Long-Term Safety Profile of Sacituzumab Govitecan vs Docetaxel in Patients With Metastatic Non–Small Cell Lung Cancer From EVOKE-01

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EVOKE-01

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Conclusions

- In this longer follow-up analysis of the EVOKE-01 study, SG had a manageable safety profile in patients with mNSCLC who progressed after platinum-based chemotherapy and anti–PD-(L)1 therapy
- The results of this analysis indicate that >90% of patients were able to recover from TEAEs and <1% of patients treated with SG required treatment discontinuation due to any of the top 10 TEAEs
- Even with longer duration of exposure, SG continued to be better tolerated than docetaxel
  - Consistent with the final analysis, occurrence of grade ≥3 TEAEs, TEAEs leading to dose reductions, and TEAEs leading to discontinuations were lower with SG vs docetaxel
  - No new treatment-related deaths were reported in either treatment arm since the prior results
  - Any-grade and grade ≥3 neutropenia were more common with docetaxel
  - Diarrhea, alopecia, and nausea were more common with SG than with docetaxel, but most cases were not severe
- SG is being investigated in combination with pembrolizumab as a first-line therapy in patients with PD-L1 expression ≥50% in a randomized phase 3 trial (EVOKE-03, NCT05609968)

Plain Language Summary

- People with NSCLC that has spread throughout their body and did not get better after chemotherapy containing platinum and immunotherapy often do not have many good treatment choices
- The treatments that are available can cause side effects that make people feel worse during their everyday life
- The EVOKE-01 study looked at 2 medicines, SG and docetaxel, to treat NSCLC that got worse after earlier treatment
- The results of this study were previously shared, but now we are presenting newer information after following patients for nearly 2 years
- Overall, patients stayed on treatment with SG longer than docetaxel and had fewer severe side effects
- Patients receiving SG had more cases of diarrhea, hair loss, and nausea, while patients receiving docetaxel had more cases of low white blood cells

Introduction

- Patients with metastatic non–small cell lung cancer (mNSCLC) progressing after platinum-based chemotherapy with or without immunotherapy have poor prognoses, and available treatment options are associated with significant adverse events (AEs) affecting patient quality of life[1-4]
- The phase 3 EVOKE-01 (NCT05089734) study compared sacituzumab govitecan (SG) vs docetaxel in patients with mNSCLC who progressed after platinum-based chemotherapy and anti–programmed cell death protein (ligand) 1 (PD-[L]1) therapy[5]
  - At final analysis (clinical cutoff date: 29 November 2023), the study did not meet statistical significance for overall survival; however, with a median follow-up of 12.7 months, SG had a tolerable safety profile
- Here, we analyze safety with longer follow-up to provide insight into the tolerability and management of treatment-emergent adverse events (TEAEs) in patients treated with SG from EVOKE-01
- The safety profile of SG will be assessed in combination with pembrolizumab as first-line therapy for mNSCLC in the phase 3 EVOKE-03 study

References: **1.** Borghaei H, et al. *Ann Oncol*. 2024;35:66-76. **2.** Neal J, et al. *J Thorac Oncol*. 2023;41:S39-S40. **3.** Paz-Ares LG, et al. *Ann Oncol*. 2021:32:S953-S954. **4.** Ahn M, et al. *Ann Oncol*. 2023;34:S1661-S1706. **5.** Paz-Ares LG, et al. *J Clin Oncol*. 2024;42:2860-2872.

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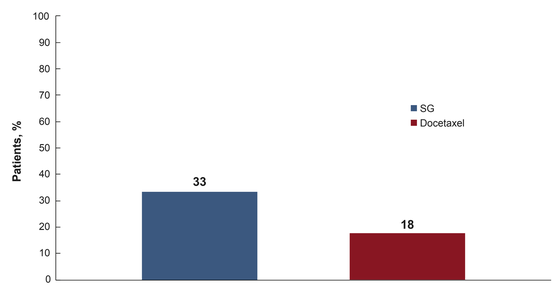
Methods

- Patients (age ≥18 years) with stage IV NSCLC that progressed after platinum-based chemotherapy and anti–PD-(L)1–containing therapy were randomly assigned (1:1) to receive either SG (n = 299; 10 mg/kg intravenously [IV], days 1 and 8) or docetaxel (n = 304; 75 mg/m^2 IV, day 1) in 21-day cycles until progression or unacceptable toxicity
  - Safety was a key secondary end point
- Safety was assessed in the safety population, which included all treated patients and was analyzed using a longer follow-up period (clinical cutoff date: 21 October 2024)
- AEs were coded according to Medical Dictionary for Regulatory Activities, version 27.0, and severity grades were defined by the Common Terminology Criteria for Adverse Events, version 5.0

Results

- The median study follow-up was 23.5 months (range, 16.8–34.8) and the study was ongoing in 64 and 56 patients in the SG and docetaxel arms, respectively
- The safety population included 584 patients with 296 patients in the SG arm and 288 patients in the docetaxel arm
- The median (range) duration of treatment exposure was 3.5 (0.0–29.5) months in the SG arm vs 2.3 (0.0–23.2) months in the docetaxel arm
- Patients treated with SG received a median (range) of 5.0 (1.0–43.0) cycles of treatment compared with 4.0 (1.0–34.0) cycles with docetaxel
- Among patients in the SG arm, 99 (33%) had a treatment exposure duration of ≥6 months vs 51 patients (18%) in the docetaxel arm (**Figure 1**)

Figure 1. Treatment Exposure for ≥6 Months



SG, sacituzumab govitecan.

