GILEAD | Medical Information

Trodelvy® (sacituzumab govitecan-hziy) Incidence and Management of Diarrhea

This document is in response to your request for information regarding Trodelvy® (sacituzumab govitecan-hziy [SG]) and the incidence and management of diarrhea.

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 SG. 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 and real-world studies that constitute the largest pooled safety populations 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]

SG can cause severe diarrhea. Monitor patients with diarrhea and give fluid and electrolytes as needed. At the onset of diarrhea, evaluate for infectious causes and, if negative, promptly initiate loperamide. If severe diarrhea occurs, withhold SG until resolved to ≤ Grade 1 and reduce subsequent doses.

Management of adverse reactions may require temporary interruption, dose reduction, or treatment discontinuation of SG as described in Tables 1 and 2 of the US Prescribing Information. Do not re-escalate the SG dose after a dose reduction for adverse reactions has been made.

Pooled Safety Analyses on the Incidence and Management of Diarrhea With SG

A total of 1063 patients from four studies of multiple epithelial tumors (ASCENT,[2] TROPiCS-02,[3] TROPHY-U-01,[4,5] and IMMU-132-01[6]) were included in this analysis.[7] These studies included patients with mTNBC, HR+/HER2- mBC, and mUC. The median (range) treatment duration of SG was 4.1 (0–63) mo.[1]

- Treatment-emergent any-grade diarrhea, Grade ≥3 diarrhea, and diarrhea that led to treatment discontinuation was reported for 64%, 11%, and 1% of patients treated with SG, respectively.[7]

- Grade ≥3 diarrhea was more common in patients with *UGT1A1 *28/*28* GT (15%) than in those with other GTs (**1/*1*, 8%; **1/*28*, 12%).[7] *UGT1A1* testing is not required as per the product label.[1]
- Median onset of any-grade and Grade ≥3 diarrhea occurred at approximately 2 wk from treatment initiation and resolved in approximately 1 wk.[7]
- Antidiarrheal treatment was administered to 477 patients (70%); loperamide ± other antidiarrheals were used by 90% of these patients. Loperamide was advised for non-infectious diarrhea at onset.[8-11] For unresolved diarrhea after 24 h, opium tincture[10] and diphenoxylate/atropine[9,10] were recommended. Subcutaneous octreotide was recommended for persistent diarrhea, and premedication with atropine was recommended for patients who experienced cholinergic response, including diarrhea, to SG.[8-11] Additional supportive measures and dietary modifications were recommended.[7-10]

A total of 969 patients with either mTNBC or HR+/HER2- mBC were included in an analysis of six clinical studies (ASCENT,[2] TROPiCS-02,[3] IMMU-132-01,[6] EVER-132-001,[12] EVER-132-002,[13] and ASCENT-J02[14]). TEAEs were analyzed by region: NA/EU, n=688; Asia, n=281.[15]

- Patients in NA/EU had higher rates of any-grade and Grade ≥3 diarrhea than did patients in Asia (absolute incidence not reported); these rates remained generally stable over time (through to approximately Weeks 68 and 72 in NA/EU and Asia, respectively). Of the patients who received an antidiarrheal during SG treatment, a higher percentage in NA/EU than in Asia received loperamide (89% vs 49%, respectively) and atropine (20% vs 5%). A higher percentage of patients in Asia received other antidiarrheal treatment vs patients in NA/EU: 73% vs 23%, respectively.[15]

Clinical Study Data on the Incidence and Management of Diarrhea With SG

ASCENT-03, an ongoing, global, open-label, randomized, phase 3 study, is comparing the efficacy and safety of SG vs chemotherapy TPC (eg, gem + carbo, paclitaxel, or nab-paclitaxel) as 1L treatment in patients (N=558) with previously untreated, locally advanced, inoperable or mTNBC who are not candidates for PD-(L)1 inhibitor therapy.[16]

- Grade ≥3 TEAEs diarrhea were reported by 9% and 1% of those in the SG and TPC arms, respectively.[16]
- In the SG arm, diarrhea led to dose reduction in 15 patients (5%) and to treatment discontinuation in 1 patient (<1%). In the TPC arm, diarrhea led to dose reduction in 3 patients (1%), and no patients required treatment discontinuation.[17]
- A total of 137 and 35 patients received antidiarrheal treatment in the SG and TPC arms, respectively. In both treatment arms, loperamide was the most common treatment: SG, 90%; TPC, 77%. Overall, multiple antidiarrheals were used in 20% of patients who received any antidiarrheal treatment in both treatment arms.[17]

