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Primary Results From Phase 3 EVOKE-03/KEYNOTE D46: Sacituzumab Govitecan + Pembrolizumab in PD-L1 TPS ≥50% Metastatic NSCLC

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Disclosures

Presenter's Disclosures

- **GM** reports advisory and consultation fees from Amgen, AstraZeneca, BMS, Gilead, MSD, Novartis, Pierre Fabre, Pfizer, Roche, Summit Therapeutics, and Takeda; travel and accommodation fees from Amgen, AstraZeneca, BMS, Demo Pharmaceuticals, Novartis, MSD, Roche, and Takeda; and acted as principal investigator in sponsored clinical trials for Amgen, AstraZeneca, BergenBio, BMS, Gilead, Merck, MSD, Novartis, Nuvalent, OSE Pharmaceuticals, Revolution Medicines, Roche, Summit Therapeutics, Syneos Health, and ZaiLab

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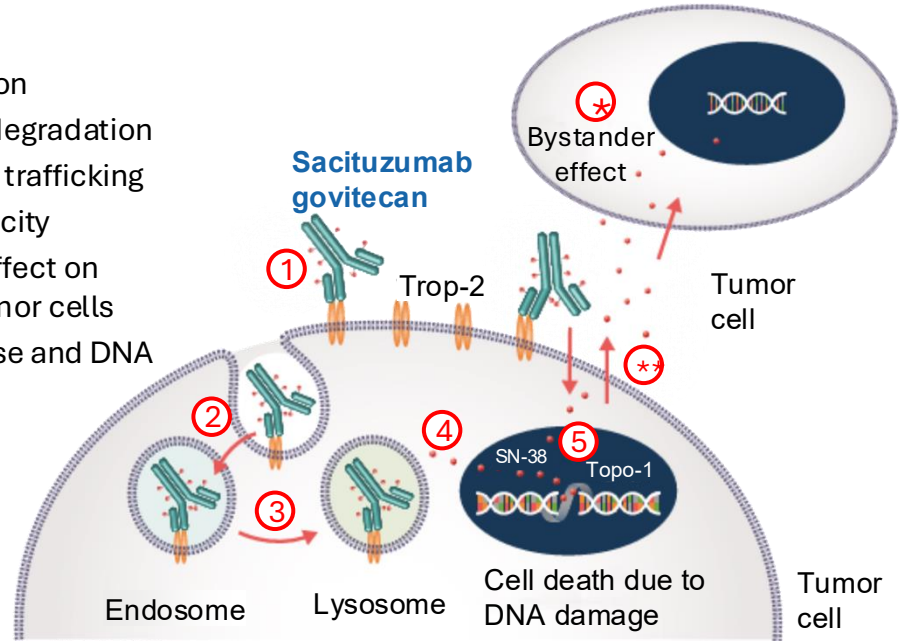
Introduction

- Despite advances with immunotherapy, >50% of patients with metastatic NSCLC (mNSCLC) do not respond to 1L pembrolizumab monotherapy[1]
- Sacituzumab govitecan (SG) is a Trop-2–directed antibody-drug conjugate with a Topo-1 (SN-38) payload being investigated for mNSCLC in the 1L setting[2]
- The Phase 2 EVOKE-02 study (NCT05186974) evaluating 1L pembrolizumab plus SG showed encouraging preliminary results across tumor histologies and among patients with PD-L1 TPS ≥50%[2]

SG Mechanism of Action

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



Objective: To report primary results from open-label, multicenter, Phase 3, randomized EVOKE-03/KEYNOTE D46 study (NCT05609968) evaluating 1L SG plus pembrolizumab in participants with mNSCLC and PD-L1 ≥50%

1L, first-line; IO, immunotherapy; mNSCLC, metastatic non–small-cell lung cancer; PD-L1, programmed death-ligand 1; SG, sacituzumab govitecan; Topo-1, topoisomerase I; TPS, tumor proportion score; Trop-2, trophoblast cell-surface antigen 2.

