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 Trodelvy® (sacituzumab govitecan-hziy [SG]) and its use 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 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).[2]

- In a post hoc subgroup analysis in patients who were BMPos, the median PFS was 2.8 (95% CI: 1.5-3.9) mo in the SG group and 1.6 (95% CI: 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.[3]

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.[4]

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.[5]

Real-World Data on SG Use in Patients With BrM

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 PFS was 3.7 (95% CI: 2.6-6.2) mo, and the median OS was 6.7 (95% CI: 56.3-NR) mo in patients who were BMPos.[6]

- In the BMPos population, 26 (81.2%) of patients discontinued SG mostly due to disease progression. AEs that led to SG dose reduction were reported in 4 (12.5%) patients, with no reports of SG-related death. ORR in the BMPos population was 6 (19.8%).[6]

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 radiotherapy (P=0.01) and BrM volume (P<0.001). No ADC agent was associated with the risk of SRN (P=0.74).[7]

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.[8]

Ongoing Clinical Study

An open-label, phase 2 study (NCT04647916) is evaluating the efficacy and safety of SG in HER2- breast cancer that has metastasized to the brain.

Clinical Data on SG Use in Patients With BrM

ASCENT Study in mTNBC

The ASCENT study, a global, open-label, randomized, confirmatory, phase 3 study, was conducted to investigate efficacy and safety of SG vs chemotherapy TPC in patients with refractory or relapsed mTNBC who received ≥2 prior chemotherapies for unresectable, locally advanced, or metastatic disease.[2]

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-day cycle (n=267) or single-agent TPC (n=262 [ie eribulin, n=139; vinorelbine, n=52; gemcitabine, and n=38; capecitabine, 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.[2]

Post hoc subgroup analysis of patients with stable BrM[3]

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.[3] Among the patients (N=529) enrolled in the ASCENT study, 61 (12%) patients were BMPos (SG, n=32; TPC, n=29). From the SG and TPC groups respectively, 2 (6%) and 6 (21%) patients did not receive treatment. Baseline characteristics were generally balanced between the ITT and BMPos groups (Table 1).

Table 1. ASCENT Subgroup Analysis in the ITT and BMPos Population: Select Baseline Patient and Disease Characteristics[3]

Characteristic	Population	
	ITT (N=529)	BMPos (n=61)
Female, n (%)	527 (99)	61 (100)
Median age, y (range)	54 (27-82)	53 (27-81)
Race, White, n (%)[a]	418 (79)	49 (80)
ECOG PS, n (%)		
0/1	229 (43)/300 (57)	23 (38)/38 (62)
No. of prior chemotherapies, n (%)		
2-3/>3	365 (69)/164 (31)	35 (57)/26 (43)
No. of prior systemic regimens, median (range)	4 (2-17)	5 (2-10)

Abbreviation: ECOG PS=Eastern Cooperative Oncology Group performance status.
[a]Self-reported.

Patient disease characteristics were generally similar between patients in the BMNeg and BMPos populations with a few exceptions.[3] *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, median (range) number of prior anticancer regimens was 4 (2-9) vs 3 (1-16), 43% vs 30% had >3 prior chemotherapies, 79% vs 65% had prior capecitabine 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 reported major tumor locations in the lung and bone, respectively.

Efficacy

In the SG vs TPC group in the BMPos population, the median PFS (95% CI) 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)[3] and the median OS (95% CI) was 7.0 (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: Tumor Response Rate (N=61)[3]

Efficacy Measure		SG (n=32)	TPC (n=29)
ORR, n (%)		1 (3)	0
Clinical benefit rate,[a] n (%)		3 (9)	1 (3)
Best overall response, n (%)	CR	0	0
	PR	1 (3)	0
	Stable disease	15 (47)	9 (31)
	Stable disease for >6 mo	2 (6)	1 (3)
	Progressive disease	11 (34)	11 (38)
	Not evaluable	5 (16)	9 (31)
Median DOR, mo (95% CI)[b]		2.9 (NE-NE)	N/A[c]
Median TTR, mo (range)		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 stable disease for ≥6 mo.
[b]Median DOR is from Kaplan-Meier estimate. CI for median is computed using the Brookmeyer-Crowley method.
[c]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.[3] In the BMPos subgroup, the most common (>20%) TEAEs 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 chemotherapy regimens for metastatic disease, as well as ≥1 endocrine therapy, taxane, and cyclin-dependent kinase 4/6 inhibitor,[9] 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.[4]

At this time, the efficacy and safety of SG in the patient subgroup with stable BrM have not been reported.[9,10]

Prospective, Single-Center Study: SG in BCBM

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 one day before surgical resection. Tumor and serum levels of SG, SN-38, and SN-38G were collected during surgery. Patients resumed treatment with SG 10 mg/kg on Days 1 and 8 of 21-day treatment cycles following recovery from surgery.[5]

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.[5]

Preliminary safety and efficacy results

In the BCBM cohort, most AEs were Grade 1 or 2, which included diarrhea, neutropenia, nausea, hypokalemia and fatigue.[5]

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

Table 3. Preliminary Efficacy Results for the BCBM Cohort[5]