PRIMED, a phase 2 study in 50 patients with unresectable, locally advanced mTNBC or HR+/HER2- mBC, is evaluating the impact of primary prophylactic G-CSF and loperamide as management of neutropenia and diarrhea, respectively.[18]

- At the primary safety analysis (median follow-up, 4.3 mo), the incidence of Grade ≥2 diarrhea was 16% (n=8; *P*=0.084); thus, the second primary endpoint was not met. At the extended safety analysis (median follow-up, 9 mo), the incidence of any-grade diarrhea was 44% (n=22). Nine patients (18%) had Grade ≥2 diarrhea, 4% had Grade 3 diarrhea, and no cases of Grade 4 diarrhea were reported. Two patients discontinued due to TEAEs of Grade 2 enteritis and Grade 3 diarrhea.

Real-World Study Data on the Incidence and Management of Diarrhea With SG

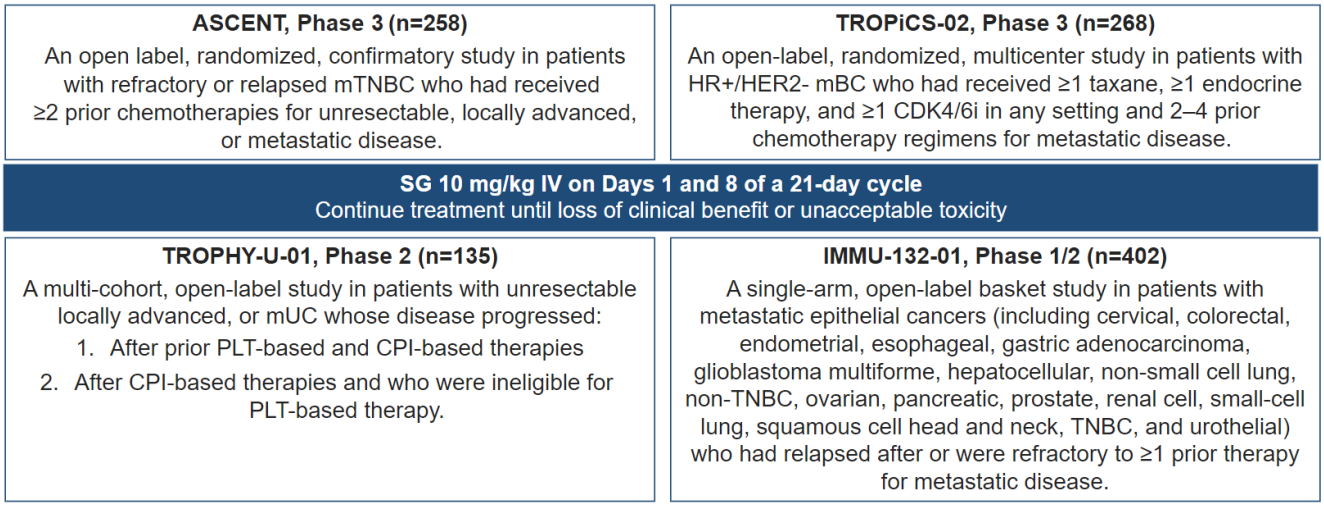
At 3 centers in Spain, 17 female patients with unresectable, locally advanced mTNBC or HR+/HER2- mBC were given atropine as a premedication to each SG infusion, according to the approved indications in Spain. The incidence of treatment-emergent any-grade, Grade 1, and Grade 2 diarrhea was 41% (n=7), 35% (n=6), and 6% (n=1), respectively. Three patients required a dose reduction of SG. No discontinuations were due to TEAEs.[19]

Pooled SG Safety Analyses on the Incidence and Management of Diarrhea With SG

Safety Analysis in Patients With Multiple Epithelial Tumors

A pooled safety analysis examined exposure to SG 10 mg/kg IV as monotherapy in 1063 patients from four studies of multiple epithelial tumors (ASCENT,[2] TROPiCS-02,[3] TROPHY-U-01,[4,5] and IMMU-132-01[6]).[7] These studies included patients with mTNBC, HR+/HER2- mBC, and mUC (Figure 1). The median (range) treatment duration of SG was 4.1 (0–63) mo.[1]

Figure 1. Pooled Clinical Studies in Patients With Multiple Epithelial Tumors[7]



Abbreviation: CPI=checkpoint inhibitor.

