GILEAD | Medical Information

Trodelvy® (sacituzumab govitecan-hziy) Use in Patients With Brain Metastases in mBC Studies

This document is in response to your request for information regarding the use of Trodelvy® (sacituzumab govitecan-hziy [SG]) in patients with brain metastases (BrM) in metastatic breast cancer (mBC) clinical studies.

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]

No information about whether SG crosses the blood-brain barrier is available in the SG US FDA-approved prescribing information.

Clinical Data on SG Use in Patients With BrM in mBC Studies

In a systematic review and meta-analysis of data pooled from 11 studies that evaluated the efficacy of SG in patients with HER2- BCBMs (N=313), after a median follow-up of 6.7 to 17.5 mo across studies, the median OS (95% CI) was 8.4 (6.7–10.5) mo. The median (95% CI) PFS was 3.8 (2.8–5.3) mo, and the median intracranial PFS (95% CI) was 2.9 (1.7–4.9) mo. The ORR (95% CI) was 10.7% (0–37.9%), and the intracranial ORR (95% CI) was 31.7% (15.5%–54.0%). The DCR (95% CI) was 45.4% (33.9%–57.5%), and the intracranial DCR (95% CI) was 55.6% (42.2%–68.1%).[2]

In the phase 3 ASCENT study, which evaluated safety and efficacy of SG in patients with mTNBC, 12% of patients had previously treated and stable BrM at baseline (BMPos: SG group, n=32; TPC group, n=29).[3]

- In a post hoc subgroup analysis in patients who were BMPos, the median (95% CI) PFS was 2.8 (1.5–3.9) mo in the SG group and 1.6 (1.3–2.9) mo in the TPC group. The safety profile among the subgroup of patients who were BMPos was consistent with the profile seen in the full ASCENT safety population.[4]

In TROPiCS-02, a phase 3 study of SG vs TPC in HR+/HER2- mBC, patients with previously treated BrM may participate if their BrM are stable for ≥4 wk. At this time, results in the stable BrM subgroup have not been reported.[5]

A phase 0/early phase 1 study evaluated the intratumoral concentrations and intracranial activity of SG in patients undergoing craniotomy for BCBM. In the BCBM cohort, most AEs

were Grade 1 or 2. The median (range) PFS was 8 (2–26.5) mo. SN-38 levels showed penetration into intracranial tumor tissue.[6]

Real-World Data on SG Use in Patients With BrM in mBC Studies

A retrospective, observational, real-world study evaluated the efficacy and safety of SG in 159 patients with mTNBC. A subgroup analysis was conducted in 22 patients (13.8%) with CNS metastases; after a median follow-up of 6 mo, the median (95% CI) rwPFS was 2.3 (1.3–3.2) mo. ORR was 13.6%, and DCR was 36.3%. rwOS was not reported for this subgroup. Among patients with CNS metastases, 31.8% required at least one dose reduction, and no patients discontinued due to AEs.[7]

A real-world study evaluated the use of SG in 103 patients with mTNBC with a focus on BrM and toxicity and included patients with active or stable BrM (n=32, 31.1%) and impaired performance status. The median (95% CI) PFS was 3.7 (2.6–6.2) mo, and the median (95% CI) OS was 6.7 (56.3–NR) mo in patients who were BMPos. ORR in the BMPos population was 19.8% (n=6).[8]

- In the BMPos population, 26 patients (81.2%) discontinued SG mostly due to disease progression. AEs that led to SG dose reduction were reported in 4 patients (12.5%), with no reports of SG-related death.[8]

A retrospective cohort study (N=98) investigated whether SRT for intact BrM used concurrently with an ADC, including SG, was associated with an increased risk of SRN. Concurrent ADC was associated with a higher risk of SRN in multivariable analyses (P<0.001) that also controlled for prior RT (P=0.01) and BrM volume (P<0.001). No ADC agent was associated with the risk of SRN (P=0.74).[9]

A retrospective study evaluated the use of SG or T-DXd in patients with mBC and active or stable BrM. Among patients treated with SG (n=12), the median (95% CI) intracranial PFS was 2.7 (1.6–10.5) mo, and the median (95% CI) OS was 6.4 (1.2–NR) mo. No statistically significant association between BrM status (active vs stable) and intracranial PFS or OS was observed (P=0.86 and P=0.63, respectively). Discontinuation of SG was most commonly due to intracranial progression (n=5 [42%]) or extracranial progression (n=3 [25%]) of disease, with 1 patient discontinuing due to treatment-associated neutropenia; overall, 7 patients (58%) had died by data cut-off. Dose reductions of SG occurred in 3 patients.[10]

A retrospective, real-world study evaluated SG in 54 patients with mTNBC and CNS metastases, including subgroups with treated/stable BrM, active BrM, or LMD. The median (95% CI) rwPFS in the overall population was 3.75 (3.06–7.89) mo, while rwOS was immature. The median CNS-specific PFS was 9.26 (4.8–16.2) mo overall and was 12.1 (4–16.2), 4.8 (2–NA), and 4.1 (2.79–NA) mo in patients with treated/stable BrM, active BrM, and LMD, respectively. No safety data were reported.[11]

In a retrospective, observational study of SG in 33 patients with HER2- mBC and CNS metastases (treated/stable BrM, active BrM, and LMD), the overall median (95% CI) CNS and extra-CNS PFS was 2.9 (2–4.3) mo and 2.6 (1.9–4) mo, respectively. Three patients (TNBC, n=2; HR+/HER2-, n=1) had bicompartmental PFS that was >10 mo; each had surgery and brain RT. No safety data were reported.[12]

In a retrospective, multicenter study of SG in 29 patients with mTNBC and BrM, the median (95% CI) OS and PFS were 8.9 (6.04–10.32) mo and 3.09 (2.4–4.11) mo, respectively. There was no statistically significant association between the number or size of CNS lesions and OS or PFS. No unexpected safety signals were reported. AEs resulted in dose delays in

15 patients (51.7%), dose reductions in 11 patients (37.9%), and discontinuations in 2 patients (7.7%).[13]

Ongoing Clinical Study

An open-label, phase 2 study (NCT04647916) is evaluating the efficacy and safety of SG in patients with HER2- breast cancer and BrM.

