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Trodelvy® (sacituzumab govitecan-hziy) Combination With Pembrolizumab for 1L Treatment in 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) for first-line (1L) treatment in patients with metastatic non-small cell lung cancer (mNSCLC).

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Trodelvy is not indicated for use in patients with mNSCLC. 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 + Pembro for 1L Treatment

EVOKE-02 is an ongoing, phase 2, multi-cohort 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]

Preliminary analyses of patients treated with SG + pembro in Cohort A (PD-L1 TPS ≥50%; n=30) and Cohort B (PD-L1 TPS <50%; n=33) showed the following[1,2]:

- In Cohort A, ORR was 69% (95% CI: 49–85%; Sq, 72.7%; Nsq, 66.7%) and DCR was 86% (95% CI: 68–96%; Sq, 81.8%; Nsq, 88.9%).
- In Cohort B, ORR was 44% (95% CI: 26–62%; Sq, 53.8%; Nsq, 36.8%) and DCR was 78% (95% CI: 60–91%; Sq, 84.6%; Nsq, 73.7%).
- The most common any-grade TEAEs were diarrhea (54%), anemia (48%), asthenia (38%), and alopecia (37%). Immune-mediated TEAEs that occurred in ≥5% of patients were pneumonitis (8%) and hyperthyroidism (5%).

In an analysis with extended follow-up for Cohort A (PD-L1 TPS ≥50%; n=30)[3]:

- Overall ORR was 66.7% (95% CI: 47.2–82.7%) and was consistent in patients with both Sq and Nsq histology.
- Median PFS was 13.1 months (95% CI: 5.5–NR).
- The most common any-grade TEAEs were diarrhea (56.7%), alopecia, anemia, and asthenia (each, 50%), and the most common immune-mediated TEAE was pneumonitis (16.7%).

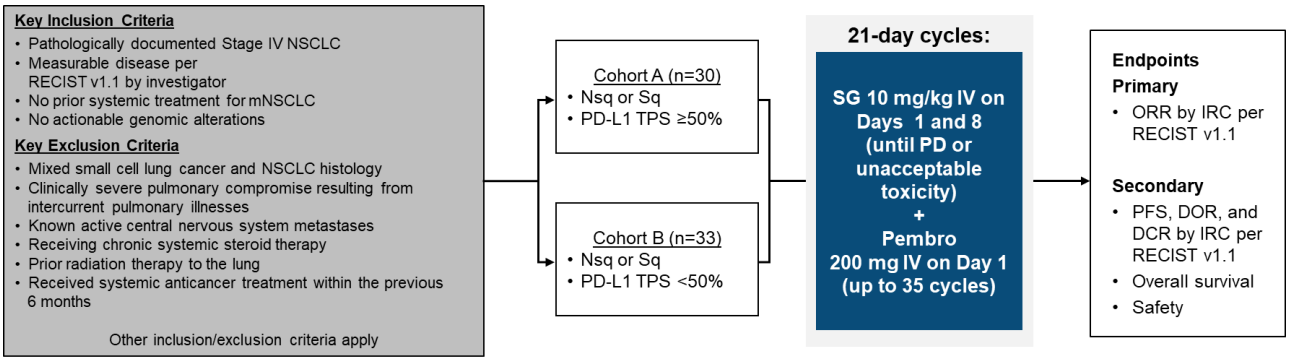
An exploratory analysis with a later data cutoff date evaluated Trop-2 expression and no patient subgroup was identified that had a greater treatment benefit (eg, ORR or PFS) with SG + pembro.[4]

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

Study Design and Demographics

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

Figure 1. EVOKE-02: Study Design[5,6]



Abbreviations: NSCLC=non-small cell lung cancer; RECIST=Response Evaluation Criteria in Solid Tumors.

Select baseline characteristics and exposure are shown in Table 1.[1,2]

Table 1. EVOKE-02 (Cohorts A and B): Select Baseline Demographics and Disease Characteristics[1,2]

Key Demographics and Characteristics		Cohort A (n=30)	Cohort B (n=33)
Age, median (range), years		67 (47–77)	68 (47–80)
Male, %		80	79
Histology, Nsq/Sq, %		60/40	61/39
Stage at diagnosis, I–III/IV, %		17/80	15/85
Treatment duration,[a] median (range), months	SG	4.1 (0–11.2+)	4.1 (0–11.9+)
	Pembro	3.6 (0–11.2+)	3.8 (0–11.7+)

[a]Patients received a median (range) of 6 (1–17+) cycles of SG and pembro.

