2024 ASCO Annual Meeting, May 31 – June 4, 2024, Chicago, IL, USA

Sacituzumab Govitecan vs Docetaxel in Patients With Metastatic Non-small Cell Lung Cancer Previously Treated With Platinum-Based Chemotherapy and PD-(L)1 Inhibitors: Primary Results From the Phase 3 EVOKE-01 Study

Luis G. Paz-Ares, MD, PhD,[1] Oscar Juan-Vidal, MD,[2] Giannis S. Mountzios, MD, PhD,[3] Enriqueta Felip, MD, PhD,[4] Niels Reinmuth, MD,[5] Filippo de Marinis, MD, PhD,[6] Nicolas Girard, MD, PhD,[7] Vipul M. Patel, MD,[8] Takayuki Takahama, MD, PhD,[9] Scott P. Owen, MD,[10] Douglas M. Reznick, MD,[11] Firas B. Badin, MD,[12] Irfan Cicin, MD,[13] Sabeen Mekan, MD,[14] Riddhi Patel, PharmD,[14] Eric Zhang, PhD,[14] Divyadeep Karumanchi, PharmD,[14] Marina Chiara Garassino, MD[15]

[1]Hospital Universitario 12 de Octubre, H12O-CNIO Lung Cancer Unit, Complutense University and Ciberoncse University and Ciberonc, Madrid, Spain; [2]Hospital Universitari i Politécnic La Fe de Valencia, Valencia, Spain; [3]Henry Dunant Hospital Center, Athens, Greece; [4]Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology, Barcelona, Spain; [5]Asklepios Lung Clinic, German Center for Lung Research (DZL), Munich-Gauting, Germany; [6]European Institute of Oncology IRCCS, Milan, Italy; [7]Institut du Thorax Curie Montsouris, Institut Curie, Paris, France; [8]Florida Cancer Specialists and Research Institute, Ocala, FL, USA; [9]Kindai University, Osaka, Japan; [10]McGill University Health Centre, Montreal, Quebec, Canada; [11]Rocky Mountain Cancer Center, Aurora, CO, USA; [12]Baptist Health Medical Group, Lexington, KY, USA; [13]Istinye University, Medical Center, Istanbul, Turkey; [14]Gilead Sciences, Inc, Foster City, CA, USA; [15]University of Chicago Comprehensive Cancer Center, Chicago, IL, USA

Background

- Docetaxel remains the standard-of-care treatment for mNSCLC that progresses after platinum-based chemotherapy and anti-PD-(L)1–containing regimens,[1] but it is associated with modest clinical outcomes[2-4]
- Sacituzumab govitecan is a Trop-2–directed ADC approved globally for 2L+ mTNBC and 2L+ HR+/HER2− mBC and approved in the US for 2L mUC via an accelerated approval program[5,6]
- Patients with heavily pretreated mNSCLC derived durable clinical benefit from sacituzumab govitecan, with an ORR of 17% in the IMMU-132-01 study[7]
- Here, we provide the primary results of EVOKE-01 (NCT05089734)—an open-label, global, multicenter, randomized, phase 3 study of sacituzumab govitecan—versus docetaxel in advanced NSCLC or mNSCLC that progressed on or after platinum-based chemotherapy and an anti-PD-(L)1–containing regimen

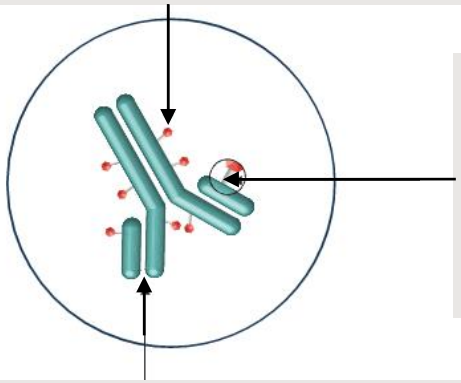
2L, second-line; 2L+, second-line and beyond; ADC, antibody-drug conjugate; HER2−, human epidermal growth factor receptor 2-negative; HR+, hormonal receptor-positive; mBC, metastatic breast cancer; mNSCLC, metastatic non-small cell lung cancer; mTNBC, metastatic triple-negative breast cancer; mUC, metastatic urothelial cancer; NSCLC, non-small cell lung cancer; ORR, objective response rate; PD-(L)1, programmed death (ligand) 1; Trop-2, trophoblast cell surface antigen 2; US, United States.

1. Hendriks LE, et al. *Ann Oncol*. 2023;34:358-376. 2. Borghaei H, et al. *J Clin Oncol*. 2021;39:723-733. 3. Mazieres J, et al. *J Thorac Oncol*. 2021;16:140-150. 4. Shi Y, et al. *Cancer Commun*. 2022;42:1314-1330. 5. TRODELVY® (sacituzumab govitecan-hziy) [prescribing information]. Foster City, CA: Gilead Sciences, Inc; April 2024. 6. TRODELVY® (sacituzumab govitecan-hziy) [summary of product characteristics]. Carrigtohill, Ireland: Gilead Sciences Ireland UC; July 2023. 7. Heist RS, et al. *J Clin Oncol*. 2017;35:2790-2797.

Sacituzumab Govitecan Is a First-in-Class Trop-2–Directed Antibody-Drug Conjugate

SN-38 payload

- SN-38 is more potent than the parent compound, irinotecan (Topo-1 inhibitor)
- SN-38 is rapidly internalized and efficiently released to the tumor with minimized effect on healthy tissues



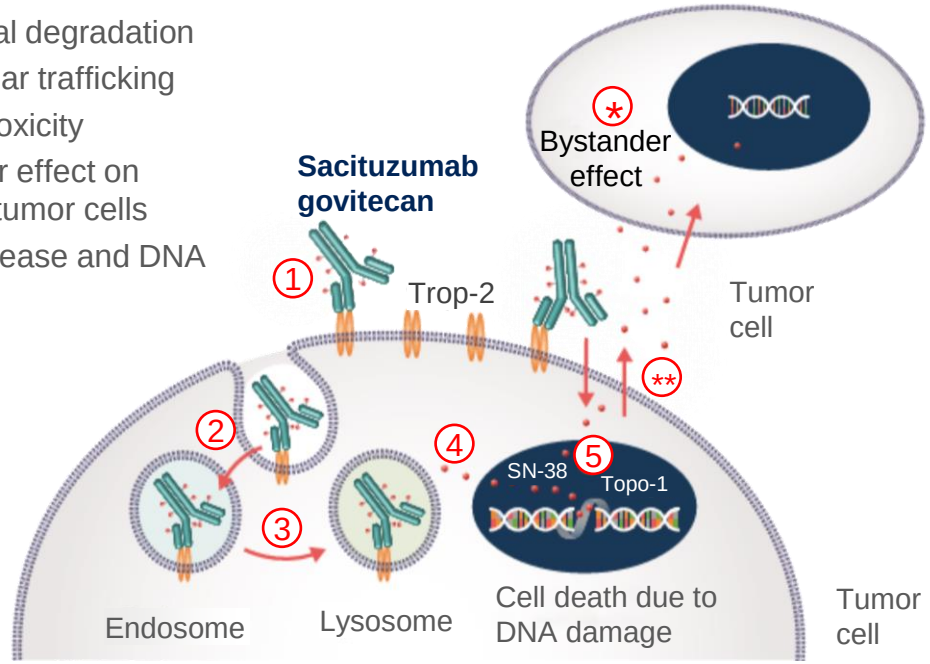
Linker for SN-38

- pH-sensitive, hydrolyzable linker for SN-38 release in targeted tumor cells and tumor microenvironment, allowing bystander effect
- High drug-to-antibody ratio (7.6:1)[1]

Humanized anti–Trop-2 antibody

- Binds with high (K_D = 0.3 nM) affinity to Trop-2, an epithelial antigen expressed on many solid tumors[2]

