ASCENT-03: Efficacy by Biomarker Subgroups With Sacituzumab Govitecan vs Chemotherapy in Participants With Previously Untreated Advanced Triple-Negative Breast Cancer Who Are Not Candidates for PD-(L)1 Inhibitors

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Key Takeaway Points: ASCENT-03 Biomarker Analysis

Median PFS was longer with SG vs chemo across all Trop-2 expression, tumor BRCA mutation, and HER2 expression subgroups, consistent with the primary analysis of ASCENT-03

These results were also consistent with those observed in prior biomarker analyses of the ASCENT study, in which SG provided longer PFS vs chemo across Trop-2, BRCA, and HER2 subgroups in 2L+ mTNBC

These results reinforce the significant, clinically meaningful benefit of SG as 1L treatment for advanced TNBC in patients who are not candidates for PD-(L)1 inhibitors across biomarker subgroups

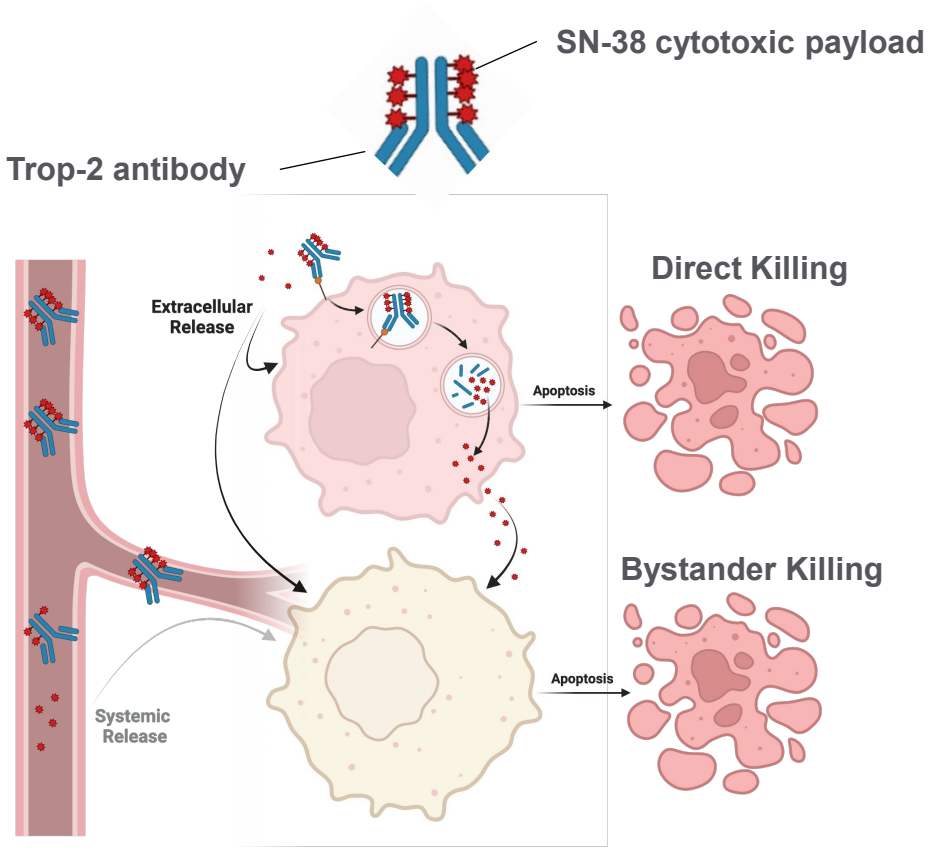
1L, first-line; **2L+**, second-line or later; **chemo**, chemotherapy; **HER2**, human epidermal growth factor receptor 2; **mTNBC**, metastatic triple-negative breast cancer; **PD-(L)1**, programmed death (ligand) 1; **PFS**, progression-free survival; **SG**, sacituzumab govitecan.

Introduction

- In ASCENT-03, SG demonstrated significant and clinically meaningful improvement in PFS vs chemo (HR, 0.62; 95% CI, 0.50-0.77; *P* < .001) in participants with previously untreated advanced TNBC who were not candidates for a PD-(L)1 inhibitor[1]

- SG is a Trop-2-directed ADC, and Trop-2 overexpression is common in breast cancer[2-4]

- Mutations in the *BRCA1* and *BRCA2* genes and HER2 expression may affect responsiveness to specific treatments used in mBC,[5-9] and therefore these biomarkers may affect treatment selection



Prespecified retrospective exploratory analyses compared efficacy of SG vs chemo in ASCENT-03 by biomarker subgroups of Trop-2 expression, BRCA status, and HER2 expression

