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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, multicohort study evaluating the efficacy and safety of SG + pembro ± chemotherapy in the 1L treatment of adult patients with advanced or mNSCLC without AGAs.[1]

After a median (range) duration of follow-up of 16.6 (8.5–23.8) months, patients treated with SG + pembro in Cohort A (PD-L1 TPS ≥50%; n=30) as well as those in Cohort B (PD-L1 TPS <50%; n=62) showed the following (all efficacy results assessed per IRC)[1]:

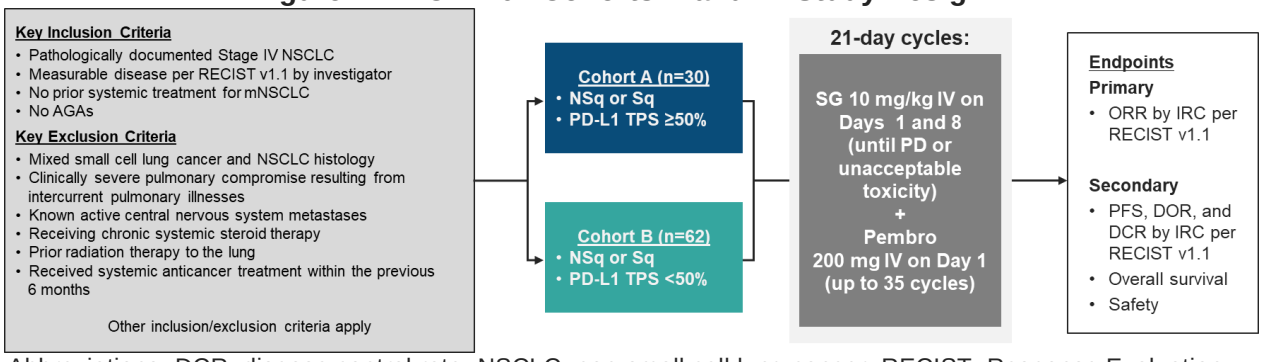
- In Cohort A, ORR was 66.7% (95% CI: 47.2–82.7%; NSq, 66.7%; Sq, 66.7%) and median PFS was 13.1 months (95% CI: 6.7–NR; NSq, NR; Sq, 10.7 months).
- In Cohort B, ORR was 29% (95% CI: 18.2–41.9%; NSq, 25%; Sq, 34.6%) and median PFS was 7 months (95% CI: 4.2–12.9; NSq, 7.4 months; Sq, 7 months).
- Within Cohorts A and B combined, 67 patients had Trop-2 expression data. ORRs were generally similar between Trop-2 subgroups according to median H-scores (<median, 33.3%; ≥median, 35.3%). Median PFS for combined cohorts was also not significantly different between subgroups according to median H-score (<median, 6.9 months; ≥median, 8.48 months; HR, 1.165; 95% CI: 0.59–2.31).
- The most common any-grade TEAEs were diarrhea (53.3%), anemia (46.7%), and alopecia (41.3%). Immune-mediated TEAEs included pneumonitis (8.7%), hyperthyroidism (3.3%), colitis (3.3%), and myocarditis (2.2%).

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 with pembro ± chemotherapy in the 1L treatment of adult patients with advanced or mNSCLC without AGAs (Figure 1). Patients from Cohorts A and B received SG + pembro. Select baseline characteristics and exposure are shown in Table 1.[1]

Figure 1. EVOKE-02 Cohorts A and B: Study Design[1,2]



Abbreviations: DCR=disease control rate; NSCLC=non-small cell lung cancer; RECIST=Response Evaluation Criteria in Solid Tumors.
Note: DCR and overall survival data were not presented in the current publication.

Table 1. EVOKE-02 Cohorts A and B: Select Baseline Demographics, Disease Characteristics, and Study Drug Exposure[1]

Key Demographics and Characteristics		Cohort A (n=30)	Cohort B (n=62)
Age, median (range), years		67 (47–77)	68 (32–80)
Male, %		80	69.4
Eastern Cooperative Oncology Group performance status, 0/1, %		20/80	33.9/66.1
Histology, NSq/Sq, %		60/40	58.1/41.9
Stage at diagnosis, I–III/IV/unknown, %		16.7/80/3.3	14.5/83.9/1.6
Brain metastasis at diagnosis, %		6.7	6.5
Tobacco use status, never/current/former, %		10/33.3/56.7	19.4/35.5/45.2
Exposure duration, median (range), months	SG	5.44 (0.03–23.36)	
	Pembro	4.86 (0.03–23.13)	
Number of cycles, median (range)	SG	8 (1–33)	
	Pembro	7.5 (1–33)	

Efficacy

The median (range) duration of follow-up was 16.6 (8.5–23.8) months, and the median follow-up durations in Cohorts A and B were 17.4 and 16.1 months, respectively. At the data cutoff date (June 3, 2024), 46.7% and 51.6% of patients in Cohorts A and B, respectively, were continuing in the study.[1]

