Sacituzumab govitecan + pembrolizumab in first-line metastatic non-small cell lung cancer: efficacy results by histology from the EVOKE-02 study

Federico Cappuzzo,[1] Jyoti Patel,[2] Byoung Chul Cho,[3] Manuel Cobo Dols,[4] Roxana Reyes Cabanillas,[5] David Vicente Baz,[6] Jose Fuentes Pradera,[7] Joel Neal,[8] Edward Garon,[9] Sabeen Mekan,[10] Farnoush Safavi,[10] Nelumka Fernando,[10] Michael Chisamore,[11] Martin Reck[12]

[1]Regina Elena Institute for Cancer Research, Rome, Italy; [2]Northwestern University Feinberg School of Medicine, Chicago, IL, USA; [3]Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea; [4]Regional and Virgen de la Victoria University Hospitals, IBIMA, Malaga, Spain; [5]Hospital Clinic de Barcelona, Barcelona, Spain; [6]Hospital Universitario Virgen Macarena, Seville, Spain; [7]Hospital Universitario Virgen de Valme, Seville, Spain; [8]Stanford Cancer Center, Stanford, CA, USA; [9]University of California Los Angeles, Los Angeles, CA, USA; [10]Gilead Sciences, Inc, Foster City, CA, USA; [11]Merck & Co., Inc., Rahway, NJ, USA; [12]Airway Research Center North, German Center for Lung Research (DZL), LungenClinic, Grosshansdorf, Germany

Conclusions

- In EVOKE-02, sacituzumab govitecan (SG) + pembrolizumab (pembro) showed promising activity regardless of histology (squamous or nonsquamous) in patients with previously untreated metastatic non-small cell lung cancer (mNSCLC) across programmed death ligand 1 (PD-L1) subgroups (PD-L1 tumor proportion score [TPS] <50% and ≥50%)
  - Within each PD-L1 subgroup, the unconfirmed objective response rates (ORRs) were numerically higher in patients with squamous vs nonsquamous mNSCLC
- The safety profile of SG + pembro was acceptable and consistent with the known safety profiles for each agent[1,2]
  - The rate of treatment-emergent adverse events (TEAEs) leading to treatment discontinuations was 17.5%
  - 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 to pembro alone in the treatment of patients with mNSCLC (squamous or nonsquamous) with PD-L1 TPS ≥50%

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, but in many patients this does not shrink their tumors. Recently, researchers showed that a new drug, sacituzumab govitecan, was effective at shrinking cancer masses when combined with pembrolizumab in treating patients with NSCLC. Lung cancers can form from different tissues, and in NSCLC, doctors classify them as squamous and nonsquamous. Patients with squamous NSCLC have shorter survival times than those with nonsquamous NSCLC. We report that sacituzumab govitecan plus pembrolizumab was effective at reducing the size or number of cancer lesions in patients with NSCLC, regardless of tissue type. This drug combination was also well tolerated and no unexpected adverse events were seen.

References: **1.** Michaleas S, et al. *ESMO Open*. 2022;7(3):100497. **2.** Sul J, et al. *Oncologist*. 2016;21:643-650. **3.** Ettinger DS, et al. *J Natl Compr Canc Netw*. 2021;19(3):254-266. **4.** Li H, et al. *Cancers*. 2024;16(4):744. **5.** Goldenberg DM, et al. *Oncotarget*. 2015;6:22496-22512. **6.** Cho BC, et al. Presented at WCLC; Sept 9-12, 2023; Singapore. **7.** Singal G, et al. *JAMA*. 2019; 321(14):1391-1399.

Acknowledgments: This study was funded by Gilead Sciences, Inc, Foster City, CA, USA. This study is in collaboration with Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA. Medical writing support for the development of this poster, under the direction of the authors, was provided by Jan Nagel, PhD, of Ashfield MedComms, an Inizio company, and funded by Gilead Sciences, Inc. Editorial and design support were provided by Ashfield MedComms and funded by Gilead Sciences, Inc.

Disclosures: FC: Roche.

