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

ASCENT-03

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The original oral slides and links to the plain language summary of this presentation and the published ASCENT-03 manuscript are available via this QR code.

Conclusions

- Sacituzumab govitecan (SG) led to a statistically significant and clinically meaningful improvement in progression-free survival (PFS) vs chemotherapy (chemo) (median, 9.7 vs 6.9 months; hazard ratio [HR], 0.62) with a 38% reduction in risk of progression or death
  - PFS benefit was observed across key prespecified subgroups
- Objective response rate (ORR) was similar between treatment groups; however, duration of response was longer with SG vs chemo
- Overall survival (OS) was immature at the time of the analysis and progression-free survival 2 (PFS2) was improved by 4.2 months with SG vs chemo
- Safety of SG was consistent with its known profile; use of prophylactic granulocyte-colony stimulation factor (G-CSF) is advised as appropriate
- Rates of treatment discontinuations due to treatment-emergent adverse events (TEAEs) (4% vs 12%) were lower with SG vs chemo
- **ASCENT-03 data support SG as a potential new standard of care for patients with previously untreated metastatic triple-negative breast cancer (mTNBC) who are not candidates for a programmed cell death (ligand) 1 (PD-[L]1) inhibitor**

Background

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

- ~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

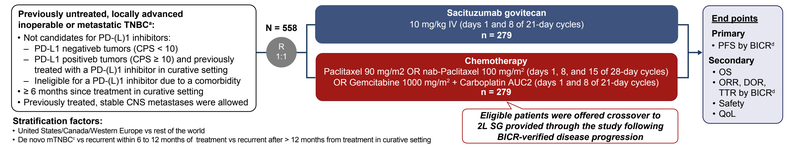
- SG is the only Trop-2–directed ADC with survival benefit in multiple phase 3 mBC studies[6-7]
- SG is approved for 2L+ mTNBC and pre-treated HR+/HER2– mBC globally[8,9]
- There is an urgent need for improved therapeutic options in earlier lines of therapy to delay progression and time to next line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

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.

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

Methods

Figure 1. ASCENT-03 Study Design

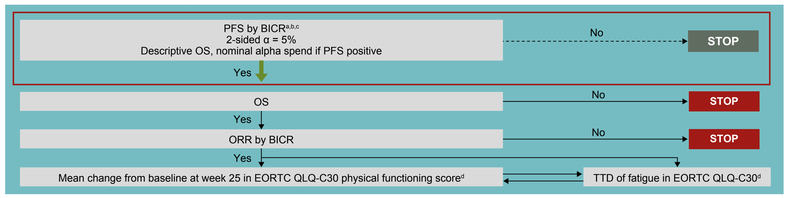


ClinicalTrials.gov identifier: NCT05382299. [a]TNBC status was centrally confirmed and determined according to standard American Society of Clinical Oncology-College of American Pathologists criteria. [b]PD-L1 CPS was centrally confirmed and defined using the PD-L1 IHC 22C3 assay (Dako, Agilent Technologies). [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.

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, PFS will be tested at 2-sided alpha of 5%
  - OS will be summarized descriptively at the time of primary PFS analysis; if 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 quality of life (QOL) end points will be performed
- At the time of the data cutoff date for primary PFS (April 2, 2025), there were 349 observed PFS events by blinded independent central review (BICR) and median follow-up was 13.2 months (range, < 0.1-29.2)
  - 75 patients (27%) in the SG group and 39 patients (14%) in the chemo group continued to receive study treatment

Figure 2. Hierarchical Testing Procedures: Intent-to-Treat Population



[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 end points 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; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30; HR, hazard ratio; ITT, intent to treat; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; TTD, time to deterioration.

Results

- The demographic and baseline characteristics are presented in **Table 1**

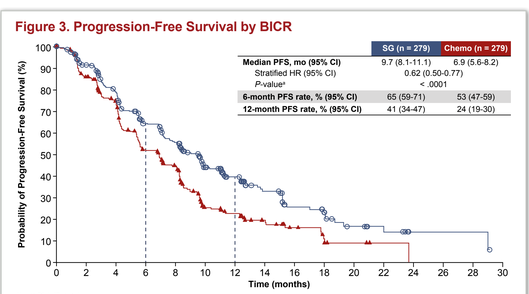
Table 1. Demographics and Baseline Characteristics

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 months	58 (21)	57 (20)
Recurrent > 12 months	134 (48)	134 (48)
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.

- 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 (**Figure 3**)

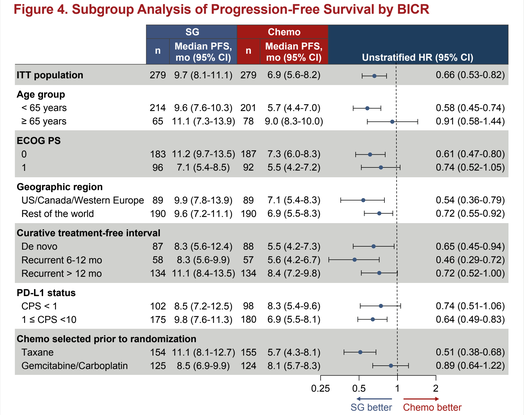
Figure 3. Progression-Free Survival by BICR



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.