Clinical Data on SG Use in Patients With BrM

Systematic Review and Meta-analysis in Patients With HER2- BCBM[2]

A systematic review and meta-analysis of data pooled from 11 studies (two prospective trials and nine observational cohorts) through November 2025 evaluated the efficacy of SG in patients with HER2- BCBMs (N=313). Outcomes included OS, PFS, ORR, DCR, and intracranial efficacy measures, including intracranial PFS, ORR, and DCR. Random-effects models were used, with heterogeneity assessed by I^2 statistics. The median age ranged from 48 to 61.5 y, and 75% of evaluable patients had stable BrM at SG treatment initiation.

After a median follow-up of 6.7 to 17.5 mo across studies, the median OS (95% CI) was 8.4 (6.7–10.5; I^2=0%) mo. The median (95% CI) PFS was 3.8 (2.8–5.3; I^2=67.8%) mo, and the median intracranial PFS (95% CI) was 2.9 (1.7–4.9; I^2=0%) mo. The ORR (95% CI) was 10.7% (0–37.9%; I^2=86.8%), and the intracranial ORR (95% CI) was 31.7% (15.5%–54.0%; I^2=58.2%). The DCR (95% CI) was 45.4% (33.9%–57.5%; I^2=0%), and the intracranial DCR (95% CI) was 55.6% (42.2%–68.1%; I^2=0%).

Safety was not reported.

ASCENT Study in mTNBC

The ASCENT study, a global, open-label, randomized, confirmatory, phase 3 study, was conducted to investigate the efficacy and safety of SG vs CT TPC in patients with refractory or relapsed mTNBC who received ≥2 prior CTs for unresectable, locally advanced, or metastatic disease. Patients with mTNBC (N=529) were enrolled and randomly assigned (1:1) to receive SG 10 mg/kg IV on Days 1 and 8 of a 21-d cycle (n=267) or single-agent TPC (n=262 [ie, eribulin, n=139; vinorelbine, n=52; gem, n=38; and cape, n=33]). Treatment was continued until the first of the following events: disease progression, unacceptable toxicity, discontinuation from the study, or death. The study protocol allowed a predefined maximum of 15% for patients with BrM for ≥4 wk. Patients with known BrM required baseline brain MRI/CT scans that were conducted every 6 wk for 36 wk and every 9 wk thereafter until disease progression led to study treatment discontinuation; confirmatory imaging was performed 4 to 6 wk after attaining responses.[3]

Post hoc subgroup analysis of patients with stable BrM[4]

A post hoc subgroup analysis evaluated the efficacy and safety of SG in patients who were BMPos, defined as having stable CNS disease for ≥4 wk by MRI, ≥2 wk from discontinuation of antiseizure medication, and corticosteroid dose (≤20 mg prednisone equivalent) that was stable or decreasing for ≥2 wk. Among the patients enrolled in the ASCENT study (N=529), 61 (12%) were BMPos (SG, n=32; TPC, n=29). From the SG and TPC groups, 2 (6%) and

6 (21%) patients, respectively, did not receive treatment. Baseline characteristics were generally balanced between the ITT and BMPos study populations (Table 1).

Table 1. ASCENT Subgroup Analysis in the ITT and BMPos Populations: Select Baseline Patient and Disease Characteristics[4]

Key Demographics and Characteristics	ITT (N=529)	BMPos (n=61)
Female, n (%)	527 (99)	61 (100)
Age, median (range), y	54 (27–82)	53 (27–81)
Race (self-reported), White, n (%)	418 (79)	49 (80)
ECOG PS, 0/1, n (%)	229 (43)/300 (57)	23 (38)/38 (62)
Number of prior CTs, 2–3/>3, n (%)	365 (69)/164 (31)	35 (57)/26 (43)
Prior systemic regimens, median (range), n	4 (2–17)	5 (2–10)

Patient disease characteristics were generally similar between patients in the BMNeg and BMPos populations with a few exceptions. *BRCA* mutations were reported in 15% vs 7% of patients who were BMPos and BMNeg, respectively. In patients who were BMPos and BMNeg, 82% vs 69% of patients were diagnosed with TNBC initially, the median (range) number of prior anticancer regimens was 4 (2–9) vs 3 (1–16), 43% vs 30% had >3 prior CTs, 79% vs 65% had prior cape therapy, and 43% vs 27% had previous checkpoint inhibitors prior to enrollment, respectively. Compared to 44% and 22% of patients who were BMNeg, 67% and 36% of patients who were BMPos had major tumor locations in the lung and bone, respectively.

Efficacy

In the SG vs TPC group in the BMPos population, the median (95% CI) PFS was 2.8 (1.5–3.9) mo vs 1.6 (1.3–2.9) mo (HR, 0.65; 95% CI: 0.35–1.22), and the median (95% CI) OS was 7 (4.7–14.7) mo vs 7.5 (4.7–11.1) mo (HR, 0.96; 95% CI: 0.55–1.68). Response rates are presented in Table 2.

