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

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EVOKE-04

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Background

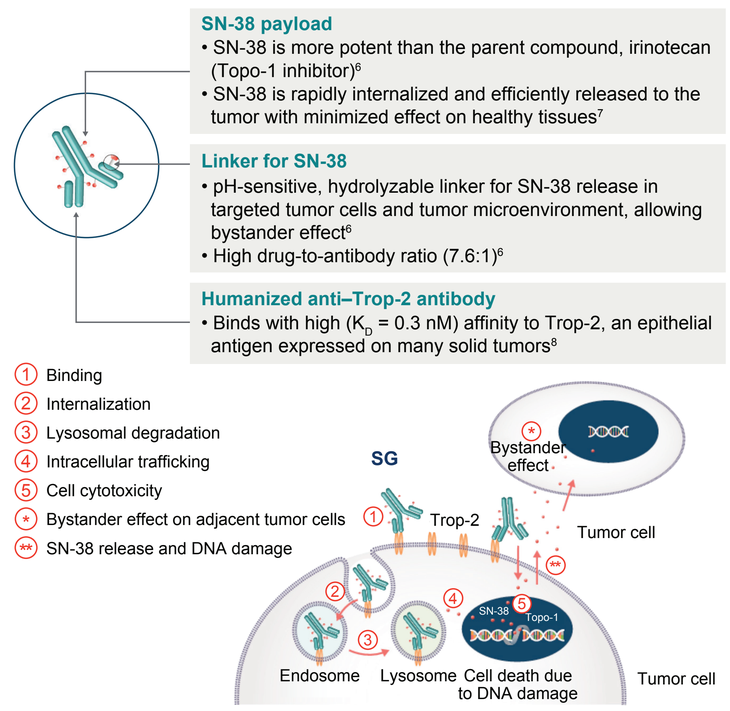
Introduction

- Treatment options are limited for patients with extensive-stage small-cell lung cancer (ES-SCLC) that has progressed after platinum-containing chemotherapy, with or without anti–programmed cell death protein (ligand) 1 (anti–PD-[L]1) therapy[1,2]
- Despite the evolving treatment landscape for ES-SCLC,[3,4] toxicities and poor clinical outcomes with the current globally approved standard of care (SOC), topotecan, highlight the unmet need for novel agents[5]

Sacituzumab Govitecan

- Sacituzumab govitecan (SG) is a first-in-class trophoblast cell surface antigen 2 (Trop-2)–directed antibody-drug conjugate (**Figure 1**)
  - SG is globally approved for the treatment of unresectable locally advanced or metastatic triple-negative breast cancer in individuals 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[9,10]

Figure 1. SG Mechanism of Action



Topo-1, topoisomerase I.

- In the phase 2, open-label TROPiCS-03 study, SG showed encouraging antitumor activity and manageable safety as a second-line treatment for participants with ES-SCLC[7]
  - At a median follow-up duration of 12.3 months, investigator-assessed objective response rate (ORR) per Response Evaluation Criteria in Solid Tumors, version 1.1 (RECIST v1.1), was 42% (95% 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
- Clinical results from TROPiCS-03 support further phase 3 investigation of SG in participants with previously treated ES-SCLC

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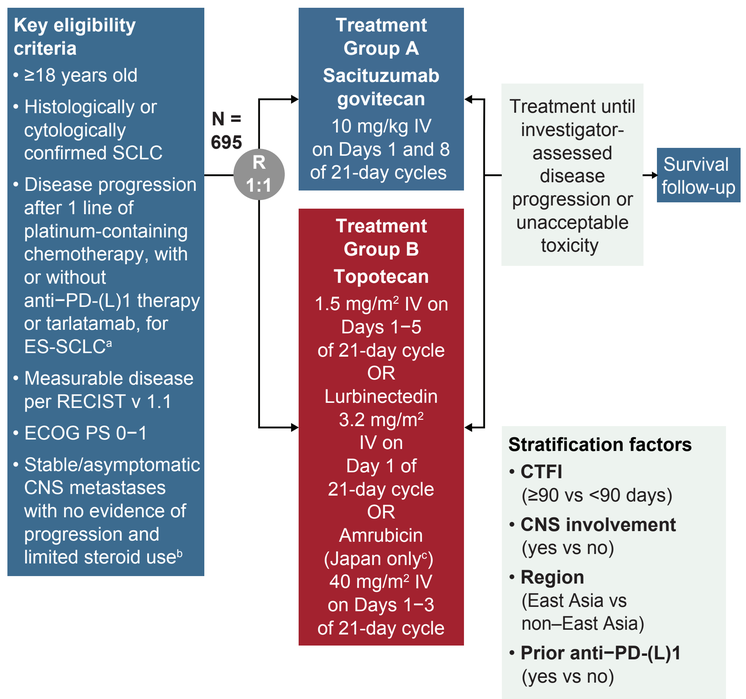
Methods