ADC, antibody-drug conjugate; **chemo**, chemotherapy; **HER2**, human epidermal growth factor receptor 2; **HR**, hazard ratio; **mBC**, metastatic breast cancer; **PD-(L)1**, programmed death (ligand) 1; **PFS**, progression-free survival; **SG**, sacituzumab govitecan; **TNBC**, triple-negative breast cancer.
1. Cortés J, et al. *N Engl J Med*. 2025;393:1912-25. 2. Goldenberg DM, et al. *Oncotarget*. 2015;6:22496-512 3. Jacot W, et al. *Cancer Med*. 2025;14:e70615. 4. Zhao W, et al. *Oncol Rep*. 2018;40:759-766. 5. Godet I, et al. *Integr Cancer Sci Ther*. 2017;4:10.15761/ICST.1000228. 6. Stoppa-Lyonnet D. *Eur J Hum Genet*. 2016;24:S3-S9. 7. Bardia A, et al. *Ann Oncol*. 2021;32:1148-1156. 8. McCann KE, et al. *Drugs Context*. 2018;7:212540. 9. Chen W, et al. *Cancer Discov*. 2026;16:235-249.

Methods

- Participants were randomized 1:1 to receive SG or chemo; the primary end point was PFS by BICR
- Participant tumors could be:
  - PD-L1− (CPS[a] < 10)
  - PD-L1+ (CPS[a] ≥ 10) but not candidates for PD-(L)1 inhibitors
- All biomarkers measured from fresh or archival (formalin-fixed paraffin-embedded) tumor samples; 41% from metastatic sites in the Trop-2 biomarker analysis set
- Exploratory, prespecified analysis of biomarker status by central testing was conducted to determine association with PFS by BICR
- The biomarker analysis set for each biomarker included all participants in the ITT population who had ≥ 1 evaluable biomarker measurement available at baseline
- At the primary data cutoff (April 2025), OS data were not mature (37% maturity); median follow-up was 13.2 months (range, < 0.1-29.2)[1]

Subgroups Analyzed

Trop-2 Expression

- Characterized by H-score, as determined by IHC[b]
- Participants grouped by Trop-2 expression quartile

tBRCA Status

- Local testing was not common, so measured by WES
- Participants grouped by tBRCA WT or mut status
- Mut indicates mutation in *BRCA1*, *BRCA2*, or both genes

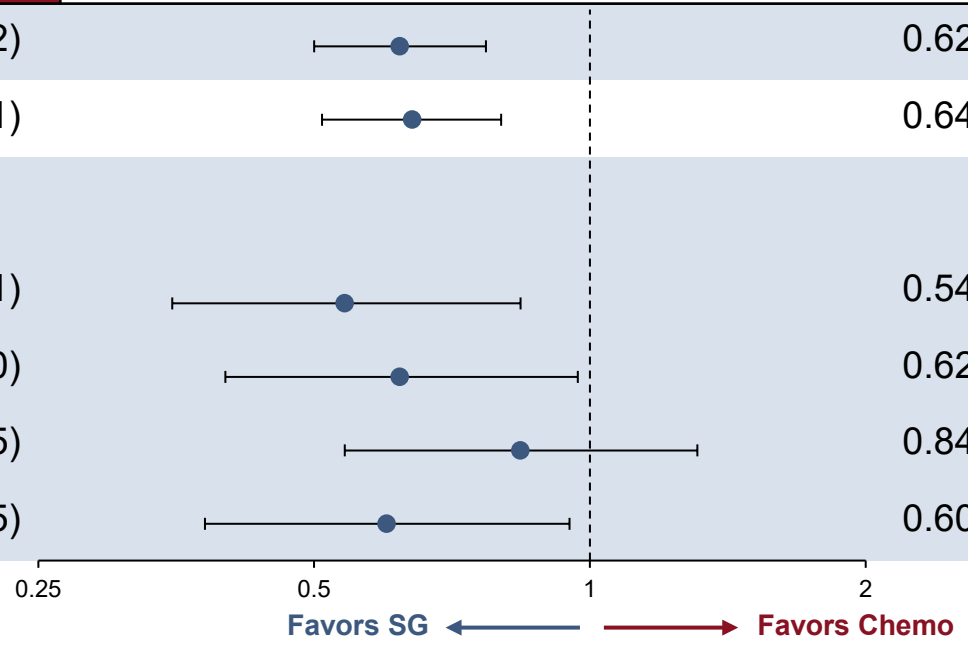
HER2 Expression

- Measured by ISH and IHC
- Participants grouped as HER2 IHC 0 or HER2 low
- HER2 low includes IHC 1+ or IHC 2+/ISH−

[a]As per 22C3 assay. [b]Scoring as follows: 0, negative or no staining of tumor cell; 1, weak or faint staining; 2, moderate staining; 3, strong staining. H-score determined by (% of 1+ tumor cells) + (2x% of 2+ tumor cells) + (3x% of 3+ tumor cells).
BICR, blinded independent central review; **chemo**, chemotherapy; **CPS**, combined positive score; **HER2**, human epidermal growth factor receptor 2; **IHC**, immunohistochemistry; **ISH**, in situ hybridization; **ITT**, intent-to-treat; **mPFS**, median progression-free survival; **mut**, mutant; **OS**, overall survival; **PD-(L)1**, programmed death (ligand) 1; **PFS**, progression-free survival; **SG**, sacituzumab govitecan; **tBRCA**, tumor BRCA; **WES**, whole exome sequencing; **WT**, wild-type.
1. Cortés J, et al. *N Engl J Med.* 2025;393:1912-25.

