ASCENT-04: Analysis of Efficacy by Biomarker Subgroups With Sacituzumab Govitecan + Pembrolizumab vs Chemotherapy + Pembrolizumab in Participants With Previously Untreated PD-L1+ Metastatic Triple-Negative Breast Cancer

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Key Takeaway Points: ASCENT-04 Biomarker Analysis

Median PFS was longer with SG + pembro vs chemo + pembro across all Trop-2 expression, tumor BRCA mutation, and HER2 expression subgroups, consistent with the primary analysis of ASCENT-04

These results were also consistent with prior results from the ASCENT study, which showed consistent PFS benefit with SG vs chemo across Trop-2, BRCA, and HER2 subgroups as treatment for 2L+ mTNBC

These results reinforce the significant, clinically meaningful benefit of SG + pembro as 1L treatment for patients with advanced PD-L1–positive TNBC across biomarker subgroups

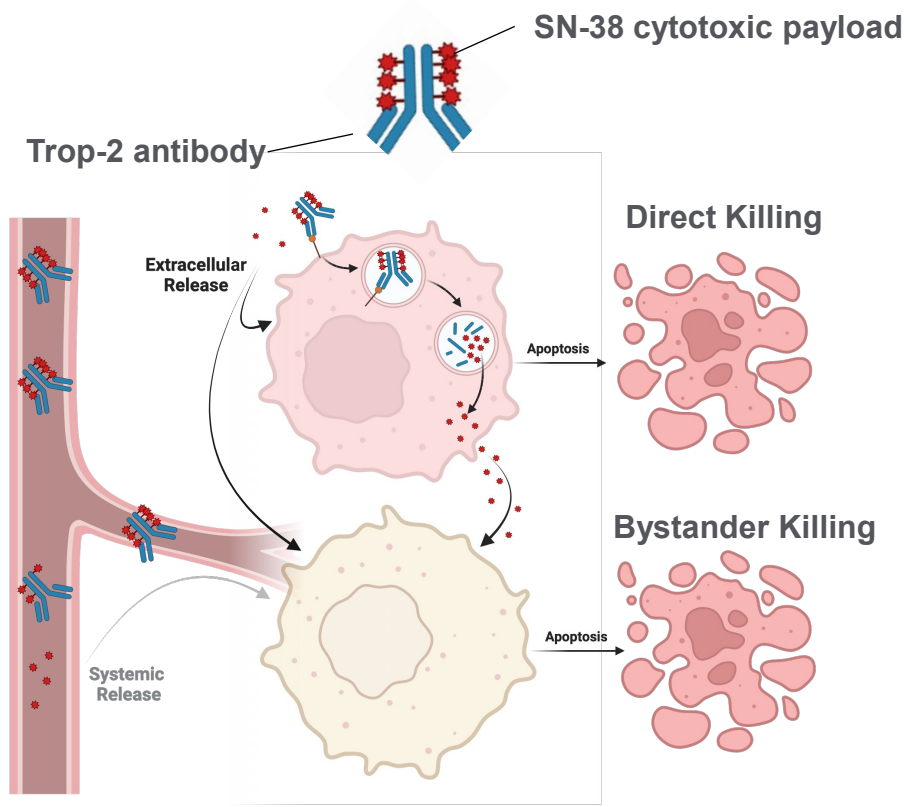
1L, first-line; **2L+**, second-line or later; **chemo**, chemotherapy; **HER2**, human epidermal growth factor receptor 2; **mTNBC**, metastatic triple-negative breast cancer; **PD-L1**, programmed death ligand 1; **pembro**, pembrolizumab; **PFS**, progression-free survival; **SG**, sacituzumab govitecan.

Introduction

- The ASCENT-04 study demonstrated significant, clinically meaningful improvement in PFS with SG + pembro vs chemo + pembro (HR, 0.65; 95% CI, 0.51-0.84; *P* < .001) in participants with previously untreated PD-L1–positive advanced TNBC[1]

- SG targets Trop-2, a surface protein overexpressed in many solid tumors, particularly in TNBC[2-4]

- Mutations in *BRCA1* and *BRCA2* and HER2 amplification or overexpression are associated with altered efficacy of some mBC treatments, although the role of these biomarkers is less established in PD-L1–positive TNBC[5-9]



Prespecified retrospective exploratory analyses evaluated the impact of Trop-2, BRCA, and HER2 biomarkers on efficacy of SG + pembro vs chemo + pembro in ASCENT-04

Chemo, chemotherapy; **HER2**, human epidermal growth factor receptor 2; **HR**, hazard ratio; **mBC,** metastatic breast cancer; **PD-L1**, programmed cell death ligand 1; **pembro**, pembrolizumab; **PFS**, progression-free survival; **SG**, sacituzumab govitecan; **TNBC**, triple-negative breast cancer.

