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Trodelvy®(sacituzumab govitecan-hziy) SG + Pembro: Incidence and Management of Diarrhea in Patients With mBC

This document is in response to your request for information regarding Trodelvy® (sacituzumab govitecan-hziy [SG]) plus pembrolizumab (pembro) and the incidence and management of diarrhea in patients with metastatic breast cancer (mBC).

This document summarizes data for SG (10 mg/kg IV on Days 1 and 8 of a 21-day treatment cycle) plus pembro from phase 2 and 3 clinical mBC studies.

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.

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

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Summary

Relevant Product Labeling[1]

Boxed Warning: 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.

Dosage Modifications for Adverse Reactions for SG in Combination with Pembrolizumab or Pembrolizumab and berahyaluronidase alfa-pmph

Interrupt or discontinue one or both drugs of the combination or reduce the dose of SG to manage adverse reactions as appropriate. Refer to the Prescribing Information for pembro or pembro and berahyaluronidase alfa-pmph for recommendations on dosage interruption or discontinuation due to adverse reactions. For SG dosage modifications, refer to Table 1 and Table 2 of the Prescribing Information.

SG + Pembro: Incidence and Management of Diarrhea in mBC

ASCENT-04, an ongoing, phase 3 study (N=443), is comparing SG + pembro vs chemotherapy treatment of physicians' choice (TPC) + pembro, as first-line (1L) treatment in patients with programmed death ligand-1 positive ([PD-L1+] combined positive score [CPS] ≥10), inoperable, locally advanced or metastatic triple-negative breast cancer (mTNBC).[2]

- The overall safety population included 221 patients who received SG + pembro and 220 patients who received TPC + pembro.
- Median duration of treatment (DOT) was 8.9 and 6.2 mo with SG and TPC, respectively. For pembro, median DOT was 8.5 mo among patients who received SG + pembro and 6.4 mo among those who received TPC + pembro.[2]
- Treatment-related diarrhea occurred more frequently with SG + pembro vs TPC + pembro for any-grade (SG + pembro, 66% vs TPC + pembro, 20%) and Grade ≥3 diarrhea (SG + pembro, 9% vs TPC + pembro, 1%);[3] exposure-adjusted incidence rates (EAIR) were 0.13 vs 0.03, respectively.[4]
- Onset of diarrhea was shorter with SG + pembro vs TPC + pembro; any-grade diarrhea had a median time to onset of 14 vs 64 d. Median time to onset of Grade ≥3 diarrhea was 17 d with SG + pembro vs 299 d with TPC + pembro.[4]
- The median duration of any-grade diarrhea was 7 vs 6 d in the SG + pembro vs TPC + pembro arms, respectively. The median duration of Grade ≥3 diarrhea was 8 d with SG + pembro vs 4 d with TPC + pembro.[4]
- Loperamide was the main antidiarrheal agent (90% vs 77% for SG + pembro vs TPC + pembro). Atropine was used more frequently with SG + pembro (12%) than TPC + pembro (3%).[4]
- Diarrhea led to dose reductions in 5% vs 1% of patients and treatment discontinuation in 0% vs <1% of patients in the SG + pembro vs TPC + pembro arms, respectively.[4,5]

SACI-IO HR+, a phase 2 study (N=104) compared SG + pembro vs SG in patients with hormone receptor-positive human epidermal growth factor receptor 2-negative (HR+/HER2-) mBC who have progressed on ≥1 line of endocrine therapy (ET) for metastatic disease, or progression on or within 12 mo of adjuvant ET, and have received 0–1 prior chemotherapy regimens for mBC.[6]

- At a median follow-up of 12.5[6] and 34.6 mo[7], the incidence of diarrhea was lower with SG + pembro vs SG. At both time points, Grade 3-4 diarrhea occurred in 3 (5.8%) vs 4 (7.7%) patients in the SG + pembro vs SG arms, respectively.

