BERLIN 2025 ESMO congress

Primary Results From ASCENT-03: A Randomized Phase 3 Study of Sacituzumab Govitecan vs Chemotherapy in Patients With Previously Untreated Metastatic Triple-Negative Breast Cancer Who Are Unable to Receive PD-(L)1 Inhibitors

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Sunday, October 19, 2025; 9:15-9:25 am
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Declaration of Interests

Javier Cortés, MD

Consulting/Advisor: Roche, AstraZeneca, Seattle Genetics, Daiichi Sankyo, Lilly, Merck Sharp & Dohme, Leuko, Bioasis, Clovis Oncology, Boehringer Ingelheim, Ellipses, Hibercell, BioInvent, Gemoab, Gilead Sciences, Menarini, Zymeworks, Reveal Genomics, Scorpion Therapeutics, Expres2ion Biotechnologies, Jazz Pharmaceuticals, AbbVie, BridgeBio, Biontech, Biocon, Circle Pharma, Delcath Systems, Hexagon Bio, Bliss Biopharmaceutical

Honoraria: Roche, Novartis, Eisai, Pfizer, Lilly, Merck Sharp & Dohme, Daiichi Sankyo, AstraZeneca, Gilead Sciences, Stemline Therapeutics, Zuellig Pharma

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Stock: MAJ3 Capital, Leuko (relative)

Travel, accommodation, expenses: Roche, Novartis, Eisai, Pfizer, Daiichi Sankyo, AstraZeneca, Gilead Sciences, Merck Sharp & Dhome, Stemline Therapeutics

Patents: Pharmaceutical combinations of A Pi3k inhibitor and a microtubule destabilizing agent. Javier Cortés Castán, Alejandro Piris Giménez, Violeta Serra Elizalde. WO 2014/199294 A (ISSUED); Her2 as a predictor of response to dual HER2 blockade in the absence of cytotoxic therapy. Aleix Prat, Antonio Llombart, Javier Cortés. US 2019/ 0338368 A1 (LICENSED)

Unmet Need in Patients With Previously Untreated mTNBC Who Are Not Candidates for PD-(L)1 Inhibitors

Unmet need

- ~60% of patients with previously untreated mTNBC are not candidates for PD-(L)1 inhibitor therapy[1]
- Median PFS observed in prior 1L mTNBC studies was < 6 months with chemo, the current standard of care[1-4]
- ~50% of the patients treated in 1L for mTNBC do not receive 2L treatment due to death or clinical deterioration[5]

Rationale for the ASCENT-03 study

- SG is the only Trop-2–directed ADC with survival benefit in multiple phase 3 mBC studies[6-7]
- SG is approved for 2L+ mTNBC and pre-treated HR+/HER2– mBC globally[8,9]
- There is an urgent need for improved therapeutic options in earlier lines of therapy to delay progression and time to next line of treatment

We present the primary results from the global, randomized phase 3 ASCENT-03 study of SG vs chemo in patients with previously untreated, advanced TNBC who are not candidates for PD-(L)1 inhibitors

1L, first line; **2L+**, second line or later; **ADC**, antibody drug conjugate; **chemo**, chemotherapy; **HER2–**, human epidermal growth factor receptor 2-negative; **HR+**, hormone receptor-positive; **mBC**, metastatic breast cancer; **mTNBC**, metastatic triple-negative breast cancer; **PD-1**, programmed cell death protein-1; **PD-L1**, programmed cell death ligand 1; **PD-(L)1**, PD-1 or PD-L1; **SG**, sacituzumab govitecan.

1. Cortés J, et al. *N Engl J Med*. 2022;387:217-26. 2. Won KA, et al. *Int J Oncol*. 2020;57:1245-61. 3. Gennari A, et al. *Ann Oncol*. 2021;32:1475-95. 4. Gennari A, et al. ESMO Metastatic Breast Cancer Living guidelines v1.2, April 2025. https://www.esmo.org/guidelines/living-guidelines/esmo-living-guideline-metastatic-breast-cancer. 5. Punie K, et al. *Oncologist*. 2025;30:oyaf034. 6. Bardia A, et al. *J Clin Oncol*. 2024;42:1738-44. 7. Rugo HS, et al. *Lancet*. 2023;402:1423-33. 8. TRODELVY® (sacituzumab govitecan-hziy) [package insert]. Foster City, CA: Gilead Sciences, Inc.; March 2025. 9. TRODELVY® (sacituzumab govitecan-hziy) [summary of product characteristics]. County Cork, Ireland: Gilead Sciences Ireland UC; November 2023.

