# Sacituzumab Govitecan vs Docetaxel in Patients With mNSCLC Non-Responsive to Last Anti-PD-(L)1–Containing Regimen: EVOKE-01

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# Background

- For mNSCLC that progresses after platinum-based chemotherapy and anti-PD-(L)1–containing regimens, docetaxel remains the standard-of-care treatment,[1] but it is associated with modest clinical outcomes[2-4]

- Sacituzumab govitecan (SG) is a Trop-2–directed ADC approved globally for patients with 2L+ mTNBC and pretreated HR+/HER2− mBC and approved in the US for patients with pretreated mUC via an accelerated approval program[5,6]

- The phase 3 EVOKE-01 study evaluated SG vs docetaxel in patients with mNSCLC progressing after platinum-based chemotherapy and anti–PD-(L)1 treatment[7]
  - Patients were randomized to receive either 10 mg/kg SG on days 1 and 8 or 75 mg/m$^2$ docetaxel on day 1 of each 21-day cycle

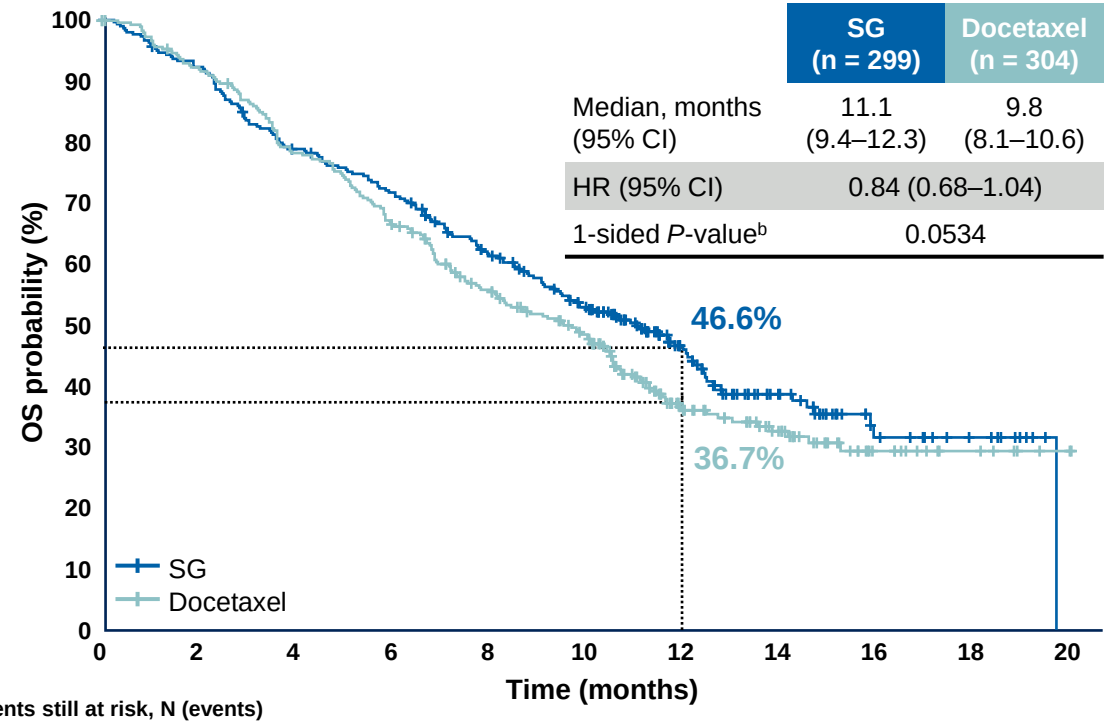
**2L+,** second line and beyond; **ADC**, antibody-drug conjugate; **HER2−**, human epidermal growth factor receptor 2–negative; **HR+**, hormonal receptor–positive; **mBC**, metastatic breast cancer; **mNSCLC**, metastatic non-small cell lung cancer; **mTNBC**, metastatic triple-negative breast cancer;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

1. Hendriks LE, et al. *Ann Oncol*. 2023;34:358-76. 2. Borghaei H, et al. *J Clin Oncol*. 2021;39:723-33. 3. Mazieres J, et al. *J Thorac Oncol*. 2021;16:140-50. 4. Shi Y, et al. *Cancer Commun*. 2022;42:1314-30. 5. TRODELVY® (sacituzumab govitecan-hziy) [prescribing information]. Foster City, CA: Gilead Sciences, Inc; April 2024. 6. TRODELVY® (sacituzumab govitecan-hziy) [summary of product characteristics]. Carrigtwohill, Ireland: Gilead Sciences Ireland UC; July 2023. 7. Paz-Ares LG, et al. *J Clin Oncol*. Published online May 31, 2024. doi:10.1200/JCO.24.00733.

