

Subgroup Analysis From the ASCENT-03 Study of Sacituzumab Govitecan vs Chemotherapy in Previously Untreated Metastatic Triple-Negative Breast Cancer: PFS by Preselected Chemotherapy, Disease Status, and Brain and Visceral Metastases

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Conclusions

- Consistent with the overall results of the ASCENT-03 study, first-line (1L) sacituzumab govitecan (SG) demonstrated clinical benefit vs chemotherapy (chemo) in this clinical subgroup analysis of participants with metastatic triple-negative breast cancer (mTNBC) who are not candidates for a programmed death (ligand) 1 (PD-[L]1) inhibitor–based therapy
 - The benefit was observed across key clinical subgroups, including preselected chemo, disease status, and presence of brain and visceral metastases at baseline
- A progression-free survival (PFS) benefit was observed with SG across all assessed subgroups by blinded independent central review (BICR) and investigator assessment
- Fewer participants developed new visceral lesions with SG vs chemo at time of progression

- Findings from this exploratory analysis in participants with PD-(L)1 inhibitor–ineligible mTNBC in ASCENT-03, in conjunction with results from the ASCENT-04 study of SG + pembrolizumab vs chemo + pembrolizumab for PD-L1+ mTNBC,¹ support the use of 1L SG as the backbone of care for patients with previously untreated, locally advanced unresectable or mTNBC, regardless of PD-L1 status

Plain Language Summary

- This additional analysis from the ASCENT-03 study explored how treatment with sacituzumab govitecan (SG) worked compared with chemotherapy in different groups of participants with advanced triple-negative breast cancer who were not eligible for treatment with a PD-(L)1 inhibitor, including those whose cancer had returned and those whose cancer had spread to the brain or other organs at the time of enrollment in the study
- Across these groups, SG generally helped participants live longer without their cancer getting worse or without them dying compared with chemotherapy
- When their cancer worsened, fewer participants treated with SG developed new areas with cancer in organs, such as the lungs or liver, compared with those treated with chemotherapy
- The results were consistent with results from the overall population in the study and support the use of SG as a first treatment option for patients with advanced triple-negative breast cancer

Introduction

- TNBC is a heterogeneous and aggressive subtype of breast cancer associated with poor outcomes²
 - Outcomes are particularly unfavorable in certain patient subgroups (eg, those defined by disease recurrence or sites of metastasis)²⁻³ due to poor prognosis and limited treatment options
- The Trop-2–targeted antibody-drug conjugate, SG, was recently approved in the European Union, United States, and other regions based on results of the phase 3 ASCENT-03 study⁴⁻⁶ and is recommended globally in multiple treatment guidelines as a preferred 1L option for patients with unresectable locally advanced or mTNBC who are not candidates for PD-1 or PD-L1 inhibitor–based therapy^{7,8}
- In the PFS primary analysis from ASCENT-03 of SG vs chemo:
 - Median PFS by BICR was 9.7 months vs 6.9 months (stratified hazard ratio [HR], 0.62; 95% CI, 0.50-0.77) and by investigator assessment was 9.6 months vs 6.8 months (stratified HR, 0.64; 95% CI, 0.52-0.79)⁴
 - Overall survival (OS) data were immature (at 37% maturity)⁴
- Given the demonstrated clinical benefit of SG, evaluating treatment outcomes across clinically relevant patient subgroups may provide insights into SG efficacy across diverse patient populations
- Here, the efficacy results in subgroups of clinical interest from ASCENT-03 are presented

