A Phase 3 Study of Sacituzumab Govitecan in Patients With Previously Treated Extensive-Stage Small Cell Lung Cancer

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Introduction

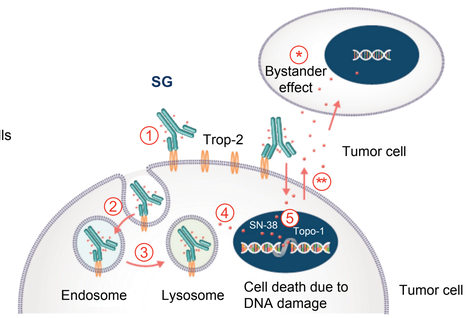
- The treatment landscape is evolving in the small cell lung cancer (SCLC) space, with recent accelerated Food and Drug Administration approvals of novel agents[1-3]
- Despite these advances and considering the toxicities and poor clinical outcomes associated with the current fully approved standard of care, topotecan, there remains an unmet need for novel agents to improve response and extend survival of patients with extensive-stage small cell lung cancer (ES-SCLC) that has progressed after platinum-containing therapy with or without anti–programmed cell death protein (ligand) 1 (PD-[L]1) therapy[4]
- Sacituzumab govitecan (SG) is a first-in-class Trop-2–directed antibody-drug conjugate (**Figure 1**) approved globally for the treatment of patients with unresectable locally advanced or metastatic triple-negative breast cancer who have received ≥2 previous systemic therapies (≥1 for metastatic disease) and metastatic hormone receptor–positive, human epidermal growth factor receptor 2 negative breast cancer after receipt of endocrine-based therapy and ≥2 additional systemic therapies[5,6]
- SG has demonstrated promising antitumor activity and manageable safety as a second-line treatment for ES-SCLC in the open-label, phase 2 TROPiCS-03 study[7]
  - At a median duration of follow-up of 12.3 months in TROPiCS-03, investigator-assessed objective response rate (ORR) per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1) was 42% (95% confidence interval [CI], 27.0–57.9), and median overall survival (OS) was 13.6 (95% CI, 6.6–14.8) months
  - Neutropenia (44%) and diarrhea (9%) were the most common grade ≥3 treatment-emergent adverse events (TEAEs), and no TEAEs led to discontinuation of SG; one treatment-related TEAE led to death
- The clinical results of TROPiCS-03 warrant further phase 3 investigation of SG in patients with previously treated ES-SCLC

Figure 1. SG Mechanism of Action

SN-38 payload
- SN-38 is more potent than the parent compound, irinotecan (Topo-1 inhibitor)
- SN-38 is rapidly internalized and efficiently released to the tumor with minimized effect on healthy tissues

Linker for SN-38
- pH-sensitive, hydrolyzable linker for SN-38 release in targeted tumor cells and tumor microenvironment, allowing bystander effect
- High drug-to-antibody ratio (7.6:1)[8]

Humanized anti–Trop-2 antibody
- Binds with high (K_D = 0.3 nM) affinity to Trop-2, an epithelial antigen expressed on many solid tumors[9]



SG, sacituzumab govitecan; Topo-1, topoisomerase I; Trop-2, trophoblast cell surface antigen 2.

References: 1. Zepzelca® (lurbinectedin) [prescribing information]. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; 2023. **2.** Imdelltra™ (tarlatamab-dlle) [prescribing information]. Thousand Oaks, CA: Amgen Inc.; 2024. **3.** Rudin CM, et al. *J Clin Oncol*. 2025;43(suppl_17): LBA8008. **4.** Hycamtin® (topotecan) [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals; 2018. **5.** TRODELVY® (sacituzumab govitecan-hziy) [prescribing information]. Foster City, CA: Gilead Sciences, Inc; March 2025. **6.** TRODELVY® (sacituzumab govitecan-hziy) [summary of product characteristics]. Carrigtohill, Ireland: Gilead Sciences Ireland UC; July 2023. **7.** Dowlati A, et al. *J Thorac Oncol*. 2025;20:799-808. **8.** Goldenberg DM, et al. *Oncotarget*. 2015;6:22496-512. **9.** Agatsuma T, et al, inventors; Daiichi Sankyo, assignee. US patent: US 9850312 B2. December 2017.

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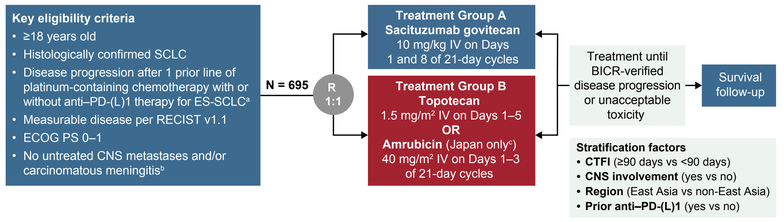
Study Design

- EVOKE-SCLC-04 (NCT06801834) is a global, multicenter, randomized, open-label, phase 3 study evaluating the efficacy and safety of SG versus standard of care (SOC) (topotecan; amrubicin in Japan) in previously treated patients with ES-SCLC
- Approximately 695 patients will be randomized 1:1 to receive SG 10 mg/kg or SOC (topotecan or amrubicin) in 21-day cycles (**Figure 2**)
- Patients will receive treatment until progressive disease (PD), death, unacceptable toxicity, or other treatment discontinuation criterion is met

Figure 2. Study Design



[a]At least 85% of participants included in the study must be pretreated with anti–PD-(L)1 therapy. [b]Patients with previously treated brain metastases may participate provided they have stable CNS disease for ≥4 weeks prior to enrollment, with all neurologic systems returned to baseline; have no evidence of new or enlarging brain metastases; and are taking ≤10 mg/day of prednisone or equivalent. [c]Participants in Japan assigned to Treatment Group B will have the option to receive topotecan or amrubicin.
BICR, blinded independent central review; CNS, central nervous system; CTFI, chemotherapy-free interval; ECOG PS, Eastern Cooperative Oncology Group performance status; ES-SCLC, extensive-stage small cell lung cancer; IV, intravenous; PD-(L)1, programmed death (ligand) 1; R, randomization; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SCLC, small cell lung cancer.