# Background: EVOKE-01 Primary Results[1]

- There was a clinically meaningful OS improvement favoring SG over docetaxel in patients with mNSCLC that was non-responsive (SD/PD) to their last anti-PD-(L)1–containing regimen[a]
  — Here we discuss this subgroup

## OS: ITT

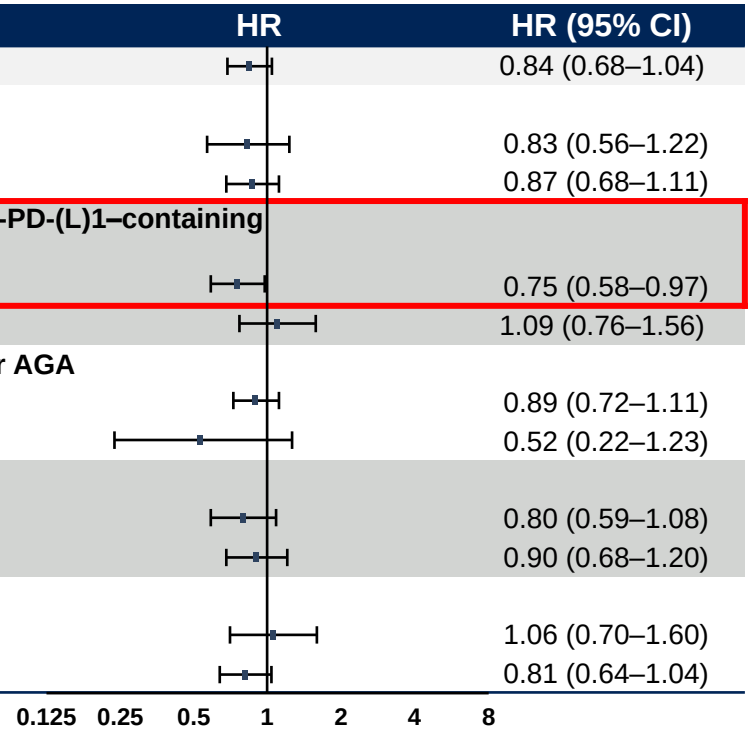



| | SG (n = 299) | Docetaxel (n = 304) |
|---|---|---|
| Median, months (95% CI) | 11.1 (9.4–12.3) | 9.8 (8.1–10.6) |
| HR (95% CI) | 0.84 (0.68–1.04) | |
| 1-sided *P*-value[b] | 0.0534 | |

**Patients still at risk, N (events)**

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| SG | 299 (0) | 275 (23) | 234 (63) | 212 (83) | 175 (112) | 140 (137) | 76 (150) | 40 (162) | 17 (166) | 10 (167) | 0 (168) |
| Docetaxel | 304 (0) | 277 (23) | 234 (65) | 201 (98) | 158 (131) | 128 (151) | 64 (178) | 41 (184) | 15 (187) | 7 (187) | 2 (187) |

## OS: Key subgroups




[a]Investigator-assessed. [b]One-sided *P*-value for significance was $P \leq 0.0223$.

**AGA**, actionable genomic alteration; **CR**, complete response; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **HR**, hazard ratio; **ITT**, intent-to-treat; **mNSCLC**, metastatic non-small cell lung cancer; **OS**, overall survival; **PD**, progressive disease; **PD-(L)1**, programmed death (ligand) 1; **PR**, partial response; **SD**, stable disease; **SG**, sacituzumab govitecan.

1. Paz-Ares LG, et al. *J Clin Oncol*. Published online May 31, 2024. doi:10.1200/JCO.24.00733.

# Patient Baseline Characteristics

## In the non-responsive (SD/PD) subgroup, baseline characteristics were well balanced between treatment groups and consistent with those of the ITT population

| Characteristic | ITT (N = 603)[1] | | Non-responsive (SD/PD)[a] (n = 383) | |
|---|---|---|---|---|
| | SG (n = 299) | Docetaxel (n = 304) | SG (n = 192) | Docetaxel (n = 191) |
| **Median age (range), years** | 66 (31–84) | 64 (32–83) | 66 (31–84) | 64 (32–83) |
| **Sex, male, n (%)** | 194 (64.9) | 216 (71.1) | 123 (64.1) | 141 (73.8) |
| **Race, n (%)** | | | | |
| Asian | 17 (5.7) | 26 (8.6) | 5 (2.6) | 11 (5.8) |
| Black | 6 (2.0) | 7 (2.3) | 3 (1.6) | 4 (2.1) |
| White | 229 (76.6) | 216 (71.1) | 157 (81.8) | 144 (75.4) |
| Other[b] | 47 (15.7) | 55 (18.1) | 27 (14.1) | 32 (16.8) |
| **ECOG PS,[c] n (%)** | | | | |
| 0 | 101 (33.8) | 89 (29.3) | 58 (30.2) | 55 (28.8) |
| 1 | 198 (66.2) | 212 (69.7) | 134 (69.8) | 134 (70.2) |
| **Disease stage at diagnosis,[d] n (%)** | | | | |
| Stage I-III | 76 (25.4) | 102 (33.6) | 50 (26.0) | 73 (38.2) |
| Stage IV | 219 (73.2) | 202 (66.4) | 139 (72.4) | 118 (61.8) |
| **Prior lines of therapy, n (%)** | | | | |
| 1 | 167 (55.9) | 167 (54.9) | 97 (50.5) | 99 (51.8) |
| 2 | 103 (34.4) | 101 (33.2) | 72 (37.5) | 69 (36.1) |
| ≥ 3 | 29 (9.7) | 36 (11.8) | 23 (12.0) | 23 (12.0) |