1. Li H, et al. *Cancers* (Basel). 2024;16(4):744. 2. Reck M, et al. *Journal of Thoracic Oncology*. 2026;21(3):103509.

EVOKE-03/KEYNOTE D46 Study Design

Key eligibility criteria

- Stage IV NSCLC (AJCC 8th)
- No prior systemic treatment for mNSCLC
- ECOG PS 0 or 1
- PD-L1 TPS ≥50%
- No ILD
- No untreated or unstable brain metastases
- EGFR/ALK/ROS-1–negative disease

Stratification

- ECOG PS (0 or 1)
- Predominant tumor histology (squamous or non-squamous)
- Geographic region (East Asia vs Western Europe/North America/Australia vs Rest of World)

Randomized
1:1
N = 620

Sacituzumab govitecan
10 mg/kg
D1, D8, Q3W
+
Pembrolizumab 200 mg
IV D1 Q3W
35 cycles

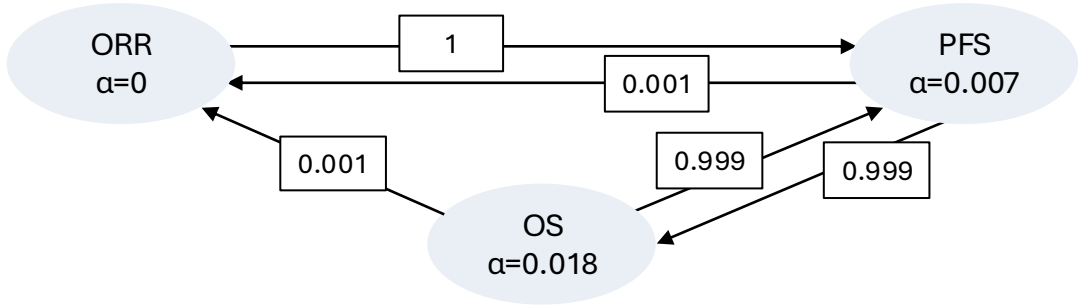
Pembrolizumab 200 mg
IV D1 Q3W
35 cycles

Primary endpoints

- PFS[a]
- OS

Secondary endpoints

- ORR[a]
- DOR[a]
- PROs
- Safety



ALK, anaplastic lymphoma kinase; BICR, blinded independent centralized review; D1, day 1; ECOG PS, Eastern Cooperative Oncology Group Performance Score; EGFR, epidermal growth factor receptor; DOR, duration of response; ILD, interstitial lung disease; IV, intravenous; mNSCLC, metastatic non–small-cell lung cancer; ORR, objective response rate; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PRO, patient-reported outcome; Q3W, every three weeks; RECIST, Response Evaluation Criteria in Solid Tumors; ROS-1, ROS proto-oncogene 1, receptor tyrosine kinase; TPS, tumor proportion score.
Data cutoff: April 3, 2026. [a]Per RECIST v1.1 as assessed by BICR.