Preliminary Results: Cohort A and Cohort B

Efficacy

The median (range) follow-up durations for Cohorts A and B were 5 (1.7–12) and 5.8 (1–12.2) months, respectively. Efficacy results were reported for 61 patients enrolled for ≥13 weeks (Table 2)[1] and reported according to PD-L1 TPS subgroup in Cohort B (Table 3). In patients who achieved a confirmed PR, the mean (standard deviation) time to response was 1.8 (0.82) months in Cohort A and 1.7 (0.6) months in Cohort B.[7]

Table 2. EVOKE-02 (Cohorts A and B): Efficacy by Investigator Assessment[1,2]

Efficacy[a]	Cohort A	Cohort B	All Patients
All histologies	n=29	n=32	N=61
ORR (BOR of CR + PR), % (95% CI)	69 (49–85)	44 (26–62)	56 (42–69)
PR (confirmed and unconfirmed), n (%)	20 (69)	14 (44)	34 (56)
PR (confirmed), n (%)	18 (62)	12 (38)	30 (49)
SD, n (%)	5 (17)	11 (34)	16 (26)
PD, n (%)	3 (10)	2 (6)	5 (8)
DCR (CR + PR + SD ≥6 weeks), % (95% CI)	86 (68–96)	78 (60–91)	82 (70–91)
DOR,[b] median (95% CI), months	NR (5.6–NR)	NR (3.5–NR)	NR (7.9–NR)
DOR rate at 6 months,[b] % (95% CI)	88 (39–98)	88 (39–98)	87 (58–97)
Sq mNSCLC	n=11	n=13	N/A
ORR, % (95% CI)	72.7 (39–94)	53.8 (25.1–80.8)	N/A
DCR (CR + PR + SD ≥6 weeks), % (95% CI)	81.8 (48.2–97.7)	84.6 (54.6–98.1)	N/A
Nsq mNSCLC	n=18	n=19	N/A
ORR, % (95% CI)	66.7 (41–86.7)	36.8 (16.3–61.6)	N/A
DCR (CR + PR + SD ≥6 weeks), % (95% CI)	88.9 (65.3–98.6)	73.7 (48.8–90.9)	N/A

[a]Patients without tumor assessment: Cohort A, n=1 (Nsq); Cohort B, n=5 (Sq, n=2; Nsq, n=3).
[b]Evaluated in patients with a confirmed CR or PR; based on Kaplan-Meier estimates.

Table 3. EVOKE-02: Cohort B PD-L1 TPS Subgroup Analysis[7]

Investigator-Assessed Efficacy	PD-L1 TPS 1–49% (n=15)	PD-L1 TPS <1% (n=17)[a]
ORR (BOR of CR + PR), % (95% CI)	53 (27–79)	35 (14–62)
DCR (CR + PR + SD ≥6 weeks), % (95% CI)	100 (78–100)	59 (33–82)

[a]Five patients did not have tumor assessment for PD-L1.

Safety[1]

TEAEs reported in the safety-evaluable population (patients who received ≥1 dose of study treatment; N=63) are shown in Table 4 and Table 5. Any-grade TEAEs were reported in all patients, with 90% related to study treatment.

Table 4. EVOKE-02 (Cohort A and B): Summary of TEAEs[1]

TEAEs, n (%)	All Patients (N=63)
Serious TEAEs	34 (54)
Related to study treatment	9 (14)
Led to treatment discontinuations	11 (18)
Led to discontinuation of SG/pembro	9 (14)/8 (13)
Led to SG dose reductions	11 (18)
Led to death[a]	4 (6)
Related to study treatment	1 (2)

[a]Causes of death: malignant lung neoplasm, respiratory tract infection, sepsis, and sudden death (each, n=1). The case of sepsis that led to death was deemed related to study treatment.

Table 5. EVOKE-02 (Cohort A and B): Any-Grade TEAEs Reported in ≥15% of Patients and Immune-Mediated TEAEs (N=63)[1]

TEAEs, %	Grade 1–2	Grade ≥3
Diarrhea	51	3
Anemia	42	6
Asthenia	38	0
Alopecia	37	0

TEAEs, %		Grade 1–2	Grade ≥3
Nausea		30	2
Constipation		24	0
Decreased appetite		22	0
Respiratory tract infection		20	5
Fatigue		19	2
Mucosal inflammation		18	0
Dyspnea		17	5
Neutropenia		9	18
Immune-mediated	Pneumonitis[a]	5	3
	Hyperthyroidism	5	0
	Colitis	2	2
	Hypothyroidism	2	0
	Maculopapular rash	0	2
	Nephritis	0	2

[a]Grade 3 pneumonitis (n=2) was the highest grade TEAE observed to date.