| Characteristic, n (%) | ITT (N = 603)[1] | | Non-responsive (SD/PD)[a] (n = 383) | |
|---|---|---|---|---|
| | SG (n = 299) | Docetaxel (n = 304) | SG (n = 192) | Docetaxel (n = 191) |
| **History of brain metastasis, n (%)** | 35 (11.7) | 39 (12.8) | 21 (10.9) | 21 (11.0) |
| **Histology[e]** | | | | |
| Non-squamous[e] | 215 (71.9) | 224 (73.7) | 142 (74.0) | 145 (75.9) |
| Squamous | 84 (28.1) | 80 (26.3) | 50 (26.0) | 46 (24.1) |
| **Best response to last anti-PD-(L)1–containing regimen[a,e]** | | | | |
| Responsive (CR/PR) | 106 (35.5) | 113 (37.2) | 0 | 0 |
| Non-responsive (SD/PD) | 192 (64.2) | 191 (62.8) | 192 (100) | 191 (100) |
| Not available | 1 (0.3) | 0 | 0 | 0 |
| **Prior therapy for AGA[e]** | | | | |
| No | 280 (93.6) | 279 (91.8) | 180 (93.8) | 177 (92.7) |
| Yes[g] | 19 (6.4) | 25 (8.2) | 12 ( 6.3) | 14 (7.3) |
| **PD-L1 result[h]** | | | | |
| < 1% | 116 (38.8) | 127 (41.8) | 80 (41.7) | 80 (41.9) |
| ≥ 1% and ≤ 49% | 119 (39.8) | 116 (38.2) | 75 (39.1) | 75 (39.3) |
| ≥ 50% | 63 (21.1) | 59 (19.4) | 36 (18.8) | 35 (18.3) |
| Missing | 1 (0.3) | 2 (0.7) | 1 (0.5) | 1 (0.5) |

[a]Investigator-assessed. [b]Other races include American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, other, and not reported. [c]ECOG PS was missing for 2 patients in the docetaxel group within both the non-responsive subgroup and ITT subgroup. [d]All patients had stage IV NSCLC at time of randomization; 4 and 3 patients in the SG group of the ITT population and the non-responsive subgroup, respectively, had unknown disease stage at diagnosis. [e]Stratification factors. [e]Non-squamous includes patients with NSCLC with "not otherwise specified" histology. [g]Patients with multiple types of AGA were counted once for each type; percentages calculated on the basis of the number of patients in the population [h]Local PD-L1 tumor testing was done if PD-(L)1 status was unknown, or if local testing was unavailable, tumor testing could be done by the central laboratory.

**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.

1. Paz-Ares LG, et al. *J Clin Oncol*. Published online May 31, 2024.

# Prior Anti–PD-(L)1 Therapy and Treatment Response

## Prior therapies were well balanced between treatment groups and representative of the ITT population

| Characteristic | ITT (N = 603) | | Non-responsive (SD/PD) (n = 383) | |
|---|---|---|---|---|
| | SG (n = 299)[a] | Docetaxel (n = 304) | SG (n = 192) | Docetaxel (n = 191) |
| **Received anti–PD-(L)1 as most recent prior therapy, n (%)** | 247 (82.6) | 261 (85.9) | 161 (83.9) | 165 (86.4) |
| Monotherapy | 44 (14.7) | 54 (17.8) | 38 (19.8) | 36 (18.8) |
| Combined with chemotherapy | 201 (67.2) | 201 (66.1) | 121 (63.0) | 126 (66.0) |
| Combined with another type of therapy | 2 (0.7) | 6 (2.0) | 2 (1.0) | 3 (1.6) |
| **Did not receive anti–PD-(L)1 as most recent prior therapy, n (%)** | 51 (17.1) | 43 (14.1) | 31 (16.1) | 26 (13.6) |
| **Median treatment duration of the last anti-PD-(L)1–containing regimen, months** | 6.2 | 7.0 | 5.6 | 5.8 |

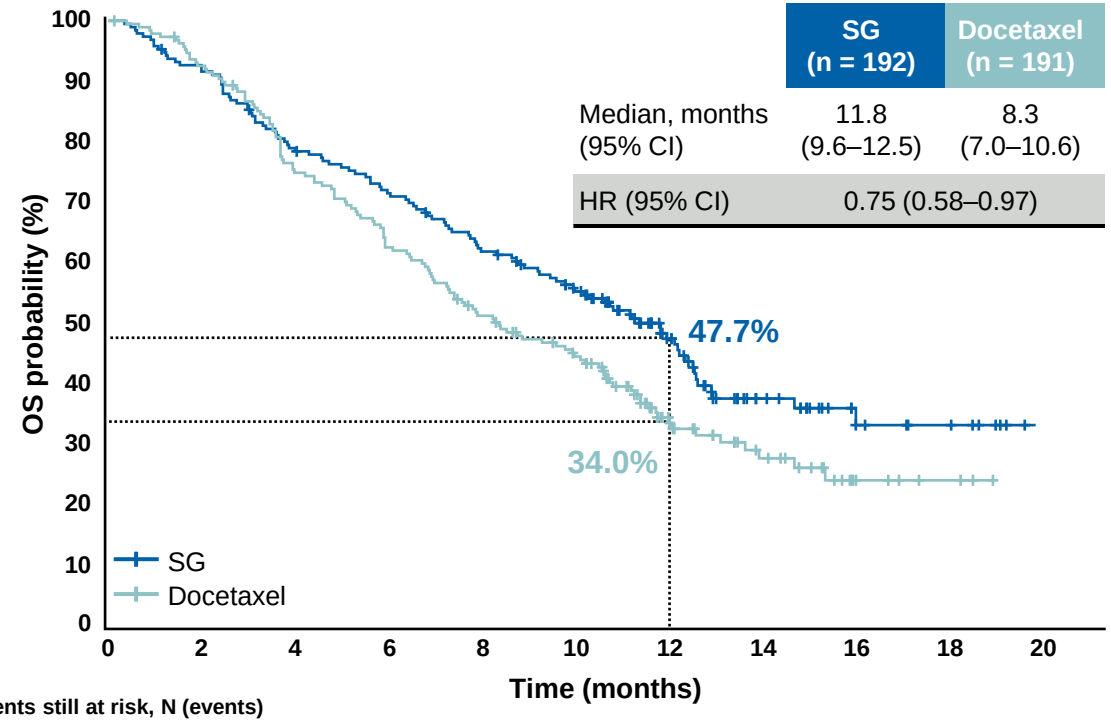
[a]One patient in the SG group did not have data available on their response to a prior anti-PD-(L)1–containing regimen.
**ITT**, intent-to-treat; **PD**, progressive disease; **PD-(L)1**, programmed death (ligand) 1; **SD**, stable disease; **SG**, sacituzumab govitecan.

