Sacituzumab Govitecan + Pembrolizumab + Carboplatin in 1L Metastatic Non-Small Cell Lung Cancer: The EVOKE-02 Study

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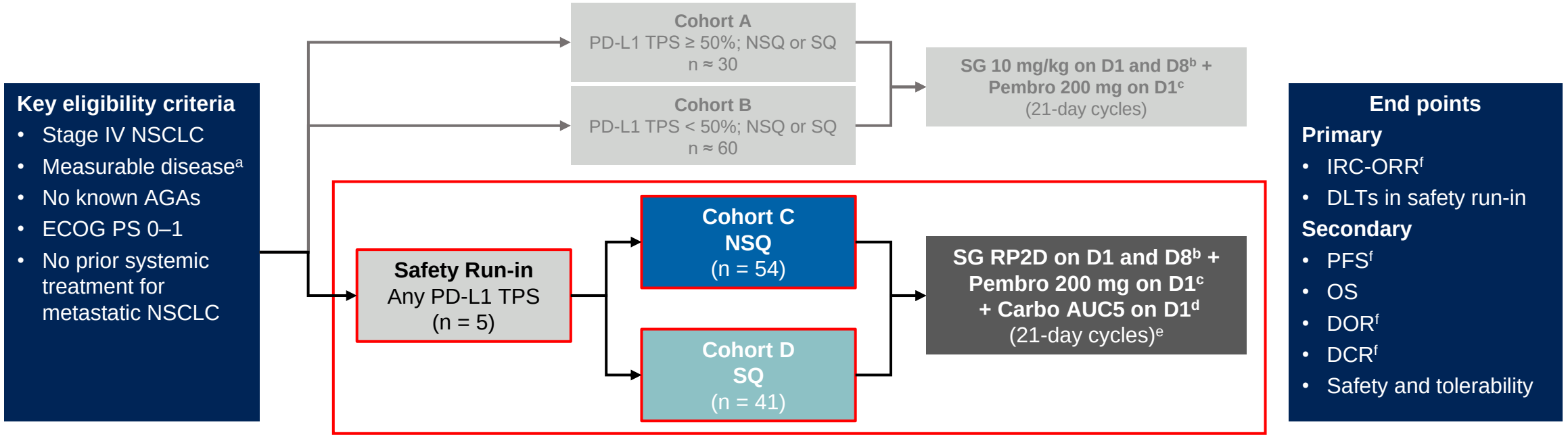
Background

- Combination regimens incorporating pembrolizumab + platinum-based chemotherapy are standard-of-care 1L treatment for mNSCLC lacking AGAs[1]; however, many patients' tumors do not respond to initial therapy[2]
- Sacituzumab govitecan (SG) is a first-in-class Trop-2–directed ADC[3]
  - SG monotherapy provided clinical activity in a phase 3 trial in 2L NSCLC[4]
  - SG has been successfully combined with pembrolizumab in 1L NSCLC,[5] and nonclinical data show enhanced antitumor activity when combining SG with platinum agents[6]
- Here, we report initial results from the ongoing, multicohort, phase 2 study, EVOKE-02 (NCT05186974)
  - Cohorts C (NSQ histology) and D (SQ histology): Patients with 1L mNSCLC (any PD-L1 TPS) receiving sacituzumab govitecan + carboplatin + pembrolizumab (CP)

1L, first line; **2L**, second line; **ADC**, antibody drug conjugate; **AGA**, actionable genomic alteration; **CP**, carboplatin + pembrolizumab; **mNSCLC**, metastatic non-small cell lung cancer; **NSCLC**, non-small cell lung cancer; **NSQ**, nonsquamous; **PD-L1**, programmed death ligand-1; **SG**, sacituzumab govitecan; **SQ**, squamous; **TPS**, tumor proportion score; **Trop-2**, trophoblast cell surface antigen 2.

