of subsequent Grade ≥ 2 neutropenia. For patients who received primary or secondary prophylaxis, neutropenia is subsequent to secondary prophylaxis. For patients who did not receive primary or secondary prophylaxis, neutropenia is the first occurrence since cycle 1 day 1. Patients who received primary prophylactic G-CSF were excluded from the secondary prophylactic G-CSF use analysis.
[c]Includes neutropenia, neutrophil count decreased, and febrile neutropenia.

Incidence of Treatment-Related Neutropenia and Growth Factor Use in Clinical Studies

Neutropenia was one of the most common all-grade and Grade ≥3 treatment-related adverse events in the four clinical studies evaluated in the pooled safety analysis. There was a higher incidence of neutropenia and febrile neutropenia with SG vs TPC in the comparator studies. They were managed with dose reduction/delay (or both) and with growth-factor support at the investigator's discretion.[3,4,6,9,19-21] See Table 5 for further details.

Table 5. Incidence of Neutropenia, Febrile Neutropenia and Growth Factor Use[3,4,6,9,19-21]

		ASCENT		TROPiCS-02		TROPHY-U-01		IMMU-132-01
						C1	C2	
		SG n=258	TPC n=224	SG n=268	TPC n=249	SG N=113	SG N=38	SG N=495
Neutropenia, n (%)	All Grade	163 (63)[a]	96 (43)[a]	188 (70)[a]	134 (54)[a]	53 (47)	17 (45)	286 (58)
	Grade ≥3	132 (51)[a]	74 (33)[a]	136 (51)[a]	94 (38)[a]	39 (34)	13 (34)	210 (42)
Febrile neutropenia, n (%)	All Grade	15 (6)	5 (2)	14 (5)	11 (4)	11 (10)	3 (8)	27 (5.5)[b]
	Grade ≥3	15 (6)	5 (2,<1)[d]	14 (5)	11 (4)	11 (10)	3 (8)	26 (5.2)[b]
Growth factor use, n (%)	Prophylaxis	NR (29)	NR (10)	94 (35)	53 (21)	NR (22)	7 (18)	175 (35)[c]
	Treatment	NR (30)	NR (17)	75 (28)	47 (19)	NR (23)	10 (26)	

[a]Included neutropenia and decreased neutrophil count.
[b]No Grade 5 events occurred. One Grade 2 event was entered per investigator assessment, though not part of NIH and NCI common terminology criteria for AEs (v4.0), febrile neutropenia is by definition ≥Grade 3.
[c]Total use of growth factor support.
[d]Incidence of febrile neutropenia was 2% and <1% for Grade 3 and 4, respectively.

In patients with available UGT1A1 GTs, all-grade and Grade ≥3 neutropenia (and febrile neutropenia) were numerically more frequent in patients homozygous for the *UGT1A1*28* allele vs those who were heterozygous or had the WT allele (Table 6).[4,5,21]

Table 6. Incidence of Neutropenia and Febrile Neutropenia by *UGT1A1* GT[3-5,21]

Study	AE	*1/*1 WT		*1/*28 Heterozygous		*28/*28 Homozygous	
		All Grade	Grade ≥3	All Grade	Grade ≥3	All Grade	Grade ≥3
ASCENT n=250[a]	n	113		96		34	
	Neutropenia, n (%)[b]	76 (67)	60 (53)	55 (57)	45 (47)	24 (71)	20 (59)
	Febrile neutropenia, n (%)	3 (3)	3 (3)	5 (5)	5 (5)	6 (18)	6 (18)
TROPHY-U-01 n=105	n	45		47		13	
	Neutropenia, %	38	31	51	34	54	54
IMMU-132-01 n=403	n	177		180		46	
	Neutropenia, n (%)	59 (33.3)	NR	69 (38.3)	NR	28 (60.9)	NR

[a]Patients with *UGT1A1* GTs in the OSP. Seven patients had *UGT1A1* GTs not listed in the table.
[b]Neutropenia and decreased neutrophil count were combined.