- PFS by investigator assessment, a sensitivity analysis, was consistent with the BICR analysis, demonstrating PFS benefit with SG (9.6 months; 95% confidence interval [CI], 8.3-10.6 months) vs chemo (6.8 months; 95% CI, 5.6-7.2 months) with an HR of 0.64 (95% CI, 0.52-0.79)
- PFS benefit of SG over chemo was observed across key prespecified subgroups (**Figure 4**)

Figure 4. Subgroup Analysis of Progression-Free Survival by BICR



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; mo, months; PD-L1, programmed cell death ligand 1; PFS, progression-free survival; SG, sacituzumab govitecan; US, United States.

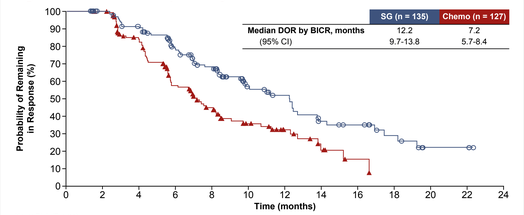
- ORRs were similar in both treatment groups (**Table 2**); however, duration of response was substantially longer with SG vs chemo (**Figure 5**)

Table 2. Tumor Response by BICR

Variable	SG (n = 279)	Chemo (n = 279)
ORR by BICR (95% CI),[a] %	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)

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.
BICR, blinded independent central review; chemo, chemotherapy; SG, sacituzumab govitecan.

Figure 5. Duration of Response by BICR



Data cutoff date: April 2, 2025.
BICR, blinded independent central review; chemo, chemotherapy; DOR, duration of response; SG, sacituzumab govitecan.

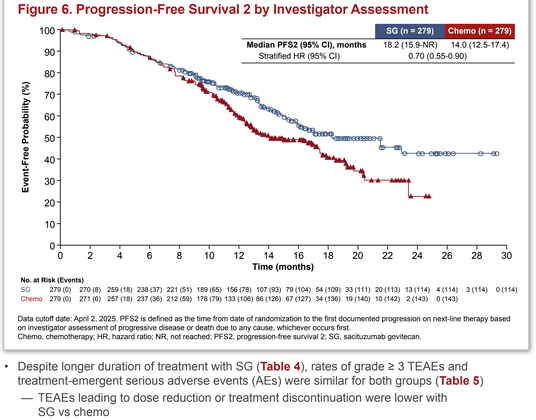
- At the time of primary analysis, OS was immature (37%; **Table 3**) and the study continues to first formal OS analysis
- Of 179 patients who initiated subsequent treatment after chemo, 147 (82%) received SG
- PFS2 was longer with SG vs chemo by investigator assessment (**Figure 6**)

Table 3. Descriptive Overall Survival

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)

Data cutoff date: April 2, 2025.
Chemo, chemotherapy; HR, hazard ratio; NR, not reached; SG, sacituzumab govitecan.

Figure 6. Progression-Free Survival 2 by Investigator Assessment



Data cutoff date: April 2, 2025. 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.
Chemo, chemotherapy; HR, hazard ratio; NR, not reached; PFS2, progression-free survival 2; SG, sacituzumab govitecan.

- Despite longer duration of treatment with SG (**Table 4**), rates of grade ≥ 3 TEAEs and treatment-emergent serious adverse events (AEs) were similar for both groups (**Table 5**)
  - TEAEs leading to dose reduction or treatment discontinuation were lower with SG vs chemo
  - 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

Table 4. Exposure

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 (range), months	8.3 (< 0.1-28.7)	6.3 (< 0.1-24.2)	5.8 (< 0.1-23.1)

Data cutoff date: April 2, 2025.
Chemo, chemotherapy; SG, sacituzumab govitecan.

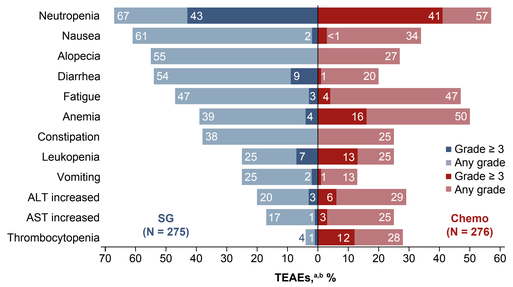
Table 5. Safety Summary

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)

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.
Chemo, chemotherapy; SAE, serious adverse event; SG, sacituzumab govitecan; TEAE, treatment-emergent adverse event.

- The AEs observed are consistent with the known safety profile of SG (**Figure 7**)

Figure 7. Safety Summary: Most Common Adverse Events



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.

References: **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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