1. Jaiyesimi IA, et al. *J Clin Oncol*. 2024;42:e1-e22. 2. Li H, et al. *Cancers*. 2024;16(4):744. 3. TRODELVY® (sacituzumab govitecan-hziy) [summary of product characteristics]. Carrigtohill, Ireland: Gilead Sciences Ireland UC; July 2023. 4. Paz-Ares LG, et al. *J Clin Oncol.* 2024;00:1-13. 5. Patel JD, et al. Presented at 2024 ASCO Annual Meeting; May 31–June 4, 2024; Chicago, IL. 6. Cardillo TM, et al. *Oncotarget.* 2024;15:144-58.

EVOKE-02: A Global, Open-Label, Multicohort Phase 2 Study



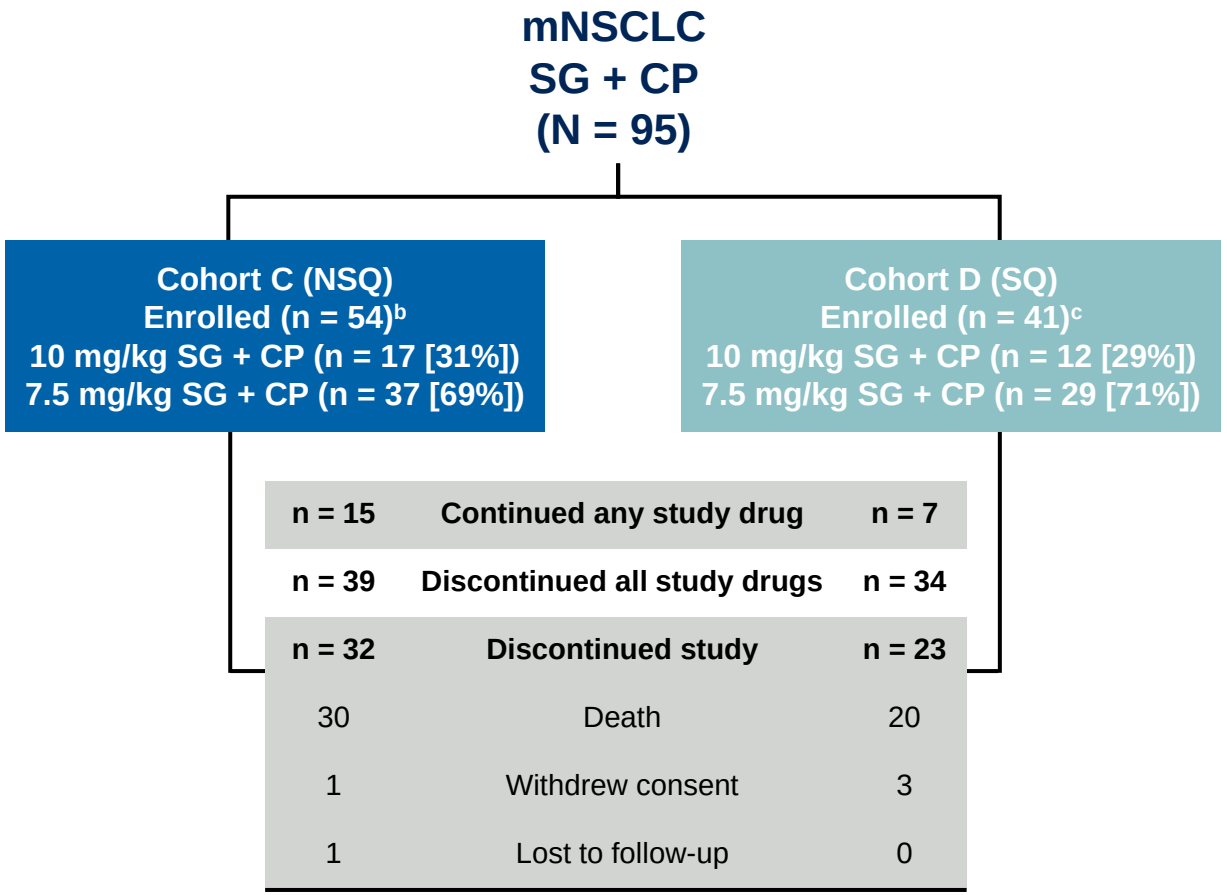
Data cutoff: 03 June 2024

	Cohort C (NSQ) (n = 51)[g]	Cohort D (SQ) (n = 41)
Follow-up, median (range), months	14.5 (12.2–22.3)	14.2 (11.0–23.0)

