ORIGINAL ARTICLE

Patient-Reported Symptoms and Quality of Life With Sacituzumab Govitecan Versus Docetaxel in Metastatic NSCLC: The Phase 3, Randomized EVOKE-01 Trial

Niels Reinmuth, MD,[a,*] Sébastien Couraud, MD, PhD,[b] Luis Paz-Ares, MD, PhD,[c] Marina Chiara Garassino, MD,[d] Shobhit Baijal, MBBS, BSc,[e] Davey Daniel, MD,[f] Pilar Garrido, MD, PhD,[g] Terufumi Kato, MD,[h] Ivor Percent, MD,[i] Achim Rittmeyer, MD,[j] Hector Soto Parra, MD,[k] Sabeen Mekan, MD,[l,m] Mira Patel, PhD,[l] Matthew Radford, PhD,[l] Eric Zhang, PhD,[l] Christopher G. Pelligra, MS,[n] Shien Guo, PhD,[o] Enriqueta Felip, MD, PhD[p]

[a]*Asklepios Lung Clinic, German Center for Lung Research (DZL), Munich-Gauting, Germany*
[b]*Respiratory Medicine and Thoracic Oncology Department, Lyon University Hospital (Hospices Civils de Lyon), Lyon Sud Hospital, Lyon, France*
[c]*Hospital Universitario 12 de Octubre, H12O-Spanish National Cancer Research Centre (CNIO) Lung Cancer Clinical Research Unit, Complutense University and Ciberonc, Madrid, Spain*
[d]*University of Chicago Comprehensive Cancer Center, Chicago, Illinois*
[e]*University Hospitals Birmingham National Health Service (NHS) Trust, Birmingham, United Kingdom*
[f]*OneOncology, Nashville, Tennessee*
[g]*Medical Oncology Department, Hospital Universitario Ramón y Cajal, Madrid, Spain*
[h]*Department of Infectious Diseases, Tokyo Metropolitan Komagome Hospital, Tokyo, Japan*
[i]*Florida Cancer Specialists, Punta Gorda, Florida*
[j]*Department of Thoracic Oncology, Lungenfachklinik Immenhausen, Immenhausen, Germany*
[k]*Medical Oncology Department, Azienda Ospedaliero Universitaria Policlinico Vittorio Emanuele, Catania, Italy*
[l]*Gilead Sciences, Inc., Foster City, California*
[m]*Current affiliation: Zymeworks, New York, New York*
[n]*Evidera, Inc., Atlanta, Georgia*
[o]*Evidera Inc., Waltham, Massachusetts*
[p]*Oncology Department, Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology, Barcelona, Spain*

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ABSTRACT

Introduction: In the phase 3 EVOKE-01 trial (NCT05089734), sacituzumab govitecan (SG) exhibited a numerical improvement in overall survival and tolerability compared with docetaxel in patients with metastatic NSCLC previously treated with platinum-based chemotherapy and programmed cell death protein (ligand) 1 inhibitors, although results were not statistically significant. This analysis evaluated health-related quality of life (HRQoL) data from EVOKE-01.

Methods: Patients (N = 603) were randomized 1:1 to SG (n = 299) or docetaxel (n = 304) in 21-day cycles. HRQoL was assessed by the NSCLC Symptom Assessment Questionnaire (NSCLC-SAQ), European Organization for Research and Treatment of Cancer Quality of Life questionnaire–Core 30 (QLQ-C30), and EuroQol 5 Dimension 3-level questionnaire. Least square mean changes from baseline at week 25, time to first meaningful deterioration or death, and time to confirmed deterioration were analyzed.

Results: SG exhibited significantly and meaningfully better effects than docetaxel on NSCLC-SAQ shortness of breath

***Corresponding author.**

Address for correspondence: Dr. Niels Reinmuth, Asklepios Lungenklinik Gauting Thorakale Onkologie, Robert-Koch-Allee 2, Gauting 82131, Germany. E-mail: n.reinmuth@asklepios.com

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(SoB), fatigue, total score, and on QLQ-C30 role functioning, fatigue, and dyspnea. Time to first meaningful deterioration or death favored SG over docetaxel for NSCLC-SAQ SoB (hazard ratio [95% confidence interval]: 0.75 [0.61–0.91]), fatigue (0.70 [0.57–0.86]), and total score (0.80 [0.66–0.97]); QLQ-C30 fatigue (0.80 [0.66–0.96]) and dyspnea (0.74 [0.60–0.90]); and EuroQol visual analog scale (0.79 [0.65–0.96]). The time to confirmed deterioration favored SG over docetaxel for NSCLC-SAQ SoB (0.59 [0.44–0.77]) and fatigue (0.70 [0.52–0.95]), and QLQ-C30 fatigue (0.75 [0.59–0.95]).

Conclusions: These exploratory results suggest that SG may benefit HRQoL over docetaxel, supporting SG as an active therapeutic agent for metastatic NSCLC post platinum-based and programmed cell death protein (ligand) 1 inhibitor therapy.

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Keywords: Sacituzumab govitecan; Docetaxel; NSCLC; Patient-reported outcome; Quality of life

Introduction

Lung cancer is the most commonly diagnosed cancer and the leading cause of cancer death worldwide, with an estimated 2.5 million new cases and 1.8 million deaths each year.[1] NSCLC accounts for approximately 84% of lung cancers, and 44% of the cases are diagnosed at stage IV.[2] Survival rates are poor for stage IV NSCLC (5-year survival: 3%–10%).[2–5]

Platinum-based chemotherapy, anti–programmed cell death protein (ligand)1 (PD-[L]1) immunotherapy, and a combination of the two are common first-line treatments for advanced or metastatic NSCLC without driver alterations.[6,7] For patients who progress on these therapies, treatment options are limited, and the current standard of care is docetaxel alone or combined with antiangiogenic drugs.[6,7] Outcomes with these treatments are suboptimal, with a median overall survival (OS) of approximately 1 year.[8–10]

Sacituzumab govitecan (SG) is a trophoblast cell-surface antigen 2–directed antibody-drug conjugate (ADC) approved in the United States for the treatment of locally advanced or metastatic breast cancer.[11] The potential use of SG for the treatment of metastatic NSCLC was recently investigated in the phase 3 EVOKE-01 trial (NCT05089734), which compared SG with docetaxel in patients with metastatic NSCLC that had progressed on or after sequential or concomitant platinum-based chemotherapy and PD-(L)1 inhibitors.[12] The median (95% confidence interval [CI]) OS, the primary end point, was 11.1 months (9.4–12.3) with SG and 9.8 months (8.1–10.6) with docetaxel; statistical significance was not reached (hazard ratio [HR] [95% CI]: 0.84 [0.68, 1.04]; $p = 0.0534$). SG was associated with less frequent grade three or higher treatment-emergent adverse events (66.6% versus 75.7%) and adverse event-related discontinuations (9.8% versus 16.7%) than docetaxel. These results suggest that, although the OS was not significantly different between the two treatments, SG may be better tolerated than docetaxel in the target patient population. Moreover, a considerable OS benefit was seen with SG versus docetaxel in a nonpredefined post hoc analysis of a subgroup of patients nonresponsive to their last anti–PD-(L)1-containing regimen (HR [95% CI]: 0.75 [0.58, 0.97]), suggesting SG may provide clinical benefits in this subset of patients.

Patient-reported outcomes (PROs) are increasingly recognized as a key component in clinical oncology research. They can provide the patient perspective on treatment benefits and risks and inform treatment decisions, regulatory approvals, and health care policy.[13,14] Here, to fully describe the experience of patients who received SG, we evaluated data on patient-reported health-related quality of life (HRQoL) and lung cancer-related symptoms from EVOKE-01.

Materials and Methods

Study Design and Participants

EVOKE-01 was a randomized, open-label, phase 3 trial conducted at 177 centers in 20 countries . Full details of the trial were reported previously.[12] Briefly, the study included adults (aged $\geq$ 18 years) with stage IV NSCLC that progressed on or after platinum-based chemotherapy and an anti–PD-(L)1–containing regimen (received in combination or sequentially). Patients with actionable genomic alterations were also included if they had received at least one tyrosine kinase inhibitor targeting the genomic alteration. Between November 17, 2021, and May 30, 2023, eligible patients were randomized 1:1 to receive intravenous infusion SG (10 mg/kg) on days 1 and 8 or docetaxel (75 mg/m^2) on day 1 of every 21-day cycle until disease progression, death, unacceptable toxicity, or fulfillment of other treatment discontinuation criteria. Randomization was stratified by squamous versus nonsquamous histology, response to last anti–PD-(L)1–containing regimen received (progressive disease or stable disease versus complete response or partial response), and receipt of previous therapy for actionable genomic alterations (yes versus no).