Fatal infections secondary to neutropenia with SG were reported in 1 patient in both TROPiCS-02 (n=272, ITT) and the TROPHY-U-01 Cohort 1 Study in mUC (n=113, ITT). In the ASCENT study (n=267, ITT), fatal infections secondary to neutropenia with SG were not reported.[3,7-11]

TROPiCS-04 Study in mUC

TROPiCS-04 is an open-label, global, multicenter, randomized, phase 3 study evaluating the efficacy and safety of SG vs TPC in patients with locally advanced unresectable or mUC who progressed after prior PLT-based and CPI therapies.[12]

In the overall study population, 32 fatal TEAEs (25/349 [7.2%] in the SG group and 7/337 [2.1%] in the TPC group) were observed in the study.[12]

Sixteen out of 25 fatal AEs in the SG group were fatal infections secondary to neutropenia, 14 of which occurred within the first month of treatment. Of the patients who experienced fatal infections with neutropenia, 81% were ≥65 y, 56% had a prior cystectomy, 81% had a prior major urinary tract procedure, 50% had prior radiotherapy, and 50% had ≥3 prior anticancer regimens. The 4 TEAEs leading to death in the TPC group were infections with neutropenia (1%) and 3 were not related to an infection.[12]

Any-grade and Grade ≥3 neutropenia occurred in 166 (48%) and 122 (35%) patients in the SG group, and in 51 (15%) and 35 (10%) patients in the TPC group, respectively.[12]

All reports of febrile neutropenia were Grade ≥3 and occurred in 41 (12%) patients treated with SG, compared to 15 (4%) patients treated with TPC. [12]

Reports of primary prophylactic G-CSF use in a post-hoc analysis are shown in Table 3. Incidence of Grade ≥3 neutropenia with or without primary prophylactic G-CSF was 32% and 48%, respectively.[12] Impact of G-CSF use on AEs is reported in Table 4.

Table 3. TROPiCS-04: G-CSF Use[22]

Safety-Evaluable Patients, n (%)	SG (n=349)	TPC (n=337)
Primary prophylaxis[a]	74 (21)	73 (22)
Secondary prophylaxis[b]	54 (15)	14 (4)
Therapeutic[c]	106 (30)	33 (10)

[a]Defined as G-CSF use on or after Cycle 1 Day 1 and prior to the onset of the first occurrence of neutropenia or no event of neutropenia.

[b]Defined as G-CSF use after resolution of Grade ≥2 neutropenia (to Grade ≤1) or after occurrence of Grade 1 neutropenia; and prior to any subsequent Grade ≥2 neutropenia or no occurrence of subsequent Grade ≥2.
[c]Defined as administration during Grade ≥2 neutropenia.

Table 4. TROPiCS-04: Impact of G-CSF Use on AEs[22]

Patients Receiving SG, n (%)	With Primary Prophylactic G-CSF (n=74)	Without Primary Prophylactic G-CSF (n=275)
AESI neutropenia[a]	32 (43)	162 (59)
AESI neutropenia Grade ≥3[a]	24 (32)	131 (48)
Febrile neutropenia	7 (9)	33 (12)
AESI serious infections secondary to neutropenia after the first AESI neutropenia[b]	1 (1)	22 (8)
Fatal infection secondary to neutropenia	2 (3)[c,d]	14 (5)

[a]Includes neutropenia, neutrophil count decreased, febrile neutropenia.
[b]Assessed as serious by investigator and started on or within 11 days after start date of AESI neutropenia.
[c]1 patient had a preexisting open wound/ulceration, underwent an invasive procedure without adequate (per protocol) healing before next SG and did not receive prophylactic G-CSF with their last SG dose; the patient died of sepsis. Another patient had rapid tumor progression with kidney damage resulting in the placement of a nephrostomy tube without adequate healing before next SG (per protocol); the patient died of septic shock.
[d]Includes 1 patient with serious infection occurring on 15 days after neutropenia, therefore outside the window of AESIs of serious infection secondary to neutropenia.

PRIMED Study in mTNBC and HR+/HER2- mBC

PRIMED is an open-label, single arm, phase 2 study, in 50 patients with unresectable locally advanced mTNBC (n=32) or HR+/HER2- mBC (n=18), evaluating the impact of primary prophylactic G-CSF as management of neutropenia and primary prophylactic loperamide as management of diarrhea.[13,14]

Safety

Primary safety analysis[13]

The primary safety analysis had a median follow-up of 4.3 mo (range 0.2-8.6). At data cut-off, 31 patients (62%) remained on treatment. Disease progression was the primary reason for treatment discontinuation in 16 patients (32%). Results were reported for 50 patients after the first 2 cycles of SG with an incidence of any-grade neutropenia (28%) (Table 7). Grade ≥3 neutropenia was reported in 8 patients (16%), meeting the primary endpoint (P<0.001). No patients experienced FN.