Table 2. ASCENT Subgroup Analysis in the BMPos Population: Response Rates (N=61)[4]

Efficacy Measure		SG (n=32)	TPC (n=29)
ORR, n (%)		1 (3)	0
CBR,[a] n (%)		3 (9)	1 (3)
Best overall response, n (%)	CR	0	0
	PR	1 (3)	0
	SD	15 (47)	9 (31)
	SD for >6 mo	2 (6)	1 (3)
	PD	11 (34)	11 (38)
	NE	5 (16)	9 (31)
DOR, median (95% CI), mo		2.9 (NE–NE)	N/A[b]
TTR, median (range), mo		1.5 (1.5–1.5)	0

Abbreviations: DOR=duration of response; TTR=time to response.
[a]Proportion of patients with a confirmed best overall response of CR or PR and SD for ≥6 mo.
[b]No patients to report.

Safety

The safety profile among the subgroup of patients who were BMPos was consistent with the profile observed in the full ASCENT safety population. In the BMPos subgroup, the most common TEAEs (with an incidence >20%) of any grade were fatigue (63% vs 52%), neutropenia (63% vs 52%), diarrhea (50% vs 13%), nausea (43% vs 26%), decreased

appetite (30% vs 17%), anemia (23% vs 35%), alopecia (23% vs 13%), and constipation (23% vs 22%) in the SG vs TPC groups, respectively.

TEAEs leading to treatment discontinuation in the BMPos subgroup occurred in 2 (7%) and 2 (9%) patients in the SG and TPC groups, respectively. In this subgroup, there were no reports of treatment-emergent death and 1 report of treatment-emergent death in the SG and TPC groups, respectively.

TROPiCS-02 Study in HR+/HER2- mBC

In TROPiCS-02, an open-label, randomized, multicenter, phase 3 study comparing the safety and efficacy of SG with TPC in patients with HR+/HER2- mBC who have received ≥2 and ≤4 prior CT regimens for metastatic disease, as well as ≥1 endocrine therapy, taxane, and cyclin-dependent kinase 4/6 inhibitor,[14] patients with previously treated BrM may participate provided they meet specific criteria, such as having clinically stable signs and symptoms for ≥4 wk, and more.[5]

At this time, the efficacy and safety of SG in the patient subgroup with stable BrM have not been reported.[14]

Prospective, Single-Center Study: SG in BCBM

Study design and demographics[6]

A prospective, single-center, window-of-opportunity, phase 0/early phase 1 study evaluated intratumoral concentrations and intracranial activity of SG in patients aged ≥18 y undergoing craniotomy for BCBM or rGBM. Patients received a single IV dose of SG 10 mg/kg 1 d before surgical resection. Patients resumed treatment with SG 10 mg/kg on Days 1 and 8 of 21-d treatment cycles following recovery from surgery. Tumor and serum levels of SG, SN-38, and SN-38G were collected during surgery.

In the BCBM cohort, 13 female patients were screened for inclusion and 1 patient failed screening; patients had a mean age (range) of 48.5 (33–70) y, 12 (93%) were White, 1 (7%) was Black/African American, 7 (54%) were HR+, 7 (54%) were HER2+, and 3 (23%) had TNBC.

Preliminary safety and efficacy results

In the BCBM cohort, most AEs were Grade 1 or 2, which included diarrhea, neutropenia, nausea, hypokalemia, and fatigue.[6]

Efficacy outcomes in the BCBM cohort are shown in Table 3.

Table 3. Preliminary Efficacy Results for the BCBM Cohort[6]

	OS, Median (Range), Mo	PFS, Median (Range), Mo	iORR, %	iPR, %	iCR, %
BCBM	35.2 (2.7–37)[a]	8 (2–26.5)	50	25	25

Abbreviations: iORR=intracranial objective response rate, iPR=intracranial partial response, iCR=intracranial complete response.
[a]Median OS for HER2+ BCBM for patients with CNS metastasis at or after diagnosis was 30 to 38 mo, respectively, and was 12.5 mo for patients with HR+ BCBM.

Primary outcome: SN-38 levels and biomarker data

In the BCBM cohort, SN-38 levels showed penetration into intracranial tumor tissue (n=13, matching tissue and serum samples; n=3, CSF samples).[6,15] SN-38 levels, molarity, and

minimum IC_{50} values are shown in Table 4.[6,15] Within the BCBM cohort, SN-38G was only detected in small amounts or not at all in the CSF.[6,15]

Table 4. Total SN-38 Levels, Molarity, and Minimum IC_{50} in Tumor Tissue, Serum, and CSF From Patients in the BCBM Cohort[6a]

Total SN-38 Tumor Tissue			Total SN-38 Serum			Total SN-38 CSF			Observed SN-38 Level, mcM	Minimum IC_{50}, mcM[b]
n	Level, Median (Range), ng/g	Molarity, mcM	n	Level, Median (Range), ng/mL	Molarity, mcM	n	Level, ng/mL	Molarity, mcM		
13	197.3 (86.5–652)	0.0523	13	2462.4 (1266.8–5659.6)	6.27	3	9.4[c]	0.035	0.662	0.000551

[a]Used brain tissue density of 1.04 g/mL. [b]Molecular weight=392.4 g/mol. [c]Median value range (5–26.5 ng/mL).