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ASCENT-03: Study Design

Patients with previously untreated, locally advanced inoperable or metastatic TNBC[a]:

- Not candidates for PD-(L)1 inhibitors:
  - PD-L1 negative[b] tumors (CPS < 10)
  - PD-L1 positive[b] tumors (CPS ≥ 10) and previously treated with a PD-(L)1 inhibitor in curative setting
  - Ineligible for a PD-(L)1 inhibitor due to a comorbidity
- ≥ 6 months since treatment in curative setting
- Previously treated, stable CNS metastases were allowed

Treatment was continued until BICR-verified progression or unacceptable toxicity

N = 558

R 1:1

Sacituzumab govitecan
10 mg/kg IV
(days 1 and 8 of 21-day cycles)
n = 279

Chemotherapy
Paclitaxel 90 mg/m^2 OR nab-Paclitaxel 100 mg/m^2
(days 1, 8, and 15 of 28-day cycles) OR
Gemcitabine 1000 mg/m^2 + Carboplatin AUC2
(days 1 and 8 of 21-day cycles)
n = 279

Eligible patients were offered crossover to 2L SG provided through the study following BICR-verified disease progression

End points

Primary
- PFS by BICR[d]

Secondary
- OS
- ORR, DOR, TTR by BICR[d]
- Safety
- QOL

Stratification factors:
- United States/Canada/Western Europe vs rest of the world
- De novo mTNBC[c] vs recurrent within 6 to 12 months of treatment vs recurrent after > 12 months from treatment in curative setting

ClinicalTrials.gov identifier: NCT05382299. [a]TNBC status was centrally confirmed and determined according to standard American Society of Clinical Oncology-College of American Pathologists criteria. [b]PD-L1 CPS was centrally confirmed and defined using the PD-L1 IHC 22C3 assay (Dako, Agilent Technologies). [c]Up to 35% de novo mTNBC. [d]Per Response Evaluation Criteria in Solid Tumors version 1.1. **2L**, second line; **AUC**, area under the curve; **BICR**, blinded independent central review; **CNS**, central nervous system; **CPS**, combined positive score; **DOR**, duration of response; **IV**, intravenous; **mTNBC**, metastatic triple-negative breast cancer; **ORR**, objective response rate; **OS**, overall survival; **PD-1**, programmed cell death protein-1; **PD-L1**, programmed cell death ligand 1; **PD-(L)1**, PD-1 or PD-L1; **PFS**, progression-free survival; **QOL**, quality of life; **R**, randomization; **SG**, sacituzumab govitecan; **TNBC**, triple-negative breast cancer; **TTR**, time to response.

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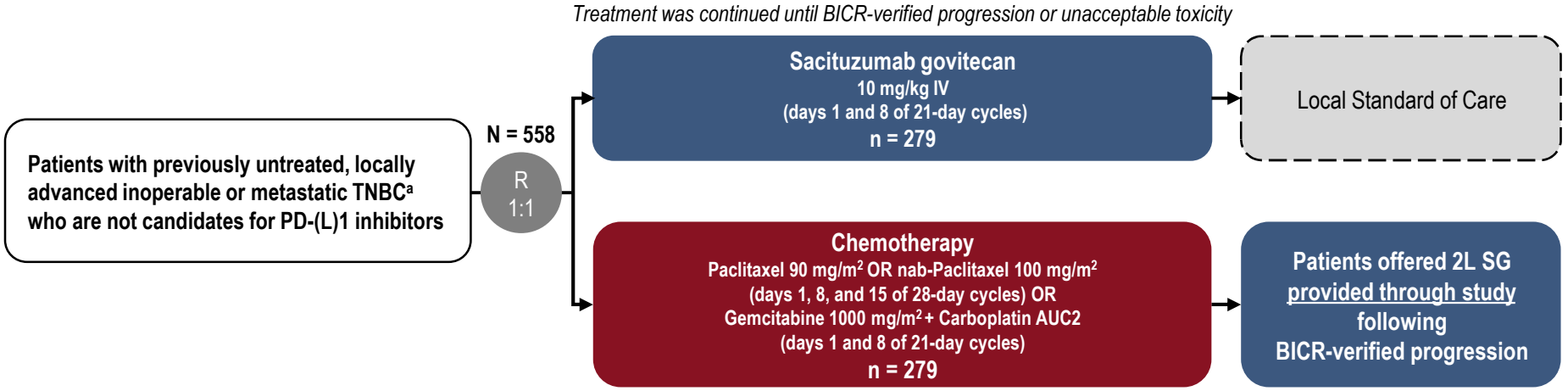
ASCENT-03: Study Design



Stratification factors:

- United States/Canada/Western Europe vs rest of the world
- De novo mTNBC[b] vs recurrent within 6 to 12 months of treatment vs recurrent after > 12 months from treatment in curative setting

ClinicalTrials.gov identifier: NCT05382299. [a]TNBC status was centrally confirmed and determined according to standard American Society of Clinical Oncology-College of American Pathologists criteria. [b]Up to 35% de novo mTNBC.
2L, second-line; **BICR**, blinded independent central review; **IV**, intravenous; **mTNBC**, metastatic triple-negative breast cancer; **PD-1**, programmed cell death protein-1; **PD-L1**, programmed cell death ligand 1; **PD-(L)1**, PD-1 or PD-L1; **R**, randomization; **SG**, sacituzumab govitecan; **TNBC**, triple-negative breast cancer.

