GILEAD | Medical Information

# Trodelvy® (sacituzumab govitecan-hziy) Use in Patients with Recurrent GBM

This document is in response to your request for information regarding Trodelvy® (sacituzumab govitecan-hziy [SG]) and its use in patients with recurrent glioblastoma (rGBM).

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.

**Trodelvy is not indicated for use in patients with rGBM. 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


### Clinical Studies in Patients With rGBM

A prospective, single-center, window-of-opportunity, phase 0 study evaluated the intratumoral concentrations and intracranial activity of SG in 25 patients undergoing craniotomy for breast cancer brain metastases (BCBM) or rGBM. Data relating to the cohort of patients with rGBM (n=12) are presented below.[1,2]

- In the 12 patients with rGBM, observed overall survival (OS) was 9.5 (1–28) months, with a median (range) of 38 (3.7–112.1) weeks. Observed progression-free survival (PFS) was 2 (0.5–13.2) months, with a median (range) of 8 (2–53) weeks.
- Across the rGBM and BCBM populations (N=25), most AEs were Grade 1 or 2. The most common AEs included fatigue (60%), diarrhea (52%), alopecia (44%), headache (40%), neutropenia (40%), and nausea (36%). Grade ≥3 AEs included neutropenia (28%), hypokalemia (8%), seizure (8%), thromboembolic event (8%), urinary tract infection (8%), and lower limb muscle weakness (8%). There was one instance of Grade 4 neutropenia. One patient in the rGBM cohort had Grade 5 pneumonia which was assessed to be unrelated to the study drug.

IMMU-132-01, a phase 1/2, single-arm basket study investigated the efficacy and safety of SG in patients with metastatic epithelial cancers, including 3 patients with GBM, who had relapsed after or were refractory to ≥1 prior therapy for metastatic disease.[3]

- No patient had a complete response (CR) or partial response (PR; objective response rate [ORR]=0%), and stable disease (SD) was observed in one (33.3%) patient in the GBM cohort. Clinical benefit rate (CBR), duration of response (DOR), OS, and PFS were not provided due to small size.
- To date, safety data specific to patients with GBM have not been published. In the overall safety population (OSP; N=495), the most common treatment-related adverse events (TRAEs) were nausea (62.6%), neutropenia (57.8%), diarrhea (56.2%), fatigue (48.3%), and alopecia (40.4%).

### Ongoing Clinical Study

A Phase 2, multicenter, prospective, open-label, single-arm study (NCT04559230) is investigating the use of SG in adult patients with histologically confirmed IDH wild-type (primary) rGBM.

# Clinical Data

## Use of SG in Patients with rGBM[1,2]

A prospective, single-center, non-randomized, window-of-opportunity, phase 0 study evaluated the intratumoral concentrations and intracranial activity of SG in 25 adult patients undergoing craniotomy for BCBM or rGBM. The secondary endpoints of efficacy (specific to the rGBM cohort) and safety are presented below.

Patients received a single IV dose of SG 10 mg/kg administered 1 day before surgical resection and resumed treatment with SG 10 mg/kg on Days 1 and 8 of 21-day treatment cycles following recovery from surgery. MRI and CT imaging assessments were conducted at screening, during the postsurgical visit, and every third cycle (from cycle 4 onward). Intracranial disease response in the rGBM cohort was assessed by Response Assessment in Neuro-Oncology (RANO 1.0). ORR, PFS, and OS were calculated from cycle 1, day 1.

In the rGBM cohort (n=12), patients had a mean (range) age of 55.2 (38–77) years and were predominantly male (75%). Nine patients (75%) had glioblastomas that were isocitrate dehydrogenase (IDH)-wildtype and 9 patients (75%) had glioblastomas that were $O^6$-methylguanine-DNA methyltransferase (MGMT) promoter unmethylated.

### Clinical Efficacy

In the 12 patients with rGBM, observed OS was 9.5 (1–28) months, with a median (range) of 38 (3.7–112.1) weeks. Observed PFS was 2 (0.5–13.2) months, with a median (range) of 8 (2–53) weeks. ORR, a non-planned exploratory analysis, was 28% (28% SD, 28% PR, and 0% CR).

### Clinical Safety

Across the rGBM and BCBM populations (N=25), most AEs were Grade 1 or 2. The most common AEs included fatigue (60%), diarrhea (52%), alopecia (44%), headache (40%), neutropenia (40%), and nausea (36%). Grade ≥3 AEs included neutropenia (28%), hypokalemia (8%), seizure (8%), thromboembolic event (8%), urinary tract infection (8%), and lower limb muscle weakness (8%). There was one instance of Grade 4 neutropenia. One patient in the rGBM cohort had Grade 5 pneumonia which was assessed to be unrelated to the study drug.

## IMMU-132-01 Study in Metastatic Epithelial Cancer[3]

### Study design and demographics

IMMU-132-01, a phase 1/2, single-arm, open-label basket study, investigated the efficacy and safety of SG in patients with metastatic epithelial cancers, including 3 patients with GBM, who had relapsed after or were refractory to ≥1 prior therapy for metastatic disease.

In the GBM cohort, SG 10 mg/kg IV was administered on Days 1 and 8 of a 21-day treatment cycle until disease progression or unacceptable toxicity, death, or withdrawal of consent.

Efficacy endpoints in the overall basket study included the following: ORR (defined as both PR and CR confirmed by investigator's assessment per RECIST version 1.1), DOR, CBR (defined as CR + PR + SD ≥6 months), PFS, and OS.

### Efficacy

No patient had a CR or PR (ORR=0%), and SD was observed in 1 (33.3%) patient in the GBM cohort. CBR, DOR, OS, and PFS were not provided due to small size.

### Safety

To date, safety data specific to patients with GBM have not been published. In the OSP (N=495), the most common TRAEs were nausea (62.6%), neutropenia (57.8%), diarrhea (56.2%), fatigue (48.3%), and alopecia (40.4%). Grade ≥3 neutropenia and febrile neutropenia occurred in 42.4% and 5.3% of patients, respectively. Adverse events led to treatment discontinuation in 41 (8.3%) patients.

## References

1. 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.
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 [Supplementary Information]. *Nat Commun.* 2024;15(6707):1-11.
3. Bardia A, Messersmith WA, Kio EA, et al. Sacituzumab govitecan, a Trop-2-directed antibody-drug conjugate, for patients with epithelial cancer: final safety and efficacy results from the phase I/II IMMU-132-01 basket trial. *Ann Oncol.* 2021;32(6):746-756.

## 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 Sciences, Inc. is providing this document to you, a US Healthcare Professional, in response to your unsolicited request for medical information.

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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