① Binding
② Internalization
③ Lysosomal degradation
④ Intracellular trafficking
⑤ Cell cytotoxicity
* Bystander effect on adjacent tumor cells
** SN-38 release and DNA damage



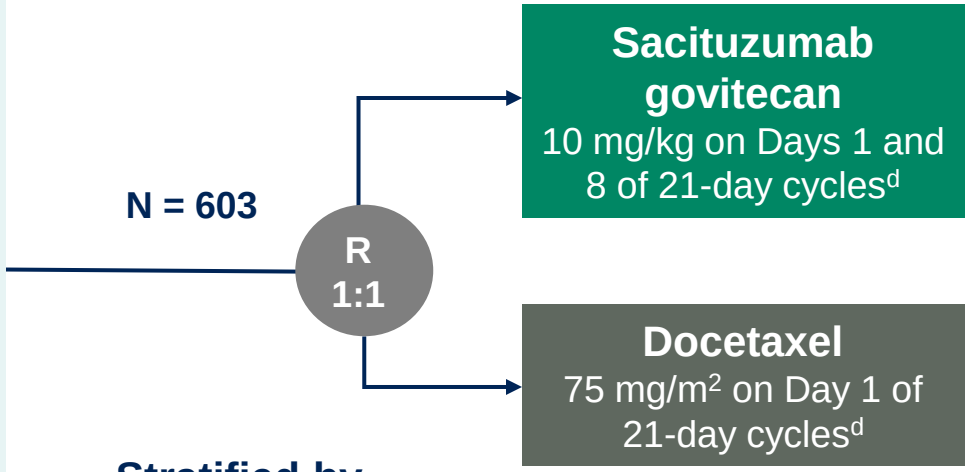
- Trop-2 is a transmembrane calcium signal transducer expressed on many solid tumors[3,4]
- SG is a first-in-class Trop-2–directed ADC that selectively delivers SN-38, an active metabolite of irinotecan[1]

ADC, antibody-drug conjugate; SG, sacituzumab govitecan; Topo-1, topoisomerase-1; Trop-2, trophoblast cell surface antigen 2. 1. Goldenberg DM, et al. *Oncotarget*. 2015;6:22496-22512. 2. Agatsuma T, et al. Patent: US 9850312 B2. Daiichi Sankyo. 2017. 3. Ambrogi F, et al. *PLoS One*. 2014;9:e96993. 4. Trerotola M, et al. *Oncogene*. 2013;32(2):222-233.

EVOKE-01: Global, Randomized, Open-Label, Phase 3 Study

Key eligibility criteria

- Measurable stage IV NSCLC
- ECOG PS 0–1
- Radiographic progression after platinum-based and anti-PD-(L)1–containing regimen[a]
- In addition, patients with known AGAs must have received ≥ 1 approved TKI[b]
  - *EGFR/ALK* test required. Testing of other AGAs recommended[c]
- Previously treated stable brain metastases were included
- No prior treatment with Topo-1 inhibitors, Trop-2–targeted therapies, or docetaxel



End points

Primary

- OS

Secondary

- PFS, ORR, DOR, and DCR by INV per RECIST v1.1
- Safety and tolerability
- QoL using NSCLC-SAQ

Stratified by

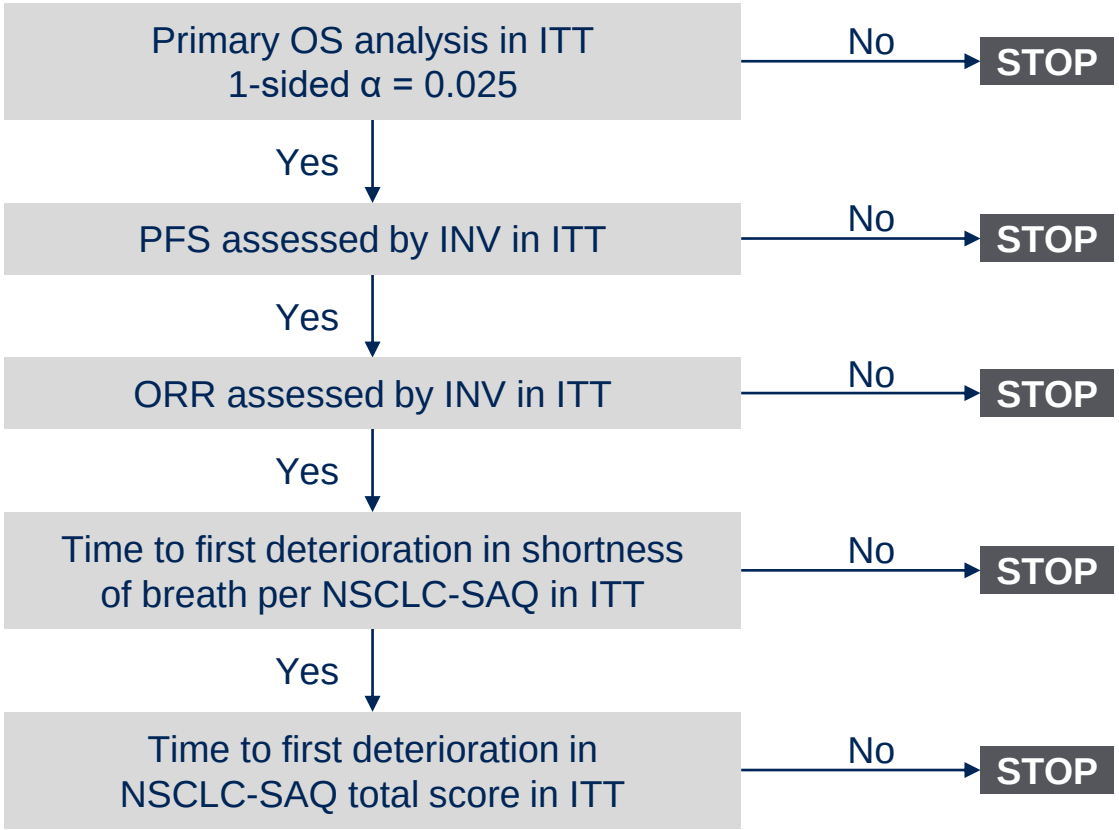
- **Histology** (squamous vs nonsquamous)
- **Response to last anti-PD-(L)1–containing regimen** (responsive [best response CR/PR] vs nonresponsive [PD/SD])
- **Received prior targeted therapy for AGA** (yes vs no)

At data cutoff (29 November 2023), the study median follow-up was 12.7 months (range, 6.0–24.0)

[a](Neo)adjuvant therapy counted if progression within 6 months of platinum treatment and while on maintenance with checkpoint inhibitor agent. [b]If local approval exists for targeted therapy to that genomic alteration. [c]Based on local SOC and availability of testing/approved targeted agent. [d]Until PD or unacceptable toxicity. AGA, actionable genomic alteration; CR, complete response; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; INV, investigator; NSCLC, non-small cell lung cancer; NSCLC-SAQ, Non-small Cell Lung Cancer Symptom Assessment Questionnaire; ORR, objective response rate; OS, overall survival; PD, progressive disease; PD-(L)1, programmed death (ligand) 1; PFS, progression-free survival; PR, partial response; QoL, quality of life; R, randomization; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease; SOC, standard of care; TKI, tyrosine kinase inhibitor; Topo-1, topoisomerase-1; Trop-2, trophoblast cell surface antigen 2.