Baseline demographics and disease characteristics are summarized in Table 1.

Table 1. Pooled Safety in Multiple Epithelial Tumors: Baseline Demographics and Disease Characteristics[7]

Key Demographics and Characteristics		All Patients (N=1063)
Age, median (range), y		59 (27–90)
Sex, n (%)	Female	840 (79)
Race, n (%)	White/Black/Asian	826 (78)/55 (5)/38 (4)
	Other or unknown	144 (14)
ECOG PS, %	0/1	36/64
Time since metastatic disease diagnosis, median (range), mo		28.7 (-0.1 to 412.6)
Number of prior lines of systemic therapy, median (range), n		5 (1–17)
Presence of visceral metastasis, n (%)		882 (83)

Key Demographics and Characteristics		All Patients (N=1063)
UGT1A1 status, n (%)	**1/*1*	416 (39)
	**1/*28*	420 (40)
	**28/*28*	112 (11)
	Other/unknown	13 (1)/102 (10)

Diarrhea incidence, onset, and duration

Treatment-emergent any-grade diarrhea, Grade ≥3 diarrhea, and diarrhea that led to treatment discontinuation was reported for 64%, 11%, and 1% of patients treated with SG, respectively.[7]

Grade ≥3 diarrhea was more common in patients with *UGT1A1 *28/*28* GT (15%) than in those with other GTs (**1/*1*, 8%; and **1/*28*, 12%).[7] *UGT1A1* testing is not required as per the product label.[1]

Median any-grade and Grade ≥3 diarrhea occurred approximately 2 wk after treatment initiation and resolved in approximately 1 wk (Table 2).[7]

Table 2. Pooled Safety in Multiple Epithelial Tumors: Time to Onset and Resolution of Diarrhea (N=1063)[7]

	Time to Onset		Time to Resolution	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Diarrhea, median (range), wk	1.9 (0.1–90)	2.1 (0.1–78.6)	1.1 (0.1–50)	1 (0.1–7.9)

Diarrhea management

SG-associated toxicities were assessed and managed in accordance with standard clinical/institutional practices and accepted treatment guidelines.[8,9,11,20]

Antidiarrheal medication

At the onset of non-infectious diarrhea, prompt initiation of loperamide 4 mg was advised, followed by 2 mg per episode (up to a dose of 16 mg/d). According to the ASCENT and IMMU-132-01 protocols, loperamide was to be discontinued 12 h after diarrhea had resolved and normal diet resumed; this was not required in TROPiCS-02 or TROPHY-U-01.[8-11]

If diarrhea did not resolve after 24 h, the TROPHY-U-01 and TROPiCS-02 protocols recommended that diphenoxylate/atropine be considered.[9,10] In addition, the TROPiCS-02 protocol also recommended opium tincture after 24 h.[10] For persistent diarrhea, subcutaneous octreotide (100–150 mcg three times daily) could be considered.[8-11]

Additional supportive measures included fluid and electrolyte substitution and oral antibiotics,[8-11] such as ciprofloxacin (for diarrhea that persisted >24 h, or in patients who exhibited an absolute neutrophil count <500/mm^3 or fever with diarrhea). The ASCENT and IMMU-132-01 protocols specified a ciprofloxacin dose of 250 to 750 mg/12 h for 7 d.[8,11] In the study protocols for TROPHY-U-01 and TROPiCS-02, several dietary modifications were recommended, including a bland diet, small frequent meals, adequate intake of clear liquids to maintain hydration, and discontinuation of lactose-containing foods/drinks and alcohol.[9,10]

Anticholinergic medication[8-11]

It was recommended that patients who experienced a cholinergic response to SG, including diarrhea, should receive premedications (eg, atropine) for future treatments.

Incidence of patients receiving any antidiarrheal medication[7]

Of the 681 patients who experienced any-grade diarrhea, 477 (70%) received antidiarrheal medication (Table 3); loperamide ± other antidiarrheals were used by 90% of these patients.