PFS by Trop-2 H-Score Quartiles[a]

Subgroup	SG		Chemo		HR (95% CI)
	n	mPFS, mo	n	mPFS, mo	
ITT Population[1,b]	279	9.7 (8.1-11.1)	279	6.9 (5.6-8.2)	0.62 (0.50-0.77)
Trop-2 BAS[c]	252	9.7 (7.8-11.1)	247	6.8 (5.4-8.1)	0.64 (0.51-0.80)
Trop-2 H-score quartiles[c]					
Q1	68	8.5 (5.6-12.7)	55	5.5 (4.2-8.1)	0.54 (0.35-0.84)
Q2	60	8.3 (5.6-12.4)	62	6.8 (4.2-9.0)	0.62 (0.40-0.97)
Q3	50	9.7 (7.6-11.3)	74	7.0 (5.3-8.5)	0.84 (0.54-1.31)
Q4	74	9.9 (6.9-NE)	56	8.1 (4.4-8.5)	0.60 (0.38-0.95)

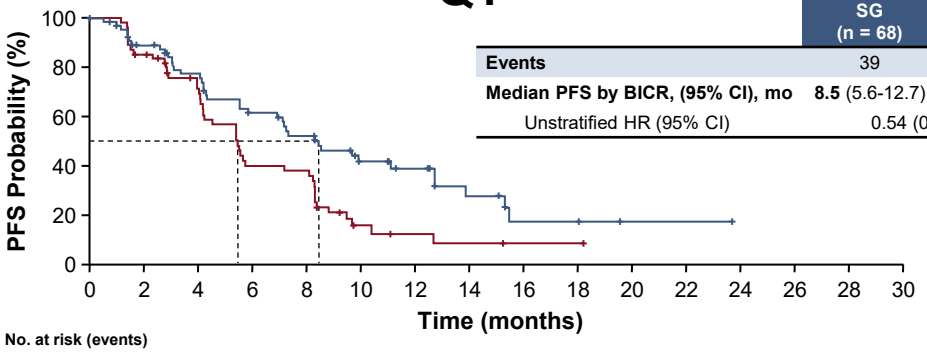


PFS was longer with SG vs chemo across all Trop-2 H-score quartile subgroups, with no clear trend of increased efficacy at higher levels of Trop-2 expression

[a]Trop-2 H-score quartiles: Q1, 0-184; Q2, 185-239; Q3, 240-283; Q4, 284-300. [b]HR value is stratified. [c]HR values are unstratified.
BAS, biomarker analysis set; **chemo**, chemotherapy; **HR**, hazard ratio; **ITT**, intent-to-treat; **mo**, months; **mPFS**, median progression-free survival; **NE**, not estimable; **PFS**, progression-free survival; **Q**, quartile; **SG**, sacituzumab govitecan.
1. Cortés J, et al. *N Engl J Med.* 2025;393:1912-25.

PFS by Trop-2 H-Score Quartiles[a]

Q1



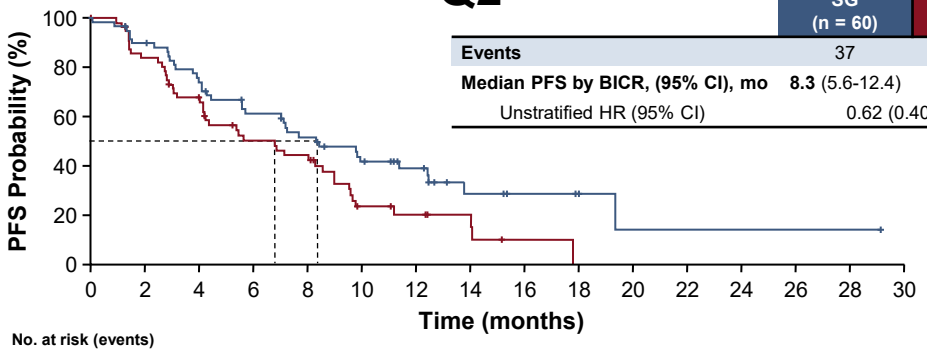
	SG (n = 68)	Chemo (n = 55)
Events	39	43
Median PFS by BICR, (95% CI), mo	**8.5** (5.6-12.7)	**5.5** (4.2-8.1)
Unstratified HR (95% CI)	0.54 (0.35-0.84)	

No. at risk (events)

SG 68 (0) 55 (7) 45 (14) 34 (23) 28 (28) 17 (33) 13 (34) 7 (37) 3 (39) 3 (39) 1 (39) 1 (39) 0 (39)

Chemo 55 (0) 46 (8) 34 (15) 19 (30) 18 (31) 5 (41) 3 (42) 2 (43) 1 (43) 1 (43) 0 (43)