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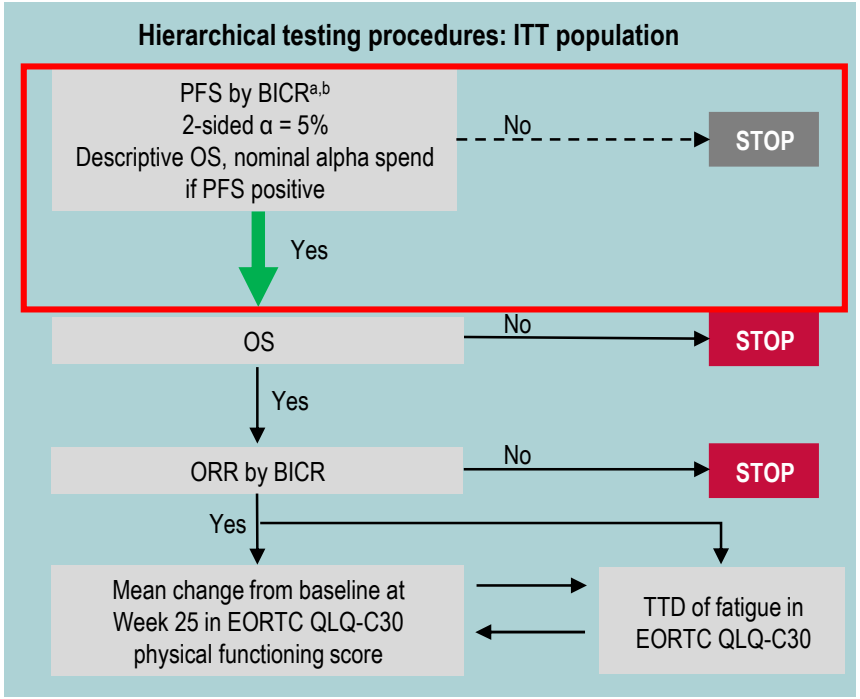
Statistical Analysis

- Enrollment was planned for ~ 540 eligible patients
- To control for overall type I error, a hierarchical testing procedure will be implemented
  - At primary analysis[c], PFS will be tested at 2-sided alpha of 5%
  - OS will be summarized descriptively at the time of primary PFS analysis; if PFS is positive, a nominal alpha will be spent without formal testing
  - If PFS is significant at primary analysis, formal sequential testing of OS, ORR, and then QOL end points will be performed[d]
- Data cutoff date for primary PFS: April 2, 2025
  - There were 349 observed PFS events by BICR
  - Median follow-up was 13.2 months (range, < 0.1-29.2)
  - At the data cutoff date, 75 patients (27%) in the SG group and 39 patients (14%) in the chemo group continued to receive study treatment



[a]If PFS is positive, descriptive OS in ITT at a nominal 2-sided alpha of 0.01% is summarized. [b]PFS by investigator was a sensitivity analysis. [c]Approximately 352 events assessed by BICR in 540 patients in the ITT population (65% maturity) to detect HR of 0.65 with > 95% power. [d]The key secondary endpoints of TTD in fatigue and mean change from baseline in physical functioning at week 25 will be tested according to the hierarchical strategy; the total 2-sided alpha will be split between the 2 tests evenly. **BICR**, blinded independent central review; **chemo**, chemotherapy; **EORTC QLQ-C30**, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30; **FA**, final analysis; **HR**, hazard ratio; **IA**, interim analysis; **ITT**, intent to treat; **ORR**, objective response rate; **OS**, overall survival; **PFS**, progression-free survival; **QOL**, quality of life; **SG**, sacituzumab govitecan; **TTD**, time to deterioration.

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Demographics and Baseline Characteristics

ITT Population	SG (n = 279)	Chemo (n = 279)
Female sex, n (%)	278 (> 99)	277 (99)
Median age, (range) yr	56 (28-84)	54 (23-86)
≥ 65 yr, n (%)	65 (23)	78 (28)
Race or ethnic group,[a] n (%)		
White	178 (64)	178 (64)
Asian	66 (24)	65 (23)
Black	10 (4)	7 (3)
Other/not specified	25 (9)	29 (10)
Geographic region, n (%)		
United States/Canada/Western Europe	89 (32)	89 (32)
Rest of the world[b]	190 (68)	190 (68)
ECOG PS, n (%)		
0	183 (66)	187 (67)
1	96 (34)	92 (33)
Curative treatment-free interval, n (%)		
De novo	87 (31)	88 (32)
Recurrent within 6-12 mo	58 (21)	57 (20)
Recurrent > 12 mo	134 (48)	134 (48)

ITT Population	SG (n = 279)	Chemo (n = 279)
PD-L1 status,[c] n (%)		
Negative	277 (99)	278 (> 99)
Positive	1 (< 1)	1 (< 1)
Metastatic sites, n (%)		
Lung	166 (59)	170 (61)
Liver	81 (29)	72 (26)
Brain	15 (5)	14 (5)
Chemo selected prior to randomization,[d] n (%)		
Taxane	154 (55)	155 (56)
Gemcitabine/carboplatin	125 (45)	124 (44)
Prior (neo)adjuvant therapies, n (%)	185 (66)	191 (68)
Taxanes	162 (58)	162 (58)
Capecitabine	50 (18)	57 (20)
Platinum agents	51 (18)	49 (18)
PD-(L)1 inhibitors	13 (5)	11 (4)

Data cutoff date: April 2, 2025. [a]As reported by the patients; other/not specified includes American Indian or Alaska Native, other races, and not provided/collection not permitted. [b]Rest 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. [c]PD-L1 status assessed using the PD-L1 IHC 22C3 assay (Dako, Agilent Technologies) at time of enrollment; tumors with a combined positive score ≥ 10 were considered PD-L1 positive and tumors with a combined positive score < 10 were considered PD-L1 negative. One patient in the SG group had PD-L1 CPS missing. [d]Actual chemo received was consistent with what was selected prior to randomization; however, 3 patients were randomized but did not receive treatment.
Chemo, chemotherapy; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **ITT**, intent to treat; **PD-1**, programmed cell death protein-1; **PD-L1**, programmed cell death ligand 1; **PD-(L)1**, PD-1 or PD-L1; **SG**, sacituzumab govitecan.