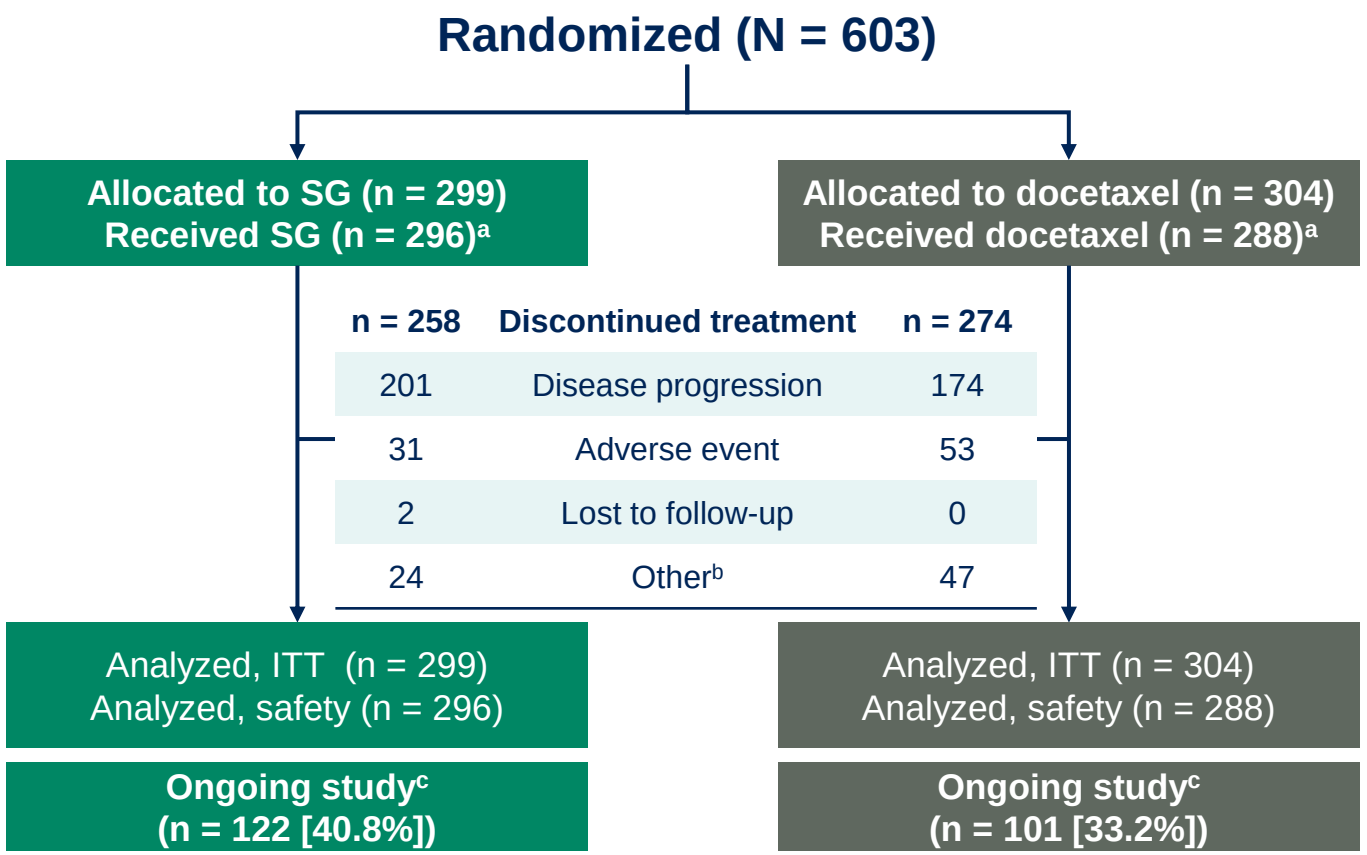
EVOKE-01 Statistical Testing Strategy

- ≈336 death events were planned to detect the OS HR of 0.7 for SG versus docetaxel at a 1-sided α of 0.025 with 90% power
- End points are tested in a hierarchical manner, starting with the primary end point OS
- The study had 1 interim and 1 final analysis, with a 1-sided α of 0.0075 spent before final analysis
- Final analysis was event-driven and occurred with a minimum 6-month follow-up
  - The 1-sided *P*-value boundary for final analysis was ≤ 0.0223



HR, hazard ratio; INV, investigator; ITT, intent-to-treat population; NSCLC-SAQ, Non-small Cell Lung Cancer Symptom Assessment Questionnaire; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; SG, sacituzumab govitecan.

Exposure and Disposition



Treatment exposure[d]

All treated patients	SG (n = 296)	Docetaxel (n = 288)
Median duration of exposure, months (range)	3.45 (0.03–18.69)	2.33 (0.03–19.75)
Median number of cycles received (range)	5 (1–28)	4 (1–29)
Exposure duration ≥ 6 months, n (%)	99 (33.4)	50 (17.4)

[a]Nineteen patients randomly allocated (3 to SG and 16 to docetaxel) but not treated (12 withdrew consent, 6 no longer met inclusion criteria, 1 death). [b]Other reasons for discontinued treatment include investigator's decision (SG, n = 5; docetaxel, n = 13), patient's decision (SG, n = 9; docetaxel, n = 18), protocol deviation (SG, n = 0; docetaxel, n = 0), and death (SG, n = 10; docetaxel, n = 16). [c]Either on-treatment or survival follow-up. [d]The safety population was defined as all patients who received ≥ 1 dose of a study treatment. ITT, intent-to-treat; SG, sacituzumab govitecan.

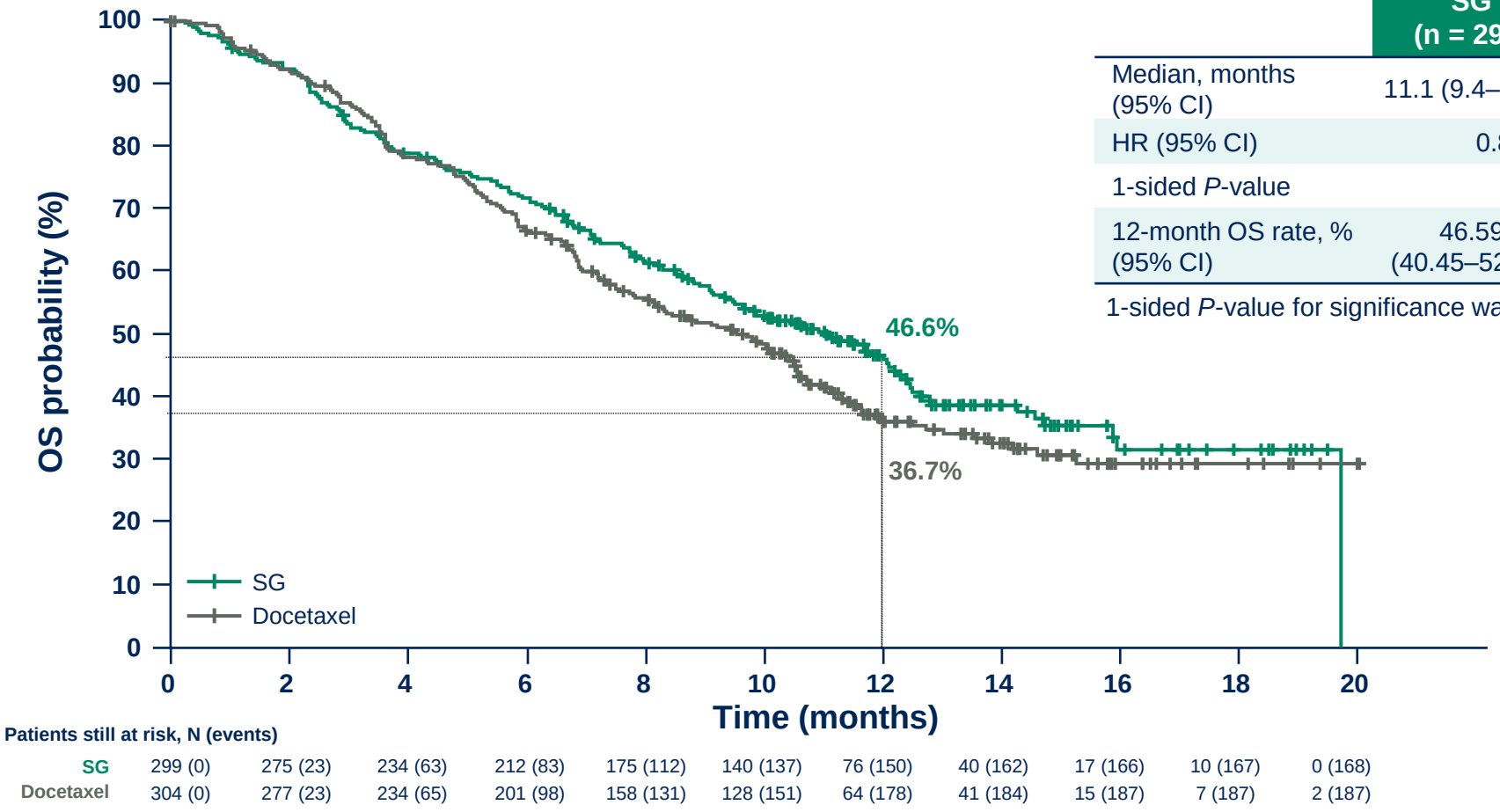
Patient Baseline Characteristics (ITT)

