Patient-Reported Outcomes (PROs) from the Phase 3 EVOKE-01 Trial of Sacituzumab Govitecan (SG) vs Docetaxel (Doc) in Metastatic Non-Small Cell Lung Cancer (mNSCLC)

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EVOKE-01

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Conclusions

- The PRO analyses showed that treatment with SG significantly and meaningfully improved lung cancer-related symptoms, particularly dyspnea and fatigue, and role functioning at week 25 compared with Doc.
- SG delayed deterioration of shortness of breath, fatigue, and overall symptoms as measured by the NSCLC-SAQ when compared with Doc.
- A worsening in diarrhea and nausea/vomiting was observed with SG compared to Doc, which is consistent with the known safety profile of SG.
- These data further support the clinical observation that SG is an active agent in the treatment of metastatic NSCLC.

Plain Language Summary

- SG is an active and tolerable treatment option for patients with previously treated metastatic NSCLC.
- In this analysis, we compared disease-related symptoms and treatment impacts between patients with lung cancer who were treated with SG and those who were treated with Doc.
- The results showed that patients treated with SG experienced improvements and delayed worsening in lung cancer symptoms, such as shortness of breath and fatigue, compared to those treated with Doc.
- Patients treated with SG experienced increased diarrhea and nausea/vomiting, both of which are known side effects of SG.
- Overall, these findings suggest that SG has the potential to improve symptoms and quality of life relative to Doc when treating advanced or metastatic NSCLC.

Introduction

- Treatment options are limited for patients with metastatic non-small cell lung cancer (NSCLC) after progression on platinum-based chemotherapy,[1] and outcomes with current standard-of-care docetaxel (Doc) are suboptimal.[2,3]
- In the phase 3 EVOKE-01 trial (NCT05089734), sacituzumab govitecan (SG), a trophoblast cell-surface antigen 2-directed antibody-drug conjugate, was compared with Doc in patients with metastatic NSCLC previously treated with platinum-based chemotherapy and PD(L)-1 inhibitors.[4]
  - SG showed numerical but not statistically significant improvement in overall survival (primary endpoint; median 11.1 vs 9.8 months) and better tolerability compared with Doc.
- To complement these clinical data, health-related quality of life (HRQoL) data are needed to evaluate patient-perceived treatment effect and tolerability of SG.
- In this analysis, we compared the effect of SG versus Doc on patient-reported outcomes (PROs) from EVOKE-01.

Methods

- In EVOKE-01, patients (age ≥18 years) with stage IV NSCLC who progressed on a platinum-based and anti-PD-(L)1–containing regimen were randomized 1:1 to SG (10 mg/kg IV, days 1 and 8) or Doc (75 mg/m^2 IV, day 1) in 21-day cycles until progression or unacceptable toxicity.
- PROs were assessed as secondary and exploratory endpoints with the NSCLC Symptom Assessment Questionnaire (NSCLC-SAQ) and European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30).
  - Primary domains of interest included NSCLC-SAQ shortness of breath and total score.
- Patients completed questionnaires on day 1 of each cycle before dosing and at the end of treatment.
- All analyses included the intent-to-treat (ITT) population, defined as all randomized patients.
- Time to first meaningful deterioration in each PRO domain from baseline or death and time to confirmed deterioration from baseline in each PRO domain were assessed.
  - A confirmed deterioration was defined as a meaningful deterioration confirmed at the following scheduled visit or by a death within 21 days after onset of deterioration.
    - For the NSCLC-SAQ, thresholds of meaningful within-patient changes used to define a deterioration were an increase of 2 points for the total score and 1 point for other domains.
    - For each EORTC QLQ-C30 domain, the meaningfulness of within-patient changes was interpreted based on published thresholds.[5,6]
  - Patients without baseline or any post-baseline assessment or with a baseline score too poor to deteriorate further were censored at randomization, and those who did not experience any worsening during follow up were censored at their last non-missing visit.
    - In the analysis of time to confirmed deterioration, death was considered as an event only if it occurred within 42 days of the last non-missing visit; otherwise, it was censored at the last non-missing visit.
  - Hazard ratios (HRs) were estimated using a stratified Cox proportional hazards regression analysis.
- Least squares (LS) mean changes from baseline at week 25 were compared between arms using a linear mixed-effect model for repeated measures analysis, with the dependent variable being change from baseline and the fixed effect covariates including treatment arm, time (discrete variable), randomization stratification factors, baseline score, and treatment arm by time interaction.