[a]Assessed by investigator per RECIST v1.1 [b]SG IV until progressive disease or unacceptable toxicity. [c]Pembro IV up to 35 cycles. [d]Carboplatin up to 4 cycles. [e]Based on safety assessment, mandatory long-acting G-CSF on D9 or short-acting G-CSF once daily for 10 days starting from D9 of each cycle. [f]Assessed by IRC per RECIST v1.1. [g]Three patients in the NSQ group had no measurable disease per IRC at baseline and were not included in the efficacy analysis. **AGA**, actionable genomic alteration; **AUC5**, area under the concentration by time curve 5; **carbo**, carboplatin; **D**, day; **DCR**, disease control rate; **DLT**, dose-limiting toxicity; **DOR**, duration of response; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **G-CSF**, granulocyte-colony stimulating factor; **IRC**, independent review committee; **IV**, intravenous; **NSCLC**, non-small cell lung cancer; **NSQ**, nonsquamous; **ORR**, objective response rate; **OS**, overall survival; **PD-L1**, programmed death ligand-1; **pembro**, pembrolizumab; **PFS**, progression-free survival; **RECIST v1.1**, Response Evaluation Criteria in Solid Tumors version 1.1; **RP2D**, recommended phase 2 dose; **SG**, sacituzumab govitecan; **SQ**, squamous; **TPS**, tumor proportion score.

Patient Disposition

- During the safety run-in (SG 10 mg/kg + CP, n = 5), de-escalation criteria were not met[a]
  - —1 DLT was observed (sepsis leading to death)
- At a subsequent planned safety evaluation, SG dose was reduced to 7.5 mg/kg owing to myelosuppression rates, mainly grade ≥ 3 neutropenia
  - —RP2D was 7.5 mg/kg for SG combined with pembrolizumab 200 mg + carboplatin AUC5



n = 15	**Continued any study drug**	**n = 7**
n = 39	**Discontinued all study drugs**	**n = 34**
n = 32	**Discontinued study**	**n = 23**
30	Death	20
1	Withdrew consent	3
1	Lost to follow-up	0

[a]Criteria for dose de-escalation was ≥ 2 patients with a predefined DLT. [b]Three (5.6%) patients in the NSQ group had no measurable disease per IRC at baseline and were not included in the full analysis set, and there were 54 patients in the safety analysis set. [c]The full analysis set and safety analysis set had 41 patients.
AUC5, area under the concentration by time curve 5; **CP**, carboplatin + pembrolizumab; **DLT**, dose-limiting toxicity; **IRC**, independent review committee; **mNSCLC**, metastatic non-small cell lung cancer; **NSQ**, nonsquamous; **RP2D**, recommended phase 2 dose; **SG**, sacituzumab govitecan; **SQ**, squamous.

Baseline Demographics and Disease Characteristics by Histology

Characteristic		Cohort C (NSQ) SG + CP (n = 54)	Cohort D (SQ) SG + CP (n = 41)
Median age (range), years		67 (46–87)	68 (42–79)
Male, n (%)		40 (74.1)	34 (82.9)
Race, n (%)	Asian	24 (44.4)	12 (29.3)
	Black	0	0
	Other and not reported	4 (7.4)	5 (12.2)
	White	26 (48.1)	24 (58.5)
Ethnicity, n (%)	Hispanic or Latino	4 (7.4)	3 (7.3)
	Not Hispanic or Latino	48 (88.9)	33 (80.5)
	Not reported	2 (3.7)	5 (12.2)
Tobacco use status, n (%)	Current	8 (14.8)	13 (31.7)
	Former	29 (53.7)	24 (58.5)
	Never	11 (20.4)	3 (7.3)
	Missing	6 (11.1)	1 (2.4)
ECOG PS, n (%)	0	15 (27.8)	14 (34.1)
	1	39 (72.2)	27 (65.9)
Disease stage IV at diagnosis,[a] n (%)		44 (81.5)	32 (78.0)
Baseline brain metastasis, n (%)		4 (7.4)	1 (2.4)
PD-L1 status,[b] n (%)	≥ 50%	8 (14.8)	4 (9.8)
	< 50%	46 (85.2)	37 (90.2)
	≥ 1% and ≤ 49%	22 (40.7)	16 (39.0)
	< 1%	24 (44.4)	21 (51.2)

[a]All patients had stage IV at screening. [b]PD-L1 status was confirmed by use of the 22C3 immunohistochemistry assay.
CP, carboplatin + pembrolizumab; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **NSQ**, nonsquamous; **PD-L1**, programmed death ligand 1; **SQ**, squamous.