Characteristic	SG (n = 299)	Docetaxel (n = 304)
Median age (range), years	66 (31–84)	64 (32–83)
Male, %	64.9	71.1
Race, %		
Asian	5.7	8.6
Black	2.0	2.3
White	76.6	71.1
Other[a]	15.7	18.1
ECOG PS,[b] %		
0	33.8	29.3
1	66.2	69.7
Disease stage at diagnosis,[c] %		
Stage I-III	25.4	33.6
Stage IV	73.2	66.4
Prior lines of therapy, %		
1	55.9	54.9
2	34.4	33.2
≥ 3	9.7	11.8
History of brain metastasis, %	11.7	12.8

Characteristic	SG (n = 299)	Docetaxel (n = 304)
Histology,[d] %		
Nonsquamous[e]	71.9	73.7
Squamous	28.1	26.3
Best response to last anti-PD-(L)1–containing regimen,[d] %		
Responsive (CR/PR)	35.5	37.2
Nonresponsive (PD/SD)	64.2	62.8
Not available	0.3	0
Prior therapy for AGA,[d] %		
No	93.6	91.8
Yes[f]	6.4	8.2
EGFR	2.0	4.3
ALK	0.3	0.3
Other[g]	5.7	4.9

[a]Other races includes American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, other, and not reported. [b]ECOG PS = 2 for 1 patient in the docetaxel group on Cycle 1, Day 1. [c]All patients had stage IV NSCLC at time of randomization. [d]Stratification factors. [e]Nonsquamous includes patients with NSCLC with "not otherwise specified" histology. [f]Patients with multiple types of AGA were counted once for each type; percentages are calculated on the basis of the number of patients in the ITT population. [g]Includes *MET, KRAS, BRAF V600E, NTRK, RET, ROS1*, and other AGAs; some patients may have multiple gene mutations, and percentages do not add up to 100%. AGA, actionable genomic alteration; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; ITT, intent-to-treat; NSCLC, non-small cell lung cancer; PD, progressive disease; PD-(L)1, programmed death (ligand) 1; PR, partial response; SD, stable disease; SG, sacituzumab govitecan.

Primary End Point: Overall Survival (ITT)



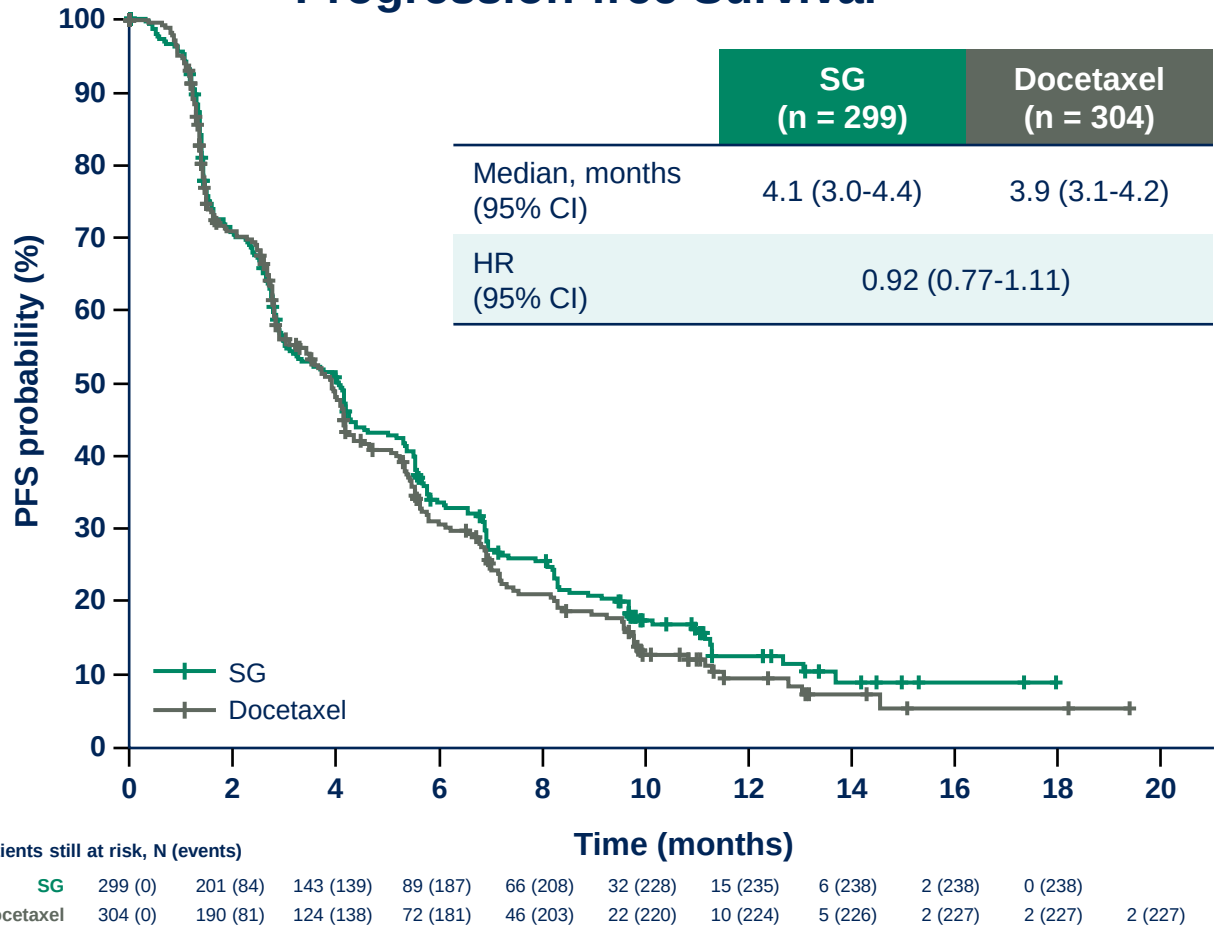
	SG (n = 299)	Docetaxel (n = 304)
Median, months (95% CI)	11.1 (9.4–12.3)	9.8 (8.1–10.6)
HR (95% CI)	0.84 (0.68–1.04)	
1-sided *P*-value	0.0534	
12-month OS rate, % (95% CI)	46.59 (40.45–52.50)	36.72 (30.88–42.57)

1-sided *P*-value for significance was $P \leq 0.0223$

CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; OS, overall survival; SG, sacituzumab govitecan.