# Efficacy: Non-Responsive (SD/PD) to Last Anti-PD-(L)1–Containing Regimen

## SG had a 3.5-month median OS improvement over docetaxel among the subgroup of patients with non-responsive (SD/PD) disease

### OS[1]

| | 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) | |

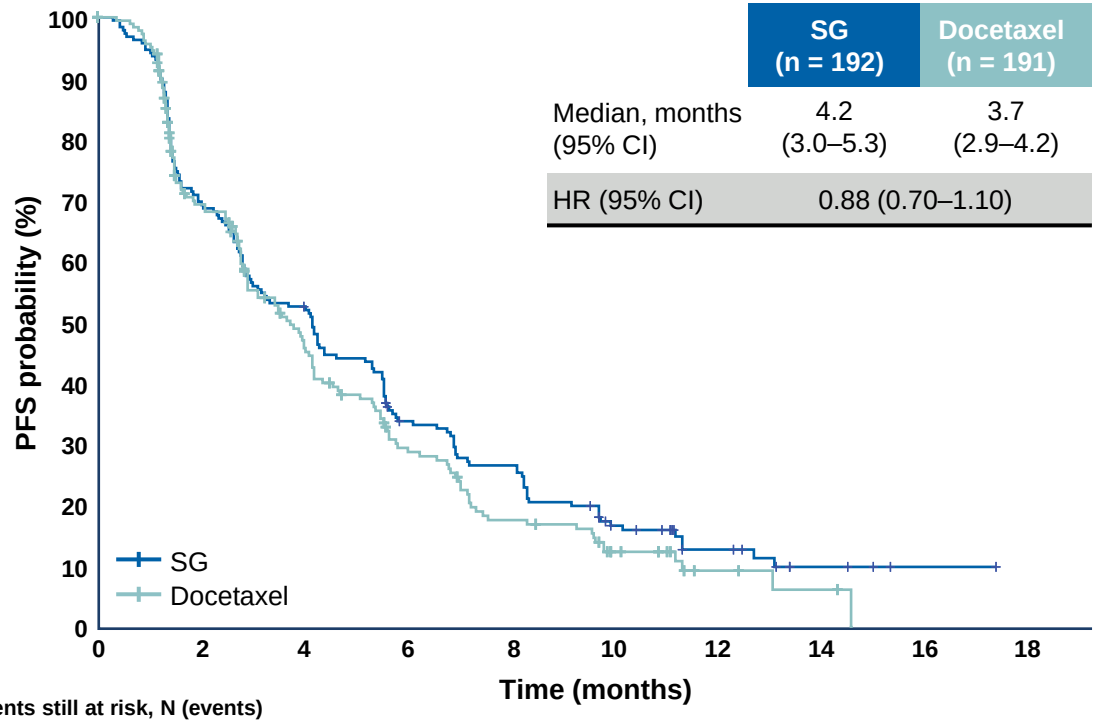



Patients still at risk, N (events)

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 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) |

### PFS[a]

| | SG (n = 192) | Docetaxel (n = 191) |
|---|---|---|
| Median, months (95% CI) | 4.2 (3.0–5.3) | 3.7 (2.9–4.2) |
| HR (95% CI) | 0.88 (0.70–1.10) | |




Patients still at risk, N (events)

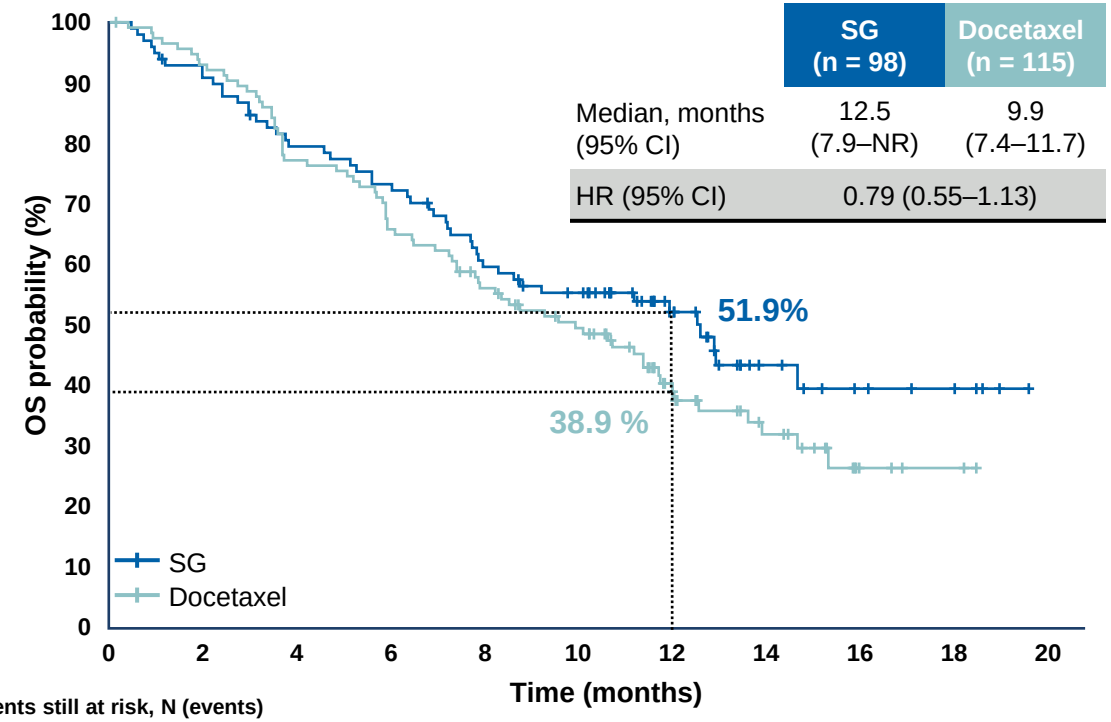
| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| SG | 192 (0) | 127 (56) | 94 (87) | 56 (120) | 44 (132) | 23 (148) | 11 (152) | 4 (154) | 1 (154) | 0 (154) |
| Docetaxel | 191 (0) | 116 (54) | 74 (90) | 43 (117) | 25 (134) | 13 (141) | 4 (143) | 2 (144) | 0 (145) | |