1. Tolaney SM, et al. *N Engl J Med*. 2026;394:354-66. 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;40:759-66. 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;32:1148-56. 8. McCann KE, et al. *Drugs Context*. 2018;7:212540. 9. Chen W, et al. *Cancer Discov*. 2026;16:235-49.

Methods

- Participants with previously untreated, locally advanced unresectable or metastatic PD-L1–positive (PD-L1 CPS[a] ≥ 10) TNBC were randomized 1:1 to receive SG + pembro or chemo + pembro; the primary end point was PFS by BICR
- This prespecified exploratory analysis was performed using central testing of fresh or archival (formalin-fixed paraffin-embedded) tumor samples; 48% from metastatic sites in the Trop-2 biomarker analysis set
- Biomarker status was analyzed descriptively for association with PFS by BICR
- At the primary data cutoff (March 2025), median follow-up was 14.0 months (range, 0.1-28.6)[1]
- Participants from the ITT population were included in the biomarker analysis set if they had ≥ 1 evaluable biomarker measurement available at baseline

Subgroups Analyzed

Trop-2 Expression

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

tBRCA Status

- Measured by WES as local testing was uncommon
- Participants grouped by t*BRCA* WT or mut status
- Mut indicates mutation in *BRCA1*, *BRCA2*, or both genes

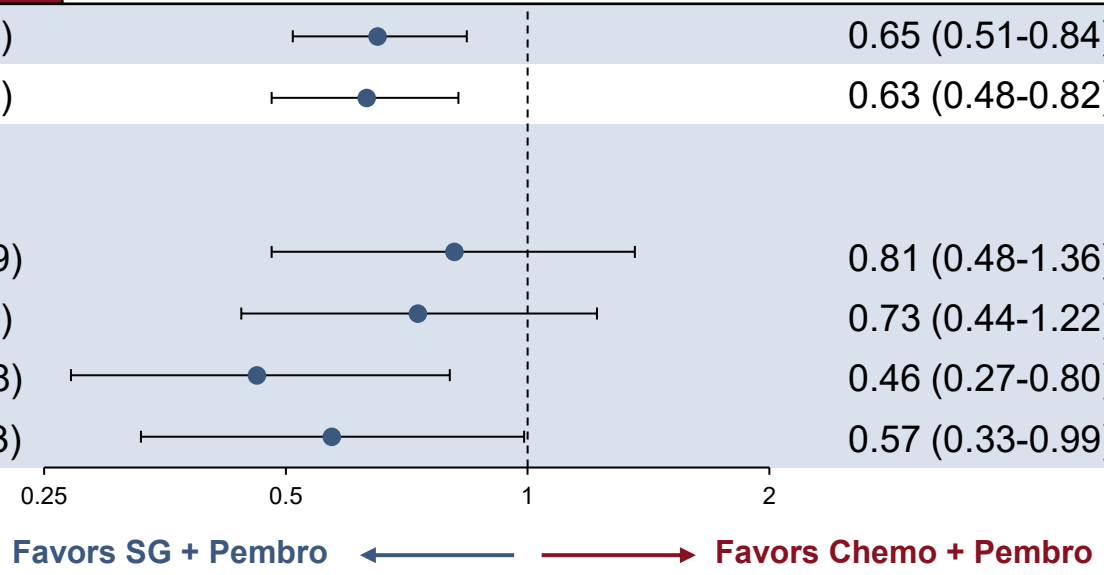
HER2 Expression

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

[a]Measured per the 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; **ITT**, intent-to-treat; **mut**, mutation; **PD-L1**, programmed cell death ligand 1; **pembro**, pembrolizumab; **PFS**, progression-free survival; **SG**, sacituzumab govitecan; **TNBC**, triple-negative breast cancer; **WT**, wild-type.
1. Tolaney SM, et al. *N Engl J Med.* 2026;394:354-66.