Q2



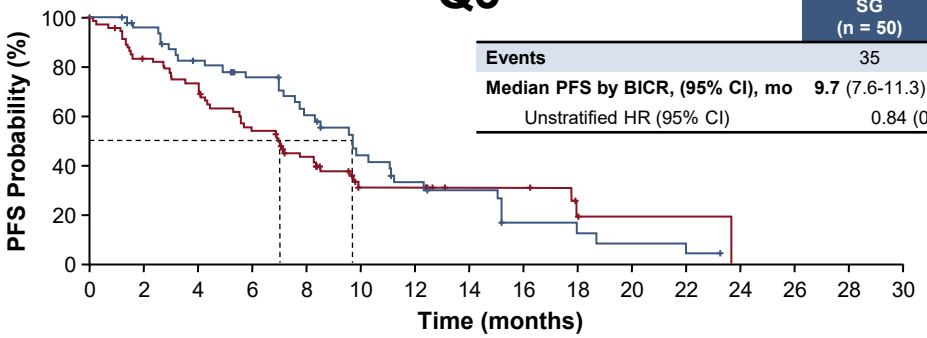
	SG (n = 60)	Chemo (n = 62)
Events	37	43
Median PFS by BICR, (95% CI), mo	**8.3** (5.6-12.4)	**6.8** (4.2-9.0)
Unstratified HR (95% CI)	0.62 (0.40-0.97)	

No. at risk (events)

SG 60 (0) 52 (6) 42 (15) 33 (22) 27 (27) 20 (32) 15 (33) 6 (36) 4 (36) 3 (36) 1 (37) 1 (37) 1 (37) 1 (37) 1 (37) 0 (37)

Chemo 62 (0) 47 (9) 37 (18) 25 (27) 22 (30) 9 (39) 6 (40) 4 (40) 1 (42) 0 (43)

Q3



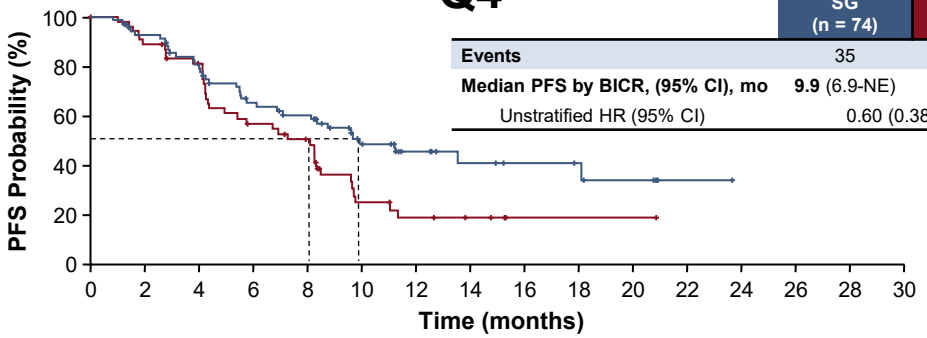
	SG (n = 50)	Chemo (n = 74)
Events	35	48
Median PFS by BICR, (95% CI), mo	**9.7** (7.6-11.3)	**7.0** (5.3-8.5)
Unstratified HR (95% CI)	0.84 (0.54-1.31)	

No. at risk (events)

SG 50 (0) 44 (2) 36 (8) 31 (11) 24 (17) 16 (23) 11 (27) 9 (28) 4 (32) 4 (32) 2 (34) 2 (34) 0 (35)

Chemo 74 (0) 58 (12) 51 (19) 38 (31) 25 (39) 12 (45) 12 (45) 7 (45) 7 (45) 3 (47) 1 (47) 1 (47) 0 (48)

Q4



	SG (n = 74)	Chemo (n = 56)
Events	35	37
Median PFS by BICR, (95% CI), mo	**9.9** (6.9-NE)	**8.1** (4.4-8.5)
Unstratified HR (95% CI)	0.60 (0.38-0.95)	

No. at risk (events)

SG 74 (0) 64 (5) 54 (13) 41 (23) 36 (26) 21 (32) 13 (33) 9 (34) 7 (34) 6 (34) 4 (35) 1 (35) 0 (35)

Chemo 56 (0) 48 (6) 40 (10) 27 (22) 22 (25) 9 (35) 6 (37) 4 (37) 1 (37) 1 (37) 1 (37) 0 (37)

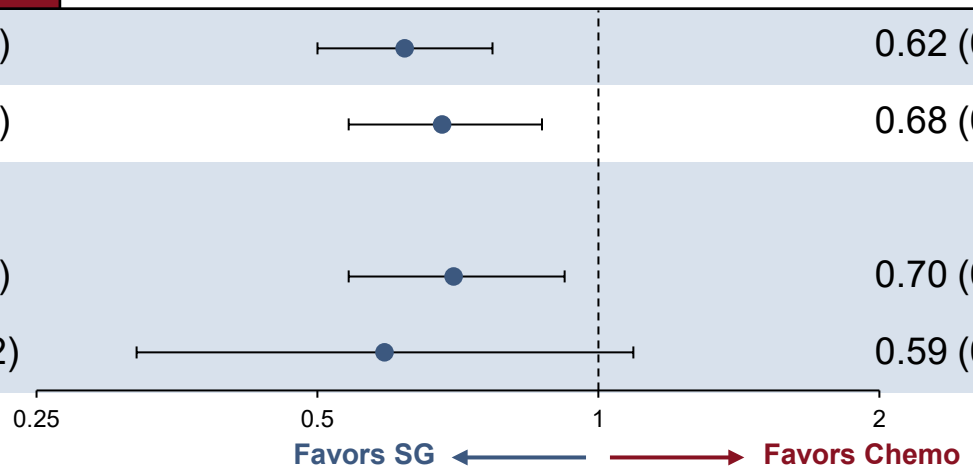
PFS curves separated early in all Trop-2 quartiles