The primary end point was OS. Time to death or meaningful deterioration in the NSCLC Symptom

Assessment Questionnaire (NSCLC-SAQ) shortness of breath domain and that in the NSCLC-SAQ total score were key secondary end points and were included in the testing hierarchy, controlling for overall Type I error rate. HRQoL assessments using the other NSCLC-SAQ domains, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) (version 3), EuroQol 5 Dimension 3-level questionnaire (EQ-5D-3L), and the PRO version of the Common Technology Criteria for Adverse Events (PRO-CTCAE) were exploratory end points.

The trial was conducted in accordance with the International Council for Harmonisation Guidelines for Good Clinical Practice and the Declaration of Helsinki, and any applicable local health authority and institutional review board requirements. All patients provided written informed consent.

PRO Measures

Patients completed the NSCLC-SAQ, EORTC QLQ-C30, EQ-5D-3L, and PRO-CTCAE on day 1 of each cycle before dosing and at the end of treatment. As treatment at a given cycle could have been delayed for some patients because of adverse or other unexpected events, PRO assessments at a given treatment cycle might not have been well aligned across all patients on the nominal time scale since day 1 of cycle 1. Thus, all scheduled and unscheduled assessment visits were remapped to nominal time points according to the windowing criteria (Supplementary Table 1).

The NSCLC-SAQ is a seven-item PRO covering the five symptom concepts of NSCLC: cough, pain, dyspnea, fatigue, and appetite.[15] Each item has a recall period of the past 7 days and uses a five-point verbal rating scale, either from 0 ("no at all") to 4 ("very severe") for intensity-related items or from 0 ("never") to 4 ("always") for frequency-related items. A total score can be derived from the five symptom domains, with a score range of 0 to 20 and a higher score indicating worse symptoms. The NSCLC-SAQ has been approved by the U.S. Food and Drug Administration (FDA) for exploratory use in drug development.[16] For all the PRO analyses in EVOKE-01, NSCLC-SAQ shortness of breath and total score were prespecified as the primary domains of interest.

The EORTC QLQ-C30 is a questionnaire developed to assess the quality of life of cancer patients. It includes 30 items covering 15 domains: global health status/quality of life, functioning (physical, role, emotional, cognitive, and social), and symptoms (fatigue, nausea/vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties).[17] Each domain score ranges from 0 to 100. A higher score in the global health status/quality of life and functioning domains indicates better quality of life or functioning, whereas a higher score in the symptom domains indicates a higher level of symptomatology or problems.

The EQ-5D-3L is a self-reported measure of functioning and well-being that assesses five dimensions of health (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), each with three levels of severity (no problems, some problems, and extreme problems).[18] A health utility index was derived on the basis of the EQ-5D-3L value set from the United Kingdom,[19] with a value of 0.00 indicating a health state equivalent to death, 1.00 indicating full health, and a negative value reflecting states perceived to be worse than death. The EQ-5D-3L questionnaire also includes a visual analog scale (EQ-VAS) that records the respondent's self-rated health on a scale of 0 (worst imaginable health state) to 100 (best imaginable health state).

The PRO-CTCAE collects patients' self-reported symptomatic treatment-related toxicity in oncology trials.[20,21] Six relevant symptom concepts (10 items in total) were selected for the current study: mouth/throat sores (severity and interference), abdominal pain (frequency, severity, and interference), rash (presence/absence), hair loss (amount), itching (severity), and numbness and tingling (severity and interference). Each item evaluating severity, frequency, amount, or interference was scored from 0 to 4, with a higher score representing a higher level of symptomatology or problems.

Thresholds of Meaningful Changes or Differences in PROs

For the NSCLC-SAQ, the thresholds of meaningful within-patient changes (responder definition) were a change of plus or minus two points (on a scale range of 0 [best]–20 [worst]) for the total score and plus or minus one point (on a scale range of 0–4) for shortness of breath (Supplementary Table 2), which were determined on the basis of anchor-based analyses of blinded EVOKE-01 data before unblinding.[22] The same threshold of one-point change was assumed for other NSCLC-SAQ domains. The minimal important difference (MID) thresholds for meaningful within-group changes and between-group differences for the NSCLC-SAQ were estimated using a distribution-based approach of 0.3 times the SD of the baseline score, which is equivalent to a small effect size. This is within the proposed range of plausible MIDs (0.2–0.5) per the guidance for health technology assessment in the European Union[23] and the MID range proposed for the EORTC QLQ-C30 domains (0.3–0.5).[24]

The responder definition and MID thresholds for meaningful within-group changes and between-group differences in QLQ-C30 domains were on the basis of

published values (Supplementary Table 2).[25–27] As no responder definition was available for the summary score, a 10-point change was assumed, consistent with the other QLQ-C30 domains.[25] In the absence of established thresholds, 0.3 times the SD of the baseline score was used as the within-group and between-group MIDs for the summary score and as the between-group MID for emotional functioning.

For the EQ-5D-3L health utility index and EQ-VAS, the responder definition and MID thresholds for meaningful within-group changes and between-group differences were on the basis of published data.[28] Norm scores for the EORTC QLQ-C30 domains were on the basis of the European general population on the basis of 11 European Union countries (N = 11,343)[29] and those for EQ-5D-3L health utility index and EQ-VAS were from the UK general population (N = 3395).[30] All norm scores were re-weighted by the sex and age distributions of the intent-to-treat analysis set of this study.

Statistical Analyses

As the primary efficacy end point was not met,[12] analyses of time to death or meaningful deterioration in NSCLC-SAQ shortness of breath and total score (key secondary end points) were considered exploratory. Therefore, no formal hypothesis testing was performed. Nominal *p* values and CI were provided to help interpret the differences between treatments. No adjustments were made for multiplicity. All statistical analyses were conducted using the Statistical Analysis System version 9.4 (SAS Institute, Cary, NC).

All PRO analyses, except for the PRO-CTCAE–related analyses, included all randomized patients (intent-to-treat population) according to the treatment arm they were allocated. PRO-CTCAE-related analyses were conducted in all randomized patients who received at least one dose of any study drug (safety population), with treatment assignments designated according to the actual treatment received.

At each visit, the proportion of patients remaining eligible for PRO assessments and the specific reasons for becoming ineligible were summarized. The completion rate was defined as the proportion of patients eligible for the assessment at a time point who submitted an evaluable assessment at that time point. An evaluable assessment for a given PRO at a given assessment visit was defined as having greater than or equal to one domain completed for the NSCLC-SAQ, greater than or equal to one of the 15 domains or summary score completed for the QLQ-C30, all five items completed for the EQ-5D-3L, no missing EQ-VAS value, or greater than or equal to one of the 10 items completed for the PRO-CTCAE.

A linear mixed-effect model for repeated measures analysis, assuming missing at random, was used to assess the change from baseline in PROs at each post-baseline visit through week 25 (dependent variable). Week 25 was prespecified as the primary time point before unblinding to ensure high completion rates for the PRO measures. The models included the intercept as a random effect and treatment arm (SG versus docetaxel), time (discrete variable), randomization stratification factors, baseline score, and treatment arm by time interaction as the fixed effect covariates. The within-group least square (LS) mean change from baseline and between-group difference in LS mean change at each postbaseline visit were estimated.

Time to death or first meaningful deterioration from baseline for a given PRO domain was calculated as the time between randomization and the first meaningful deterioration (change from baseline greater than or equal to the responder definition threshold for worsening) or death, whichever occurred first. The Kaplan-Meier product-limit method was used to estimate the time-to-event survival functions. The two treatment arms were compared using the log-rank test, stratified by randomization stratification factors. Two-sided nominal *p* values are reported. HRs (95% CIs) were estimated using a stratified Cox proportional hazards regression analysis. Patients without baseline or any postbaseline assessment or with a baseline score too poor to deteriorate further were censored at randomization. One intermittent missing visit was imputed with the last observation carried forward, whereas patients who had two or more consecutive intermittent missing visits (even if followed by a death) were censored on the date of their last nonmissing visit. Those who did not have any event of interest during follow-up were censored at their last nonmissing visit. A supplemental analysis was conducted by censoring death on the date of the last nonmissing visit before death. Sensitivity analyses of time to first meaningful deterioration or death were performed for the NSCLC-SAQ total score using different responder definition thresholds ($\geq$ three- and $\geq$ four-point increase) for meaningful deterioration.