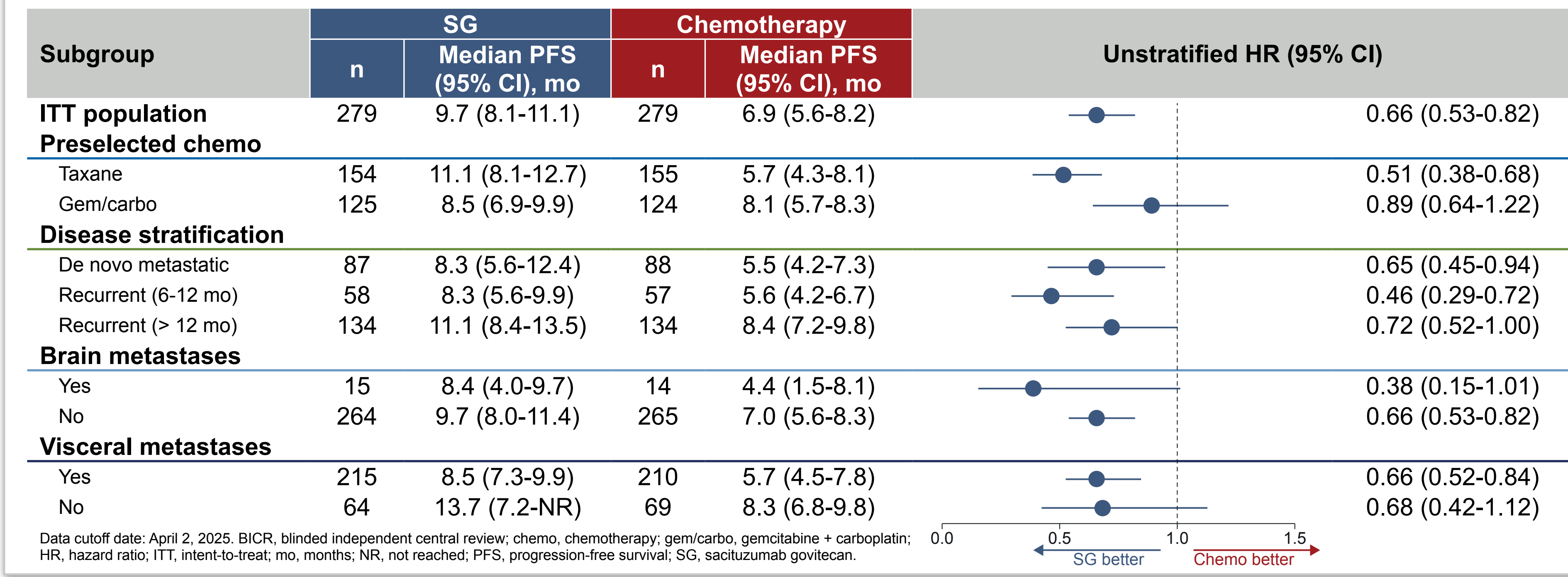
Methods

- Participants were randomized 1:1 to SG or chemo (taxane [paclitaxel, nab-paclitaxel] or gemcitabine + carboplatin [gem/carbo])
- The primary end point was PFS by BICR
- An analysis was conducted in the following prespecified subgroups:
 - Chemo selected prior to randomization (taxane, gem/carbo)
 - Disease status (de novo metastatic, recurrent disease within 6-12 months and > 12 months)
 - Presence of brain metastases at baseline (yes/no)
- A post hoc analysis by presence of visceral metastases at baseline (yes/no) was also conducted
- These analyses were not powered to detect statistically significant differences between subgroups

Results

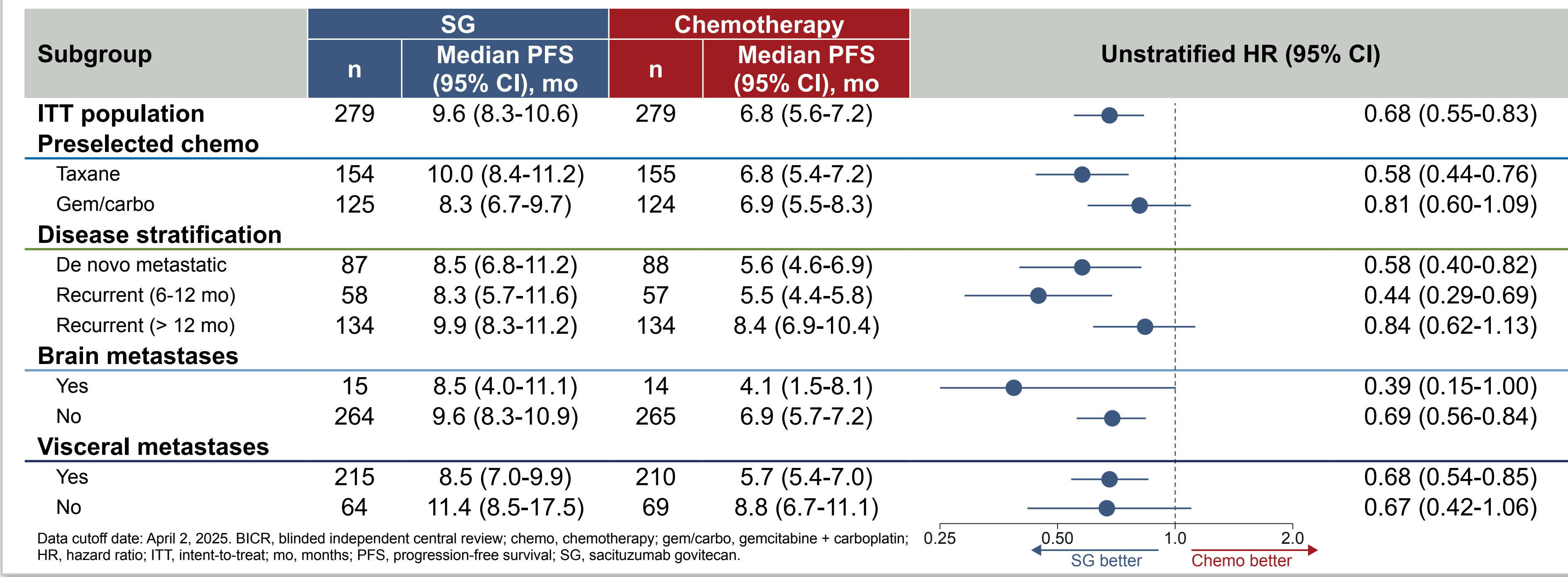
- In total, 558 participants were enrolled and randomly assigned (intent-to-treat [ITT] population) to receive SG (n = 279) or chemo (n = 279)
- Baseline characteristics were generally well balanced between the SG and chemo groups, both overall and within each assessed subgroup (**Table 1**)
 - Median age was generally consistent across subgroups, ranging from 49 to 58 years, with approximately one-quarter of participants aged ≥ 65 years in most subgroups
 - The majority of participants had an Eastern Cooperative Oncology Group performance status of 0 and lung metastases at baseline, irrespective of the subgroup
 - Recurrent disease was more common than de novo metastatic disease, with approximately half of participants experiencing disease recurrence > 12 months after prior treatment in the curative setting
 - Consistent with contemporary clinical practice, preselected chemotherapy varied by disease setting; there was a higher proportion of participants with recurrent disease preselected for gem/carbo and a higher proportion of participants with de novo disease preselected for taxane treatment