Table 3. Pooled Safety in Multiple Epithelial Tumors: Treatment of Diarrhea[7]

n (%)	Patients Who Received Any Antidiarrheal (n=477)
Any loperamide/any atropine	428 (90)/97 (20)
Loperamide alone/atropine alone	277 (58)/9 (2)
Other antidiarrheal alone	22 (5)
Multi-antidiarrheal regimen[a]	162 (34)

[a]Antidiarrheals with the same start or overlapping treatment dates were considered an antidiarrheal regimen.

Pooled Safety Analysis in Patients With mBC

A pooled safety analysis of six clinical studies[15] (ASCENT,[2] TROPiCS-02,[3] IMMU-132-01,[6] EVER-132-001,[12] EVER-132-002,[13] and ASCENT-J02[14]) examined exposure to SG 10 mg/kg IV as monotherapy in 969 patients with mTNBC or HR+/HER2- mBC; TEAEs were analyzed by region, NA/EU and Asia. Except for race (Table 4), baseline characteristics, including age, sex, and BMI, were comparable between the NA/EU and Asia groups.

Table 4. Pooled Safety in mBC: Baseline Race by Region[15]

Race, n (%)	NA/EU (n=688)	Asia (n=281)
White	517 (75)	0
Black	41 (6)	0
Asian	26 (4)	281 (100)
Other/unknown	104 (15)	0

Diarrhea incidence and management[15]

Patients in the NA/EU region had higher rates of any-grade and Grade ≥3 diarrhea compared with patients in Asia (Figure 2); these rates remained generally stable over time (through to approximately Weeks 68 and 72 in NA/EU and Asia, respectively). Diarrhea was identified as one of the most common reasons for discontinuation in the NA/EU region with an incidence of <1%.

Figure 2. Pooled Safety in mBC: Incidence of Any-Grade (≥20%) and Grade ≥3 (≥10%) Treatment-Emergent Diarrhea[15]

Of the patients who received an antidiarrheal during SG treatment, a higher percentage in the NA/EU region received loperamide and atropine than patients in Asia, while a higher percentage of patients in Asia received other antidiarrheal treatment vs patients in NA/EU (Table 5).

Table 5. Pooled Safety in mBC: Treatment of Diarrhea[15]

Patients, n (%)	Patients Who Received An Antidiarrheal During SG Treatment		Patients Who Experienced Diarrhea and Received an Antidiarrheal During SG Treatment	
	NA/EU (n=343)	Asia (n=120)	NA/EU (n=298)	Asia (n=88)
Any loperamide	304 (89)	59 (49)	271 (91)	56 (64)
Any atropine	67 (20)	6 (5)	58 (19)	5 (6)
Other antidiarrheal	80 (23)	87 (73)	76 (26)	58 (66)

Clinical Study Data on the Incidence and Management of Diarrhea With SG

ASCENT-03

Study design and demographics

ASCENT-03, an ongoing, global, open-label, randomized, phase 3 study, is comparing the efficacy and safety of SG vs TPC (eg, gem + carbo, paclitaxel, or nab-paclitaxel) as 1L treatment in patients (N=558) with previously untreated, locally advanced, inoperable or mTNBC who were ineligible for PD-(L)1 inhibitor therapy.[16] Patients with active chronic inflammatory bowel disease or gastrointestinal perforation that occurred <6 mo of enrollment were excluded from enrollment.[21] Patient baseline characteristics and prior treatments are summarized in Table 6.

No prophylactic antidiarrheal medications were provided before SG doses.[21]

Table 6. ASCENT-03: Baseline Demographics and Disease Characteristics[16]

Key Demographics and Characteristics		SG (n=279)	TPC (n=279)
Age, median (range), y		56 (28-84)	54 (23-86)
Age ≥65, n (%), y		65 (23)	78 (28)
Race or ethnic group,[a] n (%)	White/Asian/Black	178 (64)/66 (24)/10 (4)	178 (64)/65 (23)/7 (3)
	Other or not specified	25 (9)	29 (10)
Geographic region, n (%)[b]	US/Canada/Western Europe	89 (32)	89 (32)
	Rest of the world	190 (68)	190 (68)
ECOG PS, n (%)[c]	0/1	183 (66)/96 (34)	187 (67)/92 (33)
PD-L1 negative status, n (%)[d]		277 (99)	278 (>99)
Disease status, n (%)[e]	Metastatic at initial diagnosis	87 (31)	88 (32)
	Recurrent within 6–12 mo[f]	58 (21)	57 (20)
	Recurrent >12 mo[f]	134 (48)	134 (48)
Metastatic sites, n (%)	Lymph node	179 (64)	180 (65)
	Lung	166 (59)	170 (61)
	Bone	95 (34)	87 (31)
	Liver	81 (29)	72 (26)
	Brain	15 (5)	14 (5)
	Other	98 (35)	84 (30)
Prior (neo)adjuvant therapies, n (%)	Taxane	162 (58)	162 (58)
	PLT agents	51 (18)	49 (18)
	Capecitabine	50 (18)	57 (20)
	PD-(L)1 inhibitors	13 (5)	11 (4)