Extended safety analysis[14]

The extended safety analysis had a median follow-up of 9 mo (range; 0.2-13.5). At data cut-off, the incidence of any-grade neutropenia was 42% (Table 9). A total of 12 patients (24%) had Grade ≥3 neutropenia (no patients experienced FN). The overall rate of AEs associated with dose reductions and treatment interruptions was 22% and 50%, respectively. Four patients discontinued due to AEs, two of which were SG-related (Grade 2 enteritis and Grade 3 diarrhea) (Table 10). Other TEAEs can be found in Table 11.

Table 9. PRIMED: Neutropenia After 2 Cycles and Until Data Cut-Off[13,14]

Neutropenia

n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Any Grade
After 2 cycles	2(4)	4(8)	6(12)	2(4)	14(28)
Data cut-off	4(8)	5(10)	9(18)	3(6)	21(42)

Table 10. PRIMED: Dose Reductions, Treatment Interruptions, and Discontinuations due to AEs After 2 Cycles and Until Data Cut-Off[13,14]

n (%)	Dose Reductions	Treatment Interruptions	Permanent Discontinuations
After 2 cycles	7 (14)	15 (30)	0 (0)
Data cut-off	11 (22)	25 (50)	4 (8)

Table 11. PRIMED: Any-Grade and Grade ≥3 TEAEs Occurring Until Data Cut-Off[14]

TEAEs, n (%)	Any-Grade	Grade ≥3
All TEAEs	**50 (100)**	**26 (52)**
Gastrointestinal Disorders	47 (94)	6 (12)
Constipation	28 (56)	0 (0)
Diarrhea	22 (44)	2 (4)
Nausea	27 (54)	0 (0)
Intestinal Obstruction	1 (2)	1 (2)
Abdominal Upper Pain	9 (18)	2 (4)
Neutropenic Colitis	1 (2)	1 (2)
Blood and Lymphatic System Disorders	**32 (64)**	**13 (26)**
Neutropenia	21 (42)	12 (24)
Anemia	24 (48)	2 (4)
General Disorders and Administration Site Conditions	**38 (76)**	**8 (16)**
Pain	1 (2)	1 (2)
Asthenia	35 (70)	7 (14)
Infections and Infestations	**23 (46)**	**1 (2)**
Acute Pyelonephritis	1 (2)	1 (2)
Skin and Subcutaneous Tissue Disorders	**30 (60)**	**5 (10)**
Alopecia	20 (40)	4 (8)
Urticaria	2 (4)	1 (2)
Investigations	**14 (28)**	**2 (4)**
Increased Gamma-Glutamyltransferase	6 (12)	2 (4)
Hepatobiliary Disorders	**5 (10)**	**1 (2)**
Hepatic Failure	1 (2)	1 (2)

References

1. TRODELVY® Gilead Sciences Inc. Trodelvy (sacituzumab govitecan-hziy) for injection, for intravenous use. U.S. Prescribing Information. Foster City, CA.
2. Rugo HS, Tolaney SM, Bardia A, et al. Pooled safety analysis of sacituzumab govitecan in multiple solid tumor types [Poster]. Presented at: American Society of Clinical Oncology (ASCO); May 31-June 4, 2024; Chicago, IL.
3. Bardia A, Hurvitz SA, Tolaney SM, et al. Sacituzumab Govitecan in Metastatic Triple-Negative Breast Cancer. *N Engl J Med.* 2021;384(16):1529-1541.
4. Bardia A, Messersmith WA, Kio EA, et al. Sacituzumab govitecan, a Trop-2-directed antibody-drug conjugate, for patients with epithelial cancer: final safety and efficacy results from the phase I/II IMMU-132-01 basket trial. *Ann Oncol.* 2021;32(6):746-756.
5. Tagawa ST, Balar AV, Petrylak DP, et al. TROPHY-U-01: A Phase II Open-Label Study of Sacituzumab Govitecan in Patients With Metastatic Urothelial Carcinoma Progressing After Platinum-Based Chemotherapy and Checkpoint Inhibitors. *J Clin Oncol.* 2021;39(22):2474-2485.