Additionally, several assays were evaluated to investigate potential mechanisms of action for SG in the CNS and included quantification of tumor expression for Trop-2 (a marker of antigen expression), γH2AX (a marker of DNA damage), and CAIX (a marker of intratumoral hypoxia).[6]

In the BCBM cohort, 12 samples were sufficient for Trop-2 analysis, and all had an H-score of 3+. Trop-2 expression did not correlate with % SN-38 tissue-to-serum ratio (Pearson r^2, 0.018; 95% CI: -0.23 to 0.81; *P*=0.18). Expression of γH2AX (n=11) ranged from 33.1% to 81.2% (mean, 54.4%), and 5 of the 11 samples indicated high CAIX expression.[6]

Real-World Data on SG Use in Patients With BrM in mBC Studies

Retrospective, Observational Study in mTNBC[7]

Study design and demographics

A retrospective, observational, real-world study evaluated the efficacy and safety of SG in 159 patients with mTNBC treated in southern Spain between January 1, 2022 and December 31, 2023. A prespecified subgroup analysis included 22 patients (13.8%) with CNS metastases (Table 5). Patients with CNS metastases had a higher prevalence of visceral disease and de novo Stage IV disease compared to the overall population (95.2% vs 75.5% and 22.7% vs 17.6%, respectively). All patients with CNS metastases had received prior RT.

Table 5. Subgroup Analysis in Patients With CNS Metastases: Baseline Patient and Disease Characteristics[7]

Key Demographics and Characteristics		SG (n=22)
Age, median (IQR), y		45 (30–67)
Premenopausal, n (%)		11 (50)
HER2 status, n (%)	0	11 (50)
	Low	11 (50)
ECOG PS, %	0	63.6
	1	22.7
	2	9.1
	3	4.5
Visceral metastases, n (%)		21 (95.2)
Disease stage at diagnosis, n (%)	De novo Stage IV	5 (22.7)

Key Demographics and Characteristics		SG (n=22)
	Localized or Stage I–III	17 (77.3)
Previous lines of therapy, median (IQR)		2.4 (2–4)
SG cycles, median (IQR)		4.68 (1–27)
Line of SG, n (%)	First line	0
	Second line	15 (68.2)
	≥Third line	7 (31.8)
(Neo)adjuvant CT in early disease, n (%)		13 (59.1)[a]
First-line immunotherapy, n (%)		4 (18.2)

[a]Twelve patients (54.5%) achieved pathological complete response with (neo)adjuvant CT in early disease.

Results

Efficacy

In the overall population, after a median follow-up of 11.6 mo, the median (95% CI) rwPFS was 4.6 (3.7–6.3) mo, and the median (95% CI) rwOS was 10.9 (7.6–14.2) mo. ORR was 31.2%, and DCR was 68.9%.

In patients with CNS metastases, after a median follow of 6 mo, the median (95% CI) rwPFS was 2.3 (1.3–3.2) mo vs 5.1 (4.1–5.9) mo in patients without CNS metastases. ORR was 13.6%, and DCR was 36.3%. rwOS was not reported in this subgroup.

Safety

In the overall population, the most common AE was neutropenia (59.4%; Grade 3–4: 30.4%); other AEs included diarrhea (49%; Grade 3–4: 8.2%), nausea (45.3%; Grade 3–4: 0.6%), and ALT/AST elevation (24.5%; Grade 3–4: 1.9%). G-CSF was administered as primary prophylaxis in 29.6% of patients and as secondary prophylaxis in 17.6% of patients. At least one dose reduction occurred in 43.4% of patients, and 5.7% of patients discontinued SG due to AEs.

In patients with CNS metastases, the most common AE was neutropenia (45.5%; Grade 3–4: 27.2%); other AEs included diarrhea (36.8%; Grade 3–4: 9.1%), ALT/AST elevation (30%; Grade 3–4: 0%), and nausea (21.1%; Grade 3–4: 5.3%). G-CSF was administered as primary prophylaxis in 18.2% of patients and as secondary prophylaxis in another 18.2% of patients. At least one dose reduction occurred in 31.8% of patients, and no patients discontinued SG due to AEs.

Real-World Study in mTNBC[8]

Study design and demographics

An ambispective, bicentric cohort study assessed the real-world efficacy and safety of SG in patients with mTNBC treated through the French Early Access Program (May 2021 to January 2023). Of the 103 patients enrolled, the median age (range) at baseline was 55 (26–89) y, 80.6% of patients had an ECOG PS of 0 to 1, 64.1% of patients had 1 to 2 prior lines of treatment in the advanced setting, and 31.1% (n=32) were BMPos.

Results

In the BMPos population, the median (95% CI) PFS was 3.7 (2.6–6.2) mo, the median (95% CI) OS was 6.7 (56.3–NR) mo, and the ORR was 19.8% (n=6). SG treatment discontinuation was reported in 26 patients (81.2%) and was mostly due to disease

progression. AEs that led to SG dose reduction were reported in 4 patients (12.5%), with no reports of death.

Retrospective Cohort Study: ADCs With SRT for BrM[9]

Study design and demographics

A retrospective cohort study (N=98) investigated whether SRT for intact BrM used concurrently with an ADC, including SG, was associated with an increased risk of SRN. Patients who had received ≥1 course of SRT for intact BrM between January 2014, and October 2022, and ≥1 dose of ADC were eligible for inclusion (Table 6). The control cohort consisted of patients with BrM who received ADCs sequentially with SRT. Results were pooled across ADCs, and SG-specific data were not provided.