Results

Baseline characteristics

- The ITT population included 603 patients (299 SG, 304 Doc).
- Baseline characteristics were similar between arms, except for a higher proportion of patients being male (71.1% vs 64.9%) and lower proportion being White (71.1% vs 76.6%) in the Doc versus SG arm (**Table 1**).
- Baseline PRO scores were comparable between arms but worse compared with the general population for EORTC QLQ-C30 domains.[7]
- PRO completion rates were high (>85%) for most visits and comparable in both arms.

Time to deterioration from baseline

- SG delayed time to first meaningful deterioration or death in the NSCLC-SAQ shortness of breath and total scores (**Figure 1**), as well as time to confirmed deterioration in shortness of breath (**Figure 2**).
- SG was associated with lower rates of deterioration or death across most PRO domains, with HRs significantly favoring SG over Doc in terms of time to first meaningful deterioration or death for NSCLC-SAQ shortness of breath, fatigue, and total score and for EORTC QLQ-C30 fatigue and dyspnea (**Figure 3A**) and in terms of confirmed deterioration for NSCLC-SAQ fatigue and shortness of breath and for EORTC QLQ-C30 fatigue (**Figure 3B**).
- Rates of meaningful deterioration in diarrhea and nausea/vomiting were higher with SG and the corresponding HRs numerically favored Doc (**Figure 3**).

Change from baseline

- Differences in LS mean changes from baseline at week 25 significantly and meaningfully favored SG for NSCLC-SAQ fatigue, shortness of breath, and total score and for EORTC QLQ-C30 role functioning, fatigue, and dyspnea (**Table 2**).
- Numerical improvements with SG versus Doc were observed in most other symptom and functioning domains, although they were not considered meaningful except for the EORTC QLQ-C30 appetite loss and financial difficulties domains.

Results (cont'd)

Table 1. Baseline patient characteristics

Characteristic	SG (N = 299)	Doc (N = 304)
Age (years), mean (SD)	64.5 (9.2)	63.5 (9.3)
Male, n (%)	194 (64.9)	216 (71.1)
Race, n (%)		
Asian	17 (5.7)	26 (8.6)
Black/African American	6 (2.0)	7 (2.3)
White	229 (76.6)	216 (71.1)
Other[a]	47 (15.7)	55 (18.1)
Previous lines of therapy received, n (%)		
1	167 (55.9)	167 (54.9)
2	103 (34.4)	101 (33.2)
≥3	29 (9.7)	36 (11.8)
Histology, n (%)		
Nonsquamous	215 (71.9)	224 (73.7)
Squamous	84 (28.1)	80 (26.3)
Best response to last anti-PD-(L)1–containing regimen, n (%)		
Complete response/partial response	107 (35.8)	113 (37.2)
Progressive disease/stable disease	192 (64.2)	191 (62.8)

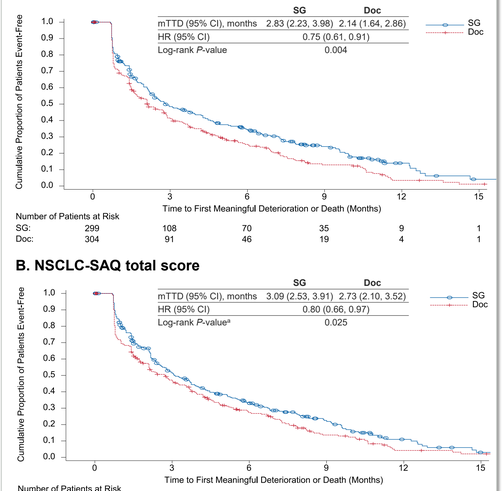
[a]Other races include American Indian/Alaska Native, Native Hawaiian/other Pacific Islander, unspecified, and not reported. All patients had stage IV NSCLC at time of randomization. Doc, docetaxel; PD-(L)-1, programmed death-(ligand) 1; SD, standard deviation; SG, sacituzumab govitecan.