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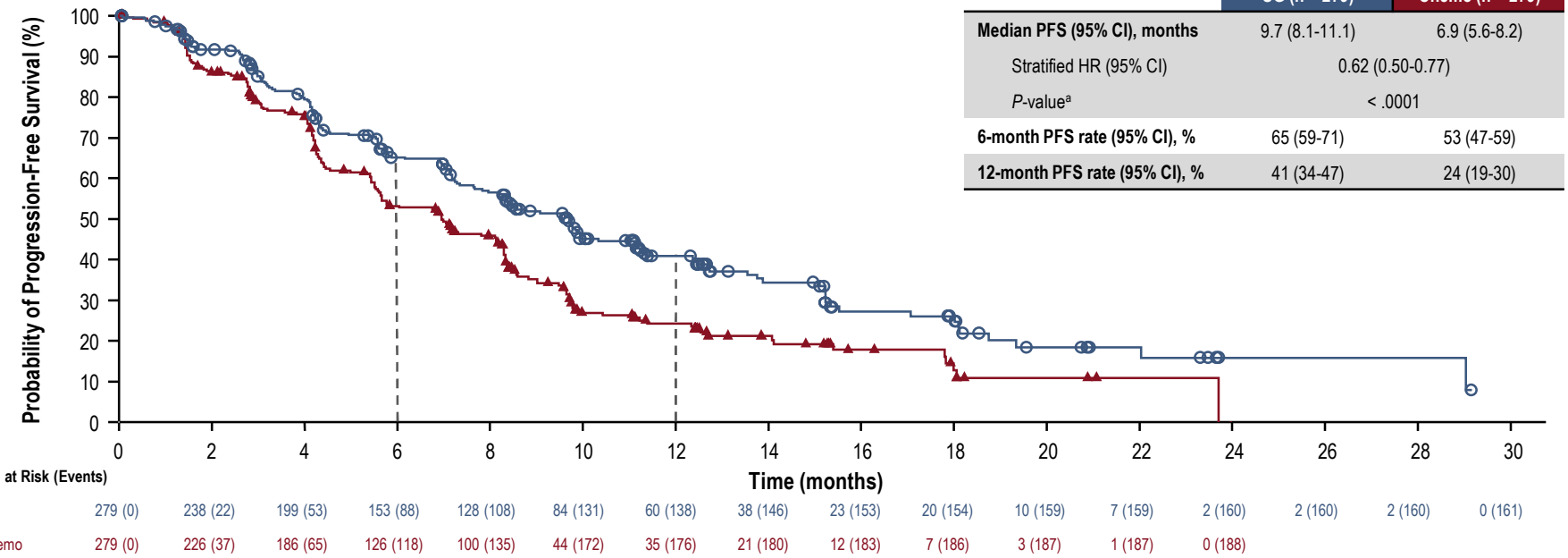
Progression-Free Survival by BICR



	SG (n = 279)	Chemo (n = 279)
Median PFS (95% CI), months	9.7 (8.1-11.1)	6.9 (5.6-8.2)
Stratified HR (95% CI)	0.62 (0.50-0.77)	
P-value[a]	< .0001	
6-month PFS rate (95% CI), %	65 (59-71)	53 (47-59)
12-month PFS rate (95% CI), %	41 (34-47)	24 (19-30)

No. at Risk (Events)																
SG	279 (0)	238 (22)	199 (53)	153 (88)	128 (108)	84 (131)	60 (138)	38 (146)	23 (153)	20 (154)	10 (159)	7 (159)	2 (160)	2 (160)	2 (160)	0 (161)
Chemo	279 (0)	226 (37)	186 (65)	126 (118)	100 (135)	44 (172)	35 (176)	21 (180)	12 (183)	7 (186)	3 (187)	1 (187)	0 (188)			

SG demonstrated statistically significant and clinically meaningful improvement in PFS vs chemo by BICR analysis, with a 38% reduction in risk of disease progression or death

Data cutoff date: April 2, 2025. [a]Two-sided *P*-value from stratified log-rank test.
BICR, blinded independent central review; **chemo**, chemotherapy; **HR**, hazard ratio; **PFS**, progression-free survival; **SG**, sacituzumab govitecan.