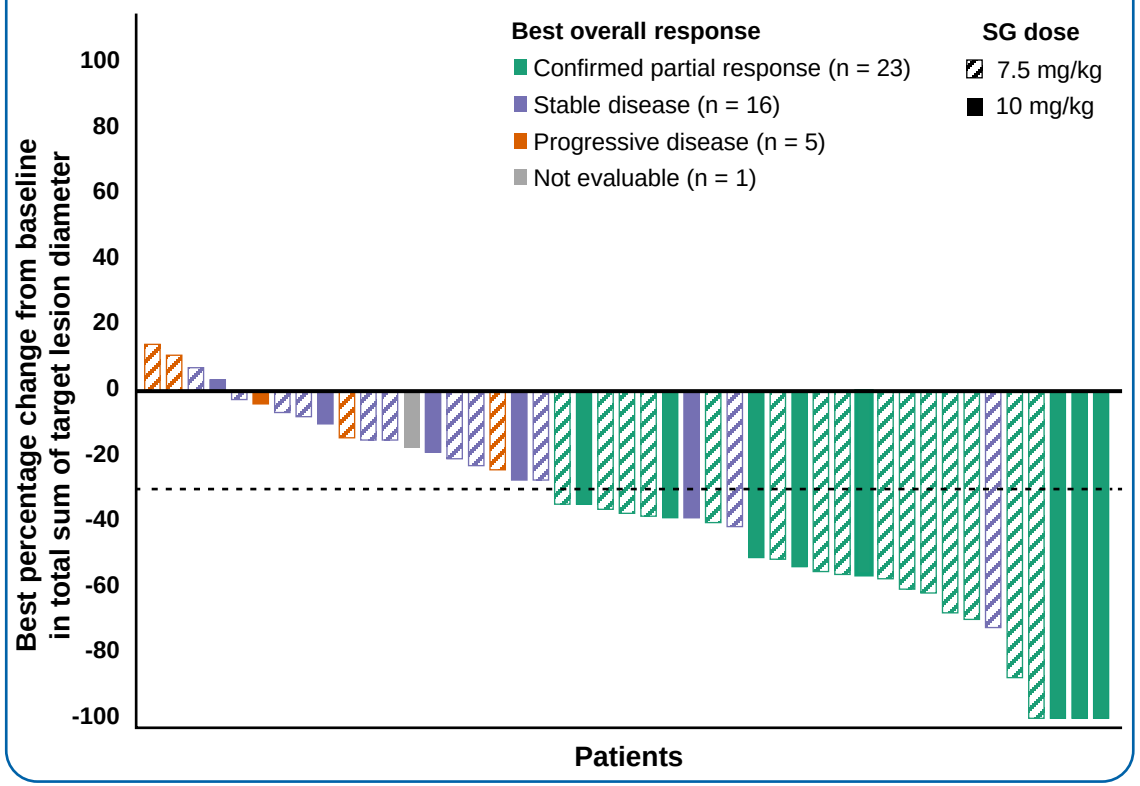
IRC[a] Efficacy by Histology

	Cohort C (NSQ) SG + CP (n = 51)[b]	Cohort D (SQ) SG + CP (n = 41)
Follow-up, median (range), months	14.5 (12.2–22.3)	14.2 (11.0–23.0)
ORR, % (95% CI)	45.1 (31.1–59.7)	39.0 (24.2–55.5)
Partial response, n (%)	23 (45.1)	16 (39.0)
Stable disease, n (%)	16 (31.4)	17 (41.5)
Progressive disease, n (%)	5 (9.8)	3 (7.3)
Not evaluable, n (%)	7 (13.7)	5 (12.2)
Time to response, median (range), months	2.7 (1.2–7.2)	1.5 (1.2–5.8)
DOR, median (95% CI), months	NR (3.2–NR)	11.5 (5.6–NR)
PFS, median (95% CI), months	8.1 (5.2–15.0)	8.3 (4.3–11.2)
PFS rate at 6 months, % (95% CI)	53.7 (37.8–67.2)	64.6 (46.0–78.2)