Baseline Demographics and Disposition

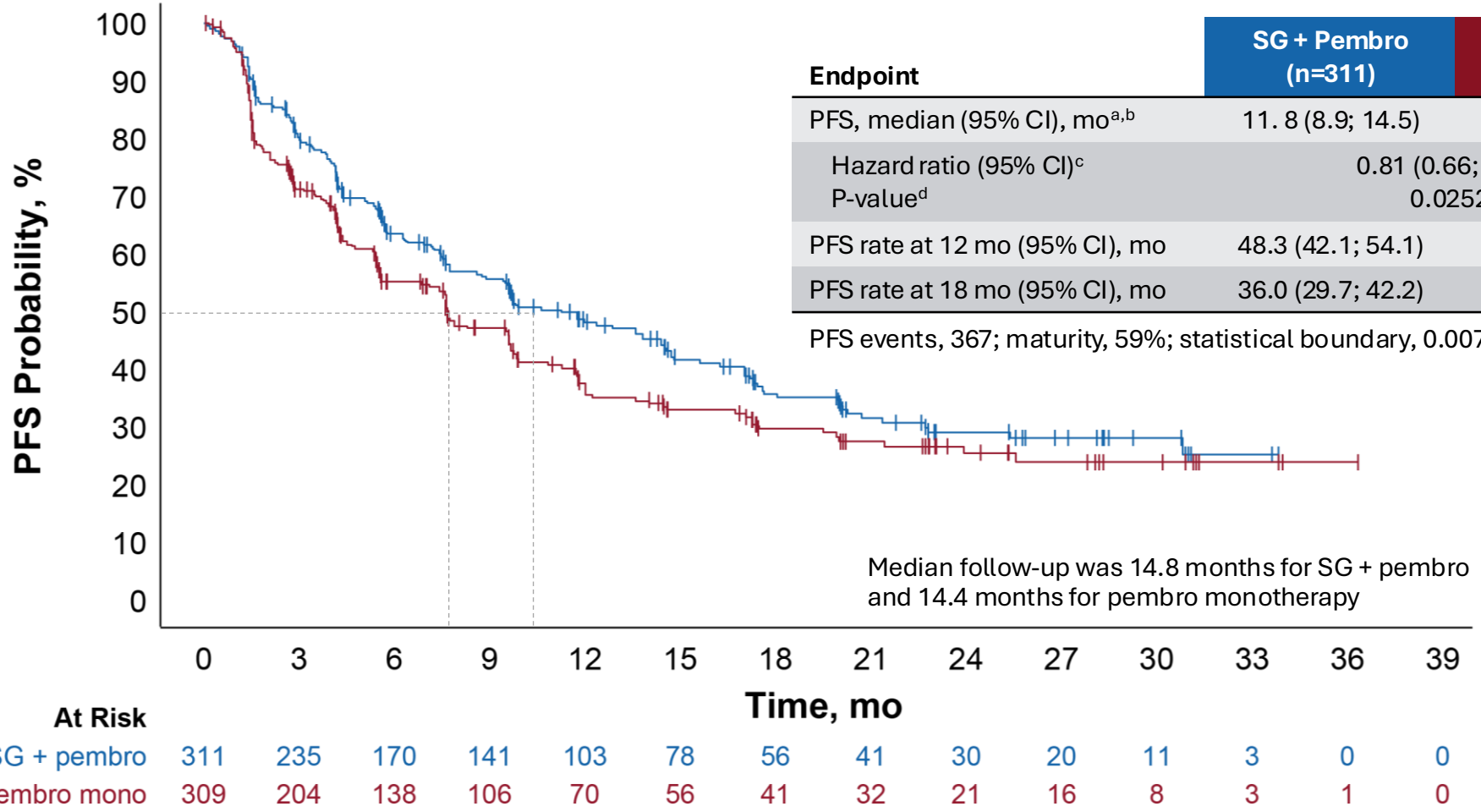
Characteristic[a]	SG + Pembro (n=311)[b]	Pembro (n=309)[b]
Median age (range), y	67 (34–87)	68 (37–86)
Male, n (%)	219 (70.4)	224 (72.5)
Geographical region[c]		
East Asia	114 (36.7)	116 (37.5)
Western Europe/North America/Australia	60 (19.3)	58 (18.8)
Rest of world	137 (44.1)	135 (43.7)
ECOG PS		
0	107 (34.4)	108 (35.0)
1	204 (65.6)	201 (65.0)
Histology		
Squamous	96 (30.9)	96 (31.1)
Non-squamous	215 (69.1)	213 (68.9)
Smoking status		
Never smoker	52 (16.7)	53 (17.2)
Current/former smoker	259 (83.3)	256 (82.8)
Cancer stage		
IIIC	1 (0.3)	0 (0.0)
IVA	158 (50.8)	168 (54.4)
IVB	152 (48.9)	141 (45.6)
Brain metastasis	27 (8.7)	30 (9.7)
Liver metastasis	49 (15.8)	49 (15.9)

All data are n (%) unless otherwise stated.

- As of April 3, 2026, 620 participants were randomized and 616 received study treatment
- Median follow-up was 14.7 months
- The median number of treatment cycles was 10 for SG and 12 for pembro in the combination arm compared with 9 for pembro monotherapy
- At the data cutoff, 70.4% of participants in the SG + pembro arm and 71.2% in the pembro monotherapy arm had discontinued any study treatment
  - Radiologic progression was the primary reason for treatment discontinuation

ECOG PS, Eastern Cooperative Oncology Group Performance Score; PD-L1, programmed death-ligand 1; pembro, pembrolizumab; SG, sacituzumab govitecan; TPS, tumor proportion score. [a]One participant in the pembro monotherapy arm had a PD-L1 TPS <50%; [b]Intention –to-treat population; [c]Geographic breakdown: East Asia - Japan, Malaysia, Philippines, Korea (Republic of), Taiwan, Thailand, China; North America/Western EU/Australia - Greece, United Kingdom, United States, Canada, Australia, Germany, Italy; Rest of World - Israel, Latvia, Poland, Romania, Turkey, Brazil, Chile, Mexico, Peru, Estonia, Lithuania.

Progression-Free Survival in the ITT Population – Primary Analysis



Endpoint	SG + Pembro (n=311)	Pembro (n=309)
PFS, median (95% CI), mo[a,b]	11. 8 (8.9; 14.5)	7.7 (5.6; 9.7)
Hazard ratio (95% CI)[c]	0.81 (0.66; 1.00)	
P-value[d]	0.0252	
PFS rate at 12 mo (95% CI), mo	48.3 (42.1; 54.1)	36.9 (30.9; 42.9)
PFS rate at 18 mo (95% CI), mo	36.0 (29.7; 42.2)	29.9 (24.0; 36.1)