Key Demographics and Characteristics	SG (n=279)	TPC (n=279)
Time since diagnosis of metastatic or locally advanced unresectable disease to randomization, median (range), mo	1.9 (0.4-26.7)	1.9 (0.1-18.9)

Abbreviation: CPS=combined positive score.
[a]Patient reported.
[b]Western Europe: Austria, Belgium, France, Germany, Italy, Netherlands, Spain, Switzerland, and United Kingdom. Rest of the world: Argentina, Australia, Brazil, Chile, China, Czech Republic, Hong Kong, Hungary, Israel, Japan, Malaysia, Mexico, Poland, Romania, Slovakia, South Africa, South Korea, Taiwan, and Turkey.
[c]Scores range from 0 to 5; higher scores indicate greater disability.
[d]PD-L1 status assessed using the PD-L1 IHC 22C3 pharmDx assay (Dako, Agilent Technologies) at the time of enrollment. One patient in the SG arm had PD-L1 CPS missing.
[e]Corresponding numbers: SG: 86 metastatic at initial diagnosis, 59 recurrent disease within 6 to 12 mo, 134 recurrent disease >12 mo; TPC: 83 metastatic at initial diagnosis, 62 recurrent disease within 6 to 12 mo, 134 recurrent disease >12 mo.
[f]From completion of treatment in the curative setting.

Safety

The median (range) duration of treatment at the time of the final progression-free survival analysis were as follows: SG, 8.3 (<0.1 to 28.7) mo; taxane, 6.3 (<0.1 to 24.2) mo; and gem + carbo, 5.8 (<0.1 to 23.1) mo. In the SG arm, diarrhea was among the most commonly reported any-grade and Grade ≥3 TEAEs (Table 7).[16]

Table 7. ASCENT-03: Any-Grade and Grade ≥3 TEAEs of Diarrhea[16a]

TEAE, n (%)	SG (n=275)		TPC (n=276)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Diarrhea	148 (54)	25 (9)	55 (20)	2 (1)

[a]TEAEs began on or after the first dose date of study drug and ≤30 d after the last dose date of study drug (including crossover treatment if applicable) or the initiation of subsequent anticancer therapy, whichever occurred first. AEs were coded according to preferred terms in the Medical Dictionary for Regulatory Activities, version 27.1, and graded for severity according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 5.0.

Time to onset and duration of diarrhea[17]

The median time to onset of diarrhea was shorter for patients treated with SG than for those treated with TPC, and the median duration of diarrhea was generally comparable between treatment arms; these results should be interpreted with caution due to the small sample size (Table 8). Any-grade and Grade ≥3 diarrhea were most frequently reported early during SG treatment.

Table 8. ASCENT-03: Time to Onset and Duration of Diarrhea[17]

Diarrhea Outcomes	SG (n=275)				TPC (n=276)			
	Any Grade		Grade ≥3		Any Grade		Grade ≥3	
	n	Median (Range), d	n	Median (Range), d	n	Median (Range), d	n	Median (Range), d
Time to onset[a]	148	13 (1–427)	25	67 (6–356)	55	26 (1–296)	2	210 (110–310)
Duration[b]	130	6 (1–273)	24	6 (1–18)	48	6 (1–370)	2	1 (1–1)

[a]Defined as the time from the first dose date of study drug to the onset date of the first TEAE.
[b]Defined as the median duration among multiple preferred terms; within each preferred term, the duration is the median duration among multiple episodes (end date of TEAE – onset date of TEAE + 1 d for each episode).

Management of diarrhea[17]

Across treatment arms, most cases of diarrhea were Grade 1/2: SG, 45%; TPC, 19%.