Secondary End Points (ITT)

Progression-free Survival[a]



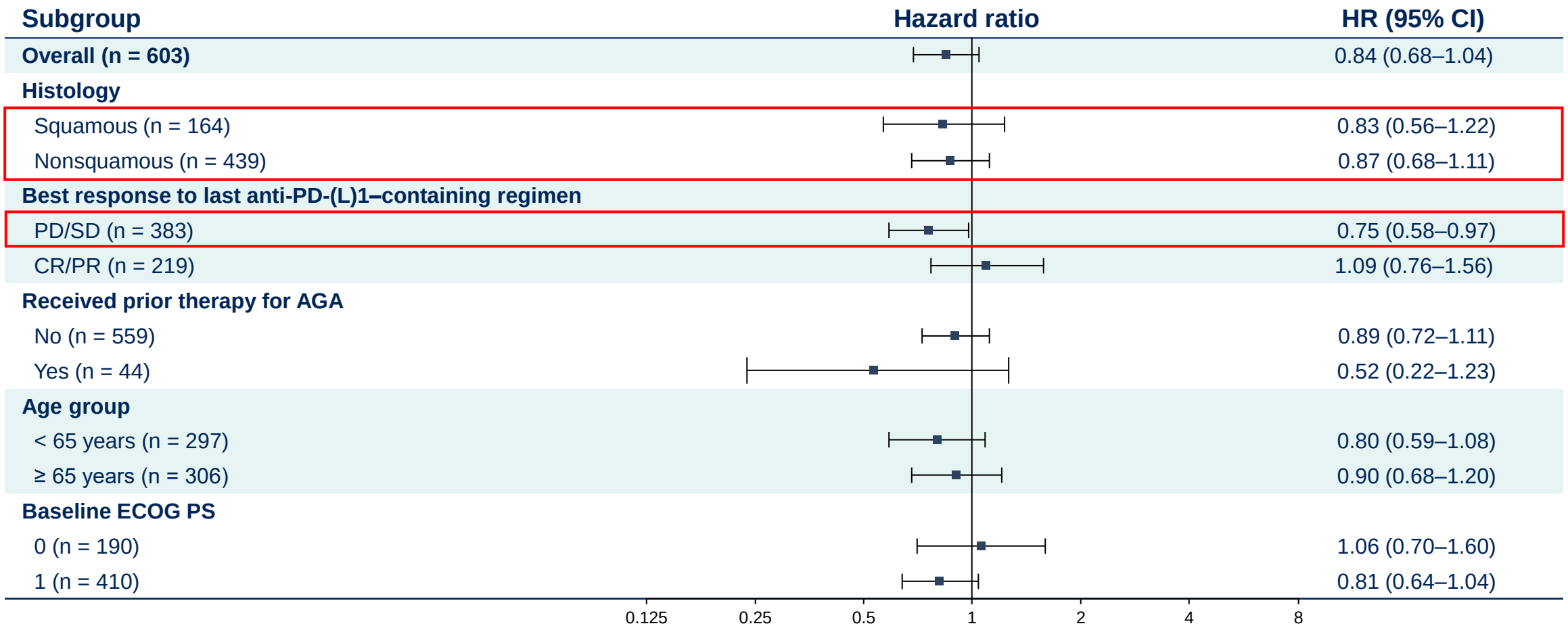
	SG (n = 299)	Docetaxel (n = 304)
Median, months (95% CI)	4.1 (3.0-4.4)	3.9 (3.1-4.2)
HR (95% CI)	0.92 (0.77-1.11)	

Objective Response Rate[a]

	SG (n = 299)	Docetaxel (n = 304)
ORR, % (95% CI)	13.7 (10.0–18.1)	18.1 (13.9–22.9)
DCR, % (95% CI)	67.6 (61.9–72.8)	67.1 (61.5–72.4)
Median DOR, months (95% CI)	6.7 (4.4–9.8)	5.8 (4.1–8.3)
DOR rate at 6 months, % (95% CI)	52.5 (35.6–66.9)	46.5 (31.9–59.8)

[a]By INV assessment. CI, confidence interval; DCR, disease control rate; DOR, duration of response; HR, hazard ratio; INV, investigator; ITT, intent-to-treat; ORR, objective response rate; PFS, progression-free survival; SG, sacituzumab govitecan.

Overall Survival: Subgroup Analyses

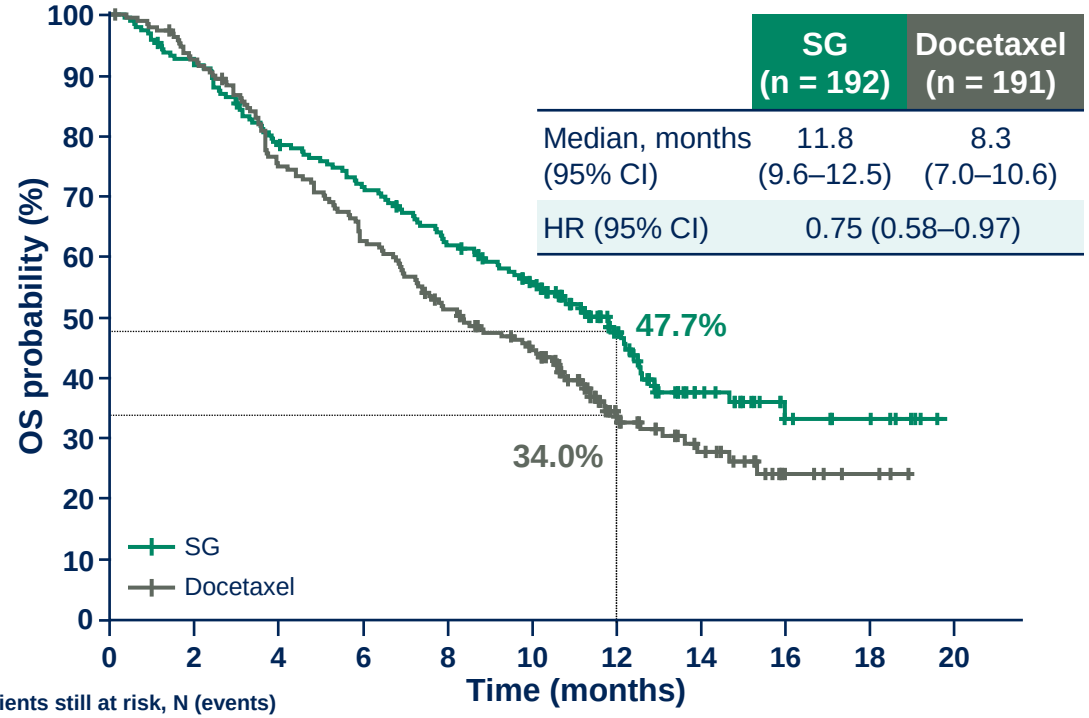


AGA, actionable genomic alteration; CI, confidence interval; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; PD, progressive disease; PD-(L)1, programmed death (ligand) 1; PR, partial response; SD, stable disease.