Table 2. LS mean changes in PRO scores from baseline at week 25

PRO domain	LS mean change from baseline (95% CI)		Difference in LS mean change (95% CI)	MID[a]
	SG	Doc		
NSCLC-SAQ				
Total score	-0.61 (-1.15, -0.07)	0.78 (0.14, 1.42)	**-1.39** (-2.21, -0.57)**	±1.2[a]
Appetite	-0.20 (-0.40, -0.01)	0.09 (-0.14, 0.33)	-0.30 (-0.60, 0.00)	±0.4[a]
Shortness of breath	-0.05 (-0.21, 0.12)	0.39 (0.20, 0.59)	**-0.44** (-0.69, -0.19)**	±0.4[a]
Pain	-0.15 (-0.32, 0.02)	-0.04 (-0.24, 0.16)	-0.12 (-0.38, 0.14)	±0.3[a]
Fatigue	-0.12 (-0.27, 0.04)	0.28 (0.10, 0.45)	**-0.39** (-0.62, -0.16)**	±0.3[a]
Cough	-0.11 (-0.27, 0.05)	-0.07 (-0.25, 0.12)	-0.04 (-0.29, 0.20)	±0.3[a]
EORTC QLQ-C30				
Summary score	-0.09 (-2.46, 2.27)	-4.93 (-7.57, -2.29)	4.84** (1.38, 8.29)	±5[a]
GHS/QoL	-2.32 (-5.72, 1.08)	-5.66 (-9.54, -1.78)	3.34 (-1.72, 8.39)	±4[b]
Physical functioning	-5.73 (-8.78, -2.69)	-9.88 (-13.30, -6.46)	4.15 (-0.31, 8.60)	±5[b]
Role functioning	-2.30 (-6.94, 2.33)	-14.43 (-19.69, -9.17)	**12.13** (5.28, 18.98)**	±6[b]
Emotional functioning	1.54 (-1.68, 4.76)	-0.47 (-4.14, 3.20)	2.01 (-2.76, 6.78)	±6.6[a]
Cognitive functioning	-3.06 (-6.23, 0.12)	-2.33 (-5.93, 1.26)	-0.72 (-5.40, 3.96)	±3[b]
Social functioning	-4.88 (-9.10, -0.67)	-8.43 (-13.23, -3.63)	3.55 (-2.69, 9.79)	±5[b]
Fatigue	-0.18 (-3.94, 3.57)	9.01 (4.72, 13.31)	**-9.20** (-14.78, -3.61)**	±5[b]
Nausea/ vomiting	2.41 (-0.67, 5.48)	0.03 (-3.52, 3.59)	2.37 (-2.25, 6.99)	±3[b]
Pain	-0.84 (-5.03, 3.35)	2.68 (-2.06, 7.42)	-3.52 (-9.70, 2.66)	±6[b]
Dyspnea	-2.29 (-6.87, 2.29)	10.44 (5.18, 15.69)	**-12.72** (-19.55, -5.90)**	±4[b]
Insomnia	-4.22 (-8.92, 0.47)	-2.56 (-7.90, 2.79)	-1.66 (-8.64, 5.31)	±4[b]
Appetite loss	-4.87 (-10.11, 0.37)	0.23 (-5.69, 6.15)	**-5.10 (-12.86, 2.67)**	±5[b]
Constipation	1.15 (-3.47, 5.77)	-3.39 (-8.70, 1.93)	4.54 (-2.36, 11.44)	±5[b]
Diarrhea	4.28 (-0.11, 8.67)	3.42 (-1.64, 8.48)	0.86 (-5.72, 7.44)	±3[b]
Financial difficulties	3.94 (0.23, 7.65)	7.03 (2.90, 11.16)	**-3.09 (-8.48, 2.29)**	±3[b]