Time to confirmed deterioration for a given PRO domain was calculated as the time between randomization and the date of a meaningful deterioration confirmed at the after scheduled visit or by a death within 21 days after deterioration onset. The Kaplan-Meier product-limit method and stratified Cox proportional hazards models were used for the analysis. The same censoring rules were followed in the analysis of time to first meaningful deterioration or death.

For the PRO-CTCAE, proportions of patients having any worsening from baseline to level 3 or 4 during treatment (for items except rash) or from “no presence”

Table 1. Baseline PRO Scores

Domain/total scores	SG		Docetaxel		Population norm, mean	Between-group MID
	n	Mean (SD)	n	Mean (SD)		
NSCLC-SAQ						
Cough	281	1.2 (1.1)	272	1.3 (1.0)	NA	±0.31
Fatigue	281	2.0 (1.0)	269	1.9 (1.0)	NA	±0.30
Fatigue item: How often low energy	281	2.0 (1.1)	269	1.9 (1.1)	NA	NA
Fatigue item: How often tire easily	281	2.1 (1.0)	269	2.0 (1.0)	NA	NA
Pain	281	1.5 (1.1)	272	1.3 (1.1)	NA	±0.34
Pain item: worst pain in the chest	281	0.8 (1.0)	271	0.8 (1.0)	NA	NA
Pain item: worst pain other than in the chest	281	1.3 (1.2)	272	1.1 (1.1)	NA	NA
Shortness of breath	281	1.8 (1.1)	269	1.6 (1.2)	NA	±0.35
Appetite	281	1.4 (1.3)	269	1.3 (1.2)	NA	±0.38
Total score	280	7.9 (3.9)	268	7.4 (3.8)	NA	±1.17
EORTC QLQ-C30						
GHS/QoL[a]	278	60.4 (21.8)	272	61.7 (21.2)	66.5	±4
Physical functioning[a]	282	71.7 (23.6)	278	72.6 (20.6)	83.8	±5
Role functioning[a]	281	69.3 (29.9)	279	70.0 (30.0)	84.2	±6
Emotional functioning[a]	279	76.5 (21.5)	272	75.2 (22.6)	79.6	±6.61
Cognitive functioning[a]	279	84.8 (20.3)	272	83.6 (22.3)	86.9	±3
Social functioning[a]	279	74.7 (27.2)	271	74.7 (27.5)	88.4	±5
Fatigue[b]	281	40.6 (25.3)	278	38.7 (26.3)	25.6	±5
Nausea and vomiting[b]	273	9.3 (17.0)	270	7.0 (15.4)	3.0	±3
Pain[b]	282	31.9 (28.8)	279	28.2 (27.7)	23.3	±6
Dyspnea[b]	281	36.5 (31.6)	278	36.0 (31.4)	16.5	±4
Insomnia[b]	277	32.5 (31.6)	279	32.6 (31.5)	25.1	±4
Appetite loss[b]	273	26.6 (32.0)	277	26.7 (31.6)	7.1	±5
Constipation[b]	267	21.2 (30.0)	262	18.3 (27.9)	10.5	±5
Diarrhea[b]	279	7.4 (17.5)	272	5.4 (14.2)	6.8	±3
Financial difficulties[b]	278	15.3 (26.5)	269	19.3 (30.4)	8.5	±3
Summary score[a]	253	74.6 (17.1)	254	75.9 (16.4)	NA	±5.03
EQ-5D-3L[a]						
Health utility index	282	0.698 (0.276)	270	0.700 (0.260)	0.79	±0.08
EQ-VAS	279	63.7 (21.4)	266	67.4 (19.7)	79.6	±7

[a]A higher score indicates better QoL or functioning.
[b]A higher score indicates a higher level of symptoms.
EORTC QLQ-30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; EQ-VAS, visual analog score of the EQ-5D-3L; GHS, global health status; MID, minimal important difference; NA, not available; NSCLC-SAQ, NSCLC Symptom Assessment Questionnaire; QoL, quality of life; SG, sacituzumab govitecan.

at baseline to "presence" during treatment (for rash only) were summarized descriptively by treatment arm.

Results

Baseline Demographics and Patient Characteristics

At data cutoff (November 29, 2023), 603 patients were randomized to the SG (n = 299) or the docetaxel (n = 304) arm (Supplementary Fig. 1) and were followed for a median of 12.7 months. The mean (SD) age was 64 (9.3) years. Most patients were men (68%) and White (74%), 73% had non-squamous histology, 45% received two or more lines of previous therapy, and 64% did not respond to their last anti–PD-(L)1-containing regimen. Most patients were from Canada/Western European Union/Australia (n = 455, 75%), 60 (10%) patients were from the United States, and 88 (15%) patients were from the rest of the world. Additional baseline demographics and clinical characteristics have been previously published.[12]

PRO Completion Rates

The proportion of patients remaining eligible for NSCLC-SAQ and PRO-CTCAE assessments declined over time in both arms, mostly because of treatment discontinuation owing to disease progression (Supplementary Fig. 2). Patients became ineligible because of adverse events or other reasons more frequently in the docetaxel than in the SG arm. At most assessment visits, completion rates remained high (approximately 90%) and comparable between arms among eligible patients (Supplementary Fig. 3).