	OS, Median (Range), Mo	PFS, Median (Range), Mo	iORR, iPR, iCR, %
BCBM	35.2 (2.7-37)[a]	8 (2-26.5)	iORR, 50%; iPR, 25%; iCR, 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).[5,11] SN-38 levels, molarity, and minimum IC50 values are shown in Table 4.[5,11] Within the BCBM cohort, SN-38G was only detected in small amounts or not at all in the CSF.[5,11]

Table 4. Total SN-38 Levels, Molarity, and Minimum IC50 in Tumor Tissue, Serum, and CSF From Patients in the BCBM Cohort[5]

Cohort	Total SN-38 Tumor Tissue			Total SN-38 Serum			Total SN-38 CSF			Observed SN-38 Level, μM	Minimum IC50, μM[b]
	n	Level, Median (Range), ng/g	Molarity, μM	n	Level, Median (Range), ng/mL	Molarity, μM	n	Level, ng/mL	Molarity, μM		
BCBM[a]	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).[5]

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.[5]

Real-World Data on SG Use in Patients With BrM

Real-World Study in mTNBC[6]

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 Eastern Cooperative Oncology Group performance status of 0 to 1, 64.1% of patients had one to two prior lines of treatment in the advanced setting, and 31.1% of patients were BMPos.

Results

In the BMPos population, the median PFS was 3.7 (95% CI: 2.6-6.2) mo, and the median OS was 6.7 (95% CI: 56.3-NR) mo. SG treatment discontinuation was reported in 26

(81.2%) patients mostly due to disease progression. AEs that led to SG dose reduction were reported in 4 (12.5%) patients, with no reports of death.

Retrospective Cohort Study: ADCs With SRT for BrM[7]

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 1, 2014, and October 24, 2022, and ≥1 dose of ADC were eligible for inclusion (Table 5). 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 5. Key Baseline Demographics, Disease Characteristics, and ADC Received: Overall and With or Without Concurrent ADC Treatment[7]

Key Demographics and Characteristics		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)
	Trastuzumab deruxtecan	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 days before or ≤21 days 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 (n=1, each).
[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 radiotherapy.

Results

The median (IQR) time from SRT to last imaging was 12.4 (0-80.4) mo. Across the entire cohort, the 24-month 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 radiotherapy and BrM volume (Table). For previously radiated lesions in patients with and without concurrent ADC therapy, the 24-month 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 6. Risk of SRN With Concurrent ADC (n=42)[7]

	Subdistribution HR (95% CI)	*P*-Value
Univariable analysis	4.01 (1.79-9.01)	<0.001
Multivariable analysis	4.31 (1.95-9.50)	<0.001
Prior radiotherapy	2.99 (1.26-7.09)	0.01
BrM volume, per cm^3	1.14 (1.09-1.19)	<0.001

Retrospective, Observational Real-World Study[8]

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 1.

Table 1. Select Baseline Patient Characteristics: Overall and by Subtype[8]

Select Patient and Treatment Characteristics		Overall (N=33)	Treated/Stable BrM (n=18)	Active BrM (n=7)	LMD (n=8)
Age at SG start, median (range)		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)		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) and 3.2 (2.0-7.1), respectively; additional results are found in Table 2. The CNS ORR by mBC type was as follows: HR+/HER2-, 11.1%; TNBC, 14.3%.

Table 2. Outcomes Overall and by Subgroup[8]

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)	

Abbreviations: DCR=disease control rate; PD=progressive disease; SD=stable disease.
[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.

References

1. TRODELVY® Gilead Sciences Inc. Trodelvy (sacituzumab govitecan-hziy) for injection, for intravenous use. U.S. Prescribing Information. Foster City, CA.
2. 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.
3. 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.
4. 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.
5. 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.
6. Loirat D, De Moura A, Korbi S, et al. 216P - Sacituzumab govitecan in metastatic triple negative breast cancer: efficacy -with afocus on brain metastases- and toxicity in a real-world cohort (ID 420). Paper presented at: ESMO Breast Cancer Congress 2023; 12/05/2023, 2023.
7. 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.
8. 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.
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. 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.
11. 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 conjugates
AE=adverse event
BCBM=breast cancer brain metastases
BICR=blinded independent central review
BMNeg=negative for brain metastasis
BMPos=positive for brain metastasis
BrM=brain metastases
CAIX=carbonic anhydrase IX
CNS=central nervous system
CR=complete response
CSF=cerebrospinal fluid
ERBB2=HER2 mutation
H-score=histochemical scoring
HER2-=human epidermal growth factor receptor 2-negative

HR=hazard ratio
HR+=hormone receptor-positive
IC50=half maximal inhibitory concentration
IDH=isocitrate dehydrogenase
LMD=leptomeningeal disease
mBC=metastatic breast cancer
mTNBC=metastatic triple-negative breast cancer
NE=not estimable
NR=not reported
ORR=objective response rate
OS=overall survival
PFS=progression-free survival
PR=partial response
rGBM=recurrent glioblastoma
RT=radiotherapy
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
TNBC=triple-negative breast cancer
TPC=treatment of physician's choice
TEAE=treatment-emergent adverse event
TRAE= treatment related adverse event
Trop-2=trophoblast cell surface antigen 2
UTI=urinary tract Infection

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 privacy@gilead.com.