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Trodelvy® (sacituzumab govitecan-hziy) Combination With Pembrolizumab and Chemotherapy for 1L Treatment of Patients With mNSCLC

This document is in response to your request for information regarding the use of Trodelvy® (sacituzumab govitecan-hziy [SG]) in combination with pembrolizumab (pembro) and chemotherapy for first-line (1L) treatment in patients with metastatic non-small cell lung cancer (mNSCLC).

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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.

Summary

EVOKE-02 Study: SG + CP for 1L Treatment

EVOKE-02 is an ongoing, multi-cohort, phase 2 study evaluating the efficacy and safety of SG in combination with pembro ± PLT agent in the 1L treatment of adult patients with advanced or mNSCLC without AGAs.[1]

- During the safety run-in (SG 10 mg/kg + CP; n=5), the de-escalation criteria (≥2 patients with a predefined DLT) were not met. At a planned follow-up safety evaluation, the SG dose was reduced to 7.5 mg/kg due to rates of myelosuppression (mainly Grade ≥3 neutropenia).
- In Cohort C (Sq; n=54), ORR was 45.1% (95% CI: 31.1–59.7%) and median PFS was 8.1 months (95% CI: 5.2–15%).
- In Cohort D (Sq; n=41), ORR was 39% (95% CI: 24.2–55.5%) and median PFS was 8.3 months (95% CI: 4.3–11.2%).
- The most common any-grade TEAEs in the SG 10 mg/kg + CP group were neutropenia (76%), anemia (75%), and diarrhea (69%).
- The most common any-grade TEAEs in the SG 7.5 mg/kg + CP group were anemia (65%), diarrhea (59%), and nausea (42%).

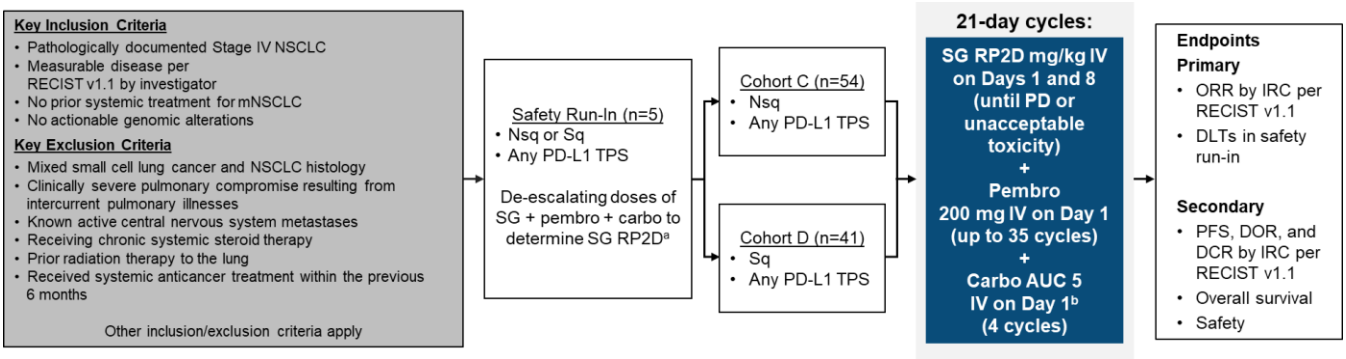
In an exploratory analysis with a later data cutoff date, Trop-2 expression ≥178 (median H-score) was associated with a numerically higher PFS and ORR; however, the association was not statistically significant.[2]

EVOKE-02 Study: SG + CP for 1L Treatment

Study Design and Demographics

EVOKE-02 is an ongoing, open-label, multicenter, multi-cohort, phase 2 study (NCT05186974) evaluating the efficacy and safety of SG in combination with pembro ± PLT agent (eg, carbo) in the 1L treatment of adult patients with advanced or mNSCLC without AGAs (Figure 1).[1]

Figure 1. EVOKE-02: Study Design[1,3]



Abbreviations: DCR=disease control rate; G-CSF=granulocyte colony-stimulating factor; NSCLC=non-small cell lung cancer; RECIST=Response Evaluation Criteria in Solid Tumors.
[a]De-escalating dose of SG (10 mg/kg, 7.5 mg/kg, and 5 mg/kg) IV on Days 1 and 8 + pembro 200 mg IV on Day 1 + carbo (AUC 5) IV on Day 1 of a 21-day cycle.
[b]Based on safety assessment, mandatory long-acting G-CSF on Day 9 or short-acting G-CSF once daily for 10 days starting from Day 9 of each cycle.

The baseline demographics and disease characteristics of patients included in a preliminary analysis of Cohorts C and D are shown in Table 1.