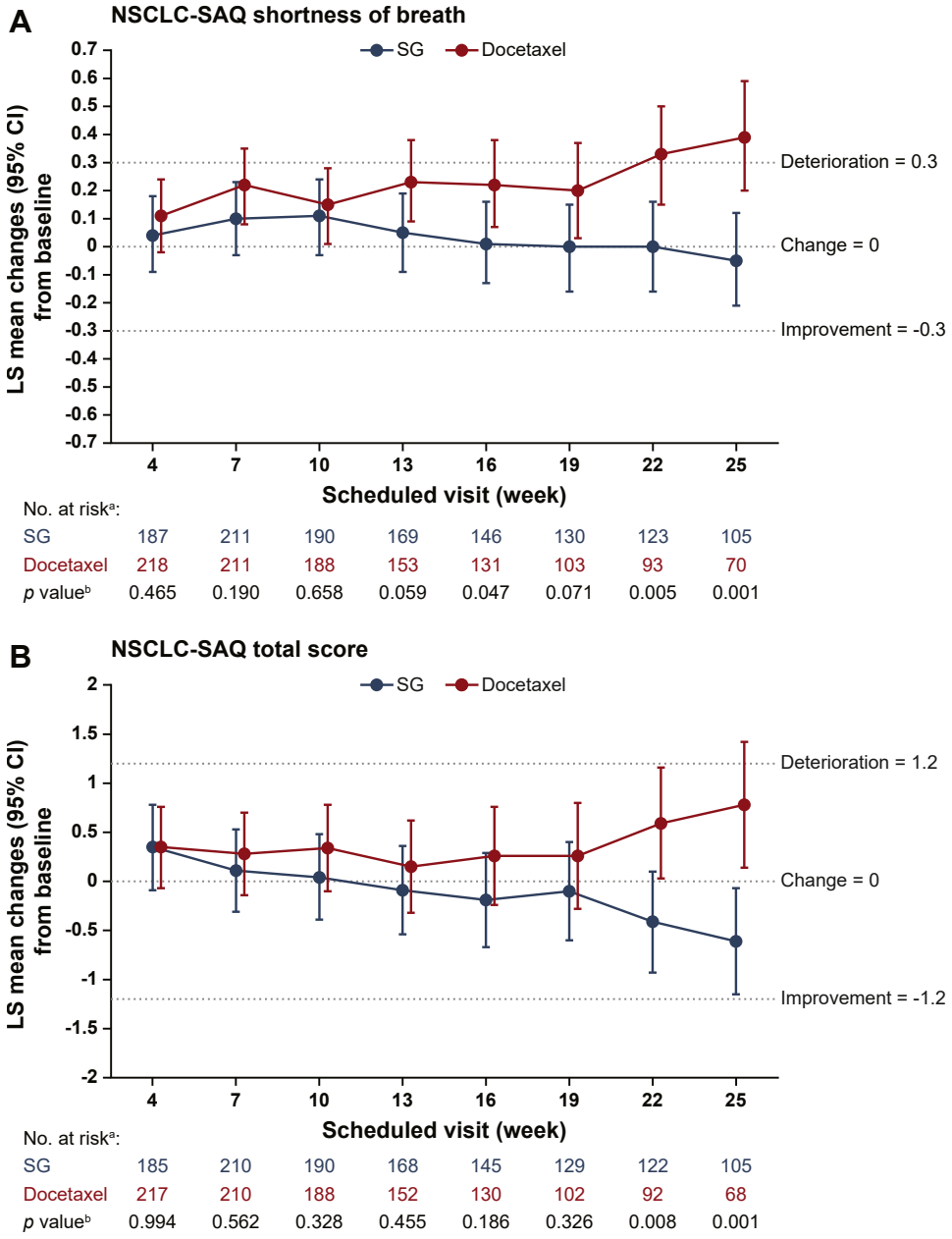


Figure 1. LS mean changes from baseline over time for NSCLC-SAQ (*A*) shortness of breath and (*B*) total score. MID thresholds of within-group improvement and worsening are presented with dotted lines. *N is the number of patients in each treatment arm with a nonmissing change from baseline in PRO score at each assessment visit; **p value for the between-group (i.e., SG versus docetaxel) difference in changes from baseline. MID, minimal important difference; NSCLC-SAQ, NSCLC Symptom Assessment Questionnaire.

Baseline PRO Scores

Baseline PRO scores were comparable between arms (Table 1). Mean baseline QLQ-C30 and EQ-5D-3L scores were meaningfully worse in both arms than age- and sex-adjusted means of the general population for most PRO domains except for QLQ-C30 emotional functioning, cognitive functioning, pain, and diarrhea. For most of the selected PRO-CTCAE items at baseline, the proportions of patients reporting any level of symptoms were numerically higher in the SG arm than in the docetaxel arm (Supplementary Fig. 4).

Change From Baseline

The LS mean change from baseline revealed that the NSCLC-SAQ shortness of breath score remained stable across visits in the SG arm (Fig. 1*A*). The score gradually increased (worsening in shortness of breath) in the docetaxel arm, with the LS mean changes from baseline

Table 2. Differences in LS Mean Changes From Baseline at Week 25

	SG		Docetaxel			
Domain/total scores	n	LS mean change (95% CI)	n	LS mean change (95% CI)	Difference in LS mean change (95% CI)	Between-group MID
NSCLC-SAQ						
Cough	105	-0.11 (-0.27 to 0.05)	68	-0.07 (-0.25 to 0.12)	-0.04 (-0.29 to 0.20)	±0.31
Fatigue	105	-0.12 (-0.27 to 0.04)	70	0.28[b] (0.10 to 0.45)	**-0.39[b] (-0.62 to -0.16)**	±0.30
Pain	105	-0.15 (-0.32 to 0.02)	68	-0.04 (-0.24 to 0.16)	-0.12 (-0.38 to 0.14)	±0.34
Shortness of breath	105	-0.05 (-0.21 to 0.12)	70	**0.39[c] (0.20 to 0.59)**	**-0.44[b] (-0.69 to -0.19)**	±0.35
Appetite	105	-0.20[a] (-0.40 to -0.01)	70	0.09 (-0.14 to 0.33)	-0.30 (-0.60 to 0.00)	±0.38
Total score	105	-0.61[a] (-1.15 to -0.07)	68	0.78[a] (0.14 to 1.42)	**-1.39[b] (-2.21 to -0.57)**	±1.17
EORTC QLQ-C30						
GHS/QoL	102	-2.32 (-5.72 to 1.08)	73	**-5.66[b] (-9.54 to -1.78)**	3.34 (-1.72 to 8.39)	±4
Physical functioning	104	**-5.73[c] (-8.78 to -2.69)**	74	**-9.88[c] (-13.30 to -6.46)**	4.15 (-0.31 to 8.60)	±5
Role functioning	104	-2.30 (-6.94 to 2.33)	74	**-14.43[c] (-19.69 to -9.17)**	**12.13[b] (5.28 to 18.98)**	±6
Emotional functioning	103	1.54 (-1.68 to 4.76)	73	-0.47 (-4.14 to 3.20)	2.01 (-2.76 to 6.78)	±6.61
Cognitive functioning	103	**-3.06 (-6.23 to 0.12)**	73	**-2.33 (-5.93 to 1.26)**	-0.72 (-5.40 to 3.96)	±3
Social functioning	103	-4.88[a] (-9.10 to -0.67)	73	**-8.43[b] (-13.23 to -3.63)**	3.55 (-2.69 to 9.79)	±5
Fatigue	104	-0.18 (-3.94 to 3.57)	74	**9.01[c] (4.72 to 13.31)**	**-9.20[b] (-14.78 to -3.61)**	±5
Nausea and vomiting	101	2.41 (-0.67 to 5.48)	71	0.03 (-3.52 to 3.59)	2.37 (-2.25 to 6.99)	±3
Pain	104	-0.84 (-5.03 to 3.35)	74	2.68 (-2.06 to 7.42)	-3.52 (-9.70 to 2.66)	±6
Dyspnea	104	**-2.29 (-6.87 to 2.29)**	73	**10.44[c] (5.18 to 15.69)**	**-12.72[c] (-19.55 to -5.90)**	±4
Insomnia	103	-4.22 (-8.92 to 0.47)	74	-2.56 (-7.90 to 2.79)	-1.66 (-8.64 to 5.31)	±4
Appetite loss	100	-4.87 (-10.11 to 0.37)	74	0.23 (-5.69 to 6.15)	**-5.10 (-12.86 to 2.67)**	±5
Constipation	99	1.15 (-3.47 to 5.77)	70	-3.39 (-8.70 to 1.93)	4.54 (-2.36 to 11.44)	±5
Diarrhea	103	4.28 (-0.11 to 8.67)	73	3.42 (-1.64 to 8.48)	0.86 (-5.72 to 7.44)	±3
Financial difficulties	102	**3.94[a] (0.23 to 7.65)**	73	**7.03[b] (2.90 to 11.16)**	**-3.09 (-8.48 to 2.29)**	±3
Summary Score	93	-0.09 (-2.46 to 2.27)	68	-4.93[c] (-7.57 to -2.29)	4.84[b] (1.38 to 8.29)	±5.03
EQ-5D-3L						
Health utility index	104	-0.06[b] (-0.10 to -0.02)	70	-0.07[b] (-0.12 to -0.02)	0.01 (-0.05 to 0.07)	±0.08
EQ-VAS	102	-0.62 (-3.47 to 2.23)	71	-2.07 (-5.33 to 1.20)	1.45 (-2.79 to 5.68)	±7

Values exceeding within-group or between-group MID thresholds are bolded. Within-group MID thresholds are provided in Supplementary Table 2.
[a]Nominal *p* less than 0.05 for within-group change or between-group difference in LS mean change from baseline.
[b]Nominal *p* less than 0.01 for within-group change or between-group difference in LS mean change from baseline.
[c]Nominal *p* less than 0.001 for within-group change or between-group difference in LS mean change from baseline.
CI, confidential interval; Doc, docetaxel; EORTC QLQ-30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS, global health status; EQ-VAS, visual analog score of the EQ-5D-3L; LS, least squares; MID, minimal important difference; NSCLC-SAQ, NSCLC Symptom Assessment Questionnaire; QoL, quality of life; SG, sacituzumab govitecan.

exceeding the within-group MID threshold for meaningful deterioration at weeks 22 and 25. The NSCLC-SAQ total score revealed no meaningful changes from baseline in both arms (Fig. 1*B*). However, a trend of improvement over time was observed in the SG arm, and a trend of worsening was observed in the docetaxel arm.

The between-group differences in LS mean changes from baseline at week 25 favored SG over docetaxel ($p < 0.01$) for NSCLC-SAQ fatigue, shortness of breath, and total score and for QLQ-C30 role functioning, fatigue, dyspnea, and summary score; between-group differences at week 25 exceeded the MID thresholds for all these domains except for the QLQ-C30 summary score (Table 2). For most other QLQ-C30 domains, the SG arm exhibited no worsening or a smaller magnitude of worsening from baseline than the docetaxel arm ($p > 0.05$ between arms); the differences between arms did not exceed the MID thresholds except for appetite loss and financial difficulties.