Table 6. Baseline Demographics, Disease Characteristics, and ADC Received: Overall and With or Without Concurrent ADC Treatment[9]

Key Demographics and Characteristics and ADCs Received		Concurrent ADC[a] (n=42)	No Concurrent ADC (n=74)	All (N=98)
Age, median (range), y		54 (27–77)	55 (34–77)	55 (27–77)
Female, n (%)		33 (78.6)	66 (89.2)	82 (83.7)
Primary cancer diagnosis,[b] breast, n (%)		30 (71.4)	55 (74.3)	71 (72.4)
ADC,[c] n (%)	SG	7 (16.7)	23 (31.1)	26 (26.5)
	Trastuzumab emtansine	21 (50)	43 (58.1)	52 (53.1)
	T-DXd	14 (33.3)	42 (56.8)	50 (51)
Lesion volume, median (range), cm^3		0.3 (0.01–43.15)	0.25 (0.01–15.6)	0.26 (0.01–43.15)
Any prior radiation,[d] n/N (%)		20/156 (12.8)	81/408 (19.9)	101/564 (17.9)

[a]SRT was considered concurrent if delivered ≤7 d before or ≤21 d after ADC administration.
[b]Other cancers in the overall population included the following: non-small cell lung cancer, *ERBB2* variant (n=13); esophageal and/or gastric cancer, *ERBB2* amplified (n=6); salivary, *ERBB2* amplified (n=4); and colon, melanoma, urothelial, and unknown (each, n=1).
[c]ADCs given concurrently or sequentially with SRT. Numbers total >100% and do not total across rows as patients could have received ≥1 course of ADC.
[d]n/N refers to the number of lesions. Lesions could have been treated with >1 type of prior RT.

Results

The median (IQR) time from SRT to last imaging was 12.4 (0–80.4) mo. Across the entire cohort, the 24-mo cumulative incidence (range) of SRN was 8.5% (6.2–11%). The use of concurrent ADC was associated with a higher risk of SRN in univariable and multivariable analyses that also controlled for prior RT and BrM volume (Table 7). For previously radiated lesions in patients with and without concurrent ADC therapy, the 24-mo risk of SRN was 42% and 9.4%, respectively. Among patients with BrM who were treated with concurrent ADC therapy, no ADC agent was associated with the risk of SRN (*P*=0.74). Grade 4 to 5 SRN after SRT was observed in 11 of 156 (7.1%) and 3 of 408 (0.7%) lesions treated with and without concurrent ADC, respectively.

Table 7. Risk of SRN With Concurrent ADC[9]

Concurrent ADC (n=42)	Subdistribution HR (95% CI)	*P*-Value
Univariable analysis	4.01 (1.79–9.01)	<0.001
Multivariable analysis	4.31 (1.95–9.5)	<0.001
Prior RT	2.99 (1.26–7.09)	0.01
BrM volume, per cm^3	1.14 (1.09–1.19)	<0.001

Retrospective Study in mBC and BrM[10]

Study design and demographics

A retrospective, real-world study evaluated the efficacy and safety of SG or T-DXd in patients with mBC and active or stable BCBMs who were treated in Germany between November 2020 and June 2023. Data were reported up to a data cut-off date of 30 November 2023. Of the patients with BrM identified for the analysis, 12 patients with TNBC were treated with SG. Patients with extracranial-only or LMD were excluded. Starting doses of SG 10 mg/kg were administered in 10 patients (83%).

Median (IQR) age was 50.5 (42–60) y in patients treated with SG. SG-treated patients received a median (range) of 2.5 (2–5) prior lines of CT, 11 (92%) had received prior RT, and 2 (17%) had undergone surgery for BrM.

Three patients (25%) received brain RT ≥45 d before SG initiation, and 2 (18%) received concurrent RT during treatment. Active and stable BrM were present in 5 (42%) and 7 patients (58%) treated with SG.

Results

Efficacy

In the SG cohort, the median (IQR) duration of treatment was 71 (37–154) d, and the intracranial DCR (95% CI) was 42% (13–71%). Intracranial PFS and OS in the overall population and by BrM subtype are summarized in Table 8.

Table 8. Outcomes Overall and by Subgroup in Patients With BrM Treated With SG[10]

Median (95% CI), Mo	SG		
	Overall (N=12)	Active BrM (n=5)	Stable BrM (n=7)
Intracranial PFS	2.7 (1.6–10.5)	2.7 (1.9–10.5)	2.1 (0.4–14.1)
OS	6.4 (1.2–NR)	8.1 (5.3–NR)	2.2 (0.4–NR)

In patients treated with SG, no statistically significant association between BrM status (active vs stable) and intracranial PFS or OS was observed (P=0.86 and P=0.63, respectively).

Before the data cut-off, SG was discontinued due to intracranial progression in 5 patients (42%), extracranial progression in 3 (25%), and a treatment-related AE in 1 (8%); overall, 7 patients (58%) died before data cut-off.

Safety

In patients treated with SG, the most common AE was neutropenia (42%). Severe Grade ≥3 AEs included neutropenia (33%) and anemia (8%). Dose reductions occurred in 3 patients due to 4 events: 2 events of neutropenia and 2 of fatigue. Treatment discontinuation occurred in 1 patient due to treatment-associated neutropenia.

Retrospective Study in mTNBC and CNS Metastases[11]

Study design and demographics

A retrospective, real-world study evaluated the efficacy of SG in patients who had mTNBC and CNS metastases and were treated in Italy. Overall, 54 patients were included (Table 9); 46 (85.2%) had treated/stable disease, 4 (7.4%) had active CNS metastases, and 4 (7.4%) had LMD.