Table 1. EVOKE-02 (Cohorts C and D): Select Baseline Demographics and Disease Characteristics[1]

Key Demographics and Characteristics	Cohort C (n=54)	Cohort D (n=41)
Age, median (range), years	67 (46–87)	68 (42–79)
Male, n (%)	40 (74.1)	34 (82.9)
Race, White/Asian/Black/other, %	48.1/44.4/0/7.4	58.5/29.3/0/12.2
Eastern Cooperative Oncology Group Performance Status, 0/1, %	27.8/72.2	34.1/65.9
Stage IV at diagnosis, n (%)	44 (81.5)	32 (78)
PD-L1 TPS, ≥50/1–49/<1, %	14.8/40.7/44.4	9.8/39/51.2
Baseline brain metastasis, n (%)	4 (7.4)	1 (2.4)
Tobacco use status, current/former/never/missing, %	14.8/53.7/20.4/11.1	31.7/58.5/7.3/2.4

Results: Cohort C and Cohort D[1]

Safety run-in

During the safety run-in (SG 10 mg/kg + CP; n=5), the de-escalation criteria (≥2 patients with a predefined DLT) were not met. One DLT of sepsis leading to death was seen. At a planned follow-up safety evaluation, the SG dose was reduced to 7.5 mg/kg due to rates of

myelosuppression (mainly Grade ≥3 neutropenia). The RP2D was 7.5 mg/kg of SG combined with pembro 200 mg and carbo AUC 5.

Preliminary efficacy

In Cohort C, 17 patients (31%) received SG 10 mg/kg + CP, and 37 patients (69%) received SG 7.5 mg/kg + CP. In Cohort D, 12 patients (29%) received SG 10 mg/kg + CP, and 29 patients (71%) received SG 7.5 mg/kg + CP. The median (range) durations of follow-up were 14.5 (12.2–22.3) and 14.2 (11–23) months for Cohorts C and D, respectively. Three patients in Cohort C did not have measurable disease per IRC at baseline and were not included in the efficacy analysis. Efficacy results overall and by PD-L1 expression for patients receiving SG 7.5 mg/kg or 10 mg/kg + CP are shown in Table 2 and Table 3, respectively.

Table 2. EVOKE-02 (Cohorts C and D): Efficacy by IRC[1]

Efficacy[a]	Cohort C (n=51)	Cohort D (n=41)
ORR, % (95% CI)	45.1 (31.1–59.7)	39 (24.2–55.5)
PR, n (%)	23 (45.1)	16 (39)
SD, n (%)	16 (31.4)	17 (41.5)
PD, n (%)	5 (9.8)	3 (7.3)
NE, n (%)	7 (13.7)	5 (12.2)
Time to response, median (range), mo	2.7 (1.2–7.2)	1.5 (1.2–5.8)
DOR, median (95% CI), mo	NR (3.2–NR)	11.5 (5.6–NR)
PFS, median (95% CI), mo	8.1 (5.2–15)	8.3 (4.3–11.2)
PFS rate at 6 months, % (95% CI)	53.7 (37.8–67.2)	64.6 (46–78.2)

[a]Patients received SG 7.5 mg/kg or 10 mg/kg.

Table 3. EVOKE-02 (Cohorts C and D): Efficacy by PD-L1 Expression[1]

Efficacy by IRC[a]	PD-L1 TPS <1% SG + CP (n=44)	PD-L1 TPS 1–49% SG + CP (n=36)	PD-L1 TPS ≥50% SG + CP (n=12)
ORR, % (95% CI)	43.2 (28.3–59)	33.3 (18.6–51)	66.7 (34.9–90.1)
PR, n (%)	19 (43.2)	12 (33.3)	8 (66.7)
SD, n (%)	15 (34.1)	16 (44.4)	2 (16.7)
PD, n (%)	3 (6.8)	4 (11.1)	1 (8.3)
NE, n (%)	7 (15.9)	4 (11.1)	1 (8.3)
PFS, median (95% CI), mo	8.3 (5.2–15)	6.8 (4–10.7)	NR (1.9–NR)

[a]Patients received SG 7.5 mg/kg or 10 mg/kg.

For patients with tumors that had PD-L1 TPS ≥1% (n=48), ORR was 41.7% (95% CI: 27.6–56.8%) and median PFS was 8.4 (95% CI: 5.3–11.2%) months.

Preliminary safety

Any-grade TEAEs were reported in all patients in each SG dose group, and a safety summary by SG dose is shown in Table 4. Grade ≥3 TEAEs occurred in 93.1% of the SG 10 mg/kg + CP group and in 86.4% of the SG 7.5 mg/kg + CP group. Grade 1 to 2 TEAEs occurred in 7% of the SG 10 mg/kg + CP group and in 14% of the SG 7.5 mg/kg + CP group. Additional TEAEs seen in ≥25% of patients are shown in Table 5.

Table 4. EVOKE-02 (Cohorts C and D): Summary of TEAEs by Dose Received[1]

TEAEs, n (%)	SG 10 mg/kg + CP (n=29)	SG 7.5 mg/kg + CP (n=66)
Serious TEAEs	18 (62.1)	36 (54.5)
Led to discontinuation of any study drug	9 (31)	12 (18.2)
Led to discontinuation of SG/pembro/carbo	9 (31)/9 (31)/7 (24.1)	9 (13.6)/12 (18.2)/4 (6.1)
Led to dose reduction of any study drug	19 (65.5)	27 (40.9)
Led to dose reduction of SG/carbo	19 (65.5)/13 (44.8)	19 (28.8)/19 (28.8)
Led to death[a]	5 (17.2)	9 (13.6)
Related to any study drug	3 (10.3)	5 (7.6)

[a]Included sepsis (n=3), pneumonia (n=1), and abdominal infection (n=1) in the SG 10 mg/kg group and pneumonia (n=3), sepsis (n=2), febrile neutropenia (n=1), bacterial sepsis (n=1), gastroenteritis (n=1), pneumococcal sepsis (n=1), and hypoglycemia (n=1) in the SG 7.5 mg/kg group.