Figure 1. Progression-Free Survival by BICR Across Subgroups



Data cutoff date: April 2, 2025. BICR, blinded independent central review; chemo, chemotherapy; gem/carbo, gemcitabine + carboplatin; HR, hazard ratio; ITT, intent-to-treat; mo, months; NR, not reached; PFS, progression-free survival; SG, sacituzumab govitecan.

Figure 2. Progression-Free Survival by Investigator Assessment Across Subgroups



Data cutoff date: April 2, 2025. BICR, blinded independent central review; chemo, chemotherapy; gem/carbo, gemcitabine + carboplatin; HR, hazard ratio; ITT, intent-to-treat; mo, months; PFS, progression-free survival; SG, sacituzumab govitecan.

Table 1. Demographic and Baseline Characteristics of Participants Across Subgroups

Characteristics	ITT Population		Preselected Chemo				Disease Stratification						Brain Metastases				Visceral Metastases			
			Taxane		Gem/Carbo		De novo metastatic		Recurrent, 6-12 months		Recurrent, > 12 months		Yes		No		Yes		No	
	SG (n = 279)	Chemo (n = 279)	SG (n = 154)	Chemo (n = 155)	SG (n = 125)	Chemo (n = 124)	SG (n = 87)	Chemo (n = 88)	SG (n = 58)	Chemo (n = 57)	SG (n = 134)	Chemo (n = 134)	SG (n = 15)	Chemo (n = 14)	SG (n = 264)	Chemo (n = 265)	SG (n = 215)	Chemo (n = 210)	SG (n = 64)	Chemo (n = 69)
Median age (range), years	56 (28-84)	54 (23-86)	57 (29-84)	56 (23-86)	53 (28-81)	52 (28-77)	57 (28-81)	57 (29-80)	51 (37-81)	49 (23-77)	57 (34-84)	56 (28-86)	55 (38-74)	56 (36-77)	56 (28-84)	54 (23-86)	55 (28-84)	53 (23-79)	57 (37-81)	58 (30-86)
≥ 65 years, n (%)	65 (23)	78 (28)	38 (25)	50 (32)	27 (22)	28 (23)	22 (25)	32 (36)	6 (10)	9 (16)	37 (28)	37 (28)	2 (13)	2 (14)	63 (24)	76 (29)	50 (23)	53 (25)	15 (23)	25 (36)
Race or ethnic group,* n (%)																				
White	178 (64)	178 (64)	97 (63)	101 (65)	81 (65)	77 (62)	47 (54)	51 (58)	41 (71)	39 (68)	90 (67)	88 (66)	9 (60)	8 (57)	169 (64)	170 (64)	134 (62)	135 (64)	44 (69)	43 (62)
Asian	66 (24)	65 (23)	40 (26)	39 (25)	26 (21)	26 (21)	24 (28)	21 (24)	10 (17)	9 (16)	32 (24)	35 (26)	6 (40)	4 (29)	60 (23)	61 (23)	55 (26)	49 (23)	11 (17)	16 (23)
Black	10 (4)	7 (3)	6 (4)	3 (2)	4 (3)	4 (3)	3 (3)	1 (1)	2 (3)	3 (5)	5 (4)	3 (2)	0	0	10 (4)	7 (3)	8 (4)	6 (3)	2 (3)	1 (1)
Other or not specified	25 (9)	29 (10)	11 (7)	12 (8)	14 (11)	17 (14)	13 (15)	15 (17)	5 (9)	6 (11)	7 (5)	8 (6)	0	2 (14)	25 (9)	27 (10)	18 (8)	20 (10)	7 (11)	9 (13)
Geographic region, n (%)																				
Canada/United States/Western Europe	89 (32)	89 (32)	59 (38)	54 (35)	30 (24)	35 (28)	28 (32)	28 (32)	19 (33)	19 (33)	42 (31)	42 (31)	1 (7)	1 (7)	88 (33)	88 (33)	62 (29)	65 (31)	27 (42)	24 (35)
