Sacituzumab Govitecan + Pembrolizumab in First-Line Metastatic Non-Small Cell Lung Cancer With PD-L1 ≥50%: Cohort A of EVOKE-02

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Conclusions

- In Cohort A of EVOKE-02, sacituzumab govitecan (SG) + pembrolizumab (pembro) showed promising activity in patients with squamous and nonsquamous histology with previously untreated metastatic non-small cell lung cancer (mNSCLC) and a programmed death-ligand 1 (PD-L1) tumor proportion score (TPS) ≥50%
  - Objective response rate was 66.7%, median duration of response was not reached, and median (95% CI) progression-free survival was 13.1 (5.5–NR) months
  - Consistent efficacy was seen across histology
- The safety profile of SG + pembro was manageable and consistent with the known safety profiles for each agent
  - The frequencies and types of immune-mediated TEAEs were consistent with the known safety profile of pembro
- These results support the approach of the ongoing phase 3 EVOKE-03 study, which is comparing the efficacy and safety of SG + pembro versus pembro alone in patients with PD-L1 TPS ≥50% squamous or nonsquamous mNSCLC

Plain Language Summary

Many patients with non-small cell lung cancer (NSCLC) that has spread throughout their body are first treated with a drug called pembrolizumab with or without chemotherapy. In many patients, their cancer continues to progress. Recently, researchers found that the drug sacituzumab govitecan when combined with pembrolizumab had promising activity in patients with NSCLC. Lung cancer tumor cells may have a protein known as PD-L1, which allows the cells to respond to pembrolizumab. Here, we report that combination treatment with sacituzumab govitecan plus pembrolizumab was effective at reducing the size or number of tumors in patients with NSCLC whose cancer cells have high levels of PD-L1. This drug combination had manageable safety, and no unexpected adverse events were seen.

References:

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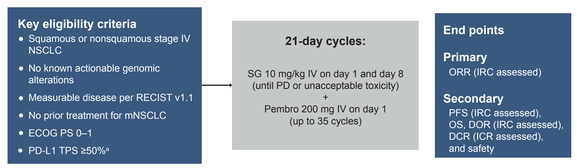
Introduction

- Pembrolizumab (pembro) ± chemotherapy is a standard first-line (1L) treatment option for patients with advanced or metatstatic non-small cell lung cancer (mNSCLC) whose tumors lack any actionable genomic alterations[1]; however, in many patients, the disease does not respond to initial treatment[2]
  - Patients treated with immunotherapy, such as pembro, in combination with chemotherapy in 1L advanced NSCLC demonstrated response rates between 43% and 63% and a median overall survival (OS) of 14.1 to 22.0 months and patients who's tumors had PD-L1 tumor proportion score (TPS) ≥50% had a 24-month OS rate of 52%[3,4]
  - Novel therapies building on the current standard of care should continue to be evaluated
- Sacituzumab govitecan (SG) is a first-in-class, Trop-2–directed, antibody-drug conjugate being investigated as a treatment for mNSCLC in 1L and second-line settings
- EVOKE-02 (NCT05186974) is an open-label, global, multicenter, multicohort, phase 2 study assessing 1L treatment with SG + pembro ± chemotherapy in patients with mNSCLC without actionable genomic alterations, irrespective of programmed death-ligand 1 (PD-L1) expression
- Preliminary data from EVOKE-02 showed that SG + pembro has promising activity in both squamous and nonsquamous histologies[5]
- Here, we report results of Cohort A of EVOKE-02: the efficacy and safety of SG + pembro in patients with mNSCLC whose tumors have a PD-L1 TPS ≥50%

Methods

- To be eligible for Cohort A, patients had to have previously untreated squamous or nonsquamous mNSCLC with no known actionable genomic alterations and a PD-L1 TPS ≥50%

Figure 1. EVOKE-02 Cohort A Study Design



[a]PD-L1 status was determined locally or at the central laboratory by 22C3 assay.
DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IRC, independent review committee; IV, intravenous; ORR, objective response rate; PD, progressive disease; PFS, progression-free survival; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

Results

Patients

- As of December 1, 2023, 30 patients were enrolled in Cohort A (**Table 1**)
- The median duration of follow-up was 11.3 (range, 8.4–17.5) months
- The median duration of exposure to SG and pembro was 7.43 (range, 0.03–16.69) months and 7.18 (range, 0.03–16.69) months, respectively

Table 1. Patient Demographics and Baseline Characteristics

	Overall (N = 30)
Median age, years (range)	67 (47–77)
Male, n (%)	24 (80.0)
Race, n (%)	
White	22 (73.3)
Asian	6 (20.0)
Black	2 (6.7)
ECOG PS, n (%)	
0	6 (20.0)
1	24 (80.0)
Histology, n (%)	
Squamous	12 (40.0)
Nonsquamous	18 (60.0)
Disease stage at diagnosis, n (%)	
I	3 (10.0)
II	0
III	2 (6.7)
IV	24 (80.0)
Unknown	1 (3.3)

Results (cont.)