SG + Pembro: Incidence and Management of Diarrhea in mBC

ASCENT-04 Study

ASCENT-04, an ongoing, global, open-label, randomized, phase 3 study is comparing the efficacy and safety of SG + pembro vs TPC (gemcitabine + carboplatin, paclitaxel, or nab-paclitaxel) + pembro as 1L treatment in patients with PD-L1+ (CPS ≥10), inoperable, locally advanced or mTNBC. A total of 443 female patients were enrolled. Patients who experienced disease progression during treatment with TPC + pembro (as verified by blinded independent central review) could crossover to receive second-line (2L) SG monotherapy.[2]

Safety

The median (range) DOT was 8.9 (<0.1 to 27.1) mo and 6.2 (<0.1 to 26.3) mo with SG and TPC, respectively. For pembro, the median (range) DOT was 8.5 (<0.1 to 26.8) mo among patients receiving SG + pembro and 6.4 (<0.1 to 25.6) mo among those receiving TPC + pembro.[2]

Diarrhea was the most frequently reported any-grade treatment-emergent adverse event (TEAE) and the second most frequently reported Grade ≥3 TEAE for patients in the SG + pembro arm.[2] Most cases of diarrhea were Grade 1 (37% vs 17%) or Grade 2 (24% vs 10%) in the SG + pembro vs TPC + pembro arms, respectively.[4]

Diarrhea was the most frequently reported any-grade treatment-related adverse event (TRAE), alongside nausea, in the SG + pembro arm. Grade ≥3 treatment-related diarrhea in the SG + pembro arm was the second most frequent TRAE;[3] see Table 1 for incidence.

Table 1. ASCENT-04: Incidence of Diarrhea[2,3]

Diarrhea, n (%)	SG + Pembro (n=221)		TPC + Pembro (n=220)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
TEAE[a]	155 (70)	22 (10)	63 (29)	5 (2)
TRAE[a,b]	145 (66)	19 (9)	45 (20)	3 (1)

[a]Data for all patients who received study treatment are included. Shown is diarrhea that began on or after the date of the first dose of study drug through 30 days after the date of the last dose of study drug, or the day before the initiation of subsequent anticancer therapy (including crossover treatment if applicable), whichever occurred first. AEs were coded according to the Medical Dictionary for Regulatory Activities, v 27.1.
[b]TRAEs are those attributed by the investigator to the study treatment.

Compared with TPC + pembro, the incidence of diarrhea remained higher for SG + pembro when adjusted for treatment exposure (Table 2).[4]

Table 2. Exposure-Adjusted Incidence Rates for Diarrhea[4]

TEAEs	SG + Pembro (n=221)		TPC + Pembro (n=220)		EAIR Difference (95% CI)
	n (%)	EAIR (95% CI)	n (%)	EAIR (95% CI)	
Diarrhea	155 (70)	0.13 (0.08–0.19)	63 (29)	0.03 (0.01– 0.07)	0.09 (0.03–0.16)

Time to onset and duration of diarrhea[4]

Median time to onset of any-grade and Grade ≥3 diarrhea was shorter for SG + pembro vs TPC + pembro, however, the duration was similar between arms (Table 3).

Table 3. Time to Onset and Duration of Neutropenia and Diarrhea[4]

	SG + Pembro (n=221)				TPC + Pembro (n=220)			
	Any-grade		Grade ≥3		Any-grade		Grade ≥3	
	n[a]	Days (range)	n[a]	Days (range)	n[a]	Days (range)	n[a]	Days (range)
Median time to onset[b]								
Diarrhea	155	14 (1–462)	22	17 (1–715)	63	64 (1–496)	5	299 (202–513)
Median duration[c]								
Diarrhea	140	7 (1–709)	22	8 (1–98)	57	6 (1–117)	5	4 (1–11)

[a]Number of patients may differ between time to onset and duration data due to events with no recorded end date or ongoing events.
[b]Time to onset of first event is calculated as time from the first dose date of any study drug to the onset date of first event.
[c]Duration is the median duration among multiple episodes of any-grade or among multiple episodes of Grade ≥3 (the end date of event of interest – the onset date of event of interest + 1 day for each episode).