Time to First Meaningful Deterioration or Death

Time to first meaningful deterioration or death was longer with SG than docetaxel for NSCLC-SAQ shortness of breath (HR [95% CI]: 0.75 [0.61–0.91]; $p = 0.004$), fatigue (0.70 [0.57–0.86]; $p = 0.001$), and total score (0.80 [0.66–0.97]; $p = 0.025$) (Fig. 2; Supplementary Fig. 5). The same was observed for QLQ-C30 fatigue (0.80 [0.66–0.96]; $p = 0.016$) and dyspnea (0.74 [0.60, 0.90]; $p = 0.003$) and for EQ-VAS (0.79 [0.65, 0.96]; $p = 0.020$) (Fig. 2). Point estimates for HRs (95% CI) for QLQ-C30 diarrhea (1.20 [0.99–1.45]; $p = 0.065$) and nausea/vomiting (1.12 [0.91–1.37]; $p = 0.284$) numerically favored docetaxel over SG.

Supplemental analysis results were similar to the main analysis when death was censored on the date of

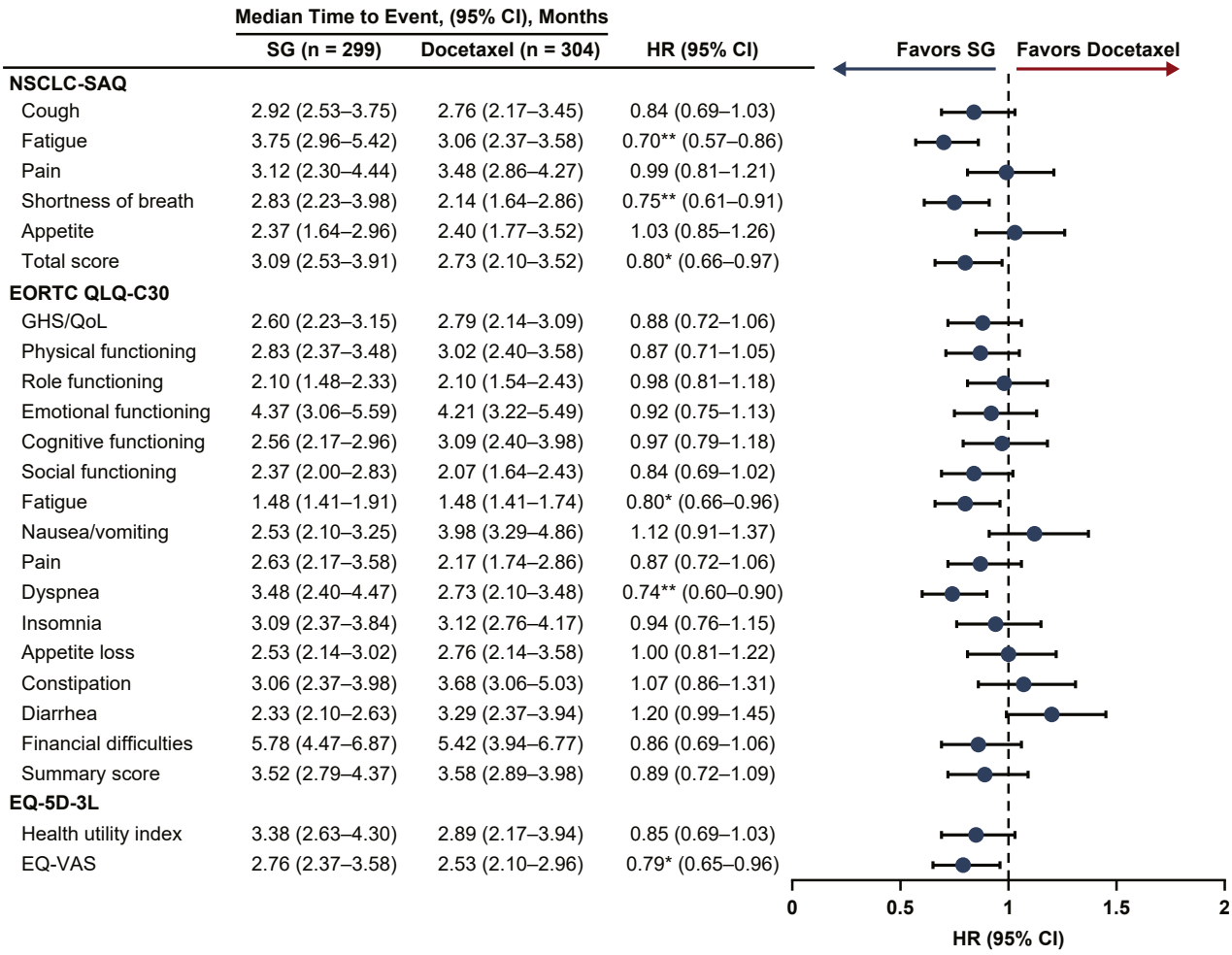


Figure 2. Forest plot for the analysis of time to first meaningful deterioration or death. *Nominal $p < 0.05$ and **nominal $p < 0.01$ from the stratified log-rank test. CI, confidence interval; Doc, docetaxel; EORTC QLQ-30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; EQ-VAS, visual analog score of the EQ-5D-3L; GHS, global health status; HR, hazard ratio; NSCLC-SAQ, NSCLC Symptom Assessment Questionnaire; QoL, quality of life; SG, sacituzumab govitecan.

the last nonmissing assessment visit. Compared with docetaxel, time to first meaningful deterioration with SG was longer for NSCLC-SAQ fatigue (HR [95% CI]: 0.73 [0.57–0.94]; $p = 0.012$) and shortness of breath (0.77 [0.61–0.98]; $p = 0.033$) and for QLQ-C30 dyspnea (0.74 [0.58–0.94]; $p = 0.015$), but shorter for QLQ-C30 nausea/vomiting (1.35 [1.05–1.73]; $p = 0.017$) and diarrhea (1.34 [1.05–1.71]; $p = 0.015$).

Sensitivity analysis results were similar when using a responder definition of either a three-point increase (HR [95% CI]: 0.80 [0.66–0.98]; $p = 0.032$) or a four-point increase (0.74 [0.60–0.91]; $p = 0.005$) as the threshold for meaningful deterioration of the NSCLC-SAQ total score.

Time to Confirmed Meaningful Deterioration

Time to confirmed meaningful deterioration was longer with SG than docetaxel for the following domains: NSCLC-SAQ shortness of breath (HR [95% CI]: 0.59 [0.44–0.77]; $p < 0.001$), NSCLC-SAQ fatigue (0.70 [0.52–0.95]; $p = 0.023$), and QLQ-C30 fatigue (0.75 [0.59–0.95]; $p = 0.016$) (Fig. 3; Supplementary Fig. 6). However, the difference between treatments for the NSCLC-SAQ total score only numerically favored SG (0.80 [0.60–1.05]; $p = 0.114$) (Fig. 3; Supplementary Fig. 6).

Worsening in PRO-CTCAE Symptom Items During Treatment

The proportions of patients with worsening of symptoms to a level of three or four during treatment were less than 20%, ranging from 10.8 % to 17.9% with SG and from 6.5% to 15.6% with docetaxel for all PRO-CTCAE items except hair loss amount and rash (Fig. 4). More than half of patients reported worsening of hair loss amount to a level of three or four in both arms (SG versus docetaxel 73.2% versus 58.8%).