Table 9. Baseline Demographics and Disease Characteristics[11]

Key Demographics and Characteristics		SG (N=54)
Age, median (range), y		54 (31–75)
ECOG PS, n (%)	0–1	48 (94.2)
	2	3 (5.8)
TNBC at initial diagnosis, n (%)		44 (81.5)
HER2 low, n (%)		12 (33.2)
BRCA1 or *BRCA2* mutation, n (%)		11 (20.4)
Number of metastatic sites, median (range)		3 (2–7)
Number of prior anticancer regimens for metastatic disease, median (range)		3 (0–5)
Lines of therapy before CNS metastases, median (range)		2 (0–4)
Prior PARPi, n (%)		10 (18.5)
Prior PD-1/PD-(L)1, n (%)		16 (29.6)
Prior surgery for CNS metastases, n (%)		4 (10.3)
Prior RT for CNS metastases, n (%)		50 (92.6)

Abbreviation: PD-(L)1=programmed death (ligand)-1.

Results

The median time from diagnosis of CNS metastases to SG initiation was 5 mo. After a median follow-up of 18.2 mo, the median (95% CI) rwPFS in the overall population was 3.75 (3.06–7.89) mo, while rwOS was immature. The median (95% CI) CNS-specific PFS was 9.26 (4.8–16.2) mo in the overall population, and the median (95% CI) CNS-specific PFS in the subgroups of patients with treated/stable BrM, active BrM, and LMD was 12.1 (4–16.2), 4.8 (2–NA), and 4.1 (2.79–NA) mo, respectively. Response rates in the overall population and by subgroup are summarized in Table 10.

Table 10. CNS Response Rates in the Overall Population and by Subgroup[11]

Efficacy Measure, n (%)	Overall (N=54)	Treated/Stable BrM (n=46)	Active BrM (n=4)	LMD (n=4)
ORR	11 (20.4)	9 (19.6)	1 (25)	1 (25)
DCR	20 (48.8)	16 (34.8)	1 (25)	3 (75)
CBR at 6 mo	18 (14.8)	8 (17.4)	0	0
SD	9 (16.6)	7 (15.2)	0	2 (50)
PD	20 (37)	16 (34.8)	3 (75)	1 (25)
Not evaluable	14 (26)	14 (30.4)	0	0

Safety was not reported.

Retrospective, Observational Real-World Study[12]

Study design and demographics

A retrospective, observational real-world study evaluated clinical outcomes with SG (≥1 dose of SG between 2018 and 2022) treatment in patients with HER2- mBC and CNS metastases. Of the 33 patients included, 23 and 10 had TNBC and HR+/HER2- mBC, respectively. Overall, 18 patients had treated/stable BrM (defined as lesions that had been previously treated with CNS-specific therapies), 7 had active BrM (defined as those with new BrM or progressed BrM that had not been treated with CNS-specific therapies since progression), and 8 had LMD (defined as metastases in the leptomeningeal space with or without BrM). One patient had CNS metastases without extra-CNS involvement. Additional baseline characteristics are shown in Table 11.

Table 11. Baseline Demographics and Disease Characteristics: Overall and by Subtype[12]

Key Demographics and Disease Characteristics		Overall (N=33)	Treated/Stable BrM (n=18)	Active BrM (n=7)	LMD (n=8)
Age at start of SG, median (range), y		56.7 (51.3–65.7)	59.59 (42.9–75.1)	59.1 (52.9–72.8)	50.88 (41.4–68.3)
Diagnosis of BrM to SG, median (range), mo		7.5 (0.6–94.8)	4.6 (0.7–94.8)	9.3 (0.6–21)	9.3 (2.7–21.5)
HER2 status at SG start, n (%)	HER2-0	22 (66.7)	9 (50)	7 (100)	6 (75)
	HER2-low	11 (33.3)	9 (50)	0 (0)	2 (25)
Metastatic lines prior to SG, median (range), n		3 (0–10)	3 (0–9)	5 (2–10)	3.5 (2–6)

Results

The overall median (95% CI) duration of follow-up was 6.7 (3.1–10) mo; responses were evaluable in 30 patients in the CNS subgroup and 29 patients in the extra-CNS subgroup. The CNS PFS was 2 (1.2–7.7) mo and 3.2 (2.2–5.1) mo in patients with HR+/HER2- and TNBC, respectively. In patients with >3 and ≤3 prior lines, the CNS PFS was 2.7 (1.2–4.8) mo and 3.2 (2–7.1) mo, respectively; additional results are found in Table 12. The CNS ORR by mBC type was as follows: HR+/HER2-, 11.1%; TNBC, 14.3%.

Table 12. Outcomes Overall and by Subgroup[12]

Response, n (%)	Overall (n=30)		Treated/Stable BrM (n=16)		Active BrM (n=7)		LMD (n=7)	
	CNS	Extra-CNS[a]	CNS	Extra-CNS[b]	CNS	Extra-CNS	CNS	Extra-CNS
Response[c]	4 (13.3)	1 (3.4)	2[d] (12.5)	0	0	0	2 (28.6)	1 (14.3)
SD	16 (53.3)	12 (41.4)	10 (62.5)	6 (40)	3 (42.9)	4 (57.1)	3 (42.9)	2 (28.6)
PD	10 (33.3)	16 (55.2)	4 (25)	9 (60)	4 (57.1)	3 (42.9)	2 (28.6)	4 (57.1)
DCR	20 (66.7)	13 (44.8)	12 (75)	6 (40)	3 (42.9)	4 (57.1)	5 (71.4)	3 (42.9)
CBR at 6 mo	8 (26.7)	4 (13.8)	6 (37.5)	2 (13.3)	1 (14.3)	1 (14.3)	1 (14.3)	1 (14.3)
PFS,[e] median (95% CI), mo	2.9 (2–4.3)	2.6 (1.9–4)	3.4 (2.2–10)	2.7 (1.9–4.2)	1.9 (1.2–16.5)	1.9 (1.5–10.1)	2.1 (0.4–7.7)	2 (0.4–6.9)
OS, median (95% CI), mo	6.9 (3.1–10.2)		10 (4.3–15.9)		3.1 (1.9–21.6)		3.8 (1.7–11.9)	