PFS events, 367; maturity, 59%; statistical boundary, 0.007

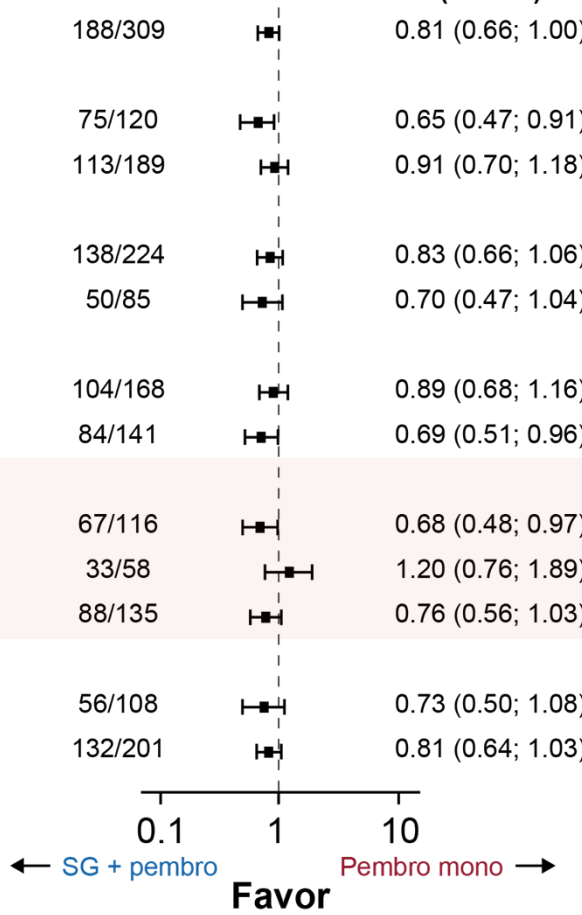
Median follow-up was 14.8 months for SG + pembro and 14.4 months for pembro monotherapy

BICR, blinded independent centralized review; mono, monotherapy; ECOG PS, Eastern Cooperative Oncology Group Performance Score; ITT, intention-to-treat; mo, months; pembro, pembrolizumab; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; SG, sacituzumab govitecan.

[a]Per RECIST v1.1 by BICR. [b]Based on Kaplan–Meier method for censored data. [c]Estimated using a Cox regression model stratified by histology (squamous vs non-squamous), ECOG PS (0 vs 1), and geographic region (East Asia vs Western Europe/North America/Australia vs rest of world). [d]One-sided P-value based on log-rank test stratified by histology (squamous vs non-squamous), ECOG PS (0 vs 1), and geographic region (East Asia vs Western Europe/North America/Australia vs rest of world).