[a]Trop-2 H-score quartiles: Q1, 0-184; Q2, 185-239; Q3, 240-283; Q4, 284-300.

BICR, blinded independent central review; **chemo**, chemotherapy; **HR**, hazard ratio; **mo**, months; **NE**, not estimable; **PFS**, progression-free survival; **Q**, quartile; **SG**, sacituzumab govitecan.

PFS by tBRCA Subgroups

Subgroup	SG		Chemo		HR (95% CI)
	n	mPFS, mo	n	mPFS, mo	
ITT Population[1,a]	279	9.7 (8.1-11.1)	279	6.9 (5.6-8.2)	0.62 (0.50-0.77)
tBRCA BAS[b]	217	9.6 (8.0-11.1)	206	7.2 (5.6-8.3)	0.68 (0.54-0.87)
tBRCA subgroup[b]					
WT	177	8.8 (7.2-9.9)	169	6.9 (5.4-8.3)	0.70 (0.54-0.92)
Mut	40	12.7 (7.2-18.7)	37	8.3 (5.6-11.2)	0.59 (0.32-1.09)

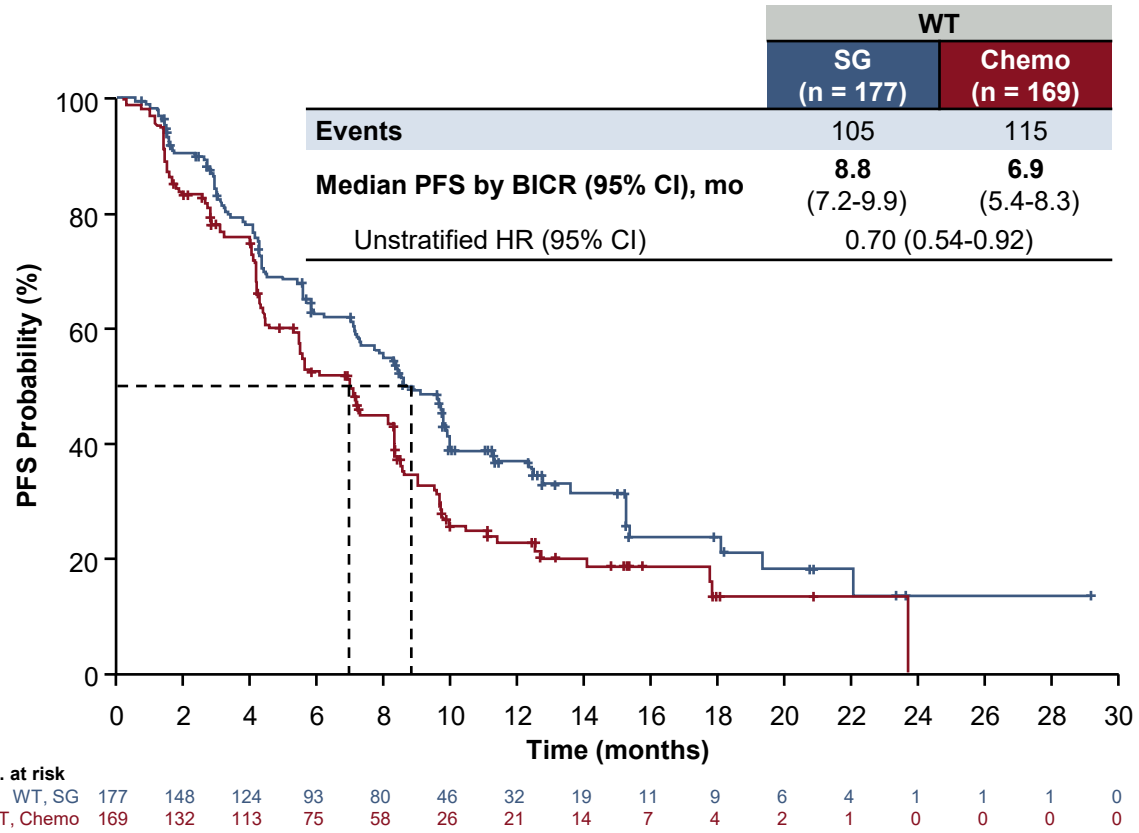


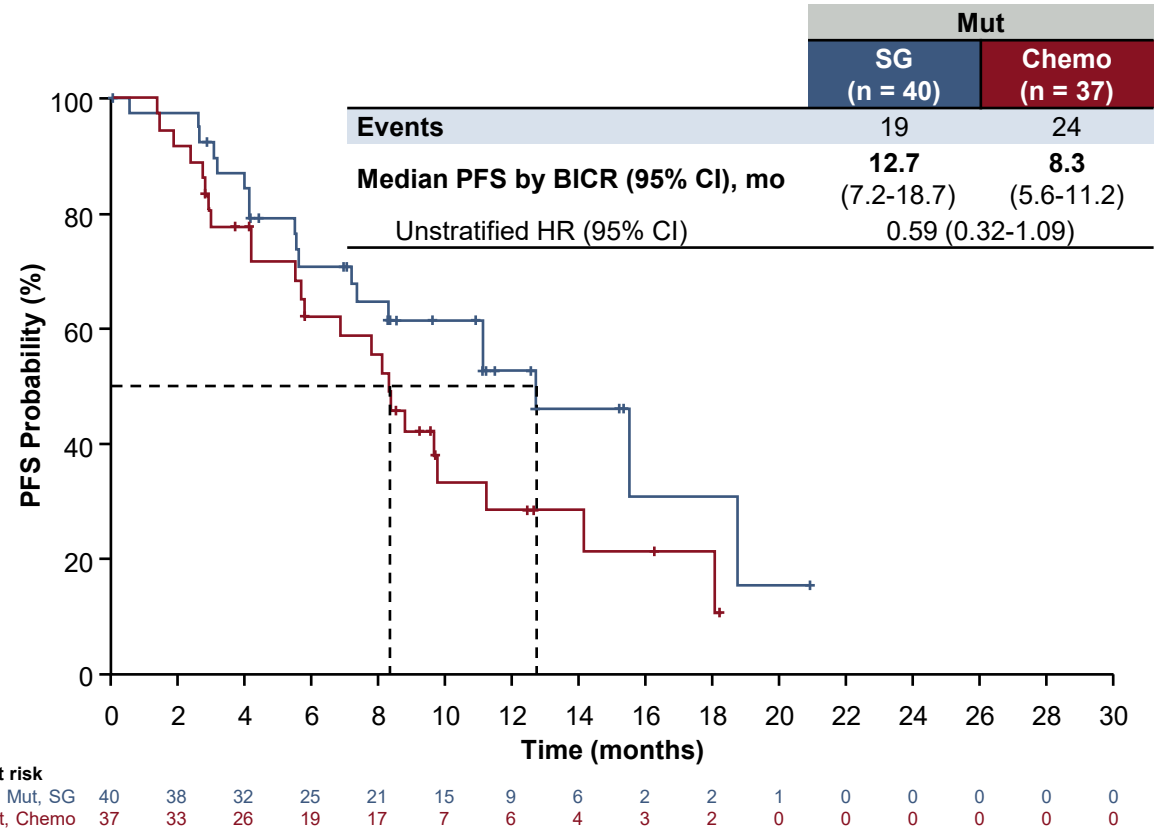
- 18% of participants treated with SG and 18% treated with chemo had tBRCA mut status in the biomarker analysis set