[a]n=29. [b]n=15. [c]CR or PR for CNS response. [d]Both received RT <2 mo before SG began.
[e]Bicompartmental median (95% CI) PFS by subgroup was as follows: overall, 2.6 (1.9–4) mo; treated/stable BrM, 2.7 (1.9–4.1) mo; active BrM, 1.8 (1.5–10.1) mo; LMD, 2.4 (0.4–5.1) mo.

Overall, 32 patients discontinued treatment due to disease progression (53.1% had both CNS and extra-CNS progression), and 1 discontinued SG due to toxicity; 5 patients died during SG treatment.

Three patients had bicompartmental PFS that was >10 mo; each had surgery and brain RT. Two of these patients had TNBC with stable BrM and received SG early (≤2 prior therapies); the third patient with HR+/HER2- mBC had 95 mo between BrM diagnosis and SG initiation.

No safety data were reported.

Retrospective, Multicenter Study in mTNBC and BrM[13]

Study design and demographics

A retrospective, multicenter study evaluated the effectiveness and safety of SG in patients with mTNBC and radiologically confirmed BrM treated at centers in the Czech Republic, Poland, and Slovakia between August 2021 up to a data cut-off date of June 2025. Overall, 29 patients were included (Table 13). In the palliative setting, prior treatments included the following: platinum compounds (n=19; 65.5%), taxanes (n=15; 51.7%), anthracyclines (n=13; 44.8%), cape (n=9; 31%), gem (n=8; 27.6%), and pembrolizumab (n=6; 20.7%). PARPi were administered in 5 patients (17.2%), vinorelbine in 2 (6.9%), hormonal agents in 4 (13.8%), anti-HER2 therapy in 1 (3.4%), and other regimens in 4 (13.8%).

Table 13. Baseline Demographics and Disease Characteristics[13]

Key Demographics and Characteristics		SG (N=29)
Age, median (range), y		48.5 (29.8–69.6)
Premenopausal, n (%)		14 (48.3)
HER2 IHC, n (%)	0	15 (51.7)
	1+	8 (27.6)
	2+	2 (6.9)
	Unknown	4 (13.8)
ECOG PS, (%)	0	7 (24.1)
	1	21 (72.4)
	≥2	1 (3.4)
Histological subtype, n (%)	Invasive ductal	26 (89.7)
	Invasive lobular	1 (3.4)
	Metaplastic	1 (3.4)
	Secretory	1 (3.4)
Patient history, n (%)	ER- or PgR+ BC	4 (13.8)
	HER2+ BC	2 (6.9)
	BRCA1 or *BRCA2* mutation	7 (24.1)
	Curative breast surgery	24 (82.8)
	Breast RT	21 (72.4)
Previous lines of palliative systemic therapy, median (range)		2 (1–3)
Prior CNS therapy, n (%)	Neurosurgical resection	4 (14.3)
	Brain RT	25 (86.21)
Number of BrM lesions, median (range)		3 (1–20)
Size of largest BrM lesion, median (range), mm		16.5 (2–50)

Results

Efficacy

After a median (range) follow-up of 6.05 (0.79–27.47) mo, 22 patients (75.9%) had died, and 26 (89.7%) had discontinued treatment with SG; of these, 25 discontinued due to disease progression. The median (95% CI) OS was 8.9 (6.04–10.32) mo, and estimated OS rates at 3, 6, 9, and 12 mo were 85.2%, 60.3%, 42.3%, and 28.2%, respectively. The median (95% CI) PFS was 3.09 (2.4–4.11) mo, and PFS rates at 3, 6, 9, and 12 mo were 53.6%, 31.4%, 22.5%, and 12%, respectively. Of the 26 patients with evaluable data, the ORR was 30.8% (n=8). CNS progression occurred in 6 patients (23.1%), and per univariable Cox proportional hazards model, there was no statistically significant association between the number or size of CNS lesions and PFS or OS (P>0.05 for each).

Safety

No unexpected safety signals were reported. Hematological AEs included neutropenia (79.3%; Grade 2: n=7; Grade 3: n=11; Grade 4: n=5), anemia (41.4%; Grade 1: n=4; Grade 2: n=6; Grade 3: n=2), thrombocytopenia (13.8%; Grade 1: n=1; Grade 2: n=1; Grade 3: n=2), and febrile neutropenia (10.3%). Febrile neutropenia included events of Grade 5 severity; however, the total number of events was not reported. Non-hematologic AEs included alopecia (50%), fatigue (48.1%; Grade 1: n=5; Grade 2: n=6; Grade 3: n=2), nausea (25%; Grade 1: n=4; Grade 2: n=3), diarrhea (17.2%; Grade 1: n=3; Grade 2: n=2), and vomiting (10.3%; Grade 1: n=2; Grade 2: n=1). Maximum Grade 2 hepatotoxicity occurred in 6.9% of patients, and Grade 4 allergic reaction to SG occurred in 3.4% of patients.

AEs resulted in dose delays in 15 patients (51.7%), and dose reductions in 11 patients (37.9%), with further reductions seen in 1 patient. Neutropenia was the main reason for dose delay (n=13) or reduction. SG was permanently discontinued due to treatment-related toxicities in 2 patients (7.7%). G-CSF was administered as primary prophylaxis in 11 patients (37.9%) and as secondary prophylaxis in an additional 12 patients (41.4%).