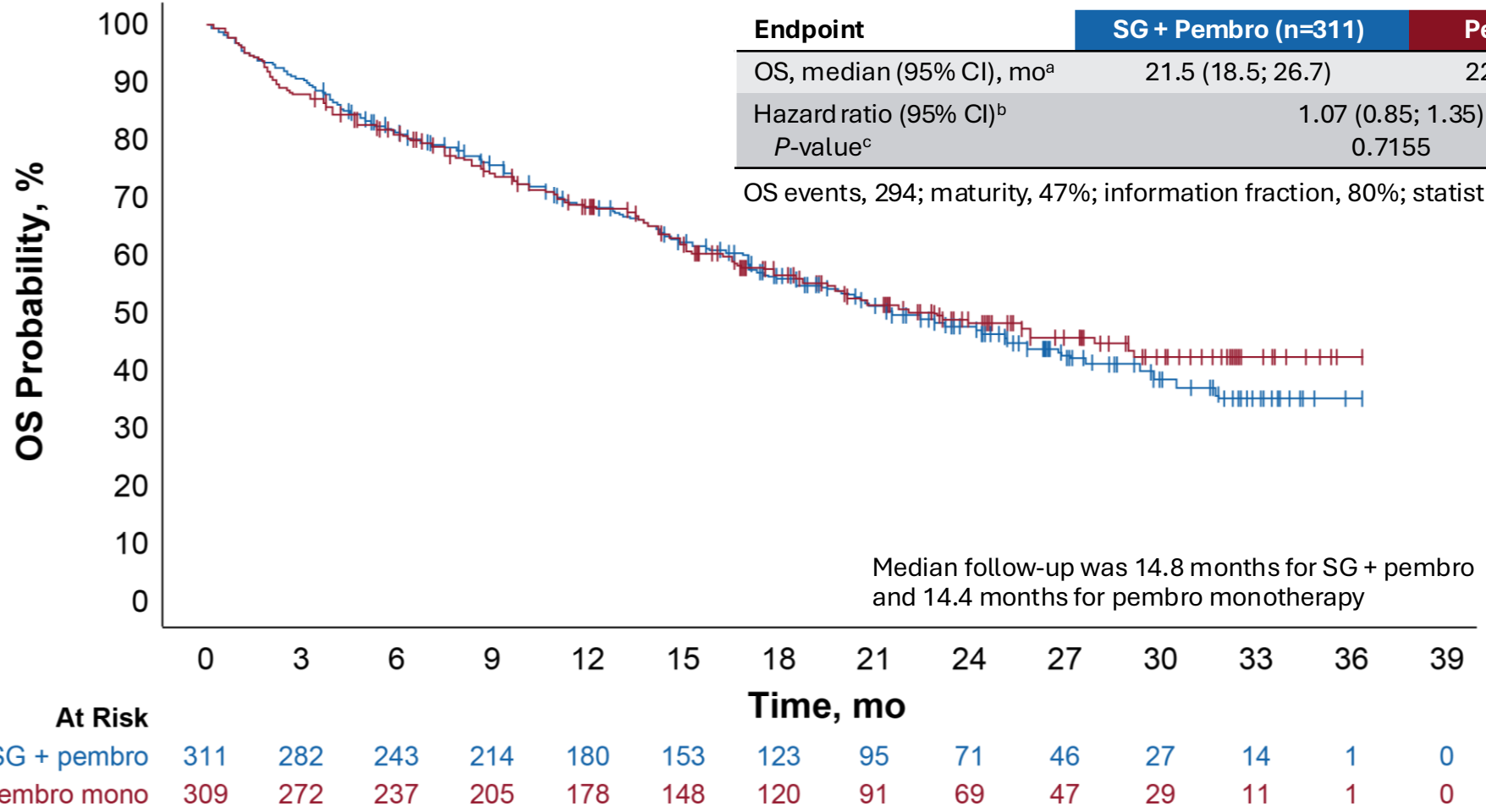
Progression-Free Survival Sub-Group Analyses

	#Events/N SG + Pembro	#Events/N Pembro mono	Hazard Ratio (95% CI)
Overall	179/311	188/309	0.81 (0.66; 1.00)
Age, years			
<65	68/126	75/120	0.65 (0.47; 0.91)
≥65	111/185	113/189	0.91 (0.70; 1.18)
Sex			
Male	129/219	138/224	0.83 (0.66; 1.06)
Female	50/92	50/85	0.70 (0.47; 1.04)
Race			
White	109/176	104/168	0.89 (0.68; 1.16)
All others	70/135	84/141	0.69 (0.51; 0.96)
Geographic Region			
East Asia	59/114	67/116	0.68 (0.48; 0.97)
Western Europe/ North America/Australia	41/60	33/58	1.20 (0.76; 1.89)
Rest of the world	79/137	88/135	0.76 (0.56; 1.03)
Baseline ECOG PS			
0	46/107	56/108	0.73 (0.50; 1.08)
1	133/204	132/201	0.81 (0.64; 1.03)
Predominant Tumor Histology			
Squamous	69/96	61/96	1.11 (0.78; 1.56)
Non-squamous	110/215	127/213	0.70 (0.54; 0.90)
Smoking Status			
Never smoker	34/52	41/53	0.59 (0.37; 0.93)
Former/current smoker	145/259	147/256	0.85 (0.67; 1.07)
Baseline Brain Metastasis Status			
Yes	19/27	17/30	
No	160/284	171/279	0.77 (0.62; 0.95)
Baseline Liver Metastasis Status			
Yes	38/49	33/49	0.92 (0.58; 1.47)
No	141/262	155/260	0.76 (0.61; 0.96)



ECOG PS, Eastern Cooperative Oncology Group Performance Score; ITT, intention-to-treat; mo, months; mono, monotherapy; pembro, pembrolizumab; SG, sacituzumab govitecan. Analysis is based on Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by histology (squamous vs non-squamous), ECOG PS (0 vs 1), and geographic region (East Asia vs Western Europe/North America/Australia vs rest of world). Subgroup analyses are based on unstratified Cox regression model with Efron's method of tie handling with treatment as a covariate. Subgroup analyses were not performed for categories representing fewer than 10% of the ITT population.