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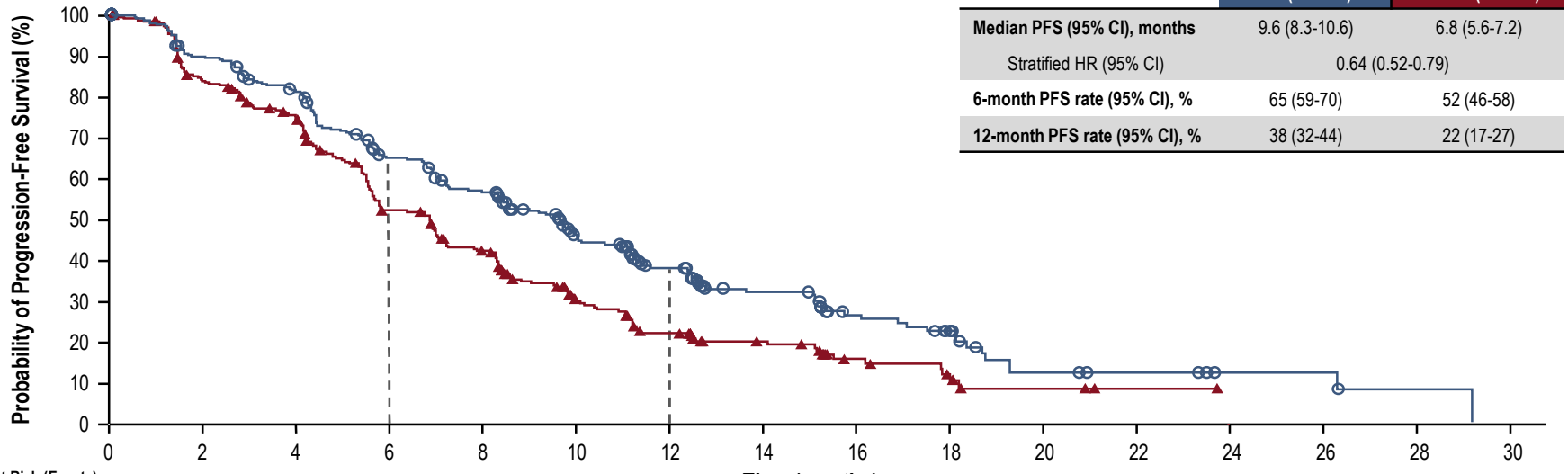
Progression-Free Survival by Investigator Assessment[a]



	SG (n = 279)	Chemo (n = 279)
Median PFS (95% CI), months	9.6 (8.3-10.6)	6.8 (5.6-7.2)
Stratified HR (95% CI)	0.64 (0.52-0.79)	
6-month PFS rate (95% CI), %	65 (59-70)	52 (46-58)
12-month PFS rate (95% CI), %	38 (32-44)	22 (17-27)

No. at Risk (Events)																
SG	279 (0)	240 (28)	213 (51)	164 (93)	140 (114)	96 (139)	66 (154)	43 (163)	27 (170)	19 (174)	8 (181)	6 (181)	3 (181)	3 (181)	1 (182)	0 (183)
Chemo	279 (0)	223 (44)	192 (69)	129 (125)	99 (149)	58 (176)	39 (191)	26 (194)	13 (199)	7 (203)	3 (204)	1 (204)	0 (204)			

SG demonstrated improved PFS vs chemo by investigator assessment, consistent with the BICR analysis

Data cutoff date: April 2, 2025. [a]Sensitivity analysis.
Chemo, chemotherapy; **HR**, hazard ratio; **PFS**, progression-free survival; **SG**, sacituzumab govitecan.

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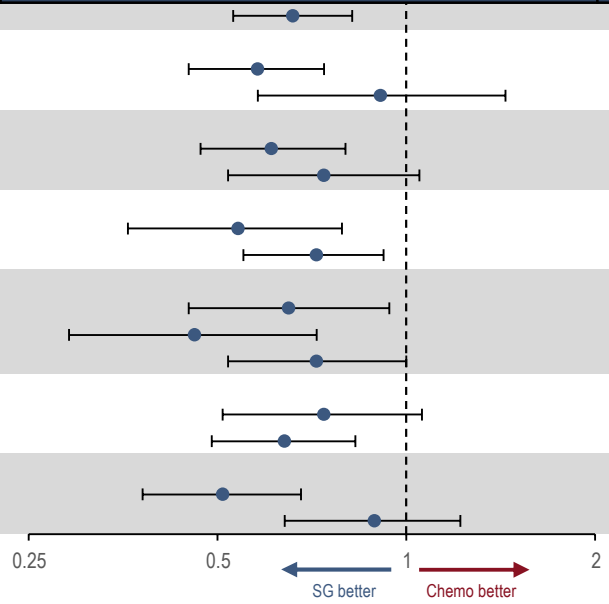
Subgroup Analysis of Progression-free Survival by BICR