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

Subgroup	SG + Pembro		Chemo + Pembro		HR (95% CI)
	n	mPFS, mo	n	mPFS, mo	
ITT Population[1,b]	221	11.2 (9.3-16.7)	222	7.8 (7.3-9.3)	0.65 (0.51-0.84)
Trop-2 BAS[c]	204	11.7 (9.3-16.8)	196	7.8 (7.3-9.3)	0.63 (0.48-0.82)
Trop-2 H-score Quartiles[c]					
Q1	48	9.3 (7.4-19.4)	47	9.0 (6.0-10.9)	0.81 (0.48-1.36)
Q2	50	9.6 (7.3-16.7)	50	7.4 (6.9-9.7)	0.73 (0.44-1.22)
Q3	55	13.5 (9.3-NE)	50	8.4 (5.6-10.8)	0.46 (0.27-0.80)
Q4	51	16.6 (8.1-NE)	49	9.2 (5.5-11.3)	0.57 (0.33-0.99)

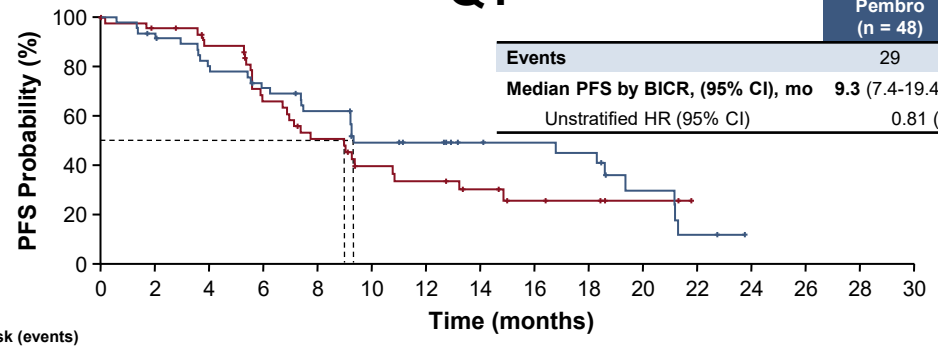


PFS was longer with SG + pembro vs chemo + pembro across all Trop-2 subgroups

[a]Trop-2 H-score quartiles: Q1, 0-224; Q2, 225-279; Q3, 280-298; Q4, 299-300. [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**, metastatic progression-free survival; **NE**, not estimable; **pembro**, pembrolizumab; **PFS**, progression-free survival; **Q**, quartile; **SG**, sacituzumab govitecan.
1. Tolaney SM, et al. *N Engl J Med.* 2026;394:354-66.

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

Q1

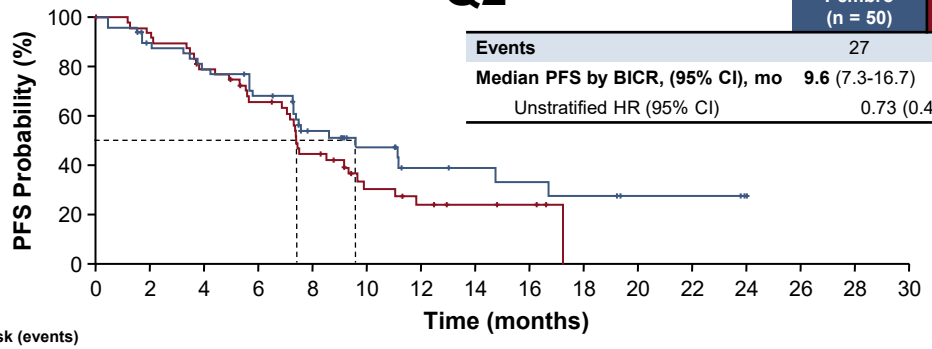


	SG + Pembro (n = 48)	Chemo + Pembro (n = 47)
Events	29	28
Median PFS by BICR, (95% CI), mo	**9.3** (7.4-19.4)	**9.0** (6.0-10.9)
Unstratified HR (95% CI)	0.81 (0.48-1.36)	

No. at risk (events)

SG + pembro	48 (0)	43 (3)	36 (9)	31 (13)	26 (17)	19 (22)	17 (22)	13 (22)	12 (22)	11 (23)	5 (26)	2 (29)	0 (29)
Chemo + pembro	47 (0)	42 (2)	37 (5)	26 (14)	19 (20)	13 (24)	11 (26)	8 (27)	5 (28)	4 (28)	2 (28)	0 (28)	