Median PFS was longer with SG vs chemo in both the tBRCA WT and mut subgroups, with numerically longer PFS in the mut subgroup vs the WT subgroup

[a]HR value is stratified. [b]HR values are unstratified.
BAS, biomarker analysis set; **chemo**, chemotherapy; **HR**, hazard ratio; **ITT**, intent-to-treat; **mo**, months; **mut**, mutant; **PFS**, progression-free survival; **SG**, sacituzumab govitecan; **tBRCA**, tumor BRCA; **WT**, wild-type.
1. Cortés J, et al. *N Engl J Med.* 2025;393:1912-25.

PFS by tBRCA Subgroups



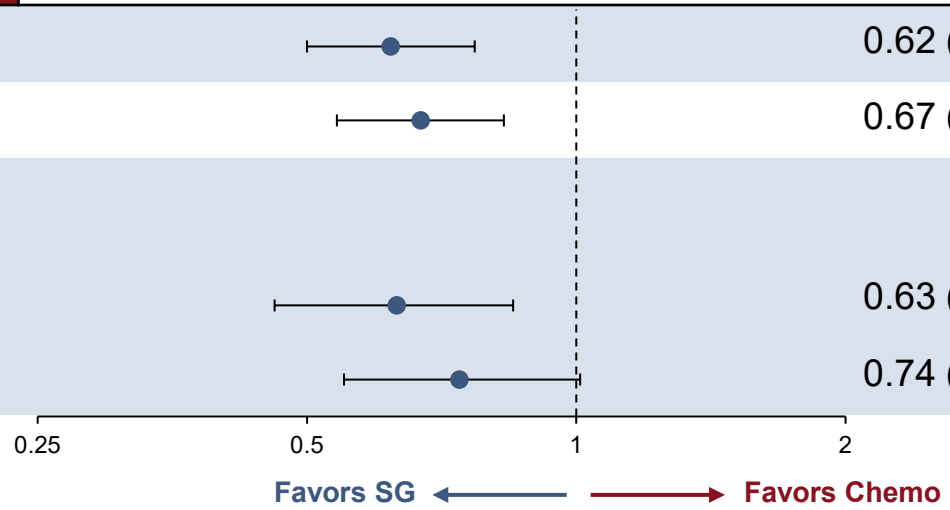


The SG and chemotherapy PFS curves separated early within the tBRCA WT and tBRCA mut subgroups and show PFS improvement with SG vs chemo regardless of tBRCA status