Overall Survival: Best Response to Last Anti-PD-(L)1–Containing Regimen

SG had a 3.5-month median OS improvement over docetaxel among subgroups with nonresponsive (SD/PD) disease

Nonresponsive (SD/PD)

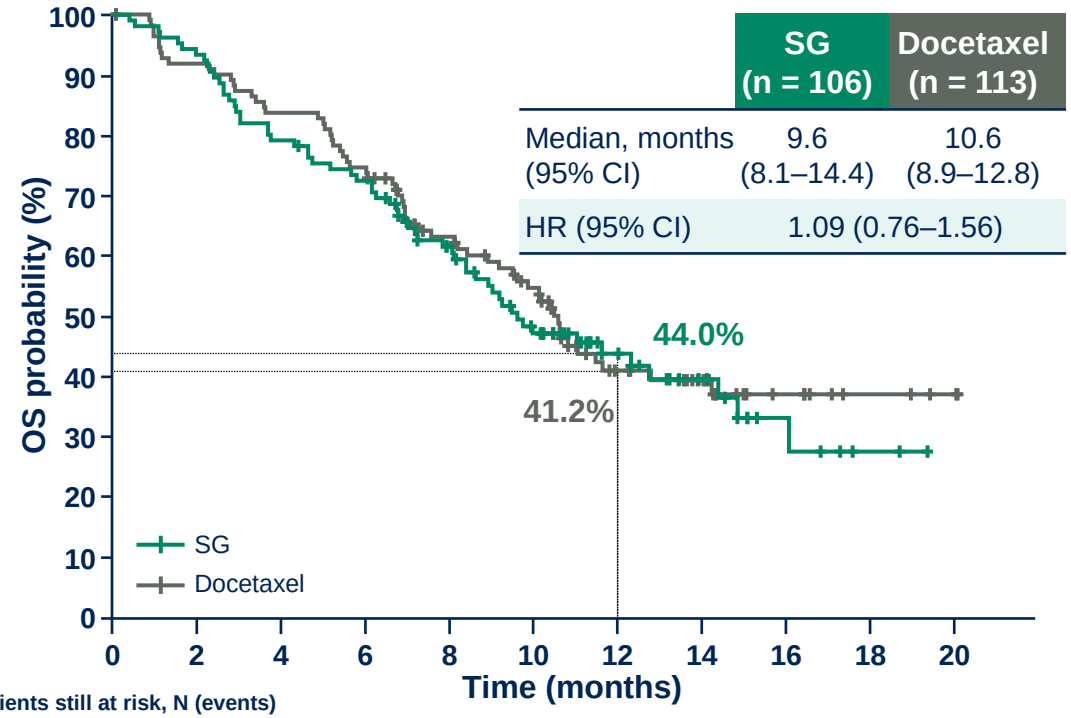


	SG (n = 192)	Docetaxel (n = 191)
Median, months (95% CI)	11.8 (9.6–12.5)	8.3 (7.0–10.6)
HR (95% CI)	0.75 (0.58–0.97)	

Patients still at risk, N (events)

SG	192 (0)	175 (16)	149 (41)	135 (54)	116 (72)	98 (84)	53 (95)	26 (105)	11 (107)	8 (107)	0 (108)
Docetaxel	191 (0)	175 (14)	141 (47)	118 (70)	95 (91)	78 (103)	36 (119)	21 (124)	6 (126)	3 (126)	0 (126)

Responsive (CR/PR)



	SG (n = 106)	Docetaxel (n = 113)
Median, months (95% CI)	9.6 (8.1–14.4)	10.6 (8.9–12.8)
HR (95% CI)	1.09 (0.76–1.56)	

Patients still at risk, N (events)

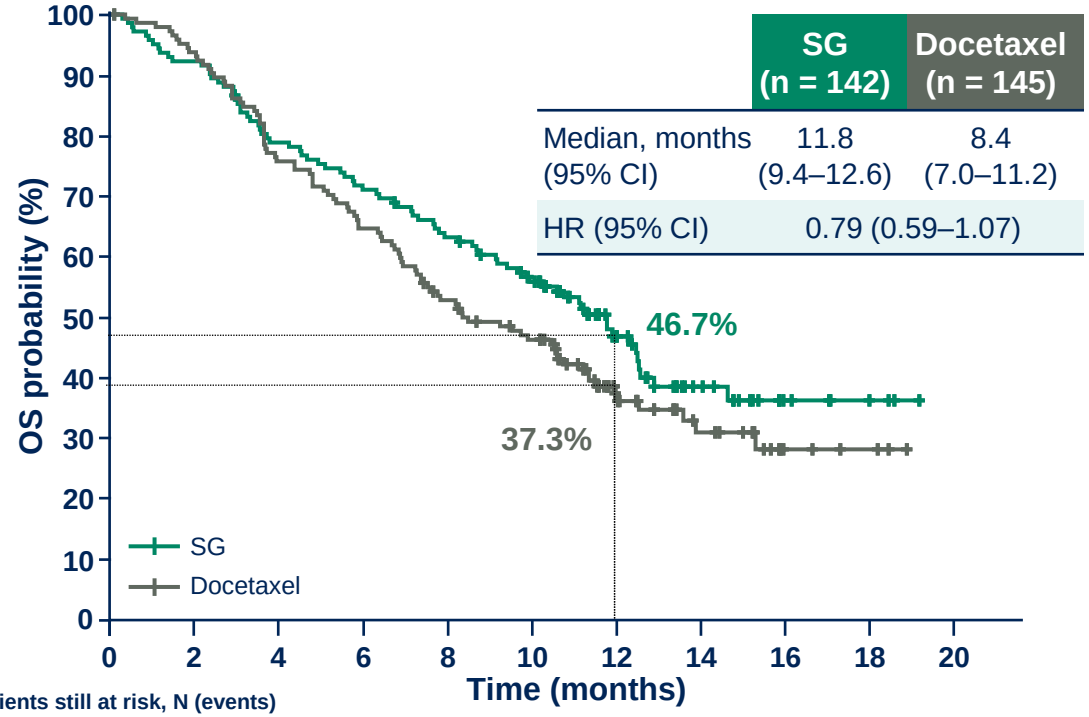
SG	106 (0)	99 (7)	84 (22)	76 (29)	58 (40)	41 (53)	22 (55)	14 (57)	6 (59)	2 (60)	0 (60)
Docetaxel	113 (0)	102 (9)	93 (18)	83 (28)	63 (40)	50 (48)	28 (59)	20 (60)	9 (61)	4 (61)	2 (61)

CI, confidence interval; CR, complete response; HR, hazard ratio; OS, overall survival; PD, progressive disease; PD-(L)1, programmed death (ligand) 1; PR, partial response; SD, stable disease; SG, sacituzumab govitecan.

Overall Survival: Nonresponsive (SD/PD) to Last Anti-PD-(L)1–Containing Regimen, by Histology

SG had similar OS improvement over docetaxel in both nonsquamous and squamous histology

Nonsquamous

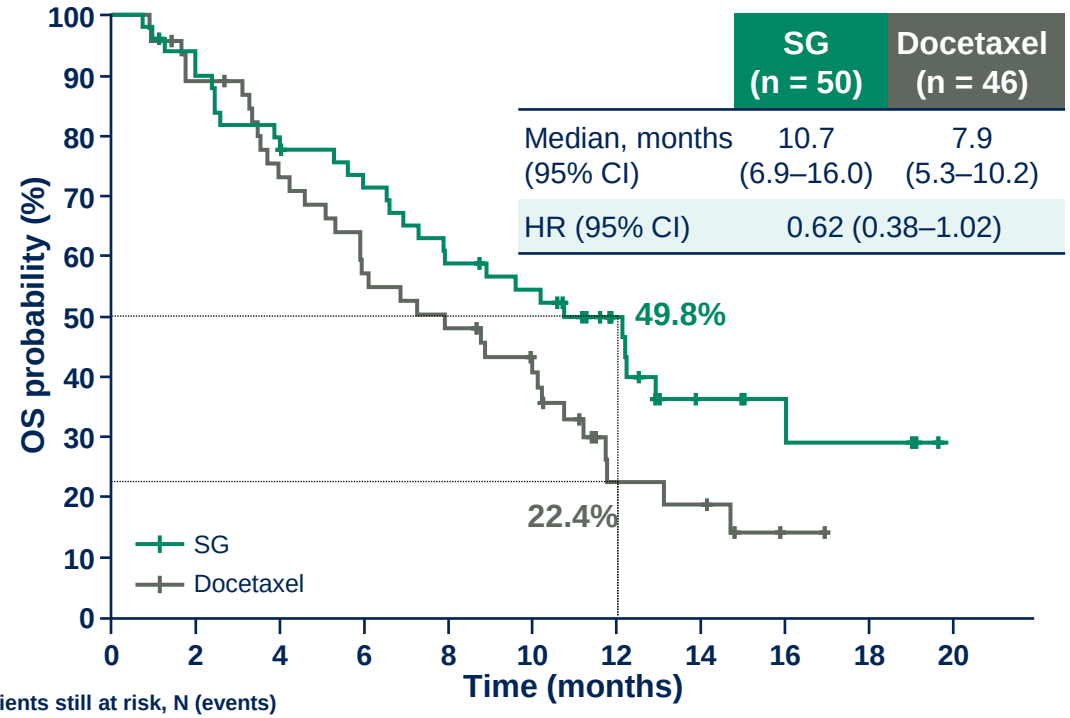


	SG (n = 142)	Docetaxel (n = 145)
Median, months (95% CI)	11.8 (9.4–12.6)	8.4 (7.0–11.2)
HR (95% CI)	0.79 (0.59–1.07)	