- Overall, the safety results in this longer follow-up population (**Table 1**) resembled those in the final analysis population
  - Any-grade TEAEs and serious TEAEs occurred at a similar frequency in the SG (>99% and 48%, respectively) and docetaxel (98% and 44%, respectively) arms
  - Patients in the SG arm had a lower incidence of grade ≥3 TEAEs (69% vs 76%) and any-grade TEAEs leading to dose reduction (30% vs 39%) and discontinuation (10% vs 17%) than those in the docetaxel arm
  - No additional treatment-related TEAEs leading to death occurred in this population compared with the final analysis population

Table 1. Safety Summary

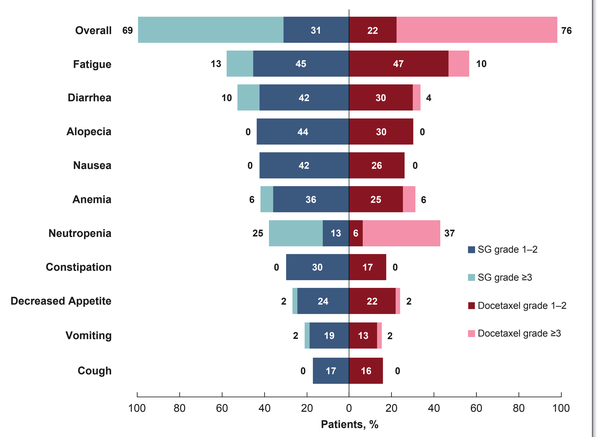
TEAEs, n (%)	SG (n = 296)	Docetaxel (n = 288)
Any grade	295 (>99)	283 (98)
Treatment related	279 (94)	263 (91)
Grade ≥3	203 (69)	219 (76)
Treatment related	159 (54)	173 (60)
Serious	141 (48)	128 (44)
Treatment related	75 (25)	60 (21)
Leading to dose reduction	88 (30)	113 (39)
Leading to discontinuation	30 (10)	48 (17)
Treatment related	22 (7)	41 (14)
Leading to death	10 (3)	12 (4)[a]
Treatment related	4 (1)	3 (1)

[a]This includes 1 less patient than reported in the final analysis, because of "death" being updated to "disease progression."
SG, sacituzumab govitecan; TEAE, treatment-emergent adverse event.

- Fatigue was the most common TEAE, and rates were comparable for SG (58%) and docetaxel (57%) (**Figure 2**)
  - Grade ≥3 fatigue was slightly higher with SG (13%) than with docetaxel (10%)
- Diarrhea was more common with SG (53%) than with docetaxel (34%)
  - Most cases were grade 1–2, and grade ≥3 diarrhea occurred in 10% and 4% of patients in the SG and docetaxel arms, respectively
- Percentages of patients with any-grade and grade ≥3 neutropenia were lower with SG (38% and 25%) than with docetaxel (43% and 37%)
- Alopecia and nausea were more frequent with SG (44% and 42%) than with docetaxel (30% and 26%); >98% of cases were grade 1–2

Results (continued)

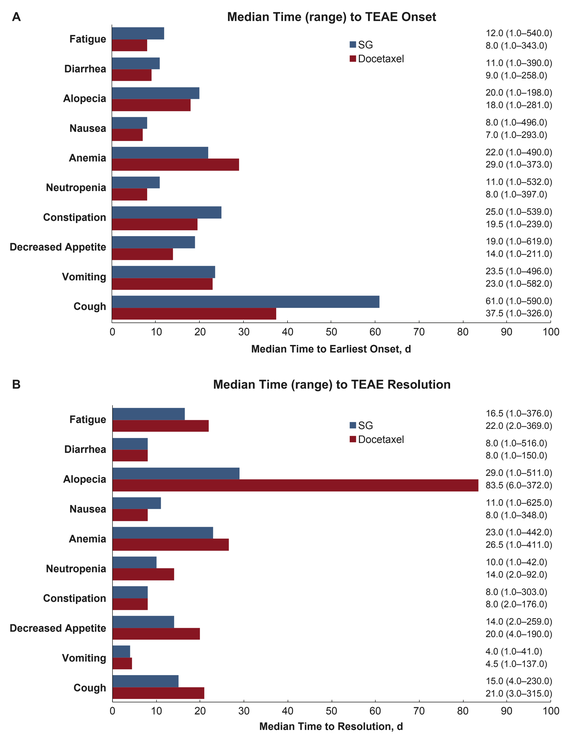
Figure 2. Ten Most Common TEAEs



SG, sacituzumab govitecan; TEAE, treatment-emergent adverse event.