[a]By investigator assessment per Response Evaluation Criteria in Solid Tumors version 1.1.
**HR**, hazard ratio; **OS**, overall survival; **PD**, progressive disease; **PD-(L)1**, programmed death (ligand) 1; **PFS**, progression-free survival; **SD**, stable disease; **SG**, sacituzumab govitecan.
1. Paz-Ares LG, et al. *J Clin Oncol*. Published online May 31, 2024. doi:10.1200/JCO.24.00733.

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

## SG showed an OS improvement over docetaxel in both SD and PD subgroups

### SD[a]

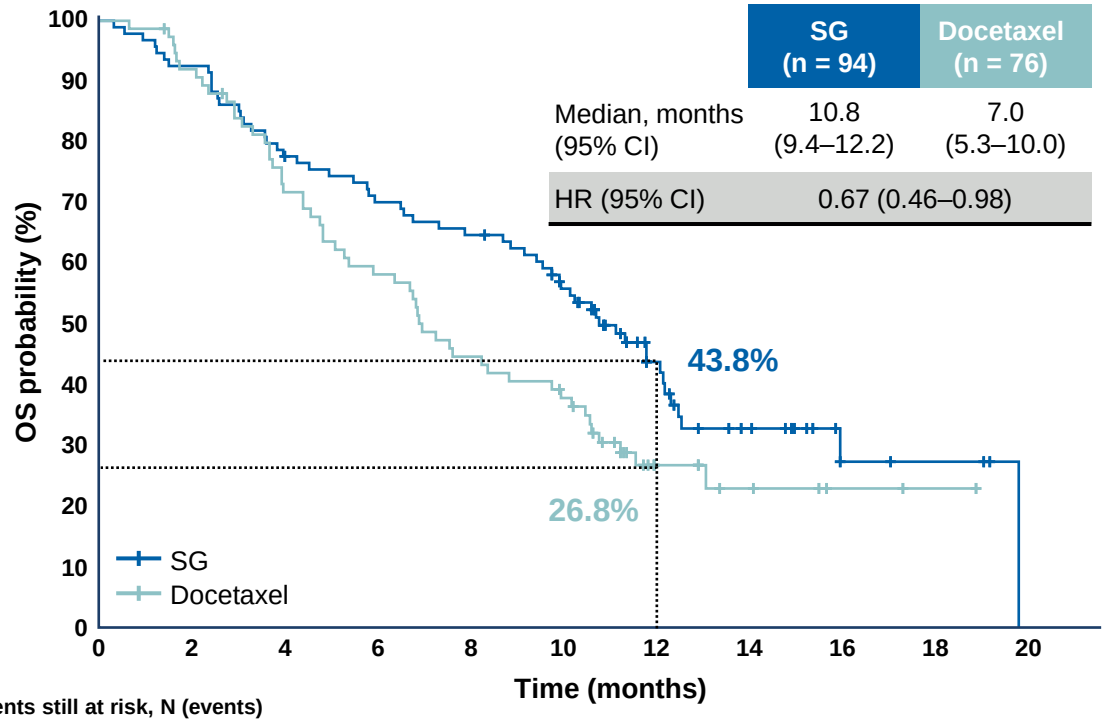



| | SG (n = 98) | Docetaxel (n = 115) |
|---|---|---|
| Median, months (95% CI) | 12.5 (7.9–NR) | 9.9 (7.4–11.7) |
| HR (95% CI) | 0.79 (0.55–1.13) | |

Patients still at risk, N (events)

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| SG | 98 (0) | 88 (9) | 76 (20) | 70 (26) | 56 (39) | 49 (43) | 28 (45) | 12 (49) | 7 (50) | 5 (50) | 0 (50) |
| Docetaxel | 115 (0) | 106 (8) | 88 (26) | 75 (39) | 62 (50) | 51 (57) | 27 (66) | 16 (70) | 4 (72) | 2 (72) | |

### PD[a]




| | SG (n = 94) | Docetaxel (n = 76) |
|---|---|---|
| Median, months (95% CI) | 10.8 (9.4–12.2) | 7.0 (5.3–10.0) |
| HR (95% CI) | 0.67 (0.46–0.98) | |

Patients still at risk, N (events)