Overall Survival in the ITT Population – Interim Analysis



Endpoint	SG + Pembro (n=311)	Pembro (n=309)
OS, median (95% CI), mo[a]	21.5 (18.5; 26.7)	22.8 (18.7; 29.0)
Hazard ratio (95% CI)[b]	1.07 (0.85; 1.35)	
P-value[c]	0.7155	

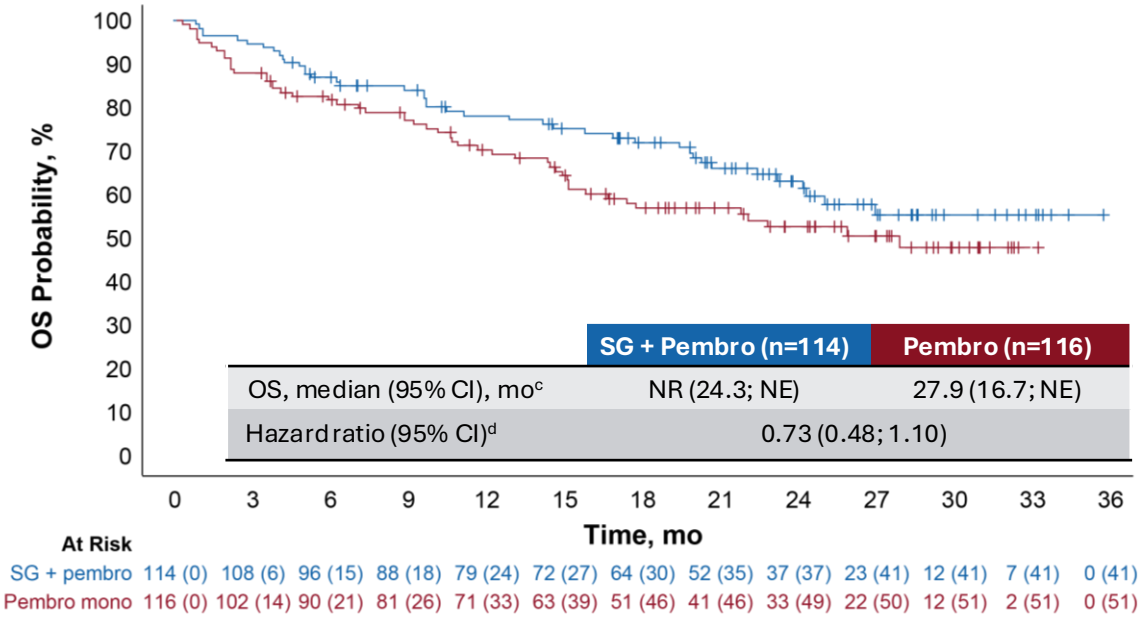
OS events, 294; maturity, 47%; information fraction, 80%; statistical boundary, 0.008

ECOG PS, Eastern Cooperative Oncology Group Performance Score; ITT, intention-to-treat; mo, months; mono, monotherapy; pembro, pembrolizumab; OS, overall survival; SG, sacituzumab govitecan.

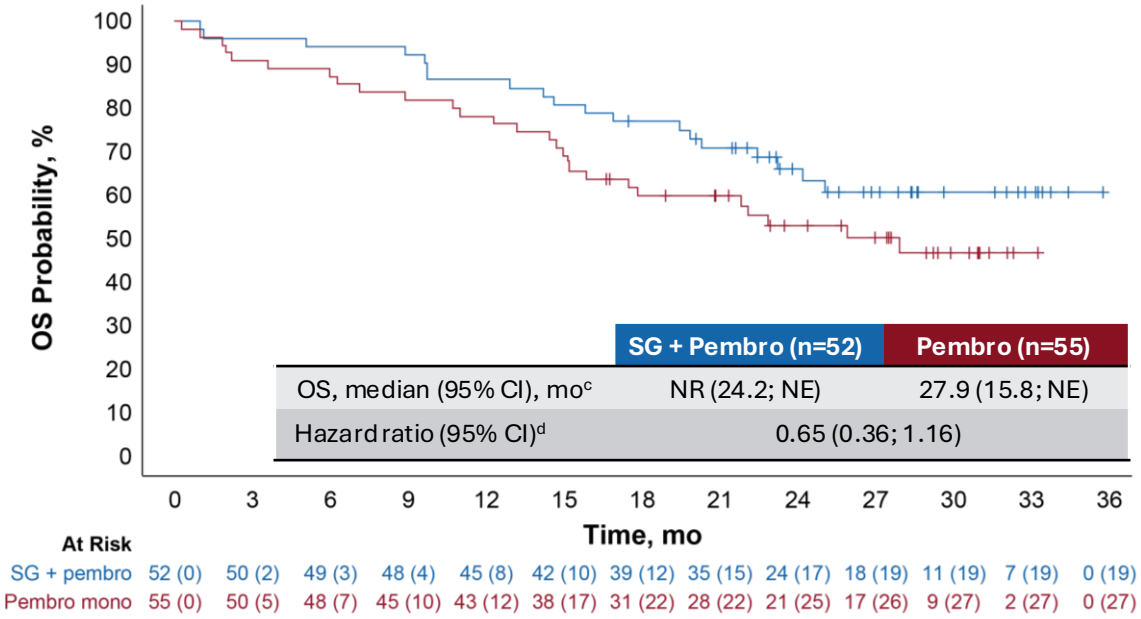
[a]Based on Kaplan–Meier method for censored data. [b]Estimated using a Cox regression model stratified by histology (squamous vs non-squamous), ECOG PS (0 vs 1), and geographic region (East Asia vs Western Europe/North America/Australia vs rest of world). [c]One-sided *P*-value based on log-rank test stratified by histology (squamous vs non-squamous), ECOG PS (0 vs 1), and geographic region (East Asia vs Western Europe/North America/Australia vs rest of world).