Q2

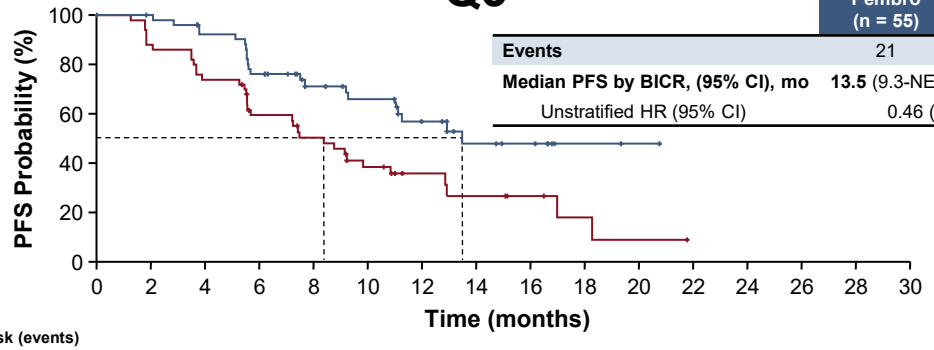


	SG + Pembro (n = 50)	Chemo + Pembro (n = 50)
Events	27	33
Median PFS by BICR, (95% CI), mo	**9.6** (7.3-16.7)	**7.4** (6.9-9.7)
Unstratified HR (95% CI)	0.73 (0.44-1.22)	

No. at risk (events)

SG + pembro	50 (0)	42 (5)	37 (10)	31 (15)	20 (21)	13 (23)	8 (25)	7 (25)	6 (26)	5 (27)	3 (27)	3 (27)	1 (27)	0 (27)
Chemo + pembro	50 (0)	45 (3)	37 (10)	29 (16)	19 (25)	10 (30)	7 (32)	5 (32)	4 (32)	0 (33)				

Q3

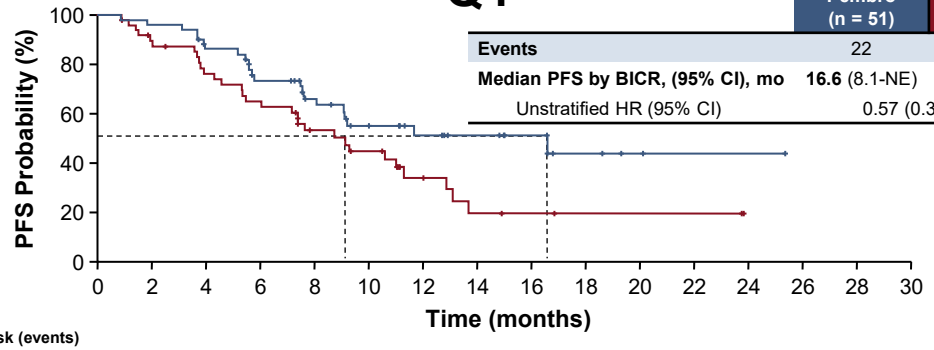


	SG + Pembro (n = 55)	Chemo + Pembro (n = 50)
Events	21	34
Median PFS by BICR, (95% CI), mo	**13.5** (9.3-NE)	**8.4** (5.6-10.8)
Unstratified HR (95% CI)	0.46 (0.27-0.80)	

No. at risk (events)

SG + pembro	55 (0)	52 (0)	46 (4)	38 (12)	28 (14)	24 (16)	17 (19)	10 (21)	7 (21)	2 (21)	1 (21)	0 (21)	
Chemo + pembro	50 (0)	44 (6)	37 (13)	27 (20)	22 (24)	15 (29)	8 (30)	6 (32)	4 (32)	2 (33)	1 (34)	0 (34)	

Q4



	SG + Pembro (n = 51)	Chemo + Pembro (n = 49)
Events	22	30
Median PFS by BICR, (95% CI), mo	**16.6** (8.1-NE)	**9.2** (5.5-11.3)
Unstratified HR (95% CI)	0.57 (0.33-0.99)	

No. at risk (events)