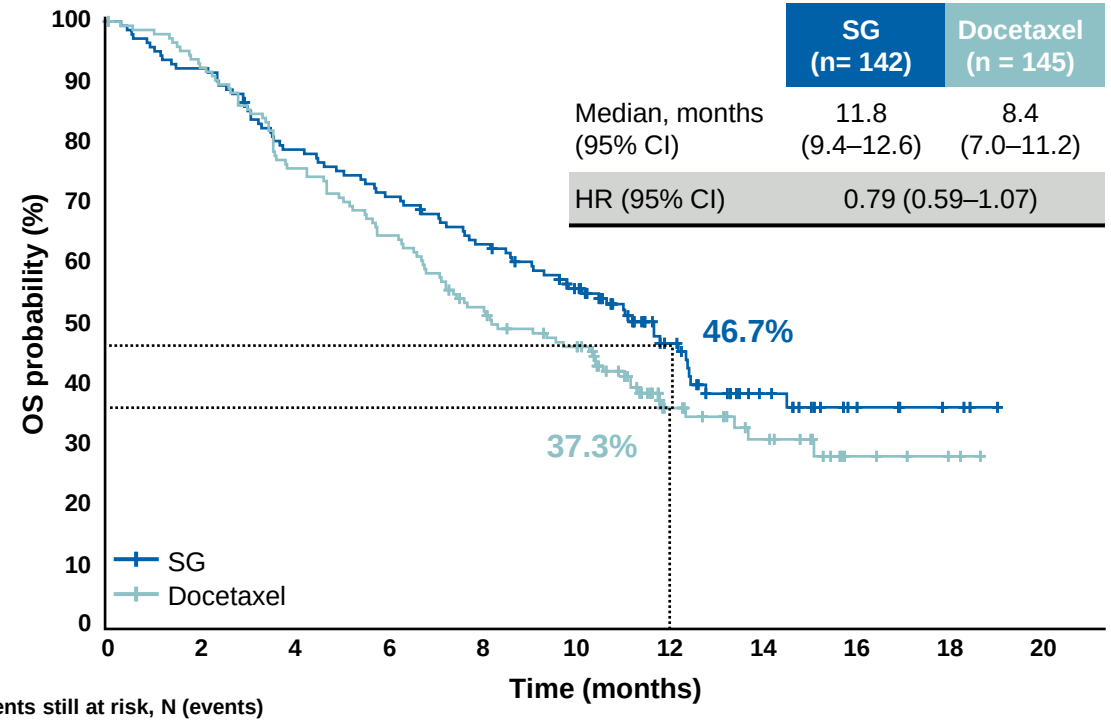
| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| SG | 94 (0) | 87 (7) | 73 (21) | 65 (28) | 60 (33) | 49 (41) | 25 (50) | 14 (56) | 4 (57) | 3 (57) | 0 (58) |
| Docetaxel | 76 (0) | 69 (6) | 53 (21) | 43 (31) | 33 (41) | 27 (46) | 9 (53) | 5 (54) | 2 (54) | 1 (54) | |

[a]Best response to last anti-PD-(L)1–containing regimen.
**HR**, hazard ratio; **NR**, not reached; **OS**, overall survival; **PD**, progressive disease; **PD-(L)1**, programmed death (ligand) 1; **SD**, stable disease; **SG**, sacituzumab govitecan.

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

## SG showed an OS improvement over docetaxel in both non-squamous and squamous histologies

### Non-squamous[1]

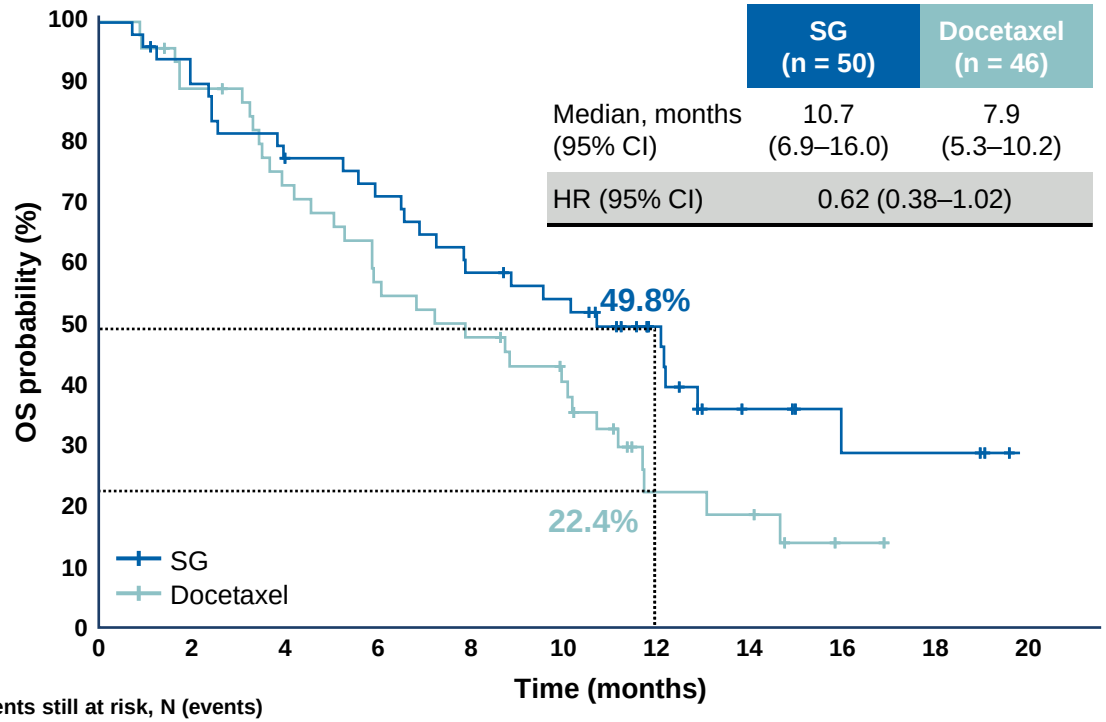



| | SG (n= 142) | Docetaxel (n = 145) |
|---|---|---|
| Median, months (95% CI) | 11.8 (9.4–12.6) | 8.4 (7.0–11.2) |
| HR (95% CI) | 0.79 (0.59–1.07) | |