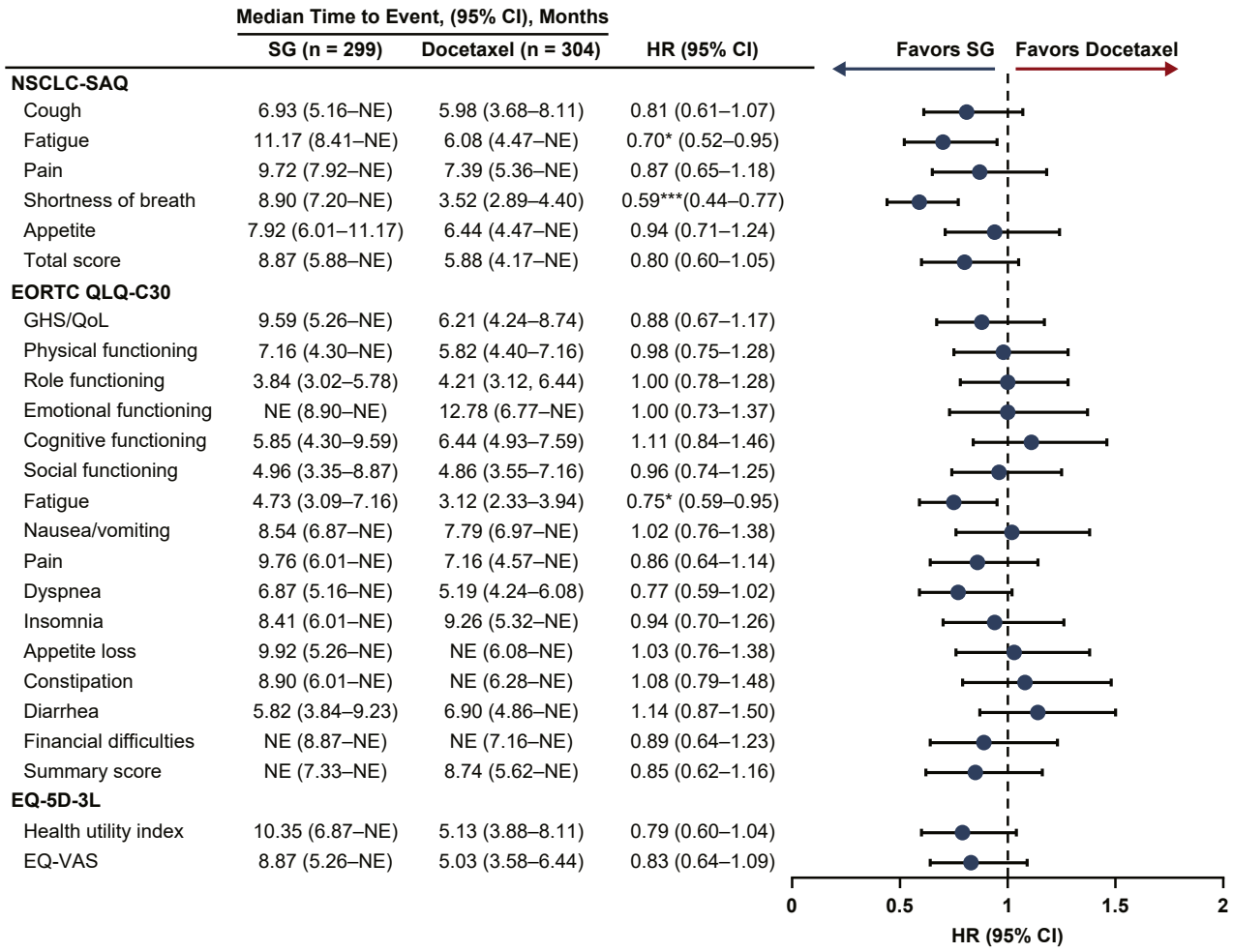


Figure 3. Forest plot for the analysis of time to confirmed deterioration. *Nominal $p < 0.05$ and ***nominal $p < 0.001$ from the stratified log-rank test. CI, confidence interval; Doc, docetaxel; EORTC QLQ-30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; EQ-VAS, visual analog score of the EQ-5D-3L; GHS, global health status; HR, hazard ratio; NE, not estimable; NSCLC-SAQ, NSCLC Symptom Assessment Questionnaire; QoL, quality of life; SG, sacituzumab govitecan.

Discussion

Results of this exploratory PRO analysis from EVOKE-01 suggest that SG may provide HRQoL benefits, compared with docetaxel, in patients with metastatic NSCLC who progressed on sequential or concomitant platinum-based chemotherapy and PD-(L)1 inhibitors. Although the OS with SG was not significantly different from that with docetaxel, SG exhibited meaningfully better effects on the overall symptom score of the NSCLC-SAQ than docetaxel after 25 weeks of treatment. A better effect with SG was consistently seen across all symptoms captured by the NSCLC-SAQ, but was more pronounced for dyspnea and fatigue. Results from the EORTC QLQ-C30 indicate consistent findings, suggesting meaningfully better effects not only on dyspnea and fatigue, but also on role functioning, appetite loss, and financial difficulties. The favorable effects on dyspnea and fatigue also resulted in a longer symptom-worsening–free survival with SG than with docetaxel, regardless of how the end point was defined (time to first or confirmed deterioration). For most PRO-CTCAE symptom items, only a small proportion of patients reported worsening to level 3 or 4 during treatment in both arms. Although worsening of hair loss amount was slightly more frequent in the SG arm, this did not seem to have any substantial adverse effects on patients' functioning and overall HRQoL.

Patients participating in EVOKE-01 had worse HRQoL than the general population at baseline, which is consistent with the impaired HRQoL typically observed in patients with advanced lung cancer,[31,32,] particularly in those who are in their later lines of therapy.[33] Given that metastatic NSCLC is incurable, the primary treatment goal is to prolong survival and maintain or enhance quality of life.[34] Symptoms such as fatigue, appetite loss, shortness of breath, and pain are highly

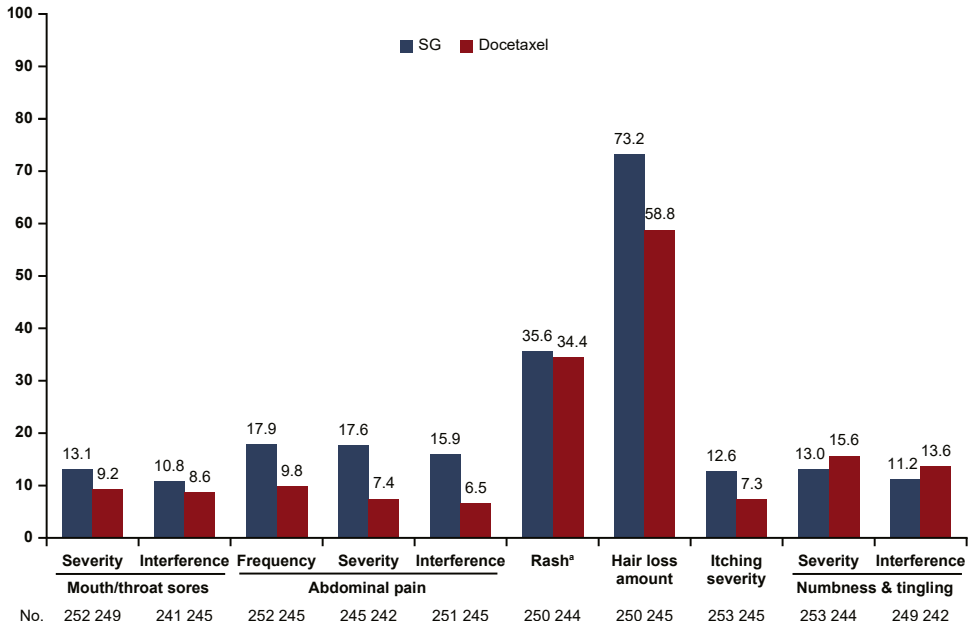


Figure 4. Percentages of patients experiencing any worsening from baseline to level three or four during treatment as assessed by the PRO-CTCAE. n represents the number of patients in the safety population with nonmissing scores at both baseline and at least one postbaseline visit. *Since rash was assessed as "no presence" or "presence," the percentage of patients whose response changed from "no presence" at baseline to "presence" during treatment was calculated. PRO-CTCAE, patient-reported outcome version of the Common Terminology Criteria for Adverse Events; SG, sacituzumab govitecan.

prevalent in patients with advanced NSCLC and reduce lung cancer-specific HRQoL.[31] As declining HRQoL is associated with shorter survival in metastatic NSCLC,[35] maintaining or improving symptoms and HRQoL in this patient population is critical. Although SG did not exhibit a statistically significant improvement in OS, the results from this analysis suggest that SG may offer a meaningful clinical benefit on HRQoL by reducing burdensome disease symptoms. This study provides valuable data for physicians and patients to use for shared decision-making.

In the current analysis, patients in the docetaxel arm exhibited significant deterioration from baseline at week 25 in global quality of life, functioning (physical, role, and social), and lung cancer symptoms (fatigue and shortness of breath). These finding aligns with previous reports of worsened overall quality of life and NSCLC symptoms, particularly fatigue, in docetaxel-treated patients with advanced NSCLC who progressed on platinum-based chemotherapy.[36–39] Compared with docetaxel, SG-treated patients experienced some worsening in symptoms related to adverse effects of SG, such as diarrhea, nausea, and vomiting; however, disease-related symptoms were mostly improved from baseline relative to the docetaxel arm, and HRQoL was generally improved or maintained from baseline with SG for global quality of life and across most functioning domains in EVOKE-01. The improvements in disease-related symptoms, along with slight worsening in treatment-related adverse effects, indicate that the observed benefits were likely because of the treatment effect of SG, rather than reduced toxicity of SG compared with docetaxel.