BICR, blinded independent central review; **chemo**, chemotherapy; **HR**, hazard ratio; **mo**, months; **mPFS**, median progression-free survival; **mut**, mutant; **PFS**, progression-free survival; **SG**, sacituzumab govitecan; **tBRCA**, tumor BRCA; **WT**, wild-type.

PFS by HER2 Subgroups

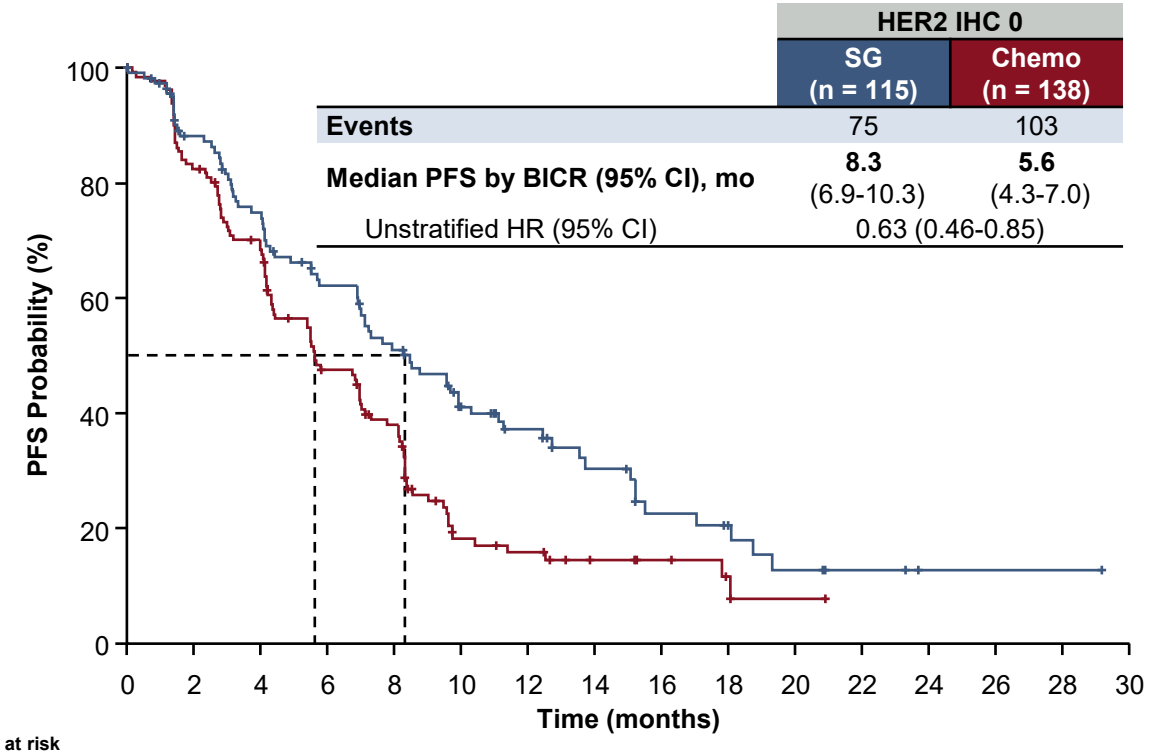
Subgroup	SG		Chemo		HR (95% CI)
	n	mPFS, mo	n	mPFS, mo	
ITT Population[1,a]	279	9.7 (8.1-11.1)	279	6.9 (5.6-8.2)	0.62 (0.50-0.77)
HER2 BAS[b]	274	9.7 (8.0-11.1)	277	6.9 (5.6-8.2)	0.67 (0.54-0.83)
HER2 2-subgroup analysis[b]					
HER2 IHC 0	115	8.3 (6.9-10.3)	138	5.6 (4.3-7.0)	0.63 (0.46-0.85)
HER2 low	159	9.8 (8.3-12.4)	139	8.3 (5.7-9.7)	0.74 (0.55-1.01)