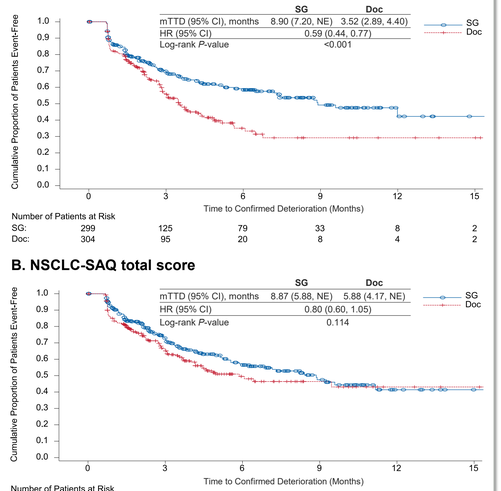
Differences exceeding the between-group MID thresholds are bolded. [a]Based on 0.3 times standard deviation of the baseline score for each domain. [b]Based on published thresholds.[6] **Nominal P<0.01 for between-group differences. CI, confidence interval; Doc, docetaxel; EORTC QLQ-30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS, global health status; LS, least squares; MID, minimal important difference; NSCLC-SAQ, Non-Small Cell Lung Cancer Symptom Assessment Questionnaire; PRO, patient-reported outcomes; QoL, quality of life; SG, sacituzumab govitecan.

Figure 1. Time to first meaningful deterioration or death



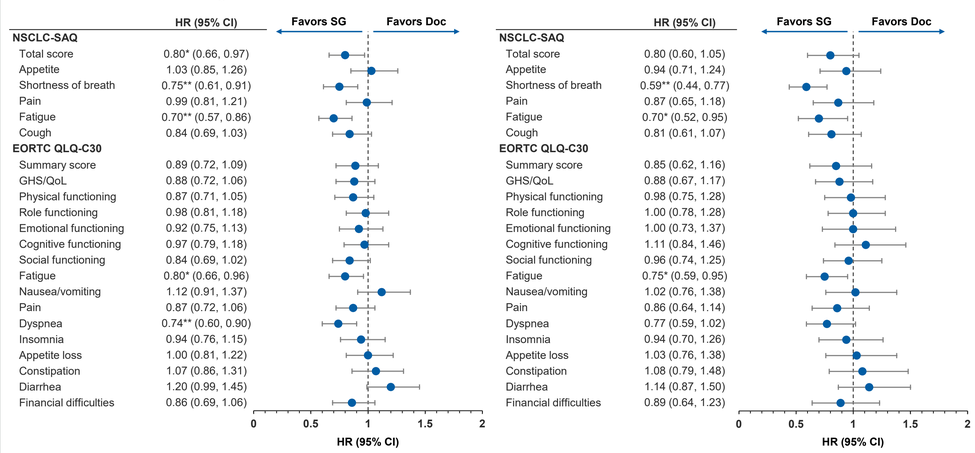
CI, confidence interval; Doc, docetaxel; HR, hazard ratio; mTTD, median time to deterioration; NSCLC-SAQ, Non-Small Cell Lung Cancer Symptom Assessment Questionnaire; SG, sacituzumab govitecan.

Figure 2. Time to confirmed deterioration



CI, confidence interval; Doc, docetaxel; HR, hazard ratio; mTTD, median time to deterioration; NE, not estimable; NSCLC-SAQ, Non-Small Cell Lung Cancer Symptom Assessment Questionnaire; SG, sacituzumab govitecan.

Figure 3. HR for time to deterioration from baseline



*Nominal P<0.05 and **nominal P<0.01 from the stratified log-rank test. CI, confidence interval; Doc, docetaxel; EORTC QLQ-30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS, global health status; HR, hazard ratio; NSCLC-SAQ, Non-Small Cell Lung Cancer Symptom Assessment Questionnaire; QoL, quality of life; SG, sacituzumab govitecan.

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