Efficacy outcomes by cohort and by PD-L1 expression and histology are shown in Table 2.[1]

Table 2. EVOKE-02 Cohorts A and B: Efficacy Outcomes Overall and by Histology and PD-L1 Expression[1]

Efficacy Outcomes	Cohort A			Cohort B				
	Overall (n=30)	NSq (n=18)	Sq (n=12)	Overall (n=62)	NSq (n=36)	Sq (n=26)	TPS 1–49% (n=33)	TPS <1% (n=29)
ORR,[a] % (95% CI)	66.7 (47.2–82.7)	66.7 (41–86.7)	66.7 (34.9–90.1)	29 (18.2–41.9)	25 (12.1–42.2)	34.6 (17.2–55.7)	36.4 (20.4–54.9)	20.7 (8–39.7)
CR, n (%)	1 (3.3)	1 (5.6)	0	0	0	0	0	0
PR, n (%)	19 (63.3)	11 (61.1)	8 (66.7)	18 (29)	9 (25)	9 (34.6)	12 (36.4)	6 (20.7)
SD, n (%)	6 (20)	4 (22.2)	2 (16.7)	23 (37.1)	16 (44.4)	7 (26.9)	14 (42.4)	9 (31)
PD, n (%)	3 (10)	1 (5.6)	2 (16.7)	9 (14.5)	4 (11.1)	5 (19.2)	3 (9.1)	6 (20.7)
NE,[b] n (%)	1 (3.3)	1 (5.6)	0	12 (19.4)	7 (19.4)	5 (19.2)	4 (12.1)	8 (27.6)
PFS,[a] median (95% CI), months	13.1 (6.7–NR)	NR (5.5–NR)	10.7 (1.2–NR)	7 (4.2–12.9)	7.4 (4.1–9.7)	7 (2.7–NR)	9.1 (5.4–NR)	4.9 (1.6–9.2)
DOR,[a] median (95% CI), months	NR (9.4–NR)	NR (4.6–NR)	NR (2.4–NR)	11.9 (6.9–NR)	7.9 (2.8–NR)	NR (2.9–NR)	Not available	Not available

Abbreviations: PR=partial response; SD=stable disease.
[a]Assessed by IRC. [b]Included not assessed.

Efficacy by Trop-2 expression

An exploratory analysis evaluated efficacy by Trop-2 expression measured on archival tumor tissue by immunohistochemistry and reported as an H-score of 0 to 300. From Cohorts A and B combined, Trop-2 expression data were available for 67 patients, and H-scores were similar between cohorts (*P*=0.155) and across NSq and Sq histologies (*P*=0.193). There were no differences in H-scores when PD-L1 TPS subgroups were compared: TPS <1% vs 1% to 49% (*P*=0.671); TPS <1% vs ≥50% (*P*=0.203); and TPS 1% to 49% vs ≥50% (*P*=0.317). In the combined cohort analysis population, ORRs by IRC were generally similar between subgroups according to median H-scores (Table 3). Higher Trop-2 expression was associated with numerically higher ORRs in patients with Sq histology relative to those with NSq histology; however, subgroup numbers were small.[1]

Table 3. EVOKE-02 Cohorts A and B (Combined; n=67): ORR per IRC According to Trop-2 Subgroups Overall and by Histology[1]

Parameter	Trop-2	ORR, n/N (%)		
		Overall	NSq	Sq
H-score (median=178)	<Median	11/33 (33.3)	5/17 (29.4)	6/16 (37.5)
	≥Median	12/34 (35.3)	6/21 (28.6)	6/13 (46.2)
I2 + I3 (median=79%)	<50%	8/21 (38.1)	5/12 (41.7)	3/9 (33.3)
	≥50%	15/46 (32.6)	6/26 (23.1)	9/20 (45)
	<75%	10/28 (35.7)	5/15 (33.3)	5/13 (38.5)
	≥75%	13/39 (33.3)	6/23 (26.1)	7/16 (43.8)
I1 + I2 + I3 (median=90%)	<50%	7/18 (38.9)	5/11 (45.5)	2/7 (28.6)
	≥50%	16/49 (32.7)	6/27 (22.2)	10/22 (45.5)
	<75%	10/24 (41.7)	5/11 (45.5)	5/13 (38.5)
	≥75%	13/43 (30.2)	6/27 (22.2)	7/16 (43.8)

Abbreviations: I=intensity score; I1=weak Trop-2 expression; I2=moderate Trop-2 expression; I3=strong Trop-2 expression.
Note: H-score was calculated as follows: I1 + I2 × 2 + I3 × 3. Patients who had 13 weeks of follow-up (defined as [data cutoff date – first dose date + 1]/7) at the time of the data cutoff were included.