Patients still at risk, N (events)

SG	142 (0)	131 (11)	111 (30)	101 (40)	88 (52)	73 (62)	38 (71)	19 (77)	7 (78)	4 (78)	0 (78)
Docetaxel	145 (0)	135 (9)	109 (35)	93 (51)	74 (68)	62 (77)	30 (87)	16 (91)	5 (92)	3 (92)	0 (92)

Squamous



	SG (n = 50)	Docetaxel (n = 46)
Median, months (95% CI)	10.7 (6.9–16.0)	7.9 (5.3–10.2)
HR (95% CI)	0.62 (0.38–1.02)	

Patients still at risk, N (events)

SG	50 (0)	44 (5)	38 (11)	34 (14)	28 (20)	25 (22)	15 (24)	7 (28)	4 (29)	4 (29)	0 (30)
Docetaxel	46 (0)	40 (5)	32 (12)	25 (19)	21 (23)	16 (26)	6 (32)	5 (33)	1 (34)		

CI, confidence interval; HR, hazard ratio; OS, overall survival; PD, progressive disease; PD-(L)1, programmed death (ligand) 1; SD, stable disease; SG, sacituzumab govitecan.

Overall Safety Summary

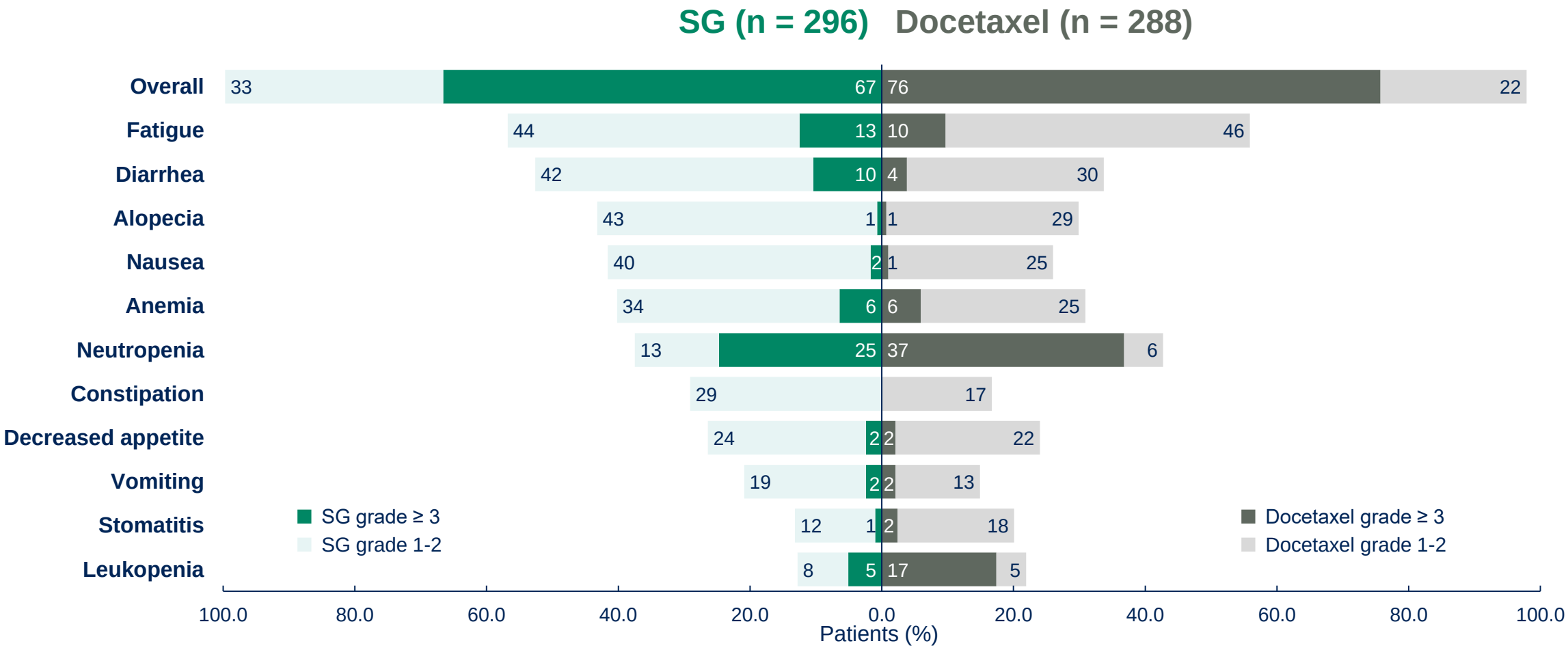
Safety-evaluable patients, n (%)	SG (n = 296)	Docetaxel (n = 288)
	TEAE	TEAE
Any grade	295 (99.7)	282 (97.9)
Grade ≥ 3	197 (66.6)	218 (75.7)
Serious	137 (46.3)	124 (43.1)
Leading to discontinuation	29 (9.8)	48 (16.7)
Leading to dose reduction	87 (29.4)	112 (38.9)
Leading to death[a]	10 (3.4)	13 (4.5)

- Overall, the incidence of grade ≥ 3 TEAEs was lower with SG
- TEAEs leading to dose reduction and discontinuation were lower with SG than docetaxel
- SG demonstrated a manageable safety profile, consistent with what is known, with no new safety signals

[a]TEAEs leading to death as determined by the investigator included cardiac failure, cerebrovascular accident, death, febrile neutropenia, hematemesis, ischemic stroke, myocardial ischemia, neutropenic colitis, sepsis and septic shock (1 each) in the SG arm; and death (n = 4), pneumonia (n = 3), cardiac failure, acute respiratory failure, cardiorespiratory arrest, intestinal obstruction, pneumonitis, and respiratory failure (1 each) in the docetaxel arm. SG, sacituzumab govitecan; TEAE, treatment-emergent adverse event.