	SG		Chemo			
	n	Median PFS, mo (95% CI)	n	Median PFS, mo (95% CI)	Unstratified HR (95% CI)	Unstratified HR (95% CI)
ITT population	279	9.7 (8.1-11.1)	279	6.9 (5.6-8.2)		0.66 (0.53-0.82)
Age group						
< 65 years	214	9.6 (7.6-10.3)	201	5.7 (4.4-7.0)		0.58 (0.45-0.74)
≥ 65 years	65	11.1 (7.3-13.9)	78	9.0 (8.3-10.0)		0.91 (0.58-1.44)
ECOG PS						
0	183	11.2 (9.7-13.5)	187	7.3 (6.0-8.3)		0.61 (0.47-0.80)
1	96	7.1 (5.4-8.5)	92	5.5 (4.2-7.2)		0.74 (0.52-1.05)
Geographic region						
United States/Canada/Western Europe	89	9.9 (7.8-13.9)	89	7.1 (5.4-8.3)		0.54 (0.36-0.79)
Rest of the world	190	9.6 (7.2-11.1)	190	6.9 (5.5-8.3)		0.72 (0.55-0.92)
Disease Status						
De novo	87	8.3 (5.6-12.4)	88	5.5 (4.2-7.3)		0.65 (0.45-0.94)
Recurrent 6-12 mo	58	8.3 (5.6-9.9)	57	5.6 (4.2-6.7)		0.46 (0.29-0.72)
Recurrent > 12 mo	134	11.1 (8.4-13.5)	134	8.4 (7.2-9.8)		0.72 (0.52-1.00)
PD-L1 status						
CPS < 1	102	8.5 (7.2-12.5)	98	8.3 (5.4-9.6)		0.74 (0.51-1.06)
1 ≤ CPS < 10	175	9.8 (7.6-11.3)	180	6.9 (5.5-8.1)		0.64 (0.49-0.83)
Chemo selected prior to randomization						
Taxane	154	11.1 (8.1-12.7)	155	5.7 (4.3-8.1)		0.51 (0.38-0.68)
Gemcitabine/carboplatin	125	8.5 (6.9-9.9)	124	8.1 (5.7-8.3)		0.89 (0.64-1.22)



PFS benefit of SG over chemo was observed across key prespecified subgroups

Data cutoff date: April 2, 2025. **BICR**, blinded independent central review; **chemo**, chemotherapy; **CPS**, combined positive score; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **HR**, hazard ratio; **ITT**, intent-to-treat; **PD-L1**, programmed cell death ligand 1; **PFS**, progression-free survival; **SG**, sacituzumab govitecan.

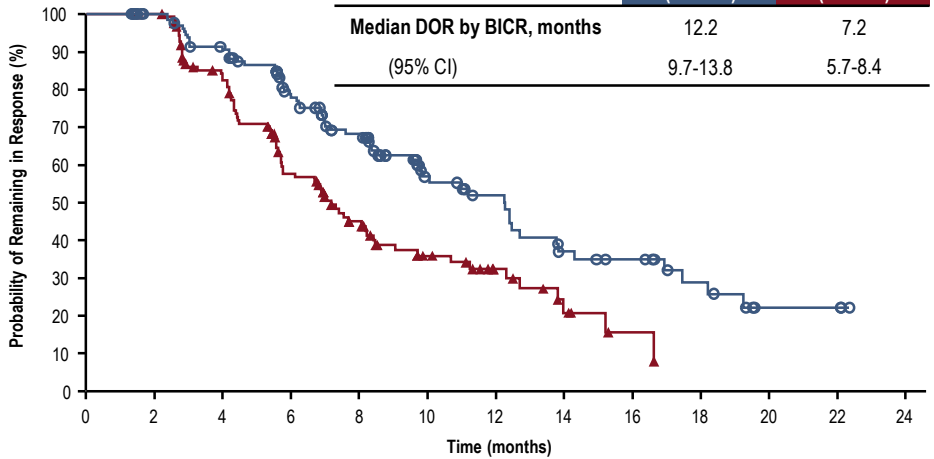
Javier Cortés, MD

Tumor Response

Variable	SG (n = 279)	Chemo (n = 279)
Objective response rate by BICR[a] (95% CI), %	48 (42-54)	46 (40-52)
Stratified odds ratio (95% CI)	1.1 (0.8-1.6)	
Best overall response by BICR, n (%)		
Complete response	20 (7)	15 (5)
Partial response	115 (41)	112 (40)
Stable disease	113 (41)	101 (36)
Stable disease ≥ 6 months	37 (13)	32 (11)
Progressive disease	14 (5)	36 (13)
Not evaluable	17 (6)	15 (5)
Time to response by BICR,[b] median (range), months	1.6 (0.7-16.7)	1.6 (0.9-6.8)

Duration of Response

	SG (n = 135)	Chemo (n = 127)
Median DOR by BICR, months	12.2	7.2
(95% CI)	9.7-13.8	5.7-8.4



Objective response rates were similar in both treatment groups; however, duration of response was substantially longer with SG vs chemo

Data cutoff date: April 2, 2025. [a]Objective response rate is defined as the proportion of patients who achieved a best overall response of complete response/partial response. [b]Time to response (months) = (date of first documented confirmed complete or partial response - date of randomization + 1)/30.4375.
Chemo, chemotherapy; **BICR**, blinded independent central review; **DOR**, duration of response; **SG**, sacituzumab govitecan.