- Time to the earliest onset of the 10 most frequent TEAEs was generally longer with SG vs docetaxel (**Figure 3A**)
  - Median time to earliest onset of anemia was shorter with SG (22.0 days) than with docetaxel (29.0 days)
  - Median time to earliest onset of neutropenia (SG: 11.0 days; docetaxel: 8.0 days) and diarrhea (SG: 11.0 days; docetaxel: 9.0 days) was comparable between treatment arms
  - Median time to earliest onset of cough was 61.0 days with SG vs 37.5 days with docetaxel
- Time to resolution of the first occurrence of TEAEs was shorter with SG than with docetaxel, or similar between treatment arms (**Figure 3B**)
  - Median time to resolution of alopecia was notably shorter with SG (29.0 days) than with docetaxel (83.5 days)

Figure 3. Time to TEAE Onset and Resolution



Time to earliest TEAE onset was defined as the number of days from first study drug administration to the first occurrence of the specific TEAE. Time to resolution of TEAE was defined as the number of days from the first occurrence of the specific TEAE to its resolution.
SG, sacituzumab govitecan; TEAE, treatment-emergent adverse event.

- Among the 10 most frequent TEAEs, required dose reductions were similar in both treatment arms, except for diarrhea (SG vs docetaxel: 6% vs 2%) and neutropenia (SG vs docetaxel: 6% vs 13%) (**Table 2**)
  - Furthermore, interruption of SG vs docetaxel was more common with fatigue (9% vs 4%), diarrhea (6% vs 1%), anemia (6% vs 1%), and neutropenia (22% vs 1%)
  - Drug discontinuation rates due to TEAEs were ≤1% across both arms, except for fatigue (2% with docetaxel)

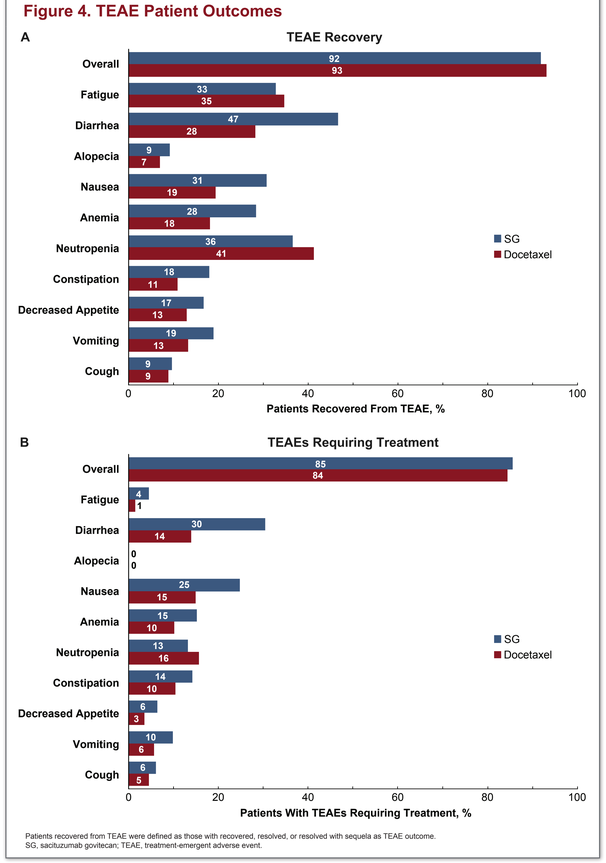
Table 2. Dose Modification Due to TEAEs

TEAEs, n (%)	Dose Reduction		Drug Interruption		Drug Discontinuation	
	SG	Docetaxel	SG	Docetaxel	SG	Docetaxel
Fatigue	22 (7)	23 (8)	26 (9)	11 (4)	<1	7 (2)
Diarrhea	19 (6)	7 (2)	18 (6)	2 (1)	<1	3 (1)
Alopecia	<1	<1	<1	<1	0	0
Nausea	4 (1)	7 (2)	5 (2)	<1	<1	<1
Anemia	2 (1)	7 (2)	17 (6)	2 (1)	0	<1
Neutropenia	18 (6)	37 (13)	64 (22)	4 (1)	<1	3 (1)
Constipation	<1	<1	<1	<1	0	0
Decreased appetite	3 (1)	4 (1)	8 (3)	3 (1)	0	<1
Vomiting	<1	<1	5 (2)	3 (1)	0	0
Cough	<1	<1	<1	<1	0	0

SG, sacituzumab govitecan; TEAE, treatment-emergent adverse event.

- Overall, similar numbers of patients recovered from TEAEs (92% and 93%) and required treatment due to TEAEs (86% and 84%) with SG and docetaxel (**Figure 4**)
  - More patients required treatment for diarrhea (30% vs 14%), nausea (25% vs 15%), and anemia (15% vs 10%) with SG vs docetaxel
  - However, the recovery rate of these TEAEs was higher with SG than with docetaxel: diarrhea, 47% vs 28%; nausea, 31% vs 19%; and anemia, 28% vs 18%

Figure 4. TEAE Patient Outcomes



Patients recovered from TEAE were defined as those with recovered, resolved, or resolved with sequela as TEAE outcome.
SG, sacituzumab govitecan; TEAE, treatment-emergent adverse event.