Extended Follow-Up: Cohort A (PD-L1 TPS ≥50%)[3]

Efficacy

In this analysis, the median (range) follow-up was 11.3 (8.4–17.5) months, and median (range) durations of exposure to SG and pembro were 7.43 (0.03–16.69) months and 7.18 (0.03–16.69) months, respectively. Efficacy by IRC is shown in Table 6.

Table 6. EVOKE-02 Cohort A Extended Follow-Up: Efficacy[3]

Efficacy by IRC	Overall (n=30)	Sq mNSCLC (n=12)	Nsq mNSCLC (n=18)
ORR, n (%) [95% CI]	20 (66.7) [47.2–82.7]	8 (66.7) [34.9–90.1]	12 (66.7) [41–86.7]
CR, n (%)	1 (3.3)	0	1 (5.6)
PR, n (%)	19 (63.3)	8 (66.7)	11 (61.1)
SD, n (%)	6 (20)	2 (16.7)	4 (22.2)
PD, n (%)	3 (10)	2 (16.7)	1 (5.6)
NE, n (%)	1 (3.3)	0	1 (5.6)
PFS, median (95% CI), months	13.1 (5.5–NR)	NR (1.2–NR)	13.1 (5.5–NR)
12-month PFS, % (95% CI)	57.2 (35.6–73.9)	58.3 (21.2–82.9)	56.3 (29.3–76.4)
DOR, median (95% CI), months	NR (8.5–NR)	NR (2.4–NR)	NR (4.6–NR)
12-month DOR, % (95% CI)	59.3 (27.4–81)	75 (31.5–93.1)	56.6 (19.7–81.9)
DCR (CR + PR + SD ≥6 weeks), n (%) [95% CI]	26 (86.7) [69.3–96.2]	10 (83.3) [51.6–97.9]	16 (88.9) [65.3–98.6]

Safety

Any-grade TEAEs were reported in all patients, with 96.7% related to study treatment. TEAEs are shown in Table 7 and Table 8.

Table 7. EVOKE-02 Cohort A Extended Follow-Up: Summary of TEAEs[3]

TEAEs, n (%)	Cohort A (n=30)
Serious TEAEs	15 (50)
Treatment-related	5 (16.7)
Led to treatment discontinuation of either study drug	6 (20)
Led to discontinuation of SG/pembro	5 (16.7)/6 (20)

TEAEs, n (%)	Cohort A (n=30)
Led to SG dose reductions	6 (20)
Led to death[a]	1 (3.3)
Treatment-related	1 (3.3)

[a]The 1 treatment-related death was due to neutropenic sepsis.

Table 8. EVOKE-02 Cohort A Extended Follow-Up: Any-Grade (≥30%), Grade 3 (≥5%), and Immune-Mediated TEAEs (n=30)[3]

TEAEs, %		Grade 1–2	Grade ≥3
Alopecia		50	0
Anemia		50	0
Asthenia		50	0
Diarrhea		46.7	10
Nausea		43.4	3.3
Constipation		33.3	0
Decreased appetite		33.3	0
Fatigue		30	0
Dyspnea		26.7	3.3
Neutropenia		13.3	16.7
Pulmonary embolism		6.6	6.7
Respiratory failure		0	10
Immune-mediated[a]	Pneumonitis	10	6.7
	Colitis	3.3	0
	Hyperthyroidism	3.3	0
	Hypothyroidism	3.3	0
	Maculopapular rash	3.3	0

[a]There were no reports of nephritis.

Subanalysis: Efficacy by Trop-2 Expression[4]

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 + pembro, there was no correlation between Trop-2 expression and best percentage change in tumor size (Spearman correlation coefficient ρ=-0.013) or BOR. Trop-2 expression ≥ median H-score was not significantly associated with improved PFS or ORR (Table 9).

Table 9. EVOKE-02 Subanalysis of Trop-2 Status: Efficacy[4]

Efficacy Outcomes		SG + Pembro	
		Trop-2 H-Score <178 (n=33)	Trop-2 H-Score ≥178 (n=34)
ORR, n (%) [95% CI]		11 (33.3) [18–51.8]	12 (35.3) [19.7–53.5]
PFS	Median (95% CI), months	6.9 (5.5–NE)	8.5 (4.2–12.9)
	Hazard ratio (95% CI)	1.17 (0.59–2.31)	

Ongoing Study: EVOKE-03

A phase 3, open-label, multicenter, randomized study (NCT05609968) is evaluating the efficacy and safety of SG in combination with pembro vs pembro monotherapy as 1L treatment in adults with mNSCLC and PD-L1 TPS ≥50%.

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Abbreviations

1L=first line
AGA=actionable genomic alteration
BOR=best overall response
CR=complete response
DCR=disease control rate
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-1
pembro=pembrolizumab
PFS=progression-free survival
PLT=platinum
PR=partial response
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

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