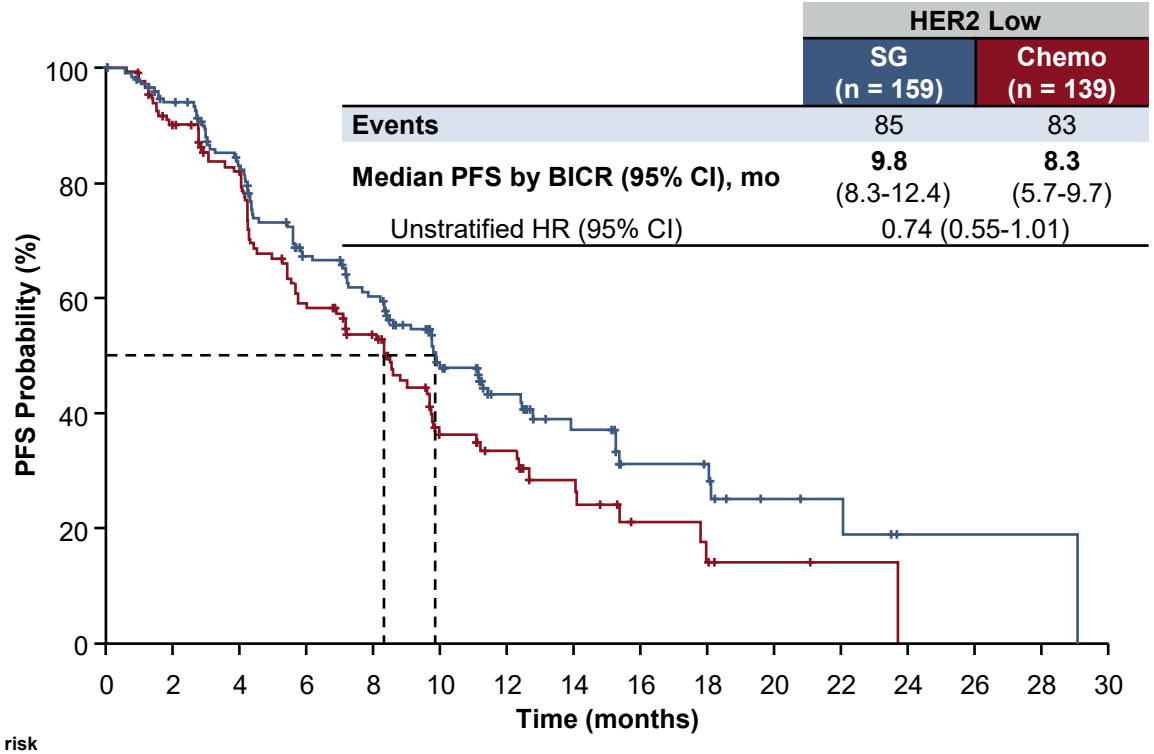


PFS was longer with SG vs chemo across the HER2 IHC 0 and HER2 low subgroups

[a]HR value is stratified. [b]HR values are unstratified.
BAS, biomarker analysis set; **chemo**, chemotherapy; **HER2**, human epidermal growth factor receptor 2; **HR**, hazard ratio; **IHC**, immunohistochemistry; **ITT**, intent-to-treat; **mo**, months; **mPFS**, median progression-free survival; **PFS**, progression-free survival; **SG**, sacituzumab govitecan.
1. Cortés J, et al. *N Engl J Med.* 2025;393:1912-25.

PFS by HER2 Subgroups





PFS curves separated early and remained separated during the study period, showing PFS benefit with SG over chemo across HER2 subgroups

BAS, biomarker analysis set; **BICR**, blinded independent central review; **chemo**, chemotherapy; **HR**, hazard ratio; **mo**, months; **mPFS**, median progression-free survival; **mut**, mutant; **PFS**, progression-free survival; **SG**, sacituzumab govitecan; **tBRCA**, tumor BRCA; **WT**, wild-type.

Conclusions

- Median PFS was longer with SG vs chemo across all biomarker subgroups, consistent with results from the primary analysis of ASCENT-03,[1] including:
  - Across all Trop-2 expression quartiles
  - Both the tBRCA WT and mut subgroups
  - Both the tumor HER2 IHC 0 and HER2 low subgroups
- Due to small sample sizes in some subgroups and the descriptive nature of this analysis, caution is needed when interpreting these results
- These results are consistent with those observed in the ASCENT study, in which SG provided longer PFS compared to chemotherapy across Trop-2, BRCA, and HER2 categories in participants with metastatic TNBC[2,3]

SG demonstrated efficacy vs chemo across Trop-2 expression, tBRCA genotypes, and HER2 expression subgroups, reinforcing the significant, clinically meaningful benefit of SG in first-line treatment for patients with previously untreated advanced TNBC who are not candidates for PD-(L)1 inhibitors

Chemo, chemotherapy; **HER2**, human epidermal growth factor receptor 2; **IHC**, immunohistochemistry; **mut**, mutant; **PD-(L)1**, programmed death (ligand) 1; **PFS**, progression-free survival; **SG**, sacituzumab govitecan; **tBRCA**, tumor BRCA; **TNBC**, triple-negative breast cancer; **WT**, wild-type.

1. Cortés J, et al. *N Engl J Med*. 2025;393:1912-25. 2. Bardia A, et al. *J Clin Oncol*. 2024;42:1738-44. 3. Bardia A, et al. *Ann Oncol*. 2021;32:1148-56.

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