OS in East Asia and China Subgroups (ITT Population; *Exploratory*)

East Asia[a]



China (Post-hoc)[b]



- Median follow-up was 18.1 months for the East Asia cohort and 22.4 months for the China cohort

ITT, intention-to-treat; mono, monotherapy; NE, not evaluable; NR, not reached; pembro, pembrolizumab; SG, sacituzumab govitecan.
[a]This analysis was not stratified. [b]This post-hoc analysis was not stratified or pre-specified. [c]Based on Kaplan–Meier method for censored data. [d]Estimated using a Cox regression model.

Summary of Secondary Efficacy Endpoints in the ITT Population

- The difference in confirmed ORR was ~12% for SG + pembro vs pembro monotherapy and the DCR was 83.3% vs 73.1%, respectively
- Median DOR was similar in both groups

Endpoint	SG + Pembro (n=311)	Pembro (n=309)
Confirmed ORR, % (95% CI)[a]	55.6 (49.9; 61.2)	43.7 (38.1; 49.4)
Best overall response, %[b,c]		
CR	7.7	3.9
PR	47.9	39.8
SD	27.7	29.4
PD	7.1	16.5
Not evaluable	1.3	2.3
Disease control, % (95% CI)[a]	83.3 (78.7; 87.3)	73.1 (67.8; 78.0)
DOR, median (95% CI), mo[a,d]	21.4 (14.9–NE)	21.3 (15.7–NE)

