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.

Relevant Product Labeling[1]

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

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. TRODELVY® Gilead Sciences Inc. Trodelvy (sacituzumab govitecan-hziy) for injection, for intravenous use. U.S. Prescribing Information. Foster City, CA.
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:

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Adverse Event Reporting

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Gilead Global Patient Safety ☎ 1-800-445-3235, option 3 or www.gilead.com/utility/contact/report-an-adverse-event

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