6. Rugo HS, Bardia A, Marme F, et al. Sacituzumab Govitecan in Hormone Receptor-Positive/Human Epidermal Growth Factor Receptor 2-Negative Metastatic Breast Cancer [Supplementary Appendix] *J Clin Oncol.* 2022;40(29):3365-3376.
7. Bardia A, Tolaney SM, Loirat D, et al. Sacituzumab govitecan versus treatment of physician's choice in patients with previously treated metastatic triple-negative breast cancer: final data from the phase 3 ASCENT study [Poster 1071]. Presented at: American Society of Clinical Oncology (ASCO) Annual Meeting; 3-7 June, 2022; Chicago, IL & Online.
8. Rugo HS, Tolaney SM, Loirat D, et al. Safety analyses from the phase 3 ASCENT trial of sacituzumab govitecan in metastatic triple-negative breast cancer. *npj Breast Cancer.* 2022;98(8).
9. Rugo HS, Bardia A, Marme F, et al. Sacituzumab Govitecan in Hormone Receptor-Positive/Human Epidermal Growth Factor Receptor 2-Negative Metastatic Breast Cancer. *J Clin Oncol.* 2022;40(29):3365-3376.
10. Tolaney SM, Bardia A, Marmé F, et al. Final overall survival analysis from the phase 3 TROPiCS-02 study of sacituzumab govitecan in patients with hormone receptor positive/HER2-negative metastatic breast cancer [Oral Presentation 1003]. Presented at: American Society of Clinical Oncology (ASCO) Annual Meeting; June 2-6, 2023; Chicago, IL.
11. Loriot Y, Petrylak DP, Kalebasty AR, et al. TROPHY-U-01, a phase II open-label study of sacituzumab govitecan in patients with metastatic urothelial carcinoma progressing after platinum-based chemotherapy and checkpoint inhibitors: updated safety and efficacy outcomes. *Ann Oncol.* 2024;35(4):392-401.
12. Powles T, Tagawa S, Vulsteke C, et al. Sacituzumab govitecan in advanced urothelial carcinoma: TROPiCS-04, a phase III randomized trial. *Annals of Oncology.* 2025;36(5):561-571.
13. Perez-Garcia JM, Gion M, Ruiz-Borrego M, et al. Prevention of sacituzumab govitecan-related neutropenia and diarrhea in patients with triple-negative or HR+/HER2- advanced breast cancer (PRIMED): a phase 2 trial [Poster 1101]. American Society of Clinical Oncology (ASCO); May 31-June 4, 2024; Chicago, IL.
14. Perez-Garcia JM, Gion M, Ruiz-Borrego M, et al. Efficacy analysis and updated safety from the phase 2 PRIMED study of prophylactic granulocyte-colony stimulating factor (G-CSF) and loperamide for patients with HER2-negative advanced breast cancer treated with sacituzumab govitecan [Poster P1-02-06]. San Antonio Breast Cancer Symposium (SABCS); December 10-13, 2024; San Antonio, TX.
15. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Hematopoietic Growth Factors, Version 1.2025 - October 11, 2024.
16. Smith TJ, Bohlke K, Lyman GH, et al. Recommendations for the Use of WBC Growth Factors: American Society of Clinical Oncology Clinical Practice Guideline Update. *J Clin Oncol.* 2015;33(28):3199-3212.
17. Klastersky J, de Naurois J, Rolston K, et al. Management of febrile neutropaenia: ESMO Clinical Practice Guidelines. *Ann Oncol.* 2016;27(suppl 5):v111-v118. http://www.ncbi.nlm.nih.gov/pubmed/27664247
18. Petrylak DP, Tagawa ST, Jain RK, et al. Early results of TROPHY-U-01 cohort 2: sacituzumab govitecan in platinum-ineligible patients with metastatic urothelial cancer who progressed after prior checkpoint inhibitor therapy [Poster]. Presented at: American Society of Clinical Oncology (ASCO) Meeting; 29 May-2 June, 2020; Chicago, IL.
19. Tagawa ST, Balar AV, Petrylak DP, et al. Updated outcomes in TROPHY-U-01 cohort 1, a phase 2 study of sacituzumab govitecan in patients with metastatic urothelial cancer who progressed after platinum-based chemotherapy and a checkpoint inhibitor [Poster 526]. Presented at: American Society of Clinical Oncology (ASCO) Genitourinary Cancers Symposium; 16-18 February, 2023; San Francisco, CA.
20. Petrylak DP, Tagawa ST, Jain RK, et al. TROPHY-U-01 Cohort 2: A Phase II Study of Sacituzumab Govitecan in Cisplatin-Ineligible Patients With Metastatic Urothelial Cancer Progressing After Previous Checkpoint Inhibitor Therapy. *J Clin Oncol.* 2024;42(29):3410-3420. https://www.ncbi.nlm.nih.gov/pubmed/39186707
21. Rugo HS, Tolaney SM, Loirat D, et al. Impact of UGT1A1 Status on the Safety Profile of Sacituzumab Govitecan in the Phase 3 ASCENT Study in Patients With Metastatic