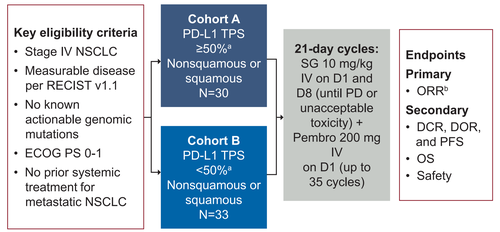
Correspondence: Federico Cappuzzo: f.cappuzzo@gmail.com

Introduction

- Pembro ± chemotherapy is a standard-of-care frontline (1L) treatment option for patients with mNSCLC and without actionable genomic mutations[3]; however, the disease does not respond to initial treatment for many patients[4]
- SG is a first-in-class Trop-2–directed antibody-drug conjugate[5]
- SG is being evaluated in the EVOKE-02 study (NCT05186974), which is an ongoing, multicenter, phase 2 trial with 4 cohorts; 2 of the cohorts (Cohorts A and B) are assessing the efficacy and safety of SG + pembro as 1L therapy in patients with squamous or nonsquamous mNSCLC without actionable genomic mutations
- Preliminary results for Cohorts A and B of EVOKE-02 demonstrated encouraging response rates and duration of response (DOR)[6]
  - Among patients with PD-L1 tumor proportion score (TPS) ≥50% (Cohort A), the ORR was 69%, the disease control rate (DCR) was 78%, and the median DOR was not reached
  - Among patients with PD-L1 TPS <50% (Cohort B), the ORR was 44%, the DCR was 78%, and the median DOR was not reached
- NSCLC prognosis can be influenced by histology; patients with squamous histology have a shorter median overall survival than patients with nonsquamous histology[7]
- Therefore, we conducted this analysis of EVOKE-02 to examine efficacy by histology (squamous vs nonsquamous) and present safety results from Cohorts A and B

Methods

Figure 1. EVOKE-02 Cohorts A and B study design



[a]PD-L1 status was determined locally or at the central laboratory by 22C3 assay prior to initiating treatment. [b]Per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1).
D1, day 1; D8, day 8; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; OS, overall survival; PD, progressive disease; PFS, progression-free survival.

- For this analysis, response was assessed by investigators in efficacy-evaluable patients (those with ≥13 weeks of follow-up as of the data cutoff date)

Results

Patient Baseline Characteristics

- As of June 16, 2023, 30 patients in Cohort A and 33 patients in Cohort B were enrolled (**Table 1**)
- Across both cohorts, 25 (39.7%) patients had squamous mNSCLC and 38 (60.3%) patients had nonsquamous mNSCLC

Efficacy

- In Cohort A, the unconfirmed ORR was 72.7% (8/11) in patients with squamous mNSCLC and 66.7% (12/18) in patients with nonsquamous mNSCLC
- In Cohort B, the unconfirmed ORR was 53.8% (7/13) and 36.8% (7/19), respectively, in patients with squamous and nonsquamous mNSCLC (**Table 2**)
- Median DOR was not reached in either cohort

Table 1. Patient Demographics and Baseline Characteristics

Characteristic	Cohort A PD-L1 TPS ≥50% (n=30)	Cohort B PD-L1 TPS <50% (n=33)
Median age (range), years	67 (47-77)	68 (47-80)
Sex, n (%)		
Male	24 (80.0)	26 (78.8)
Race, n (%)		
Asian	6 (20.0)	5 (15.2)
Black	2 (6.7)	1 (3.0)
White	22 (73.3)	27 (81.8)
ECOG PS, n (%)		
0	6 (20.0)	8 (24.2)
1	24 (80.0)	25 (75.8)
Histology, n (%)		
Squamous	12 (40.0)	13 (39.4)
Nonsquamous	18 (60.0)	20 (60.6)
Disease stage at diagnosis, n (%)		
I-III	5 (16.7)	5 (15.2)
IV	24 (80.0)	28 (84.8)
PD-L1 TPS, n (%)		
≥50%	30 (100.0)	0
1-49%	0	16 (48.5)
<1%	0	17 (51.5)