Rest of the world ^b	190 (68)	190 (68)	95 (62)	101 (65)	95 (76)	89 (72)	59 (68)	60 (68)	39 (67)	38 (67)	92 (69)	92 (69)	14 (93)	13 (93)	176 (67)	177 (67)	153 (71)	145 (69)	37 (58)	45 (65)
ECOG PS, n (%)																				
0	183 (66)	187 (67)	102 (66)	107 (69)	81 (65)	80 (65)	55 (63)	57 (65)	43 (74)	43 (75)	85 (63)	87 (65)	4 (27)	8 (57)	179 (68)	179 (68)	138 (64)	142 (68)	45 (70)	45 (65)
1	96 (34)	92 (33)	52 (34)	48 (31)	44 (35)	44 (35)	32 (37)	31 (35)	15 (26)	14 (25)	49 (37)	47 (35)	11 (73)	6 (43)	85 (32)	86 (32)	77 (36)	68 (32)	19 (30)	24 (35)
Disease stratification, n (%)																				
De novo	87 (31)	88 (32)	58 (38)	62 (40)	29 (23)	26 (21)	87 (100)	88 (100)	0	0	0	0	2 (13)	2 (14)	85 (32)	86 (32)	64 (30)	58 (28)	23 (36)	30 (43)
Recurrent within 6-12 months	58 (21)	57 (20)	27 (17)	26 (17)	31 (25)	31 (25)	0	58 (100)	57 (100)	0	0	0	3 (20)	4 (29)	55 (21)	53 (20)	46 (21)	49 (23)	12 (19)	8 (12)
Recurrent > 12 months	134 (48)	134 (48)	69 (45)	67 (43)	65 (52)	67 (54)	0	0	0	0	134 (100)	134 (100)	10 (67)	8 (57)	124 (47)	126 (48)	105 (49)	103 (49)	29 (45)	31 (45)
Metastatic sites, n (%)																				
Lung	166 (59)	170 (61)	88 (57)	89 (57)	78 (62)	81 (65)	49 (56)	47 (53)	39 (67)	41 (72)	78 (58)	82 (61)	10 (67)	13 (93)	156 (59)	157 (59)	166 (77)	170 (81)	0	0
Liver	81 (29)	72 (26)	45 (29)	46 (30)	36 (29)	26 (21)	24 (28)	22 (25)	19 (33)	17 (30)	38 (28)	33 (25)	6 (40)	5 (36)	75 (28)	67 (25)	81 (38)	72 (34)	0	0
Brain	15 (5)	14 (5)	9 (6)	7 (5)	6 (5)	7 (6)	2 (2)	2 (2)	3 (5)	4 (7)	10 (7)	8 (6)	15 (100)	14 (100)	0	0	15 (7)	14 (7)	0	0
Chemo selected prior to randomization, n (%)																				
Taxane	154 (55)	155 (56)	154 (100)	155 (100)	0	0	58 (67)	62 (70)	27 (47)	26 (46)	69 (51)	67 (50)	9 (60)	7 (50)	145 (55)	148 (56)	119 (55)	118 (56)	35 (55)	37 (54)
Gemcitabine plus carboplatin	125 (45)	124 (44)	0	0	125 (100)	124 (100)	29 (33)	26 (30)	31 (53)	31 (54)	65 (49)	67 (50)	6 (40)	7 (50)	119 (45)	117 (44)	96 (45)	92 (44)	29 (45)	32 (46)

Data cutoff date: April 2, 2025. *As reported by the participants; other/not specified includes American Indian or Alaska Native, other races, and not provided/collection not permitted. ^bRest of the world includes Argentina, Australia, Brazil, Chile, China, Czech Republic, Hong Kong, Hungary, Israel, Japan, Malaysia, Mexico, Poland, Republic of Korea, Romania, Slovakia, South Africa, Taiwan, and Turkey. Chemo, chemotherapy; ECOG PS, Eastern Cooperative Oncology Group performance status; gem/carbo, gemcitabine + carboplatin; ITT, intent-to-treat; SG, sacituzumab govitecan.

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