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[1]




| | 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)

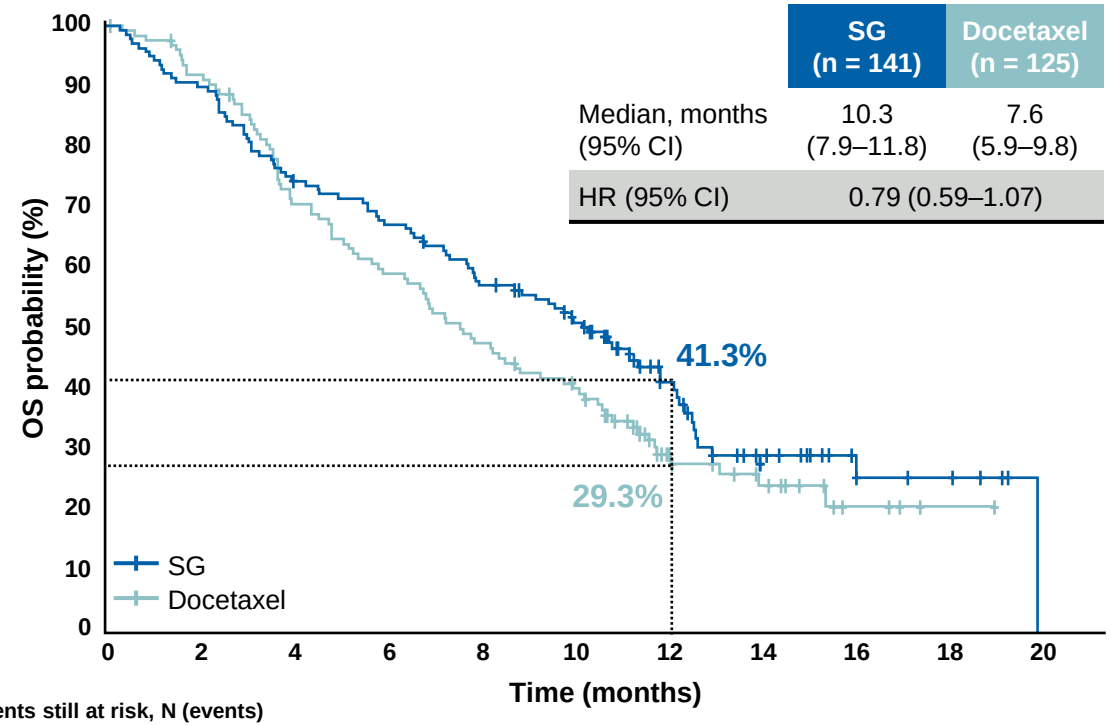
| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| SG | 50 (0) | 44 (5) | 38 (11) | 34 (14) | 28 (20) | 25 (22) | 15 (24) | 7 (28) | 4 (29) | 4 (29) | 0 (30) |
| Docetaxel | 46 (0) | 40 (5) | 32 (12) | 25 (19) | 21 (23) | 16 (26) | 6 (32) | 5 (33) | 1 (34) | | |

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

1. Paz-Ares LG, et al. *J Clin Oncol.* Published online May 31, 2024. doi:10.1200/JCO.24.00733.

# Overall Survival Analysis: Primary or Secondary Resistance to Treatment With Last Anti-PD-(L)1–containing Regimen (SD/PD)