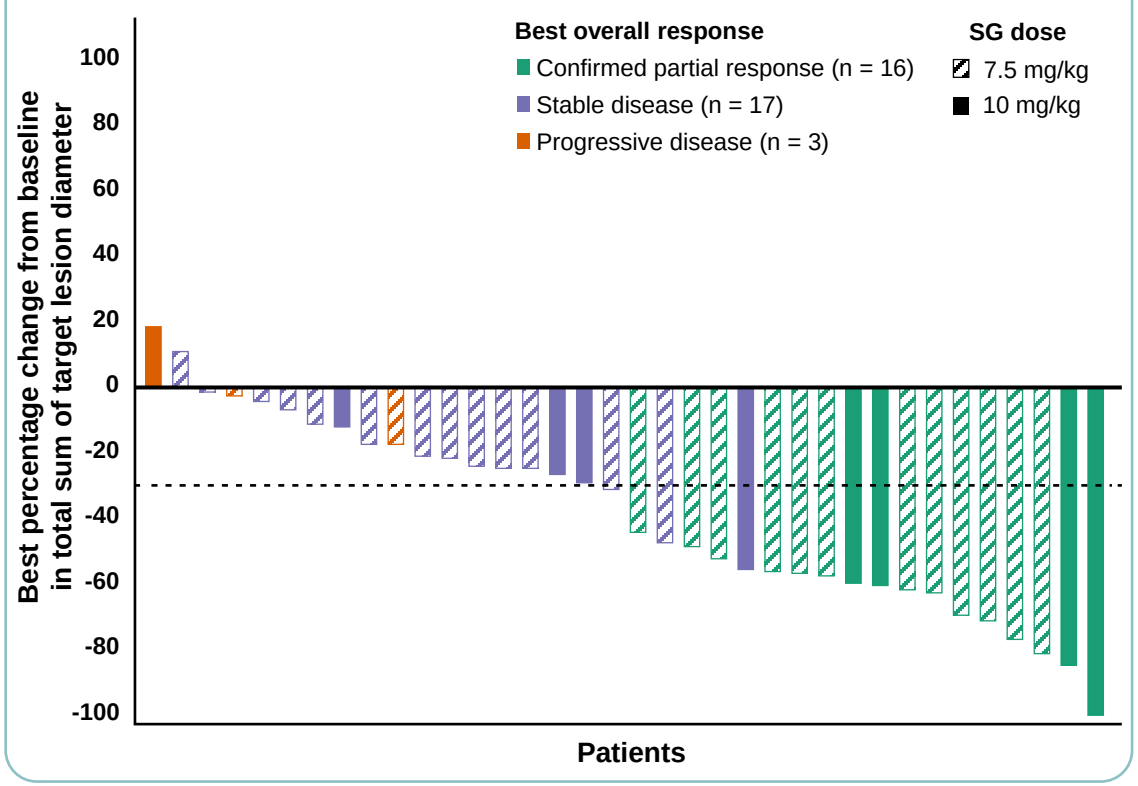
Patients received SG 7.5 mg/kg or 10 mg/kg.
[a]IRC assessment per Response Evaluation Criteria in Solid Tumors version 1.1. [b]Three patients in the NSQ group had no measurable disease per IRC at baseline and were not included in the efficacy analysis.
CP, carboplatin + pembrolizumab; **DOR**, duration of response; **IRC**, independent review committee; **NR**, not reached; **NSQ**, nonsquamous; **ORR**, objective response rate; **PFS**, progression-free survival; **SG**, sacituzumab govitecan; **SQ**, squamous.