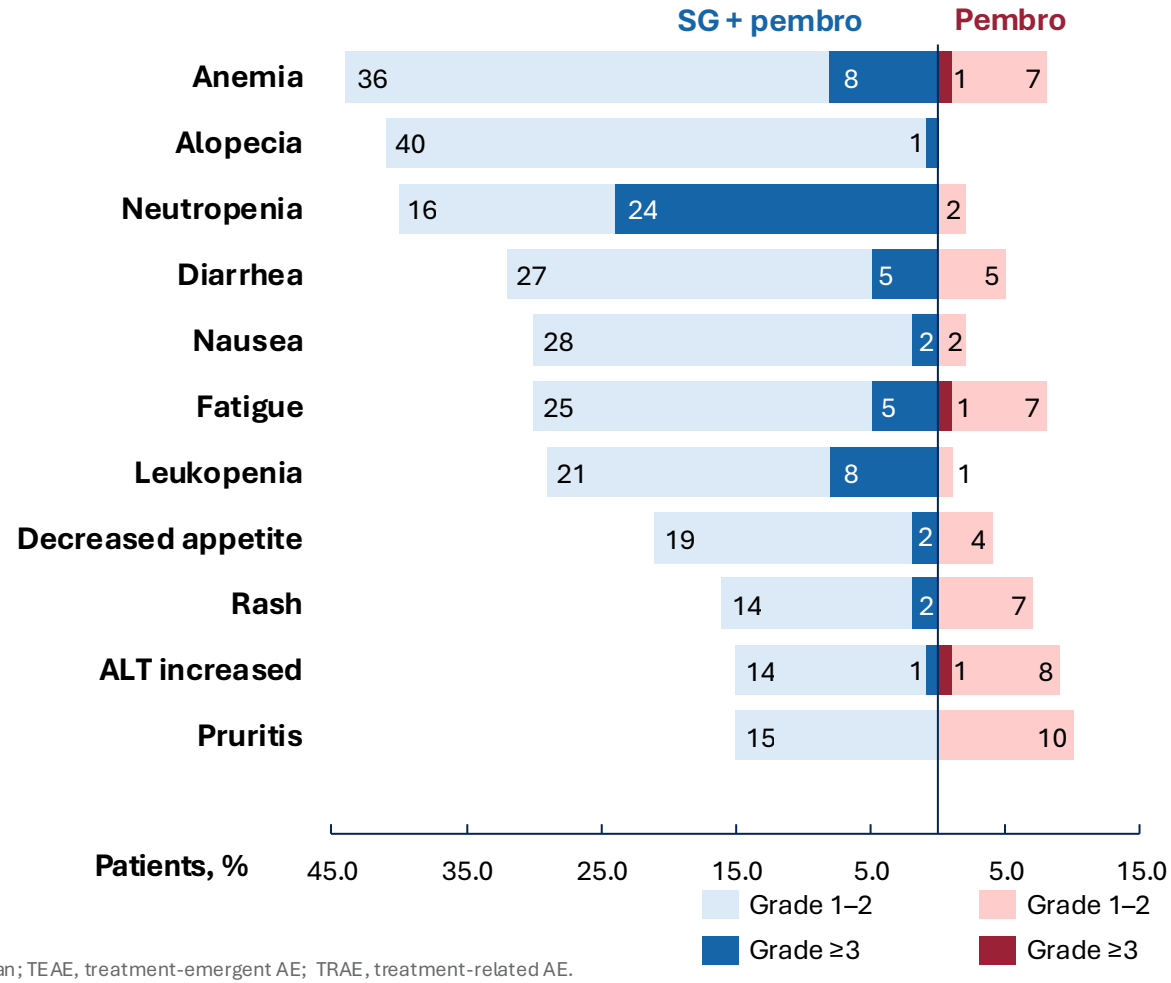
BICR, blinded independent central review; CR, complete response; DCR, disease control rate; DOR, duration of response; ITT, intention-to-treat; mo, months; NE, not estimated; ORR, objective response rate; PD, progressive disease; pembro, pembrolizumab; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; SG, sacituzumab govitecan.
[a]Per RECIST v1.1 by BICR. [b]CR and PR are confirmed responses. [c]No post-baseline assessment was available for 8.4% of participants in the SG + pembrolizumab group and for 8.1% of participants in the pembrolizumab monotherapy group. Europe/North America/Australia vs rest of world). [d]Based on Kaplan–Meier method for censored data.

Safety Summary (Safety Population)

- Median duration of study drug exposure was 8.5 months for SG + pembro and 6.2 months for pembro monotherapy
- SG + pembro had a safety profile consistent with each agent, with no new or additional toxicities observed

Adverse Events, n (%)	SG + Pembro (n=307)	Pembro (n=309)
Any grade TEAEs	**302 (98.4)**	**294 (95.1)**
Grade ≥3	226 (73.6)	139 (45.0)
Serious TEAEs	**164 (53.4)**	**122 (39.5)**
Treatment-related	94 (30.6)	41 (3.3)
TEAEs leading to discontinuation of any drug	**95 (30.9)**	**62 (20.1)**
TEAEs leading to death	**35 (11.4)**	**30 (9.7)**
Treatment-related[b]	5 (1.6)	4 (1.3)

TRAEs Occurring >15% of Participants[a]



AESI, adverse event of special interest; ALT, alanine transaminase; pembro, pembrolizumab; SG, sacituzumab govitecan; TEAE, treatment-emergent AE; TRAE, treatment-related AE.

[a]AESI for SG occurring in ≥2% of participants included hypersensitivity, neutropenia, serious infections secondary to neutropenia,and severe diarrhea. [b]Overall, nine treatment-related deaths were reported. Five treatment-related fatal AEs were reported for the SG + pembro arm (immune-mediated lung disease, n=1; pneumonia, n=2; interstitial lung disease, n=1; and pneumonitis, n=1), not all were attributed by investigator to SG; four were reported for pembro arm (pneumonitis, pulmonary embolism, myocarditis, and immune-mediated lung disease; n=1 each).

Conclusions

- Although SG + pembro demonstrated a numerically longer PFS versus pembro monotherapy at PFS primary analysis, the study did not meet its primary endpoint because the difference was not statistically significant
  - Confirmed ORR and disease control rate were numerically higher with SG + pembro than with pembro monotherapy (55.6% vs 43.7%, ~12% difference; 83.3% vs 73.1%, respectively); median DOR was similar between treatment groups
- At the interim OS analysis, a statistically significant difference for this dual primary endpoint was not met
- The safety profile of SG plus pembro was consistent with the known profiles of each agent, and no new or additional toxicities were observed with the combination

DOR, duration of response; pembro, pembrolizumab; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; SG, sacituzumab govitecan.

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Thank You.