These results are in line with previous studies comparing docetaxel with other advanced NSCLC therapies on HRQoL effects in later-line settings. Ramucirumab plus docetaxel, nintedanib plus docetaxel, and pembrolizumab were found to have comparable effects to docetaxel on global quality of life and lung cancer symptoms in patients with previously treated advanced NSCLC.[36,40,41] Nivolumab, atezolizumab, and tislelizumab reduced overall symptom burden and individual symptoms (e.g., fatigue, dyspnea, or pain), compared with docetaxel in patients with advanced NSCLC who progressed on platinum-based chemotherapy.[37–39,42] PRO results from the phase 3, randomized TROPION-Lung01 trial in patients with previously treated advanced or metastatic NSCLC revealed that datopotamab deruxtecan, a Trop-2–directed ADC, was associated with delayed time to deterioration in lung cancer-specific symptoms compared with docetaxel, suggesting improved QoL in patients receiving datopotamab deruxtecan.[43]

The concepts of pain, fatigue, shortness of breath, and appetite loss were assessed using the NSCLC-SAQ and EORTC QLQ-C30 separately. Results on both the change from baseline and time to first deterioration or confirmed deterioration were consistent between the

two measures across all these concepts, supporting the robustness of the findings. In addition, the sensitivity analysis results, using a responder definition of either a three-point or four-point increase, corroborated the main analysis results, further confirming the robustness of the findings. Another strength of the study is that EVOKE-01 was conducted in multiple countries, with 90% of patients ex-United States, making the results generalizable to patient populations outside the United States.

In this study, patients in the docetaxel arm more frequently became ineligible for PRO assessment than those in the SG arm because of discontinuations related to adverse events or other reasons (e.g., loss to follow-up or consent withdrawal) over the course of the study, potentially resulting in attrition bias. As a result, the effect of SG relative to docetaxel on PRO end points may have been underestimated because patients who discontinued owing to adverse events or dropped out early were likely to have worse HRQoL than those remaining on treatment. In addition, the impact of missing PRO data among eligible patients on the analysis findings was not fully investigated. However, as the completion rates were high across visits and comparable between treatment arms, the impact should have been small.

HRQoL monitoring and PRO reporting are essential means to adequately assess the benefit-risk of novel treatment approaches in oncology. As SG and other Trop-2–directed ADCs are currently investigated in various combinations in clinical trials, future areas of research should include prospective studies to evaluate the HRQoL of patients with lung cancer receiving those treatments. In addition, detailed assessment of highly symptomatic patients enrolled in clinical studies and real-world data describing both patient- and physician-reported burden of disease could help refine treatment choices in routine clinical practice.

In summary, results of this PRO analysis from EVOKE-01 revealed that SG was associated with better HRQoL and patient-reported symptoms than docetaxel, particularly in dyspnea, fatigue, and role functioning, despite not reaching statistical significance for OS improvement. The findings suggest that SG may provide beneficial effects on HRQoL and NSCLC symptoms compared with docetaxel. SG is an active therapeutic agent in lung cancer, currently being evaluated in combination with pembrolizumab as a first-line treatment for metastatic NSCLC with PD-L1 tumor proportion score greater than or equal to 50% in a phase 3 study (EVOKE-03; ClinicalTrials.gov identifier: NCT05609968).

CRediT Authorship Contribution Statement

Niels Reinmuth: Resources, Supervision, Validation, Visualization, Writing - review & editing.

Sébastien Couraud: Resources, Supervision, Validation, Visualization, Writing - review & editing.

Luis Paz-Ares: Resources, Supervision, Validation, Visualization, Writing - review & editing.

Marina Chiara Garassino: Resources, Supervision, Validation, Visualization, Writing - review & editing.

Shobhit Baijal: Resources, Supervision, Validation, Visualization, Writing - review & editing.

Davey Daniel: Resources, Supervision, Validation, Visualization, Writing - review & editing.

Pilar Garrido: Resources, Supervision, Validation, Visualization, Writing - review & editing.

Terufumi Kato: Resources, Supervision, Validation, Visualization, Writing - review & editing.

Ivor Percent: Resources, Supervision, Validation, Visualization, Writing - review & editing.

Achim Rittmeyer: Investigation, Resources, Writing - review & editing.

Hector Soto Parra: Resources, Supervision, Validation, Visualization, Writing - review & editing.

Sabeen Mekan: Conceptualization. Funding acquisition, Investigation, Project administration, Supervision, Writing - review & editing.

Mira Patel: Conceptualization, Methodology, Writing - original draft, Writing - review & editing.

Matthew Radford: Conceptualization, Funding acquisition, Project administration, Supervision, Writing - original draft, Writing - review & editing.

Eric Zhang: Writing - review & editing.

Christopher G. Pelligra: Conceptualization, Formal analysis, Methodology, Project administration, Supervision, Validation, Visualization, Writing - original draft, Writing - review & editing.

Shien Guo: Conceptualization, Methodology, Writing - review & editing.

Enriqueta Felip: Resources, Supervision, Validation, Visualization, Writing - review & editing.

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Dr. Garrido reports receiving personal payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing, or educational events from Johnson & Johnson, Medscape, MSD Oncology, Novartis, Takeda, and TouchTime; receiving personal support for attending meetings and/or travel from AstraZeneca, Johnson & Johnson, Pfizer, and Roche; receiving support for participation on a data safety monitoring board or advisory board from AbbVie, Amgen, AstraZeneca, Bayer, BeiGene, Boehringer Ingelheim, Bristol Myers Squibb, Daiichi Sankyo, GlaxoSmithKline, Johnson & Johnson, Lilly, MSD Oncology, Novartis, PharmaMar, Pierre Fabre, Pfizer, Regeneron, Roche, Sanofi, and Takeda. 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Data Sharing Statement

Gilead Sciences shares anonymized individual patient data on request or as required by law or regulation with qualified external researchers on the basis of submitted curriculum vitae and reflecting non conflict of interest. The request proposal must also include a statistician. Approval of such requests is at Gilead Science's discretion and is dependent on the nature of the request, the merit of the research proposed, the availability of the data, and the intended use of the data. Data requests should be sent to datasharing@gilead.com.

Supplementary Data

Note: To access the supplementary material accompanying this article, visit the online version of the *JTO Clinical and Research Reports* at www.jtocrr.org and at https://doi.org/10.1016/j.jtocrr.2025.100929.

References

1. Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2024;74:229-263.
2. Ganti AK, Klein AB, Cotarla I, Seal B, Chou E. Update of incidence, prevalence, survival, and initial treatment in patients with non-small cell lung cancer in the US. *JAMA Oncol*. 2021;7:1824-1832.
3. Jeon DS, Kim HC, Kim SH, et al. Five-year overall survival and prognostic factors in patients with lung cancer: results from the Korean Association of Lung Cancer Registry (KALC-R) 2015. *Cancer Res Treat*. 2023;55:103-111.
4. Yang CY, Lin YT, Lin LJ, et al. Stage shift improves lung cancer survival: real-world evidence. *J Thorac Oncol*. 2023;18:47-56.
5. Canadian Cancer Society. Survival statistics for non-small cell lung cancer. https://cancer.ca/en/cancer-information/cancer-types/lung/prognosis-and-survival/non-small-cell-lung-cancer-survival-statistics. Accessed January 29, 2025.
6. Siringo M, Baena J, Bote de Cabo H, et al. Future perspectives in the second line therapeutic setting for non-oncogene addicted non-small-cell lung cancer. *Cancers (Basel)*. 2023;15:5505.
7. Singh N, Jaiyesimi IA, Ismaila N, et al. Therapy for stage IV non-small-cell lung cancer without driver alterations: ASCO living guideline, version 2023.1. *J Clin Oncol*. 2023;41:e51-e62.
8. Paz-Ares L, Goto Y, Wan-Teck Lim D, et al. Canakinumab in combination with docetaxel compared with docetaxel alone for the treatment of advanced non-small cell lung cancer following platinum-based doublet chemotherapy and immunotherapy (CANOPY-2): a multicenter, randomized, double-blind, phase 3 trial. *Lung Cancer*. 2024;189:107451.
9. Neal J, Pavlakis N, Kim SW, et al. CONTACT-01: a randomized phase III trial of atezolizumab + cabozantinib versus docetaxel for metastatic non-small cell lung cancer after a checkpoint inhibitor and chemotherapy. *J Clin Oncol*. 2024;42:2393-2403.
10. Garon EB, Visseren-Grul C, Rizzo MT, Puri T, Chenji S, Reck M. Clinical outcomes of ramucirumab plus docetaxel in the treatment of patients with non-small cell lung cancer after immunotherapy: a systematic literature review. *Front Oncol*. 2023;13:1247879.
11. Gilead Sciences. TRODELVY® (sacituzumab govitecan-hziy) for injection, for intravenous use (prescribing information). https://www.gilead.com/-/media/files/pdfs/medicines/oncology/trodelvy/trodelvy_pi.pdf. Accessed August 7, 2025.
12. Paz-Ares LG, Juan-Vidal O, Mountzios GS, et al. Sacituzumab govitecan versus docetaxel for previously treated advanced or metastatic non-small cell lung cancer: the