IRC[a] Response by Dose

Cohort C (NSQ) SG + CP (n = 51)[b]



Cohort D (SQ) SG + CP (n = 41)[c]



- Response was observed in patients who received either dose

The dotted line represents 30% reduction.
[a]IRC assessment per Response Evaluation Criteria in Solid Tumors version 1.1. [b]Three (5.6%) patients in the NSQ group had no measurable disease per IRC at baseline and were not included in the efficacy analysis and 7 (13.7%) patients in the NSQ group were not evaluable. [c]5 (12.2%) patients in the SQ group were not evaluable.
CP, carboplatin + pembrolizumab; **IRC**, independent review committee; **NSQ**, nonsquamous; **SG**, sacituzumab govitecan; **SQ**, squamous.

Overall Efficacy by PD-L1 Expression[a]

	PD-L1 TPS < 1% SG + CP (n = 44)	PD-L1 TPS 1–49% SG + CP (n = 36)	PD-L1 TPS ≥ 50% SG + CP (n = 12)
ORR, % (95% CI)	43.2 (28.3–59.0)	33.3 (18.6–51.0)	66.7 (34.9–90.1)
Partial response, n (%)	19 (43.2)	12 (33.3)	8 (66.7)
Stable disease, n (%)	15 (34.1)	16 (44.4)	2 (16.7)
Progressive disease, n (%)	3 (6.8)	4 (11.1)	1 (8.3)
Not evaluable, n (%)	7 (15.9)	4 (11.1)	1 (8.3)
PFS, median (95% CI), months	8.3 (5.2–15.0)	6.8 (4.0–10.7)	NR (1.9–NR)

- For patients with tumors that had PD-L1 TPS ≥ 1% (n = 48), ORR was 41.7% (95% CI, 27.6–56.8) and median PFS was 8.4 (95%CI, 5.3–11.2) months

Patients received SG 7.5 mg/kg or 10 mg/kg.
[a]IRC assessment per Response Evaluation Criteria in Solid Tumors version 1.1.
CP, carboplatin + pembrolizumab; **IRC**, independent review committee; **NR**, not reached; **ORR**, objective response rate; **PD-L1**, programmed death ligand 1; **PFS**, progression-free survival; **SG**, sacituzumab govitecan; **TPS**, tumor proportion score.