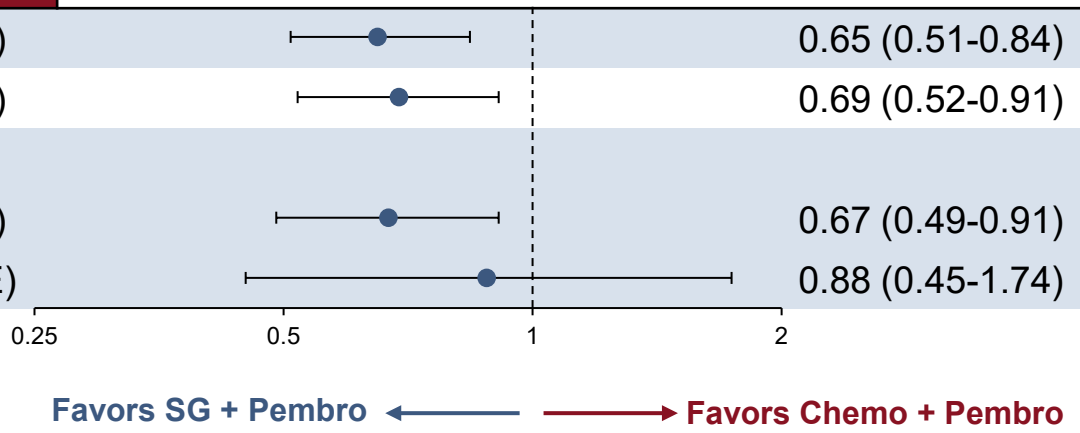
SG + pembro	51 (0)	49 (2)	42 (7)	33 (13)	25 (16)	18 (20)	13 (21)	10 (21)	8 (21)	4 (22)	2 (22)	1 (22)	1 (22)	0 (22)
Chemo + pembro	49 (0)	41 (5)	34 (11)	29 (16)	19 (21)	15 (24)	8 (27)	4 (30)	3 (30)	2 (30)	2 (30)	2 (30)	0 (30)	

SG + pembro treatment was associated with consistently improved PFS vs chemo + pembro across Trop-2 expression quartiles, with trends toward greater separation of KM curves in Q3 and Q4

[a]Trop-2 H-score quartiles: Q1, 0-224; Q2, 225-279; Q3, 280-298; Q4, 299-300.
BICR, blinded independent central review; **chemo**, chemotherapy; **HR**, hazard ratio; **KM**, Kaplan-Meier; **mo**, months; **NE**, not estimable; **pembro**, pembrolizumab; **PFS**, progression-free survival; **Q**, quartile; **SG**, sacituzumab govitecan.

PFS by tBRCA Subgroups

Subgroup	SG + Pembro		Chemo + Pembro		HR (95% CI)
	n	mPFS, mo	n	mPFS, mo	
ITT Population[1,a]	221	11.2 (9.3-16.7)	222	7.8 (7.3-9.3)	0.65 (0.51-0.84)
tBRCA BAS[b]	169	11.1 (9.2-16.7)	163	7.8 (7.2-9.3)	0.69 (0.52-0.91)
tBRCA subgroup[b]					
WT	130	9.6 (7.6-16.7)	131	7.4 (6.9-9.2)	0.67 (0.49-0.91)
Mut	39	16.6 (7.5-NE)	32	12.9 (7.1-NE)	0.88 (0.45-1.74)



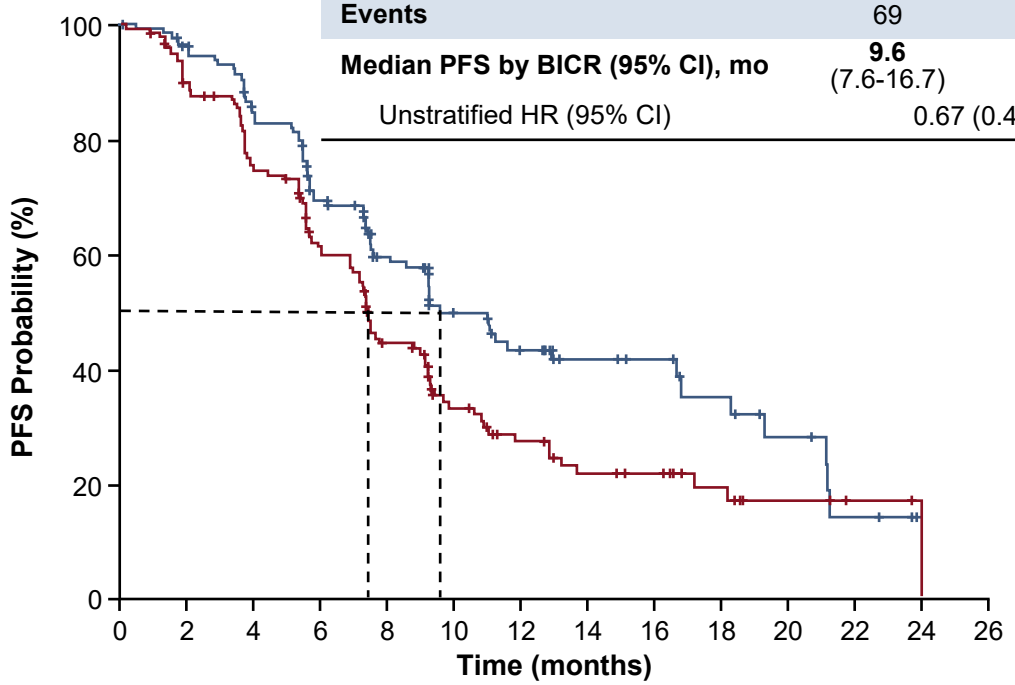
- From the biomarker analysis set, 23% of participants in the SG + pembro group and 20% in the chemo + pembro group had tBRCA mut tumors