Management of diarrhea

Dose reduction, interruption, and discontinuation of SG was protocol specified for treatment-related AEs. SG dose could be withheld for treatment-related gastrointestinal AEs, including diarrhea. The SG dose could not be re-escalated following a dose reduction. For pembro and TPC, dose modifications were per the approved prescribing information for each drug.[3]

Diarrhea led to dose reduction in 5% and 1% of patients in the SG + pembro and TPC + pembro arms, respectively, and to treatment discontinuation in <1% of patients in the TPC + pembro arm.[4,5]

Among patients who received antidiarrheals, diarrhea was managed mostly with loperamide (SG + pembro, 90% and TPC + pembro, 77%); atropine was more frequently used in the SG + pembro group (12%) vs the TPC + pembro group (3%).[4]

SACI-IO HR+ Study[6,7]

The ongoing phase 2, SACI-IO HR+ study is investigating SG + pembro vs SG monotherapy in patients with HR+/HER2- mBC who have progressed on ≥1 line of ET for metastatic disease or have progressed on or within 12 mo of adjuvant ET and have received 0 or 1 prior chemotherapy regimens for mBC.

Safety

At a median follow-up of 12.5 and 34.6 mo, the incidence of Grade ≥2 and 3–4 diarrhea was lower with SG + pembro vs SG monotherapy (Table 4).

Table 4. SACI-IO HR+: Incidence of Diarrhea[6,7]

TEAE	Median Follow-up	SG + Pembro (n=52)		SG (n=52)	
		Grade ≥2, n (%)	Grade 3-4, n (%)	Grade ≥2, n (%)	Grade 3-4, n (%)
Diarrhea	12.5 mo	12 (23.1)	3 (5.8)	20 (38.5)	4 (7.7)
	34.6 mo	13 (25)	3 (5.8)	21 (40.4)	4 (7.7)

Ongoing SG Clinical Studies: SG + Pembro in mBC

The phase 2 SACI-IO TNBC study (NCT04468061) is investigating the efficacy and safety of SG ± pembro in patients with PD-L1 negative mTNBC who have received no prior systemic therapy for mBC.

References

1. TRODELVY® Gilead Sciences Inc. Trodelvy (sacituzumab govitecan-hziy) for injection, for intravenous use. U.S. Prescribing Information. Foster City, CA.
2. Tolaney S, De Azambuja E, Kalinsky K, et al. Sacituzumab govitecan plus pembrolizumab for advanced triple-negative breast cancer. *N Engl J Med.* 2026;394:354-366.
3. Tolaney S, De Azambuja E, Kalinsky K, et al. Sacituzumab govitecan plus pembrolizumab for advanced triple-negative breast cancer [Supplement]. *N Engl J Med.* 2026;394:354-366.

4. Kalinsky K, Schmid P, de Azambuja E, et al. Safety analysis of phase 3 ASCENT-04 study of sacituzumab govitecan + pembrolizumab vs chemotherapy + pembrolizumab for previously untreated PD-L1+ metastatic triple-negative breast cancer [Poster PS5-02-28]. Presented at: San Antonio Breast Cancer Symposium (SABCS); December 9-12, 2025; San Antonio, TX.
5. Kalinsky K, Schmid P, de Azambuja E, et al. Safety analysis of phase 3 ASCENT-04 study of sacituzumab govitecan + pembrolizumab vs chemotherapy + pembrolizumab for previously untreated PD-L1+ metastatic triple-negative breast cancer [Abstract PS5-02-28]. Presented at: San Antonio Breast Cancer Symposium (SABCS); December 9-12, 2025; San Antonio, TX.
6. Garrido-Castro AC, Kim S-E, Desrosiers J, et al. SACI-IO HR+: A randomized phase II trial of sacituzumab govitecan with or without pembrolizumab in patients with metastatic hormone receptor-positive/ HER2-negative breast cancer [Oral presentation LBA1004]. Presented at: American Society of Clinical Oncology (ASCO) Annual Meeting; 31 May-4 June, 2024; Chicago, IL.
7. Garrido-Castro AC, Li T, Kim SE, et al. SACI-IO HR+: Final results from a randomized phase II trial of sacituzumab govitecan with or without pembrolizumab in hormone receptor-positive/HER2-negative metastatic breast cancer [Oral presentation 424RO]. Presented at: European Society for Medical Oncology Breast Cancer (ESMO BC); May 6–8, 2026; Berlin, Germany.

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

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

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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

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