Javier Cortés, MD

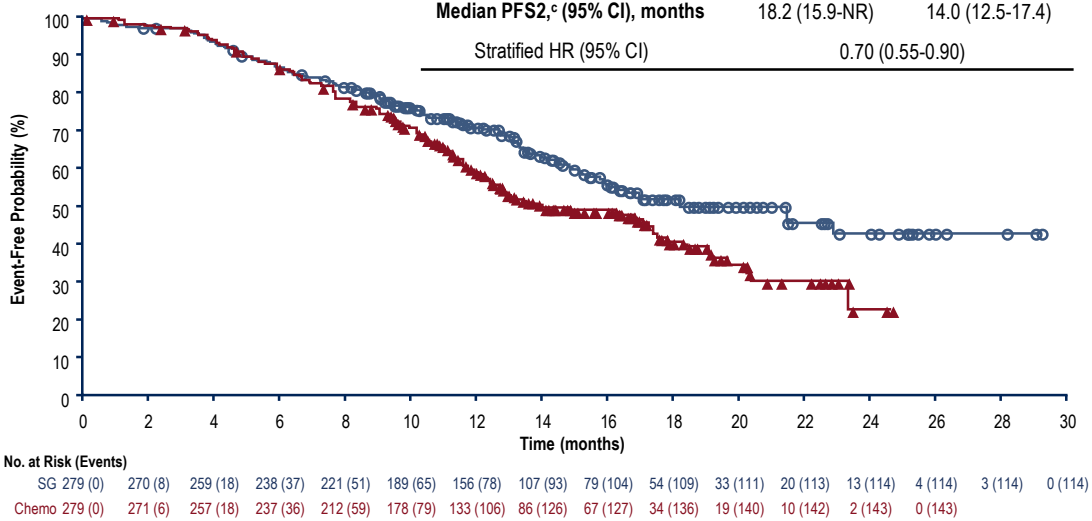
Descriptive Overall Survival and PFS2

- **Overall survival not yet mature[a]**
- Study continues to first formal OS analysis
- Of 179 patients who initiated subsequent treatment after chemo, 147 (82%) received SG

Overall survival	SG (n = 279)	Chemo (n = 279)
Number of events, %	103 (37)	103 (37)
Median (95% CI) , months	21.5 (17.7-NR)	20.2 (18.2-NR)
Stratified HR (95% CI)	0.98 (0.75-1.30)	
OS rate (95% CI), %		
12-month	75 (70-80)	73 (67-78)
24-month	46 (36-56)	42 (29-54)

Progression-Free Survival 2[b]

	SG (n = 279)	Chemo (n = 279)
Median PFS2,[c] (95% CI), months	18.2 (15.9-NR)	14.0 (12.5-17.4)
Stratified HR (95% CI)	0.70 (0.55-0.90)	



At the time of primary analysis, overall survival was immature and PFS2 was longer with SG vs chemo by investigator assessment

Data cutoff date: April 2, 2025. [a]At the time of this analysis, OS data maturity was 37%. [b]PFS2 is defined as the time from date of randomization to the first documented progression on next-line therapy based on investigator assessment of progressive disease or death due to any cause, whichever occurs first. [c]By investigator assessment.
2L, second line; **chemo**, chemotherapy; **HR**, hazard ratio; **NR**, not reached; **OS**, overall survival; **PFS2**, progression-free survival 2; **SG**, sacituzumab govitecan.

Javier Cortés, MD

Exposure and Safety Summary

Safety population	SG (n = 275)	Chemo (n = 276)	
Treatment component	**SG**	**Taxane**	**Gemcitabine/ Carboplatin**
All treated patients, n	275	154	122
Median duration of treatment, months (range)	8.3 (< 0.1-28.7)	6.3 (< 0.1-24.2)	5.8 (< 0.1-23.1)

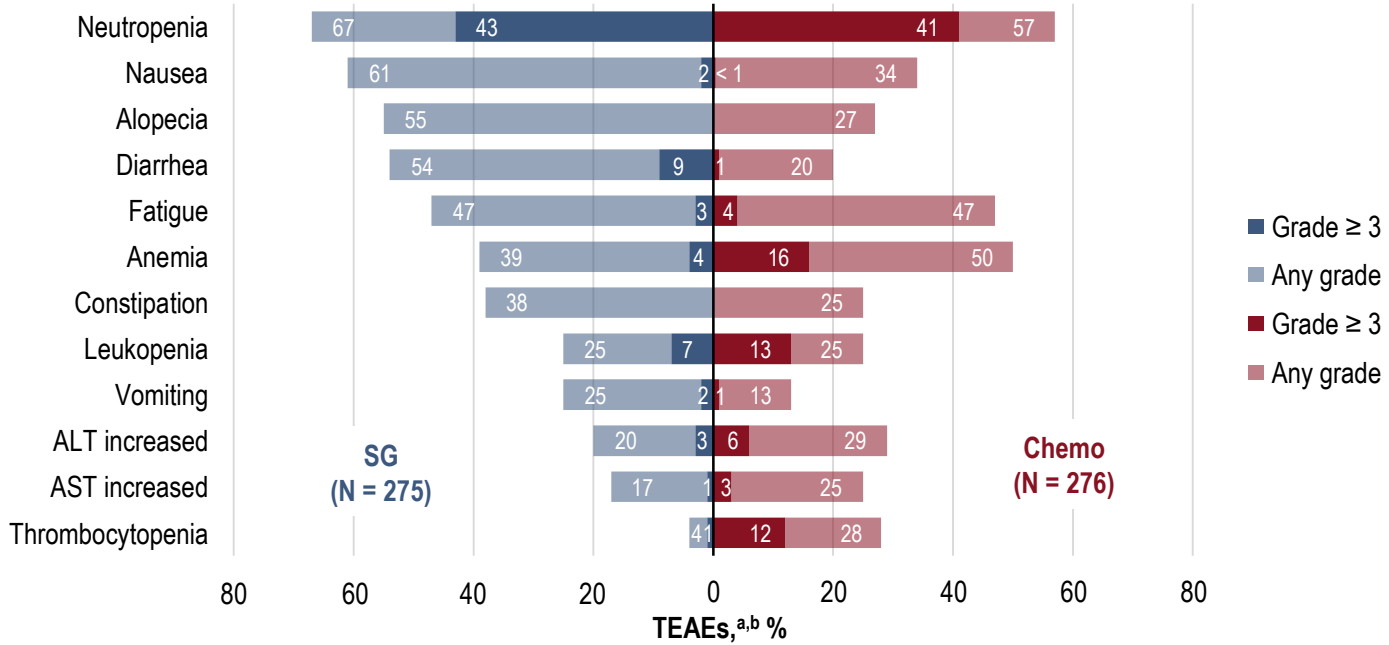
TEAEs, n (%)	SG (n = 275)	Chemo (n = 276)
Any TEAE	273 (99)	269 (97)
Grade ≥ 3 TEAEs	181 (66)	171 (62)
Treatment-related	167 (61)	147 (53)
Treatment-emergent SAE	71 (26)	67 (24)
Treatment-related	46 (17)	37 (13)
TEAEs leading to treatment discontinuation	10 (4)	33 (12)
TEAEs leading to dose interruption	181 (66)	171 (62)
TEAEs leading to dose reduction	101 (37)	124 (45)
TEAEs leading to death	7 (3)	1 (< 1)
Treatment-related	6 (2)	1 (< 1)