Treatment-Emergent Adverse Events

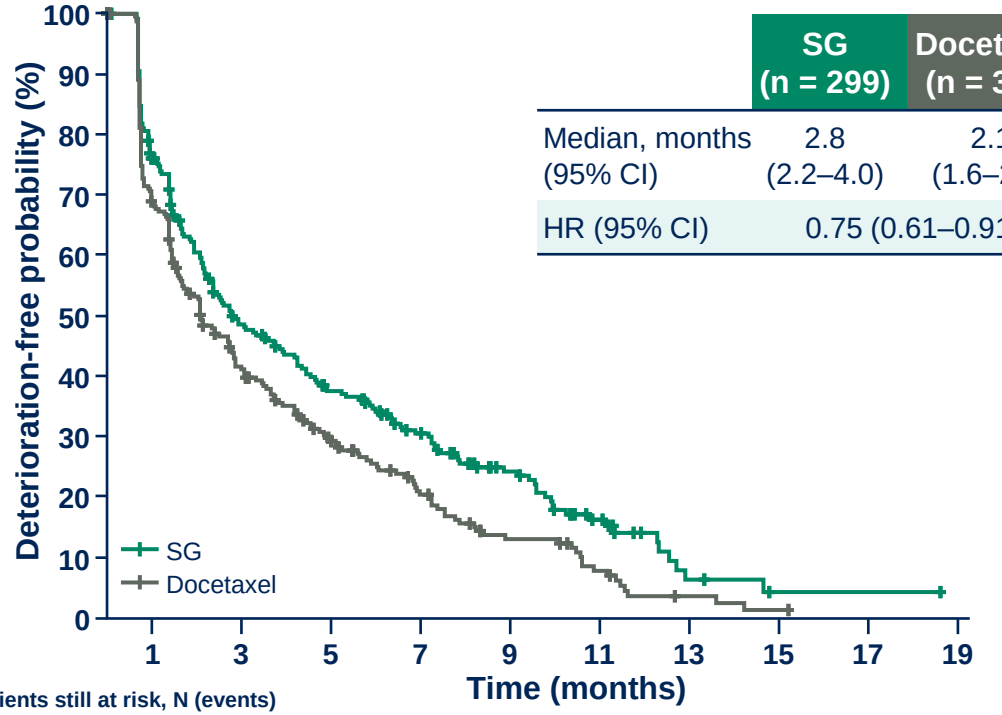
In ≥ 20% of patients receiving SG or docetaxel



SG, sacituzumab govitecan.

Secondary End Points: NSCLC–Symptom Assessment Questionnaire (SAQ) (ITT)

TTD in shortness-of-breath domain

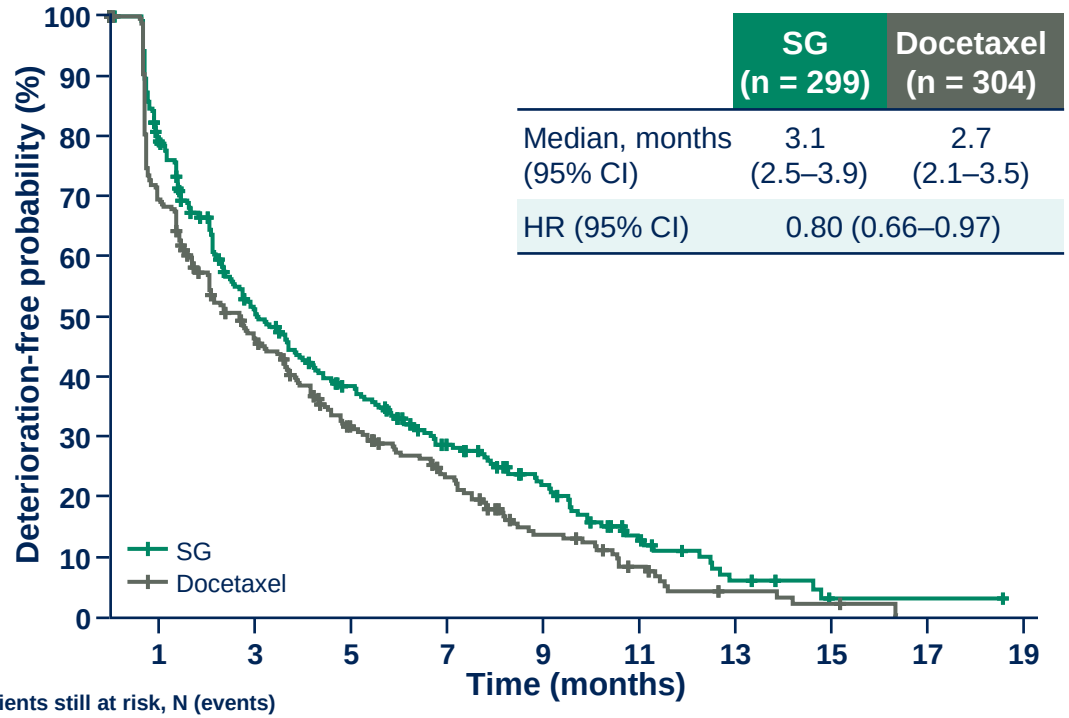


	SG (n = 299)	Docetaxel (n = 304)
Median, months (95% CI)	2.8 (2.2–4.0)	2.1 (1.6–2.9)
HR (95% CI)	0.75 (0.61–0.91)	

Patients still at risk, N (events)

SG	183 (56)	108 (121)	79 (145)	57 (159)	35 (170)	17 (181)	4 (188)	1 (189)	1 (189)	0 (189)
Docetaxel	168 (70)	91 (137)	59 (162)	35 (179)	19 (191)	10 (198)	3 (203)	1 (205)		

TTD in NSCLC-SAQ total score



	SG (n = 299)	Docetaxel (n = 304)
Median, months (95% CI)	3.1 (2.5–3.9)	2.7 (2.1–3.5)
HR (95% CI)	0.80 (0.66–0.97)	

Patients still at risk, N (events)

SG	207 (50)	123 (122)	86 (153)	57 (174)	37 (185)	17 (199)	6 (207)	1 (209)	1 (209)	0 (209)
Docetaxel	178 (71)	110 (130)	68 (165)	44 (182)	22 (199)	11 (207)	4 (212)	2 (214)	0 (215)	

CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; NSCLC-SAQ, Non-small Cell Lung Cancer Symptom Assessment Questionnaire; SG, sacituzumab govitecan; TTD, time to deterioration.

Conclusions

- EVOKE-01 did not meet the statistical significance for the primary end point of OS in ITT
  - A numerical improvement in median OS favoring SG was observed, with a 16% reduction in risk of death (HR [95% CI], 0.84 [0.68–1.04]) and a higher 12-month OS rate (SG, 46.6%; docetaxel, 36.7%)
  - Improvement in OS with SG was seen in both squamous and nonsquamous histologies
- A prespecified subgroup analysis showed meaningful improvement in OS of 3.5 months (HR [95% CI], 0.75 [0.58–0.97]) with SG in mNSCLC that was nonresponsive (SD/PD) to last anti-PD-(L)1–containing regimen
- SG had a favorable safety profile and was better tolerated than docetaxel
  - Grade ≥ 3 AEs and AEs leading to discontinuation were lower among patients receiving SG than docetaxel
- Patients reported improvement in NSCLC-related symptoms, reflective of better tolerability and disease control with SG
- SG is an active and tolerable treatment option for patients with previously treated mNSCLC
  - SG is being evaluated in combination with immunotherapy in the first-line setting (EVOKE-02, NCT05186974; EVOKE-03, NCT05609968)

AE, adverse event; CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat population; mNSCLC, metastatic NSCLC; NSCLC, non-small cell lung cancer; OS, overall survival; PD, progressive disease; PD-(L)1, programmed death (ligand) 1; SD, stable disease; SG, sacituzumab govitecan.

Acknowledgments

- We want to thank the patients and their caregivers for their participation and commitment to clinical research
- Thank you to the clinical trial investigators and their team members, without whom this work would not have been possible
- This study was sponsored by Gilead Sciences, Inc
- Medical writing and editorial support were provided by Jan Nagel and Celia Nelson of Ashfield MedComms, an Inizio company, and funded by Gilead Sciences, Inc

Scan QR codes for a copy of the slides and access to a plain language summary infographic

Presentation slides

Copies of this slide deck obtained through Quick Response (QR) Code are for personal use only and may not be reproduced without permission from ASCO® or the author of these slides.

Plain language summary

Copies of a plain language summary of this presentation obtained through Quick Response (QR) Code are for personal use only and may not be reproduced without permission from ASCO® or the author of these slides.