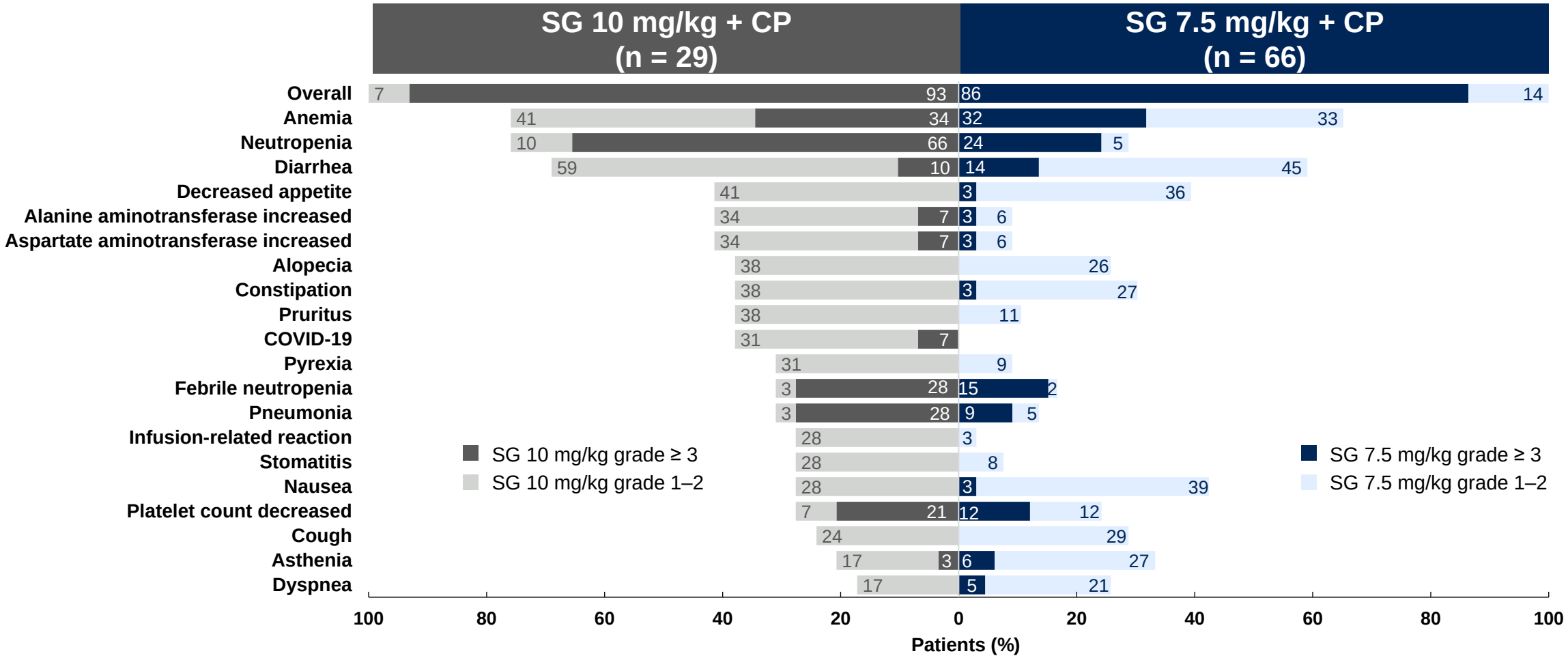
Overall Safety Summary by Dose

TEAEs, n (%)	SG 10 mg/kg + CP (n = 29)	SG 7.5 mg/kg + CP (n = 66)
Any grade	29 (100)	66 (100)
Grade ≥ 3	27 (93.1)	57 (86.4)
Serious	18 (62.1)	36 (54.5)
Leading to discontinuation of any study drug	9 (31.0)	12 (18.2)
Leading to discontinuation of SG	9 (31.0)	9 (13.6)
Leading to discontinuation of pembrolizumab	9 (31.0)	12 (18.2)
Leading to discontinuation of carboplatin	7 (24.1)	4 (6.1)
Leading to dose reduction of any study drug	19 (65.5)	27 (40.9)
Leading to dose reduction of SG	19 (65.5)	19 (28.8)
Leading to dose reduction of carboplatin	13 (44.8)	19 (28.8)
Leading to death[a]	5 (17.2)	9 (13.6)
Related to any study drug leading to death	3 (10.3)	5 (7.6)

- The incidence of grade ≥ 3 TEAEs and TEAEs leading to discontinuation was lower with SG 7.5 mg/kg
- Overall safety results are similar between NSQ and SQ histologies