Study Design

- EVOKE-SCLC-04 (NCT06801834) is a global, Phase 3, randomized, open-label, multicenter study investigating the efficacy and safety of SG versus SOC (topotecan, lurbinectedin [in countries/regions where approved], or amrubicin [Japan only]) in participants with previously treated ES-SCLC (**Figure 2**)
- Participants who meet eligibility criteria (**Table 1**) will be randomized 1:1 to receive SG 10 mg/kg or SOC (topotecan, lurbinectedin, or amrubicin) in 21-day cycles
  - Randomization must occur on or within 3 days prior to dosing on Day 1 of Cycle 1
  - Randomization stratification factors include chemotherapy-free interval (CTFI), central nervous system (CNS) involvement, geographic region, and prior anti–PD-(L)1 therapy
- Study endpoints are shown in **Table 2**

Figure 2. EVOKE-SCLC-04 Study Design



[a]At least 85% of participants included in the study must be pretreated with anti–PD-(L)1 therapy. [b]Participants with previously treated brain metastases may participate provided they have stable CNS disease for ≥4 weeks before 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.

Table 1. Key Eligibility Criteria

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

[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 before 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 small-cell lung cancer; IV, intravenous; PD-(L)1, programmed cell death (ligand) 1; R, randomization; RECIST v1.1, Response Evaluation Criteria in Solid Tumors, version 1.1; SCLC, small-cell lung cancer; SG, sacituzumab govitecan.

Table 2. Study Endpoints

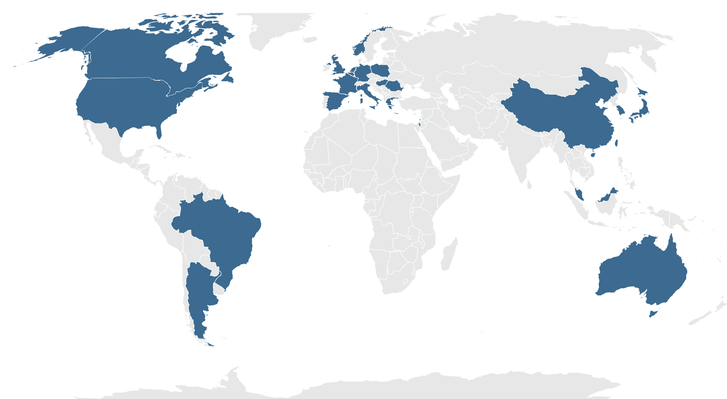
	Endpoints	Assessed by
Primary	• Overall survival	
Secondary	• Progression-free survival	• Investigator per RECIST v1.1 criteria
	• Objective response rate	• Investigator per RECIST v1.1 criteria
	• Duration of response	• Investigator per RECIST v1.1 criteria
	• Time to first deterioration in shortness-of-breath domain	• NSCLC-SAQ
	• Time to first deterioration in physical functioning domain	• EORTC QLQ-C30
	• Safety and tolerability	• Incidence of TEAEs and clinical laboratory abnormalities

EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality-of-Life Questionnaire–Core 30; RECIST v1.1, Response Evaluation Criteria in Solid Tumors, version 1.1; NSCLC-SAQ, Non–Small Cell Lung Cancer Symptoms Assessment Questionnaire; TEAE, treatment-emergent adverse event.

Trial Status

- The study commenced on April 4, 2025, and is actively recruiting, with plans to enroll 695 participants
- Approximately 275 study sites are planned globally (active countries are represented in **Figure 3**)
- Updated study information can be found at ClinicalTrials.gov, NCT06801834, https://clinicaltrials.gov/study/NCT06801834

Figure 3. Trial Status



Plain Language Summary

- Many people with extensive-stage small-cell lung cancer (ES-SCLC) will find their disease getting worse, even after being treated with standard platinum-containing medicines
- Investigations showed that the drug sacituzumab govitecan shrank ES-SCLC tumors and had promising survival outcomes in people who have already been treated with standard medicines
- The EVOKE-SCLC-04 study is currently enrolling participants worldwide and plans to look at whether sacituzumab govitecan works better and is safer than the standard medicines (topotecan, lurbinectedin, and amrubicin) currently approved to treat ES-SCLC that has worsened after receiving previous treatment
- Participants will be divided into 2 treatment groups
  - The experimental group will be given sacituzumab govitecan
  - The control group will be given topotecan or lurbinectedin; Japanese participants in this group will have the option to take either topotecan or amrubicin
- Investigators will assess whether tumors shrink, how long participants live, and if the treatments are safe

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