Trodelvy® (sacituzumab govitecan) Crossing the Blood-Brain Barrier

This document is in response to your request for information regarding Trodelvy® (sacituzumab govitecan [SG]) and its ability to cross the blood-brain barrier.

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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.

Product Labeling[1]

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

Indications and Usage

Locally advanced or metastatic breast cancer

SG is indicated for the treatment of adult patients with unresectable locally advanced or metastatic triple-negative breast cancer who have received ≥2 prior systemic therapies, ≥1 of them for metastatic disease.

SG is indicated for the treatment of adult patients with unresectable locally advanced or metastatic hormone receptor-positive, human epidermal growth factor receptor 2-negative (immunohistochemistry [IHC] 0, IHC 1+ or IHC 2+/in situ hybridization-negative) breast cancer who have received endocrine-based therapy and ≥2 additional systemic therapies in the metastatic setting.

Data on the Ability of SG to Cross the Blood-Brain Barrier

Prospective, Single-Center Study: SG in BCBM and rGBM[2]

Study design and demographics

A prospective, single-center, non-randomized, window-of-opportunity, phase 0 study (NCT03995706) evaluated the intratumoral concentrations and intracranial activity of SG in adult patients undergoing craniotomy for breast cancer brain metastases (BCBM) or recurrent glioblastoma (rGBM). Patients received a single IV dose of SG 10 mg/kg administered 1 day before surgical resection. A pre-surgical interval of roughly 24 hours was

allowed to measure intracranial penetration. Tumor specimens and cerebrospinal fluid were collected intra-operatively alongside blood serum to assess levels of SN-38 and its metabolites. Patients resumed treatment with SG 10 mg/kg IV on Days 1 and 8 of 21-day treatment cycles following recovery from surgery.

Thirteen patients were in the BCBM cohort and had a mean (range) age of 48.5 (33–70) years; 93% were White, and 7% were Black/African American; 54% were hormone receptor positive (HR+); 54% were human epidermal growth factor receptor 2 positive (HER2+); and 23% had triple-negative breast cancer.

Twelve patients were in the rGBM cohort and had a mean (range) age of 55.2 (38–77) years; 75% were male, 83% were White, and 17% were of unknown race; 75% had glioblastomas that were isocitrate dehydrogenase wild type, and 75% had glioblastomas that were O^6-methylguanine-DNA methyltransferase (MGMT) promoter unmethylated.

SN-38 levels and biomarker data

From the BCBM cohort, 13 matching samples of tissue and serum and 3 cerebrospinal fluid (CSF) samples were collected. From the rGBM cohort, 11 matching samples of tissue and serum and 1 CSF sample were collected. SN-38 levels and molarity are shown in Table 1.

Table 1. Total SN-38 Levels and Molarity in Tumor Tissue, Serum, and CSF From Patients in the BCBM and rGBM Cohorts[2]

Cohort	Total SN-38 Tumor Tissue			Total SN-38 Serum			Total SN-38 CSF		
	n	Level, Median (Range, IQR), ng/g	Molarity, µM	n	Level, Median (Range, IQR), ng/mL	Molarity, µM	n	Level, ng/mL	Molarity, µM
BCBM	13	197.3 (86.5–652, 230.1)	0.0523	13	2462.4 (1266.8–5659.6, 2483.2)	6.27[b]	3	9.4[c]	0.035
rGBM	11[a]	104.5 (8.6–259.1, 182.7)	0.28	11[a]	2465.7 (115–5363.1, 1992.9)	6.28	1	5.1	0.0129

[a]One patient had insufficient samples for SN-38 analysis. [b]Using brain tissue density of 1.04 g/mL. [c]Median value.

Additionally, several pre-specified exploratory analyses were conducted to investigate potential mechanisms of action for SG, including quantification of tumor expression for trophoblast cell surface antigen 2 (Trop-2; marker of antigen expression), γ-H2AX (marker of DNA damage) and carbonic anhydrase IX (CAIX; marker of intratumoral hypoxia).

In the BCBM cohort, 11 samples were sufficient for Trop-2 analysis, and all had an H-score of 3+. In the rGBM cohort, 9 samples were sufficient for Trop-2 analysis; H-scores were 3+ (n=1), 2+ (n=2), 1+ (n=4), and 0 (n=2). Trop-2, γ-H2AX, and CAIX expression is shown in Table 2.

Table 2. Trop-2, γH2AX, and CAIX Expression in Tumor Tissue From Patients in the BCBM and rGBM Cohorts[2]

Cohort		%SN-38 Tissue-to-Serum Ratio vs:		
	n	Trop-2 Expression, Pearson r (r^2; 95% CI; *P*)	γH2AX Expression, Pearson r (r^2; 95% CI; *P*)	High[a] CAIX Expression, n samples (%)
BCBM	11	0.42 (0.018; -0.23 to 0.81; 0.18)	0.25 (0.065; -0.41 to 0.74; 0.45)	5 (45%)
rGBM	9	0.85 (0.73; 0.29–0.97; 0.013)	0.002 ($3.7e^{-6}$; -0.75 to 0.75; 0.99)	3[b] (38%)

[a]>10% positive tumor cells. [b]3/8 samples.

References

1. Gilead Sciences Inc. Placeholder for local label.
2. 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.

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

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