Study End Points

Primary End Points
- Objective response rate (ORR) – as assessed by blinded independent central review (BICR) according to the RECIST v1.1
- Overall survival (OS)

Secondary End Points
- Progression-free survival (PFS) – as assessed by BICR according to the RECIST v1.1
- Duration of response (DOR) – as assessed by BICR according to the RECIST v1.1
- Time to first deterioration in shortness-of-breath domain – as assessed by Non-Small Cell Lung Cancer Symptom Assessment Questionnaire (NSCLC-SAQ)
- Time to first deterioration in physical functioning domain – as assessed by the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire – Core Questionnaire (QLQ-C30)
- Safety and tolerability – as assessed by incidence of TEAEs and clinical laboratory abnormalities

Randomization

- Patients who meet eligibility criteria will be randomized 1:1 to receive SG or standard of care (topotecan or amrubicin) (**Table 1**)
- Randomization will occur on or within 3 days prior to dosing on or before the first treatment at Day 1 of Cycle 1
- Randomization stratification factors:
  - Chemotherapy-free interval (CTFI) (≥90 days vs <90 days)
  - Central nervous system (CNS) involvement (yes vs no)
  - Geographic region (East Asia vs non-East Asia)
  - Prior anti–PD-(L)1 therapy (yes vs no)

Table 1. Key Eligibility Criteria

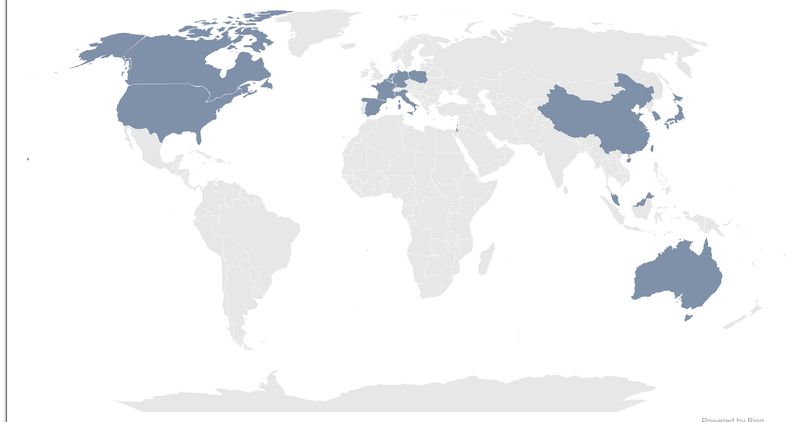
Inclusion	Exclusion
• Age ≥18 years at enrollment and able to understand and give written informed consent • Histologically confirmed diagnosis of SCLC • ECOG PS of 0 or 1 • Measurable disease by computed tomography or magnetic resonance imaging as assessed by investigator per RECIST v1.1 • Documentation of radiological disease progression after 1 prior line of platinum-containing chemotherapy (≥2 cycles of treatment) with or without anti–PD-(L)1 therapy for ES-SCLC	• CTFI[a] of <30 days (independent of maintenance immunotherapy) • Any prior treatment with irinotecan, topotecan, SG, SN-38, exatecan derivatives, and similar agents targeting topoisomerase I • Untreated CNS metastases and/or carcinomatous meningitis[b]

[a]Defined as the time from the last dose of platinum-containing chemotherapy to the occurrence of progressive disease. [b]Participants with previously treated brain metastases may participate provided they have stable CNS disease for ≥4 weeks prior to enrollment, with all neurologic systems returned to baseline; have no evidence of new or enlarging brain metastases; and are taking ≤ 10 mg/day of prednisone or equivalent.
CNS, central nervous system; CTFI, chemotherapy-free interval; ECOG PS, Eastern Cooperative Oncology Group performance status; ES-SCLC, extensive stage SCLC; PD-(L)1, programmed death (ligand) 1; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SCLC, small cell lung cancer; SG, sacituzumab govitecan.

Trial Status

- The study commenced on April 4, 2025
- Approximately 200 study sites are planned globally (active countries represented in **Figure 3**)
- Updated information on this trial can be found at ClinicalTrials.gov, reference number NCT06801834, https://clinicaltrials.gov/study/NCT06801834

Figure 3. Study Locations



Plain Language Summary

- Many people with extensive-stage small cell lung cancer (ES-SCLC) will experience their disease worsening even after being treated with prior standard platinum-containing medicines
- Researchers observed that the drug sacituzumab govitecan shrank ES-SCLC tumors and had promising survival outcomes in patients who have already received standard treatments
- The EVOKE-SCLC-04 study is being conducted worldwide and plans to check whether sacituzumab govitecan works better and is safer than standard medicines called topotecan or amrubicin, which are the current fully approved treatments for patients with ES-SCLC that has gotten worse after prior treatment
- Participants will be split into 2 groups
  - The experimental group will receive sacituzumab govitecan
  - The control group will receive topotecan, and patients in the control group who are from Japan will have the option to take either topotecan or amrubicin
- Researchers will assess whether tumors shrink, how long participants live, and if the treatments are safe