## Primary resistance[a] to last anti-PD-(L)1–containing regimen

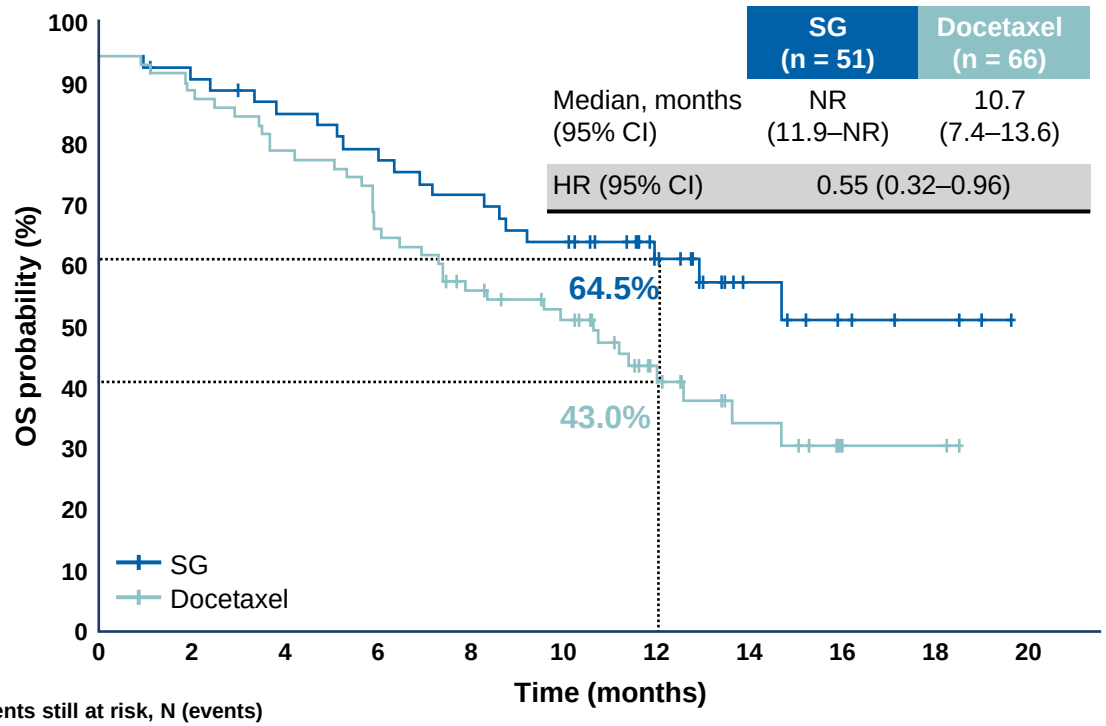



| | SG (n = 141) | Docetaxel (n = 125) |
|---|---|---|
| Median, months (95% CI) | 10.3 (7.9–11.8) | 7.6 (5.9–9.8) |
| HR (95% CI) | 0.79 (0.59–1.07) | |

**Patients still at risk, N (events)**

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| SG | 141 (0) | 127 (14) | 105 (36) | 94 (46) | 79 (60) | 65 (68) | 32 (78) | 17 (87) | 6 (88) | 5 (88) | 0 (89) |
| Docetaxel | 125 (0) | 113 (10) | 86 (36) | 72 (50) | 58 (64) | 47 (73) | 20 (84) | 12 (87) | 4 (88) | 1 (88) | |

## Secondary resistance[a] to last anti-PD-(L)1–containing regimen




| | SG (n = 51) | Docetaxel (n = 66) |
|---|---|---|
| Median, months (95% CI) | NR (11.9–NR) | 10.7 (7.4–13.6) |
| HR (95% CI) | 0.55 (0.32–0.96) | |

**Patients still at risk, N (events)**

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| SG | 51 (0) | 48 (2) | 44 (5) | 41 (8) | 37 (12) | 33 (16) | 21 (17) | 9 (18) | 5 (19) | 3 (19) | 0 (19) |
| Docetaxel | 66 (0) | 62 (4) | 55 (11) | 46 (20) | 37 (27) | 31 (30) | 16 (35) | 9 (37) | 2 (38) | 2 (38) | |

[a]Primary resistance per SITC-based criteria for PD-(L)1 inhibitors: patients with PD or SD (< 6 months on treatment); secondary resistance SD (≥6 months on treatment), no patients in subgroup had CR or PR.[1]

**CR,** complete response; **HR**, hazard ratio; **NR**, not reached; **OS**, overall survival; **PD**, progressive disease; **PD-(L)1**, programmed death (ligand) 1; **PR**, partial response; **SD**, stable disease; **SITC**, Society for Immunotherapy of Cancer; **SG**, sacituzumab govitecan.

1. Kluger HM, et al. *J Immunother Cancer.* 2023;11:e005921.

# Overall Safety Summary: Non-Responsive (SD/PD) Subgroup

| TEAEs (safety-evaluable patients), n (%) | SG (n = 189) | Docetaxel (n = 182) |
|---|---|---|
| Any grade | 189 (100.0) | 177 (97.3) |
| Grade ≥ 3 | 128 (67.7) | 132 (72.5) |
| Serious | 92 (48.7) | 78 (42.9) |
| Leading to dose reduction | 58 (30.7) | 60 (33.0) |
| Leading to discontinuation | 16 (8.5) | 24 (13.2) |
| Leading to death[a] | 5 (2.6) | 7 (3.8) |

- Consistent with the ITT population,[1] rates of grade ≥ 3 TEAEs and TEAEs leading to dose reductions or discontinuations were lower with SG than with docetaxel

[a]TEAEs leading to death in the non-responsive subgroup as determined by the investigator included cerebrovascular accident, febrile neutropenia, hematemesis, neutropenic colitis, and sepsis (1 each) in the SG arm; and death (n = 4), pneumonia (n = 2), and pneumonitis (n = 1) in the docetaxel arm.
**ITT**, intent-to-treat; **PD**, progressive disease; **SD**, stable disease; **SG**, sacituzumab govitecan; **TEAE**, treatment-emergent adverse event.
1. Paz-Ares LG, et al. *J Clin Oncol*. Published online May 31, 2024. doi:10.1200/JCO.24.00733.

# Conclusions

- In patients with mNSCLC, the EVOKE-01 study did not meet the primary end point of OS in the ITT population[1]
  - — Observed a numerical improvement favoring SG vs docetaxel (HR, 0.84; 95% CI, 0.68–1.04)[1]
- In patients non-responsive to their last anti-PD-(L)1–containing regimen, a meaningful OS improvement of 3.5 months (HR [95% CI], 0.75 [0.58–0.97]) was seen with SG vs docetaxel
  - — This analysis was preplanned and not alpha-controlled
  - — No major differences in baseline characteristics were observed to explain the OS benefit
- In the non-responsive group, OS improvement was consistent across different post hoc analyses
  - — Best response to last anti-PD-(L)1–containing regimen (SD vs PD)
  - — Histology (squamous vs non-squamous)
  - — Duration of response to last anti-PD-(L)1–containing regimen (primary vs secondary resistance)
- SG had a favorable safety profile and was better tolerated than docetaxel in the non-responsive subgroup, consistent with the ITT population

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

1. Paz-Ares LG, et al. *J Clin Oncol*. Published online May 31, 2024. doi:10.1200/JCO.24.00733.

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