A total of 137 (50%) and 35 (13%) patients received antidiarrheal treatment in the SG and TPC arms, respectively; loperamide was the most common treatment in both arms (SG, 90%; TPC, 77%). In both treatment arms, multi-antidiarrheal regimens were used in 20% of the patients who received any antidiarrheal treatment. In the SG arm, diarrhea led to dose reduction in 15 patients (5%) and to treatment discontinuation in 1 patient (<1%). In the TPC arm, diarrhea led to dose reduction in 3 patients (1%), and no patients required treatment discontinuation.

Exploratory analysis: EAIRs[17]

EAIRs, defined as the number of patients with ≥1 specified TEAE per PYE, were calculated as the patients with a specific event divided by the total PYE in each arm. PYE was defined as the sum of each patient's time at risk (exposure duration). Due to the exploratory nature of this post hoc analysis, all results presented in Table 9 should be considered nominal.

The incidence of diarrhea remained higher for SG than for TPC when adjusted for treatment exposure. Additional EAIR data by treatment arm are presented in Table 9.

Table 9. ASCENT-03 Exploratory Safety Analysis: EAIRs[17]

TEAE	SG (n=275)		TPC (n=276)		EAIR Difference (95% CI)
	n (%)	EAIR (95% CI)	n (%)	EAIR (95% CI)	
Diarrhea	148 (54)	1.42 (1.2–1.67)	55 (20)	0.41 (0.31–0.54)	1.01 (0.76–1.28)

Note: EAIR values <0 indicate a difference that favors SG, and values >0 indicate a difference that favors TPC.

PRIMED Study in mTNBC and HR+/HER2- mBC

Study design and demographics[18]

PRIMED is an ongoing, open-label, single-arm, phase 2 study evaluating the impact of primary prophylactic G-CSF and loperamide as management of neutropenia and diarrhea, respectively, in 50 patients with unresectable, locally advanced mTNBC (n=32) or HR+/HER2- mBC (n=18) who were treated with SG. Patients received primary prophylactic loperamide (2 mg twice daily or 4 mg once daily on Days 2, 3, 4, 9, 10, and 11) during the first two SG cycles; additional loperamide could be given thereafter at the healthcare provider's discretion. The primary endpoint was the incidence of either Grade ≥3 neutropenia or Grade ≥2 diarrhea during the first two SG cycles. Patient baseline characteristics and prior treatments are summarized in Table 10.

Table 10. PRIMED: Baseline Demographics, Disease Characteristics, and Prior Treatments[18]

Key Demographics and Characteristics and Prior Treatments		mTNBC (n=32)	HR+/HER2- mBC (n=18)	Overall (N=50)
Age, median (range), y		51 (31–74)	53.5 (37–72)	52 (31–74)
ECOG PS, n (%)	0/1	18 (56.2)/14 (43.8)	12 (66.7)/6 (33.3)	30 (60)/20 (40)
HER2 expression, n (%)	0	19 (59.4)	11 (61.1)	30 (60)
	1+	8 (25)	2 (11.1)	10 (20)
	2+/ISH [-]	5 (15.6)	5 (27.8)	10 (20)
Visceral disease, n (%)		20 (62.5)	15 (83.3)	35 (70)
Prior (neo)adjuvant chemotherapy, n (%)		19 (59.4)	5 (27.8)	24 (48)
Prior chemotherapy regimens for advanced disease, n (%)	0[a]	8 (25)	2 (11.1)	10 (20)
	1	18 (56.2)	11 (61.1)	29 (58)
	2	6 (18.8)	5 (27.8)	11 (22)

Key Demographics and Characteristics and Prior Treatments		mTNBC (n=32)	HR+/HER2- mBC (n=18)	Overall (N=50)
Most common (≥20% in any arm) active principle for previous anticancer treatment, n (%)	Taxane	32 (100)	18 (100)	50 (100)
	Anthracyclines	20 (62.5)	12 (66.7)	32 (64)
	Immunotherapy	11 (34.4)	0	11 (22)
	Endocrine therapy[b]	7 (21.9)	18 (100)	25 (50)
	CDK4/6 inhibitor[b]	1 (3.1)	18 (100)	19 (38)

Abbreviation: ISH=in situ hybridization.
[a]Systemic treatment in the curative setting was considered as a line of therapy if development of unresectable locally advanced or metastatic disease occurred within 12 mo of chemotherapy or immunotherapy completion.
[b]The treatment of those in the TNBC arm with an endocrine therapy or CDK4/6 inhibitor occurred when the patient's disease was not TNBC.