randomized, open-label Phase III EVOKE-01 study. *J Clin Oncol*. 2024;42:2860–2872.
13. Mercieca-Bebber R, King MT, Calvert MJ, Stockler MR, Friedlander M. The importance of patient-reported outcomes in clinical trials and strategies for future optimization. *Patient Relat Outcome Meas*. 2018;9:353–367.
14. Bellino S, La Salvia A. The importance of patient reported outcomes in oncology clinical trials and clinical practice to inform regulatory and healthcare decision-making. *Drugs R D*. 2024;24:123–127.
15. Bushnell DM, Atkinson TM, McCarrier KP, et al. Non-small cell lung cancer symptom assessment questionnaire: psychometric performance and regulatory qualification of a novel patient-reported symptom measure. *Curr Ther Res Clin Exp*. 2021;95:100642.
16. US Food and Drug Administration. Qualification of Non-small Cell Lung Cancer Symptom Assessment Questionnaire (NSCLC-SAQ): a patient-reported outcome instrument. https://www.fda.gov/media/119250/download?attachment. Accessed August 14, 2024.
17. Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst*. 1993;85:365–376.
18. Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol Group. *Ann Med*. 2001;33:337–343.
19. Dolan P. Modeling valuations for EuroQol health states. *Med Care*. 1997;35:1095–1108.
20. Kluetz PG, Kanapuru B, Lemery S, et al. Informing the tolerability of cancer treatments using patient-reported outcome measures: summary of an FDA and critical path institute workshop. *Value Health*. 2018;21:742–747.
21. Kluetz PG, Chingos DT, Basch EM, Mitchell SA. Patient-reported outcomes in cancer clinical trials: measuring symptomatic adverse events with the National Cancer Institute's patient-reported outcomes version of the common terminology criteria for adverse events (PRO-CTCAE). *Am Soc Clin Oncol Educ Book*. 2016;35:67–73.
22. Patel M, Radford M, Mekan S, Guo S, Pelligra CG. Psychometric Validation and Meaningful Within-Patient Change (MWPC) Thresholds for the Non-small Cell Lung Cancer Symptom Assessment Questionnaire (NSCLC-SAQ) Using Data From the EVOKE-01 Study (Poster PCR54). Poster Presented at: ISPOR Europe 2024. 2024. Barcelona, Spain.
23. HTA CG. Guidance on outcomes for joint clinical assessments. https://health.ec.europa.eu/document/download/a70a62c7-325c-401e-ba42-66174b656ab8_en?filename=hta_outcomes_jca_guidance_en.pdf. Accessed November 8, 2024.
24. Musoro JZ, Coens C, Sprangers MAG, et al. Minimally important differences for interpreting EORTC QLQ-C30 change scores over time: a synthesis across 21 clinical trials involving nine different cancer types. *Eur J Cancer*. 2023;188:171–182.
25. Osoba D, Rodrigues G, Myles J, Zee B, Pater J. Interpreting the significance of changes in health-related quality-of-life scores. *J Clin Oncol*. 1998;16:139–144.
26. Cocks K, King MT, Velikova G, Martyn St-James M, Fayers PM, Brown JM. Evidence-based guidelines for determination of sample size and interpretation of the European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30. *J Clin Oncol*. 2011;29:89–96.
27. Cocks K, King MT, Velikova G, et al. Evidence-based guidelines for interpreting change scores for the European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30. *Eur J Cancer*. 2012;48:1713–1721.
28. Pickard AS, Neary MP, Cella D. Estimation of minimally important differences in EQ-5D utility and VAS scores in cancer. *Health Qual Life Outcomes*. 2007;5:70.
29. Nolte S, Liegl G, Petersen MA, et al. General population normative data for the EORTC QLQ-C30 health-related quality of life questionnaire based on 15,386 persons across 13 European countries, Canada and the Unites States. *Eur J Cancer*. 2019;107:153–163.
30. Janssen B, Szende A. Population norms for the EQ-5D. In: Szende A, Janssen B, Cabases J, eds. *Self-Reported Population Health: an International Perspective Based on EQ-5D*. Dordrecht, Netherlands: Springer; 2014:19–30.
31. Iyer S, Taylor-Stokes G, Roughley A. Symptom burden and quality of life in advanced non-small cell lung cancer patients in France and Germany. *Lung Cancer*. 2013;81:288–293.
32. Polanski J, Jankowska-Polanska B, Rosinczuk J, Chabowski M, Szymanska-Chabowska A. Quality of life of patients with lung cancer. *Onco Targets Ther*. 2016;9:1023–1028.
33. Wintner LM, Giesinger JM, Zabernigg A, et al. Quality of life during chemotherapy in lung cancer patients: results across different treatment lines. *Br J Cancer*. 2013;109:2301–2308.
34. Mieras A, Pasman HRW, Klop HT, et al. What goals do patients and oncologists have when starting medical treatment for metastatic lung cancer? *Clin Lung Cancer*. 2021;22:242–251.e5.
35. Billingy NE, Tromp VNMF, van den Hurk CJG, Becker-Commissaris A, Walraven I. Health-related quality of life and survival in metastasized non-small cell lung cancer patients with and without a targetable driver mutation. *Cancers (Basel)*. 2021;13:4282.
36. Barlesi F, Garon EB, Kim DW, et al. Health-related quality of life in KEYNOTE-010: a Phase II/III study of pembrolizumab versus docetaxel in patients with previously treated advanced, programmed death ligand 1-expressing NSCLC. *J Thorac Oncol*. 2019;14:793–801.
37. Huang D, Zhou C, Barnes G, et al. The effects of tislelizumab treatment on the health-related quality of life of patients with advanced non-small cell lung cancer. *Cancer Med*. 2023;12:17403–17412.
38. Reck M, Taylor F, Penrod JR, et al. Impact of nivolumab versus docetaxel on health-related quality of life and symptoms in patients with advanced squamous non-small cell lung cancer: results from the CheckMate 017 study. *J Thorac Oncol*. 2018;13:194–204.
39. Reck M, Brahmer J, Bennett B, et al. Evaluation of health-related quality of life and symptoms in patients with advanced non-squamous non-small cell lung cancer

treated with nivolumab or docetaxel in CheckMate 057. *Eur J Cancer*. 2018;102:23–30.
40. Novello S, Kaiser R, Mellemgaard A, et al. Analysis of patient-reported outcomes from the LUME-Lung 1 trial: a randomised, double-blind, placebo-controlled, Phase III study of second-line nintedanib in patients with advanced non-small cell lung cancer. *Eur J Cancer*. 2015;51:317–326.
41. Pérol M, Ciuleanu TE, Arrieta O, et al. Quality of life results from the phase 3 REVEL randomized clinical trial of ramucirumab-plus-docetaxel versus placebo-plus-docetaxel in advanced/metastatic non-small cell lung cancer patients with progression after platinum-based chemotherapy. *Lung Cancer*. 2016;93:95–103.
42. Bordoni R, Ciardiello F, von Pawel J, et al. Patient-reported outcomes in OAK: A Phase III study of atezolizumab versus docetaxel in advanced non-small-cell lung cancer. *Clin Lung Cancer*. 2018;19:441–449.e4.
43. Ahn MJ, Tanaka K, Paz-Ares L, et al. Datopotamab deruxtecan versus docetaxel for previously treated advanced or metastatic non-small cell lung cancer: the randomized, open-label phase III TROPION-Lung01 study. *J Clin Oncol*. 2025;43:260–272.