All treatment-related deaths with SG were due to infections; 5 infections were secondary to neutropenia. None of the 5 patients, who had risk factors for febrile neutropenia, received prophylaxis with G-CSF

Rates of grade ≥ 3 TEAEs and treatment-emergent SAEs were similar for both groups.
TEAEs leading to dose reduction or treatment discontinuation were lower with SG vs chemo

Data cutoff date: April 2, 2025. TEAEs were defined as any AEs that began or worsened on or after the first dose date of study drug up to 30 days after the last dose date of study drug or the initiation of subsequent anticancer therapy (including crossover treatment), whichever occurs first.
AE, adverse event; **chemo**, chemotherapy; **G-CSF**, granulocyte-colony stimulation factor; **SAE**, serious adverse event; **SG**, sacituzumab govitecan; **TEAE**, treatment-emergent adverse event.

Safety Summary: Most Common Adverse Events



The AEs observed are consistent with the known safety profile of SG

Data cutoff date: April 2, 2025. [a]TEAEs were included if they occurred in ≥ 20% of patients in either group. [b]Combined preferred terms of Neutropenia includes neutrophil count decreased, Fatigue includes asthenia, Anemia includes hemoglobin decreased and red blood cell count decreased, Leukopenia includes white blood cell count decreased, and Thrombocytopenia includes platelet count decreased.
AE, adverse event; **ALT**, alanine aminotransferase; **AST**, aspartate aminotransferase; **chemo**, chemotherapy; **SG**, sacituzumab govitecan; **TEAE**, treatment-emergent adverse event.

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Conclusions

- SG led to a statistically significant and clinically meaningful improvement in PFS vs chemo (median, 9.7 vs 6.9 months; HR, 0.62)
  - PFS benefit was observed across key prespecified subgroups

PFS by BICR

38% reduction in risk of progression or death

- ORR was similar between treatment groups; however, duration of response was longer with SG vs chemo
- OS was immature at the time of the analysis and PFS2 was improved with SG vs chemo

PFS2 per investigator

Median PFS2 was 4.2 months longer with SG vs chemo

- Safety of SG was consistent with its known profile; use of prophylactic G-CSF is advised as appropriate
- Rates of treatment discontinuations (4% vs 12%) were lower with SG vs chemo

Treatment Discontinuation

Lower rate of treatment discontinuation due to TEAEs with SG vs chemo

ASCENT-03 data support SG as a potential new standard of care for patients with previously untreated mTNBC who are not candidates for a PD-(L)1 inhibitor

Data cutoff date: April 2, 2025. **Chemo**, chemotherapy; **G-CSF**, granulocyte-colony stimulation factor; **HR**, hazard ratio; **mTNBC**; metastatic triple-negative breast cancer; **ORR**, objective response rate; **OS**, overall survival; **PD-1**, programmed cell death protein-1; **PD-L1**, programmed cell death ligand 1; **PD-(L)1**, PD-1 or PD-L1; **PFS**, progression-free survival; **SG**, sacituzumab govitecan; **TEAEs**, treatment-emergent adverse events.

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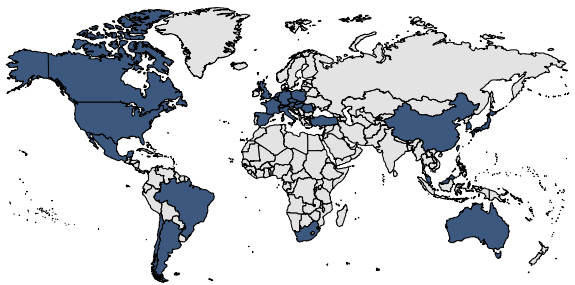
Acknowledgments



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ORIGINAL ARTICLE

Sacituzumab Govitecan in Untreated, Advanced Triple-Negative Breast Cancer

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