Table 5. EVOKE-02 (Cohorts C and D): TEAEs in ≥25% of Patients by Dose Received[1]

TEAEs, %	SG 10 mg/kg + CP (n=29)		SG 7.5 mg/kg + CP (n=66)	
	Grade 1–2	Grade ≥3	Grade 1–2	Grade ≥3
Diarrhea	59	10	45	14
Anemia	41	34	33	32
Decreased appetite	41	0	36	3
Constipation	38	0	27	3
Alopecia	38	0	26	0
Pruritus	38	0	11	0
ALT increased	34	7	6	3
AST increased	34	7	6	3
COVID-19	31	7	0	0
Pyrexia	31	0	9	0
Nausea	28	0	39	3
Stomatitis	28	0	8	0
Infusion-related reaction	28	0	3	0
Cough	24	0	29	0
Asthenia	17	3	27	6
Dyspnea	17	0	21	5
Neutropenia	10	66	5	24
Platelet count decreased	7	21	12	12
Pneumonia	3	28	5	9
Febrile neutropenia	3	28	2	15

Subanalysis: Efficacy by Trop-2 Expression[2]

An exploratory analysis with a later data cutoff date evaluated efficacy outcomes according to Trop-2 expression. Trop-2 membrane expression on archival tumor tissue was assessed with immunohistochemistry and expressed as an H-score of 0 to 300. Trop-2 expression was assessed for association with ORR and PFS. Clinical outcomes were evaluated in 184 patients with evaluable archival tissue. With a median Trop-2 H-score of 178, outcomes were assessed in H-score groups of <178 and ≥178. To boost the numbers for subgroup analyses, Trop-2 subgroups from Cohorts A + B + C + D were combined to correlate with evaluated efficacy outcomes.

In patients who received SG + CP, there was no correlation between Trop-2 expression and best percentage change in tumor size (Spearman correlation coefficient ρ=-0.01) or best overall response. Trop-2 expression ≥ median H-score resulted in numerically higher but not statistically significant PFS and ORR (Table 6).

Table 6. EVOKE-02 Subanalysis of Trop-2 Status: Efficacy[2]

Efficacy Outcomes		SG + CP	
		Trop-2 H-Score <178 (n=30)	Trop-2 H-Score ≥178 (n=32)
ORR, n (%) [95% CI]		10 (33.3) [17.3–52.8]	14 (43.8) [26.4–62.3]
PFS	Median (95% CI), months	5.5 (3.9–8.5)	8.7 (5.6–NE)
	Hazard ratio (95% CI)	0.68 (0.35–1.31)	

References

1. Gray JE, Neal JW, Patel JD, et al. Sacituzumab govitecan + pembrolizumab + carboplatin in 1L metastatic non–small cell lung cancer: the EVOKE-02 study [Oral Presentation OA08.07]. Presented at: 2024 World Conference on Lung Cancer (WCLC); September 7-10, 2024; San Diego, CA.
2. Patel J, Zavodovskaya M, Chul Cho B, et al. Trop-2 expression and association with efficacy in patients treated with sacituzumab govitecan + pembrolizumab +/- carboplatin in the EVOKE-02 study of non-small cell lung cancer (Poster LB399). Presented at: American Association for Cancer Research (AACR); April 25-30, 2025; Chicago, IL, USA.
3. ClinicalTrials.gov. Study of sacituzumab govitecan combinations in first-line treatment of participants with advanced or metastatic non-small-cell lung cancer (NSCLC) (EVOKE-02). ClinicalTrials.gov Identifier: NCT05186974. Available at: https://www.clinicaltrials.gov/ct2/show/NCT05186974.

Abbreviations

1L=first-line
AGA=actionable genomic alteration
AUC=area under the concentration-time curve
carbo=carboplatin
BEP=biomarker-evaluable population
CP=carboplatin + pembrolizumab
DLT=dose-limiting toxicity
DOR=duration of response
H-score=histochemical-score
IRC=independent review committee
mNSCLC=metastatic non-small cell lung cancer
NE=not evaluable
NR=not reached
Nsq=nonsquamous
ORR=objective response rate
PD=progressive disease
PD-L1=programmed cell death-ligand 1
pembro=pembrolizumab
PFS=progression-free survival
PLT=platinum
PR=partial response
RP2D=recommended phase 2 dose
SD=stable disease
SG=sacituzumab govitecan-hziy
Sq=squamous
TEAE=treatment-emergent adverse event
TPS=tumor proportion score
Trop-2=trophoblast cell surface antigen-2

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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