Efficacy

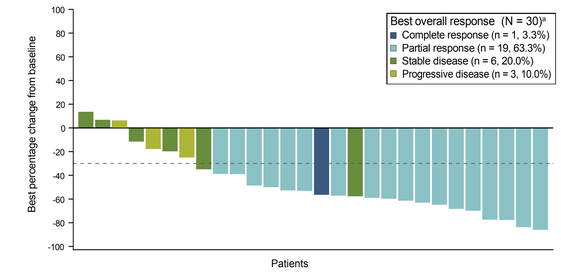
- The overall ORR per IRC assessment was 66.7% (95% confidence interval [CI], 47.2–82.7%), with 1 complete response and 19 partial responses (**Table 2**)
- The ORR was 66.7% both in patients with squamous and nonsquamous histology
- A majority of patients had reduction in total sum of target lesion diameters (**Figure 2**)

Table 2. Efficacy of SG + Pembro in Patients With PD-L1 TPS ≥50% mNSCLC

	Overall (N = 30)	Squamous mNSCLC (n = 12)	Nonsquamous mNSCLC (n = 18)
ORR, n (%) [95% CI]	20 (66.7) [47.2–82.7]	8 (66.7) [34.9–90.1]	12 (66.7) [41.0–86.7]
CR	1 (3.3)	0	1 (5.6)
PR	19 (63.3)	8 (66.7)	11 (61.1)
SD	6 (20.0)	2 (16.7)	4 (22.2)
PD	3 (10.0)	2 (16.7)	1 (5.6)
NE	1 (3.3)	0	1 (5.6)
Median PFS, months (95% CI)	13.1 (5.5–NR)	NR (1.2–NR)	13.1 (5.5–NR)
12-month PFS rate, % (95% CI)	57.2 (35.6–73.9)	58.3 (21.2–82.9)	56.3 (29.3–76.4)
Median DOR, n months (95% CI)	20 NR (8.5–NR)	8 NR (2.4–NR)	12 NR (4.6–NR)
12-month DOR rate, % (95% CI)	59.3 (27.4–81.0)	75.0 (31.5–93.1)	56.6 (19.7–81.9)
DCR,[a] n (%) [95% CI]	26 (86.7) [69.3–96.2]	10 (83.3) [51.6–97.9]	16 (88.9) [65.3–98.6]

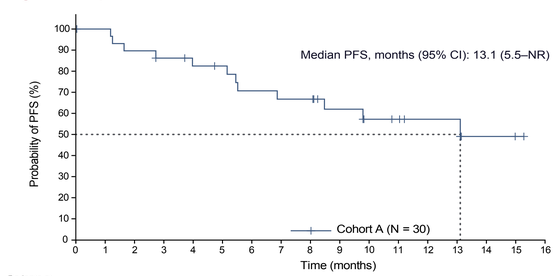
Efficacy end points were per RECIST v1.1 criteria, as confirmed by independent review committee.
[a]Defined as the proportion of patients with CR, PR, or SD for ≥6 weeks.
CR, complete response; DCR, disease control rate; NE, not evaluable; NR, not reached; PR, partial response; SD, stable disease.

Figure 2. Best Percentage Change From Baseline in Total Sum of Target Lesion Diameters



Per RECIST v1.1 criteria, as assessed by independent review committee.
[a]One patient with partial response and one patient who was not evaluable were not included in the plot.
The dotted line represents 30% reduction.

Figure 3. Kaplan-Meier Estimates of PFS



The dotted line represents the median PFS.

Safety

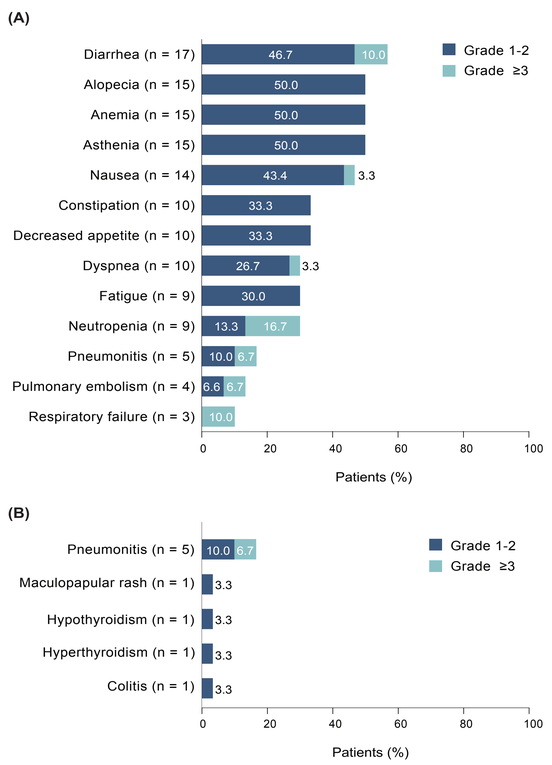
Table 3. Safety Summary

	Overall (N = 30)
Any-grade TEAE, n (%)	30 (100.0)
Treatment-related	29 (96.7)
Grade ≥3 TEAE, n (%)	20 (66.7)
Treatment-related	12 (40.0)
Serious AE, n (%)	15 (50.0)
Treatment-related	5 (16.7)
TEAE leading to dose reduction for SG, n (%)	6 (20.0)
TEAE leading to discontinuation of either study drug, n (%)	6 (20.0)
TEAE leading to discontinuation of SG	5 (16.7)
TEAE leading to discontinuation of pembro	6 (20.0)
TEAE leading to death, n (%)	1 (3.3)[a]
Treatment-related	1 (3.3)[a]

[a]One patient died owing to treatment-related neutropenic sepsis.
AE, adverse event.

- The most common TEAEs of any grade and grade ≥3 are presented in **Figure 4A**
- Immune-mediated TEAEs of any grade are presented in **Figure 4B**

Figure 4. Safety Summary



(A) Most common any-grade (reported in ≥30% of patients) TEAEs and grade ≥3 (reported in ≥5% of patients) TEAEs.
(B) Immune-mediated TEAEs (no patients had a TEAE of nephritis).