PFS by IRC was not significantly different between Trop-2 subgroups according to the median H-score, and PFS according to histology is shown in Table 4.[1]

Table 4. EVOKE-02 Cohorts A and B: PFS per IRC According toTrop-2 Subgroups in Combined Cohorts and by Histology[1,3]

Parameter	Trop-2	PFS, Median (95% CI), Months		
		Cohorts A and B	NSq	Sq
H-score (median=178)	<Median	n=33; 6.9 (5.5–NE)	n=17; 6.9 (5.5–NE)	n=16; NE (1.4–NE)
	≥Median	n=34; 8.48 (4.2–12.9)	n=21; 11.07 (3.4–NE)	n=13; 6.97 (1.2–NE)
	HR (95% CI)	1.165 (0.588–2.31)	0.889 (0.351–2.249)	1.745 (0.626–4.865)

Most patients in each cohort showed a reduction in the best percent change from baseline in the total sum of the target lesion's diameter. There was no association between Trop-2 H-score and the percent change in tumor size in either cohort (A, rs=-0.056; B, rs=-0.182) or in the combined cohorts (A and B, rs=-0.013).[1]

Safety[1]

Any-grade TEAEs were reported for all patients in the safety analysis set (patients who received ≥1 dose of any study drug; Table 5). The most common any-grade TEAEs were diarrhea (53.3%), anemia (46.7%), and alopecia (41.3%). Immune-mediated TEAEs that occurred in >1 patient were pneumonitis (8.7%), hyperthyroidism (3.3%), colitis (3.3%), and myocarditis (2.2%). Additional TEAE data are summarized in Table 6.

Table 5. EVOKE-02 Cohorts A and B (Combined): Summary of Safety[1]

Outcomes, n (%)	Cohorts A and B (N=92)
Any-grade TEAEs	92 (100)
Grade ≥3 TEAEs	70 (76.1)
TEAEs related to any study drug	84 (91.3)
Grade ≥3 TEAEs related to any study drug	42 (45.7)
Serious TEAEs	58 (63)
Serious TEAEs related to any study drug	19 (20.7)
TEAEs that led to discontinuation of any study drug	25 (27.2)
TEAEs that led to discontinuation of SG	22 (23.9)
TEAEs that led to discontinuation of pembro	21 (22.8)
TEAEs that led to SG dose reduction	16 (17.4)
TEAEs that led to dose interruptions of any study drug	65 (70.7)
TEAEs that led to dose interruption of SG	64 (69.6)
TEAEs that led to dose interruption of pembro	51 (55.4)
TEAEs that led to death	8 (8.7)
TEAEs related to any study drug that led to death	3 (3.3)[a]

[a]Neutropenic sepsis, n=2; sepsis, n=1.

Table 6. EVOKE-02 Cohorts A and B: Grade 1–2 (≥20%), Grade ≥3 (≥5%), and Immune-Mediated TEAEs[1]

TEAEs, %	Grade 1–2	Grade ≥3
Diarrhea	45.7	7.6
Anemia	42.4	4.3
Alopecia	41.3	0
Asthenia	30.4	1.1
Nausea	30.4	1.1
Constipation	23.9	0

TEAEs, %		Grade 1–2	Grade ≥3
Decreased appetite		22.8	4.3
Fatigue		22.8	3.3
Decreased weight		21.7	2.2
Cough		21.7	0
Respiratory tract infection		17.4	5.4
Dyspnea		12	5.4
Neutropenia		10.9	17.4
Decreased neutrophil count		4.3	9.8
Pneumonia		3.3	10.9
Immune-mediated	Pneumonitis	5.4	3.3
	Hyperthyroidism	3.3	0
	Colitis	2.2	1.1
	Myocarditis	1.1	1.1

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%.

References

1. Reck M, Patel JD, Gray JE, et al. First-line sacituzumab govitecan plus pembrolizumab in metastatic NSCLC: PD-L1 TPS <50% and ≥50% cohorts of the EVOKE-02 study [Published online ahead of print October 29, 2025]. *J Thorac Oncol.* 2025;30:S1556-0864(25)02890-4. https://www.ncbi.nlm.nih.gov/pubmed/41173143
2. 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.
3. Reck M, Patel JD, Gray JE, et al. First-line sacituzumab govitecan plus pembrolizumab in metastatic NSCLC: PD-L1 TPS <50% and ≥50% cohorts of the EVOKE-02 study [Supplementary Materials]. *J Thorac Oncol.* 2025;30:S1556-0864(25)02890-4. https://www.ncbi.nlm.nih.gov/pubmed/41173143

Abbreviations

1L=first line
AGA=actionable genomic alteration
CR=complete response
DOR=duration of response
H-score=histochemical score
HR=hazard ratio
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
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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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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