Table 2. Response rates for frontline SG + pembro among patients with squamous and nonsquamous mNSCLC

Efficacy by investigator assessment	Squamous mNSCLC		Nonsquamous mNSCLC	
	Cohort A PD-L1 TPS ≥50% (n=11)	Cohort B PD-L1 TPS <50% (n=13)	Cohort A PD-L1 TPS ≥50% (n=18)	Cohort B PD-L1 TPS <50% (n=19)
ORR,[a] n (%)	**8 (72.7)**	**7 (53.8)**	**12 (66.7)**	**7 (36.8)**
95% CI	39.0-94.0	25.1-80.8	41.0-86.7	16.3-61.6
Best overall response,[a] n (%)				
PR	8 (72.7)	7 (53.8)	12 (66.7)	7 (36.8)
Confirmed PR	7 (63.6)	6 (46.2)	11 (61.1)	6 (31.6)
SD	1 (9.1)	4 (30.8)	4 (22.2)	7 (36.8)
PD	2 (18.2)	0	1 (5.6)	2 (10.5)
Not assessed	0	2 (15.4)	1 (5.6)	3 (15.8)
DCR,[b] n (%) [95% CI]	9 (81.8) [48.2-97.7]	11 (84.6) [54.6-98.1]	16 (88.9) [65.3-98.6]	14 (73.7) [48.8-90.9]

[a]Unconfirmed responses per RECIST v1.1, except where otherwise stated. [b]Complete response + PR + SD (for ≥6 weeks if confirmed).
CI, confidence interval; PR, partial response; SD, stable disease.

Safety Summary

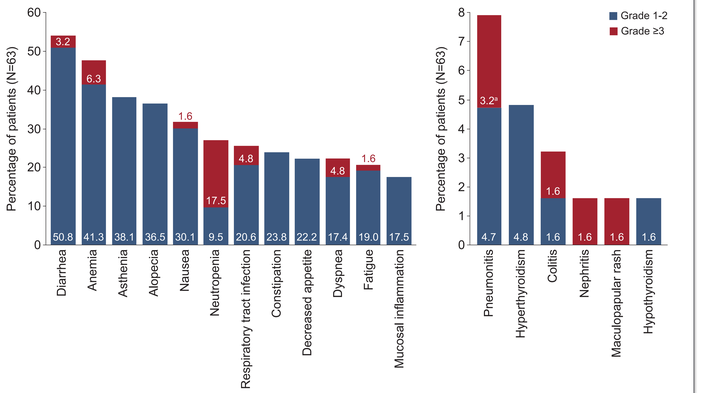
- An overview of treatment-emergent adverse events (TEAEs) in the safety population (N=63) is shown in **Table 3**
- The rate of TEAEs leading to treatment discontinuation was 17.5%
- Four patients (6.3%; all in Cohort B) had a TEAE that led to death: sudden death, respiratory tract infection, sepsis (treatment-related), and malignant lung neoplasm
- The most common (≥15%) TEAEs are shown in **Figure 2A**; immune-mediated TEAEs are shown in **Figure 2B**

Table 3. Safety summary

Patients, n (%)	Safety population (N=63)
Any-grade TEAE	63 (100)
Grade ≥3 TEAE	44 (69.8)
TEAE related[a] to any study drug	57 (90.5)
Serious TEAEs	34 (54.0)
TEAE leading to discontinuation of any study drug	11 (17.5)
TEAE leading to discontinuation of SG	9 (14.3)
TEAE leading to discontinuation of pembro	8 (12.7)
TEAE leading to death	4 (6.3)
Related to any study drug[a,b]	1 (1.6)

[a]Investigator-assessed; [b]Sepsis.

Figure 2. Treatment-emergent adverse events. A) Any-grade TEAEs in ≥15% of patients. B) Immune-mediated TEAEs



[a]Grade ≥3 pneumonitis occurred in 2 patients (3.2%), and both events were grade 3.