Safety

Primary safety analysis

The primary safety analysis had a median (range) follow-up time of 4.3 (0.2–8.6) mo. Results were reported for 50 patients during the first 2 cycles of SG: Grade ≥2 diarrhea, 8 patients (16%; *P*=0.084); thus, the second primary endpoint was not met (Table 11).[18]

Extended safety analysis

The extended safety analysis had a median (range) duration of follow-up of 9 (0.2–13.5) mo. At data cutoff, 9 patients (18%) continued treatment and 33 (66%) discontinued SG primarily due to disease progression. Twenty-nine patients (58%) received ≥1 dose of loperamide after Cycle 2 (median [range] duration, 5.6 [1.5–12.6] mo).[18]

The incidence of any-grade and Grade ≥2 diarrhea was 44% and 18%, respectively, and no Grade 4 diarrhea or treatment-related serious AEs were reported (Table 11). The overall rate of dose reductions and treatment interruptions was 22% and 50%, respectively. Four patients discontinued SG due to AEs; of these, 2 were SG-related: Grade 2 enteritis and Grade 3 diarrhea (Table 12).[18] An additional case of Grade ≥3 neutropenic colitis resulted in permanent SG discontinuation.[22] The average relative dose intensity of SG was 95%.[18]

Table 11. PRIMED: Diarrhea During First 2 Cycles and Extended Safety Analysis[18,23]

Diarrhea, n (%)	Any Grade	Grade 1	Grade 2	Grade ≥2	Grade 3	Grade ≥3	Grade 4
During first 2 cycles	17 (34)	NR	6 (12)	8 (16)[a]	2 (4)	NR	0
Extended safety analysis	13 (26)	13 (26)	7 (14)	NR	NR	2 (4)	NR

Abbreviation: NR=not reported.
[a]Primary endpoint.

Table 12. PRIMED: Dose Reductions, Treatment Interruptions, and Discontinuations[18]

n (%)	Dose Reduction	Treatment Interruption	Permanent Discontinuation
During first 2 cycles	7 (14)	15 (30)	0
Extended safety analysis	11 (22)	25 (50)	4 (8)

Real-World Study Data on the Incidence and Management of Diarrhea With SG

Real-World Safety of SG and Prophylactic Atropine Use[19]

At three Spanish centers, 17 female patients with unresectable, locally advanced mTNBC (n=13) or HR+/HER2- mBC (n=4) received atropine (0.5 mg subcutaneously) as a premedication to each SG infusion, according to the approved indications in Spain. Patient baseline characteristics are summarized in Table 13.

Table 13. Baseline Demographics and Disease Characteristics (Echarri et al)[19]

Key Demographics and Characteristics		SG + Atropine (N=17)
Age, median (range), y		50 (29–72)
ECOG PS, n (%)	0/1/2	2 (11.8)/9 (52.9)/6 (35.3)
Germline *BRCA* mutation, n (%)	Negative/positive	15 (88.2)/2 (11.8)
PD-L1 expression, n (%)	Negative/positive	3 (17.6)/14 (82.1)

Abbreviation: *BRCA*=breast cancer gene.

Of the 17 patients who received prophylactic atropine, 7 patients developed any-grade diarrhea, 6 patients developed Grade 1 diarrhea, and 1 patient developed Grade 2 diarrhea. Constipation was not reported as a common TEAE. Three patients each required an SG dose reduction, and there were no discontinuations due to TEAEs.

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Abbreviations

1L=first line
AE=adverse event
carbo=carboplatin
CDK4/6i=cyclin-dependent 4/6 inhibitor
EAIR=exposure-adjusted incidence rate
ECOG PS=Eastern Cooperative Oncology Group Performance Status
EU=Europe
G-CSF=granulocyte colony-stimulating factor
gem=gemcitabine
GT=genotype
HER2-=human epidermal growth factor receptor 2-negative

HR+=hormone receptor-positive
mBC=metastatic breast cancer
mTNBC=metastatic triple-negative breast cancer
mUC=metastatic urothelial cancer
NA=North America
PD-(L)1=programmed death (ligand) 1
PLT=platinum
PYE=patient year of exposure
SG=sacituzumab govitecan-hziy
TEAE=treatment-emergent adverse event
TNBC=triple-negative breast cancer
TPC=treatment of physicians' choice
UGT1A1=uridine diphosphate glucuronosyl transferase family 1 member A1

Product Label

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