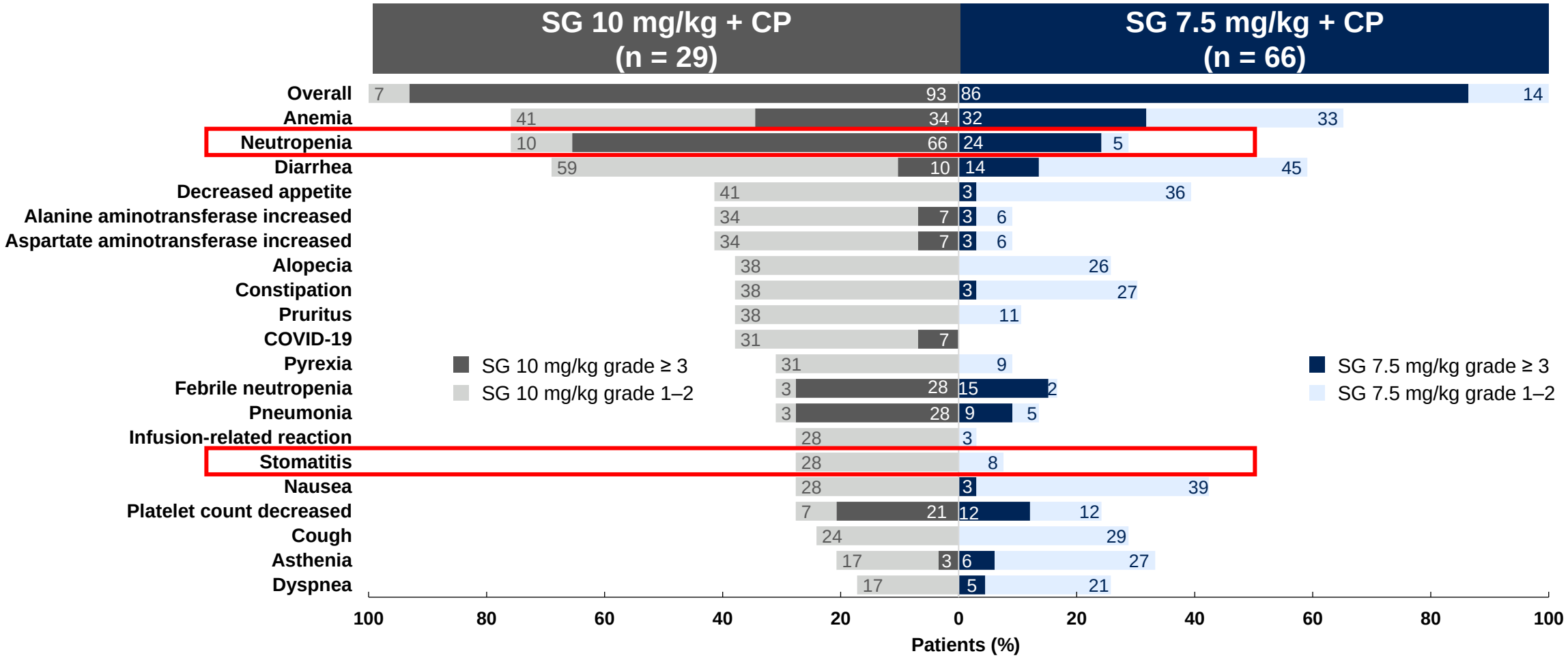
[a]TEAEs leading to death included sepsis (n=3), pneumonia (n=1), and abdominal infection (n=1) in the SG 10 mg/kg group and pneumonia (n=3), sepsis (n=2), febrile neutropenia (n=1), bacterial sepsis (n=1), gastroenteritis (n=1), pneumococcal sepsis (n=1), and hypoglycemia (n=1) in the SG 7.5 mg/kg group.
CP, carboplatin + pembrolizumab; **NSQ**, nonsquamous; **SG**, sacituzumab govitecan; **SQ**, squamous; **TEAE**, treatment-emergent adverse event.

Treatment-Emergent Adverse Events in ≥ 25% of Patients



CP, carboplatin + pembrolizumab; **SG**, sacituzumab govitecan.

Treatment-Emergent Adverse Events in ≥ 25% of Patients



CP, carboplatin + pembrolizumab; **SG**, sacituzumab govitecan.

Conclusions

- SG + carboplatin + pembrolizumab demonstrated encouraging efficacy in patients with non-AGA–driven metastatic NSCLC
  - Efficacy was seen across NSQ and SQ histologies and PD-L1 status
  - Responses were observed at both doses of SG
- Recommended dose for SG is 7.5 mg/kg in combination with pembrolizumab 200 mg and carboplatin AUC5
  - TEAEs were manageable with the appropriate supportive measures
- SG continues to be studied in various combinations in first-line metastatic NSCLC
  - Combination with pembrolizumab (EVOKE-02; phase 2, all PD-L1 expression levels, NCT05186974)
  - Combination with pembrolizumab (EVOKE-03; phase 3, PD-L1 TPS ≥50%, NCT05609968)
  - Combination with zimberelimab ± domvanalimab (VELOCITY-Lung; phase 2, all PD-L1 expression levels, NCT05633667)

AGA, actionable genomic alteration; **AUC5**, area under the concentration by time curve 5; **NSCLC**, non-small cell lung cancer; **NSQ**, nonsquamous; **PD-L1**, programmed death ligand 1; **SG**, sacituzumab govitecan; **SQ**, squamous; **TEAE**, treatment-emergent adverse event; **TPS**, tumor proportion score.

Acknowledgments

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- Thank you to the clinical trial investigators and their team members, without whom this work would not have been possible