References

1. TRODELVY® Gilead Sciences Inc. Trodelvy (sacituzumab govitecan-hziy) for injection, for intravenous use. U.S. Prescribing Information. Foster City, CA.
2. Gazzoni G, Libonati N, Michelon I, et al. Intracranial activity of sacituzumab govitecan in HER2-negative breast cancer brain metastases: A systematic review and meta-analysis [Abstract e14009]. *Journal of Clinical Oncology.* 2026;44(16_suppl):e14009.
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. Hurvitz SA, Bardia A, Punie K, et al. Subgroup analyses from the phase 3 ASCENT study of sacituzumab govitecan in metastatic triple-negative breast cancer. *NPJ Breast Cancer.* 2024;10(1):33.
5. 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.
6. Balinda HU, Kelly WJ, Kaklamani VG, et al. Sacituzumab govitecan in patients with breast cancer brain metastases and recurrent glioblastoma: a phase 0 window-of-opportunity trial. *Nat Commun.* 2024;15(6707):1-11.
7. Falcón-González A, Llabrés-Valenti E, Henao-Carrasco F, et al. Real-world effectiveness and safety of Sacituzumab Govitecan in metastatic triple-negative breast cancer: results from the

multicenter retrospective observational SACISUR cohort in Southern Spain. *Front Oncol.* 2026;16:1717135.
8. Loirat D, De Moura A, Korbi S, et al. Sacituzumab govitecan in metastatic triple negative breast cancer: efficacy -with a focus on brain metastases- and toxicity in a real-world cohort. Presented at: European Society for Medical Oncology (ESMO BC); May 11-13, 2023; Berlin, Germany.
9. Lebow E, Pike L, Seidman A, Moss N, Beal K, Yao Y. Symptomatic necrosis with antibody-drug conjugates and concurrent stereotactic radiotherapy for brain metastases. *JAMA Oncol.* 2023;9(12):1729-1733.
10. Dannehl D, Jakob D, Mergel F, et al. The efficacy of sacituzumab govitecan and trastuzumab deruxtecan on stable and active brain metastases in metastatic breast cancer patients-a multicenter real-world analysis. *ESMO Open.* 2024;9(5):102995.
11. Caputo R, Piezzo M, Martinelli C, et al. Real-world outcomes with sacituzumab govitecan in patients with triple-negative breast cancer and central nervous system metastases. Presented at: San Antonio Breast Cancer Symposium (SABCS); December, 9-12, 2025; San Antonio, TX.
12. Grinda T, Morganti S, Hsu L, et al. Real-world outcomes with sacituzumab govitecan among breast cancer patients with central nervous system metastases. *NPJ Breast Cancer.* 2025;11(1):22.
13. Zubrowska J, Pieniazek M, Polakiewicz-Gilowska A, et al. Real-world outcomes of sacituzumab govitecan in patients with pretreated triple-negative breast cancer and brain metastases: data from CEBCC-102 study. *J Neurooncol.* 2026;176(2):167.
14. 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.
15. Balinda HU, Kelly WJ, Kaklamani VG, et al. Sacituzumab govitecan in patients with breast cancer brain metastases and recurrent glioblastoma: a phase 0 window-of-opportunity trial [Supplementary Information]. *Nat Commun.* 2024;15(6707):1-11.

Abbreviations

γH2AX=phosphorylated form of histone H2AX
ADC=antibody drug conjugate
AE=adverse event
BCBM=breast cancer brain metastases
BMNeg=negative for brain metastasis
BMPos=positive for brain metastasis
BrM=brain metastases
CAIX=carbonic anhydrase IX
cape=capecitabine
CBR=clinical benefit rate
CNS=central nervous system
CR=complete response
CSF=cerebrospinal fluid
CT=chemotherapy
DCR=disease control rate
ECOG PS=Eastern Cooperative Oncology Group performance status
ER=estrogen receptor
ERBB2=HER2 mutation
Extra-CNS=lesions or disease outside of the central nervous system
G-CSF=granulocyte colony-stimulating factor
gem=gemcitabine
H-score=histochemical scoring
HER2-=human epidermal growth factor receptor 2-negative
HR=hazard ratio
HR+=hormone receptor-positive
I^2=i-squared
IC_{50}=half maximal inhibitory concentration
IHC=immunohistochemistry
ITT=intent-to-treat
LMD=leptomeningeal disease
mBC=metastatic breast cancer
mTNBC=metastatic triple-negative breast cancer
NA=not available
NE=not estimable
NR=not reached
ORR=objective response rate
OS=overall survival
PARPi=poly(ADP-ribose) polymerase inhibitors
PD=progressive disease
PFS=progression-free survival
PgR=progesterone receptor
PR=partial response
rGBM=recurrent glioblastoma
RT=radiotherapy
rwOS=real-world overall survival
rwPFS=real-world progression-free survival
SD=stable disease
SG=sacituzumab govitecan-hziy
SN-38=active metabolite of irinotecan; topoisomerase I inhibitor

SN-38G=glucuronidation metabolite of SN-38
SRN=symptomatic radiation necrosis
SRT=stereotactic radiotherapy
T-DXd=trastuzumab deruxtecan
TEAE=treatment-emergent adverse event
TNBC=triple-negative breast cancer
TPC=treatment of physician's choice
Trop-2=trophoblast cell surface antigen 2

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 🖱 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 gilead.privacy@gilead.com.