Triple-Negative Breast Cancer [Poster PS11-09]. Presented at: San Antonio Breast Cancer Symposium (SABCS) Virtual; 08-11 December, 2020.
22. Grivas P, Powles T, Vulsteke C, et al. TROPiCS-04: A Randomized Phase 3 Study of Sacituzumab Govitecan vs Chemotherapy in Pretreated Advanced Urothelial Carcinoma. [Oral Presentation LBA9]. Presented at ESMO Asia; December 6-8; Singapore. 2024.

Abbreviations

AE=adverse event
AESI=adverse event of special interest
ANC=absolute neutrophil count
ASCO=American Society of Clinical Oncology
CPI=checkpoint inhibitor
EAIR=exposure adjusted incidence rate
ESMO=European Society of Medical Oncology
FN=febrile neutropenia
G-CSF=granulocyte colony-stimulating factor
GT=genotype
HR+/HER2- mBC=hormone receptor-positive/human epidermal growth factor receptor 2-negative metastatic breast cancer
mTNBC=metastatic triple-negative breast cancer
mUC=metastatic urothelial cancer
NCCN=National Comprehensive Cancer Network
NR=not reported
OSP=overall safety population
PLT=platinum
SG=sacituzumab govitecan-hziy
TEAE= treatment-emergent adverse event
TPC=treatment of physician's choice
UGT1A1=uridine diphosphate-glucuronosyl transferase 1A1
WT=wild-type

Product Label

For the full indication, important safety information, and boxed warning(s), please refer to the Trodelvy US Prescribing Information available at:
www.gilead.com/-/media/files/pdfs/medicines/oncology/trodelvy/trodelvy_pi

Follow-Up

For any additional questions, please contact Trodelvy Medical Information at:

☎1-888-983-4668 or 🖱 www.askgileadmedical.com

Adverse Event Reporting

Please report all adverse events to:

Gilead Global Patient Safety ☎ 1-800-445-3235, option 3 or
🖱 https://www.gilead.com/utility/contact/report-an-adverse-event

FDA MedWatch Program by ☎ 1-800-FDA-1088 or ✉MedWatch, FDA, 5600 Fishers Ln, Rockville, MD 20852 or 🖱 www.accessdata.fda.gov/scripts/medwatch

Data Privacy

The Medical Information service at Gilead Sciences may collect, store and use your personal information to provide a response to your medical request. We may share your information with other Gilead Sciences colleagues to ensure that your request is addressed

appropriately. If you report an adverse event or concern about the quality of a Gilead or Kite product, we will need to use the information you have given us in order to meet our regulatory requirements in relation to the safety of our medicines.

It may be necessary for us to share your information with Gilead's affiliates, business partners, service providers and regulatory authorities located in countries besides your own. Gilead Sciences has implemented measures to protect the personal information you provide. Please see the Gilead Privacy Statement (www.gilead.com/privacy-statements) for more information about how Gilead handles your personal information and your rights. If you have any further questions about the use of your personal information, please contact privacy@gilead.com.