Median PFS was longer with SG + pembro vs chemo + pembro in both tBRCA subgroups

[a]HR value is stratified. [b]HR values are unstratified.
BAS, biomarker analysis set; **chemo**, chemotherapy; 2; **HR**, hazard ratio; **ITT**, intent-to-treat; **mo**, months; **mPFS**, median progression-free survival; **mut**, mutant; **NE**, estimable; **pembro**, pembrolizumab; **PFS**, progression-free survival; **SG**, sacituzumab govitecan; **tBRCA**, tumor BRCA; TNBC, triple-negative breast cancer; **WES**, whole exome sequencing; **WT**, wild-type.
1. Tolaney SM, et al. *N Engl J Med.* 2026;394:354-66.

PFS by tBRCA Subgroups

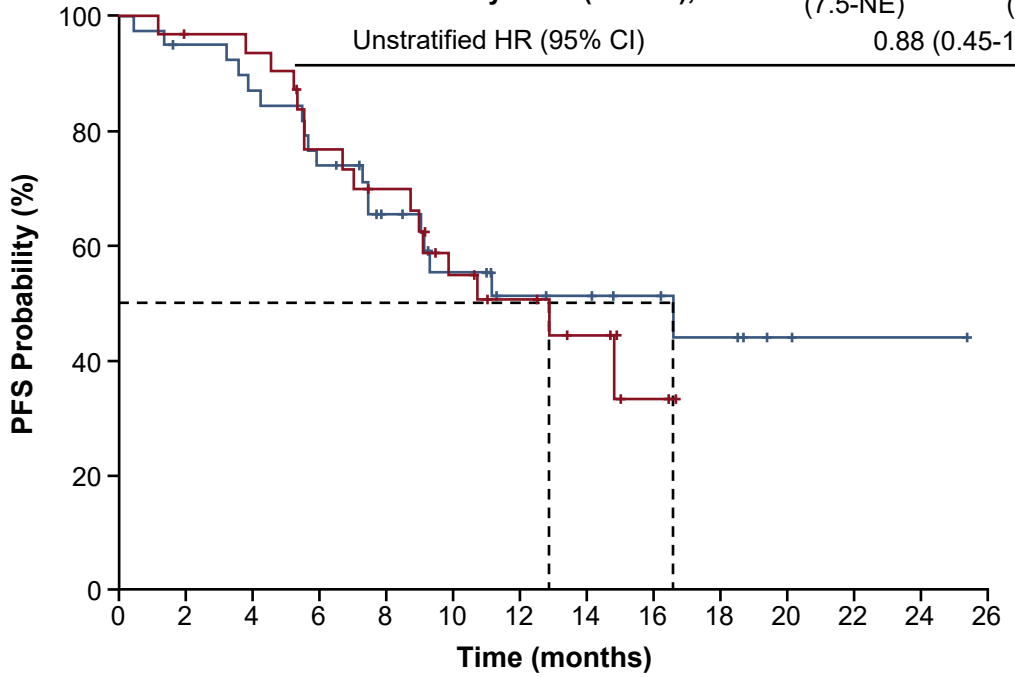
	WT	
	SG + Pembro (n = 130)	Chemo + Pembro (n = 131)
Events	69	90
Median PFS by BICR (95% CI), mo	**9.6** (7.6-16.7)	**7.4** (6.9-9.2)
Unstratified HR (95% CI)	0.67 (0.49-0.91)	



No. at risk

WT, SG + pembro	130	119	100	78	58	42	30	19	17	11	7	3	0	0
WT, Chemo + pembro	131	113	92	71	47	30	21	15	13	8	4	2	1	0

	Mut	
	SG + Pembro (n = 39)	Chemo + Pembro (n = 32)
Events	18	16
Median PFS by BICR (95% CI), mo	**16.6** (7.5-NE)	**12.9** (7.1-NE)
Unstratified HR (95% CI)	0.88 (0.45-1.74)	



No. at risk

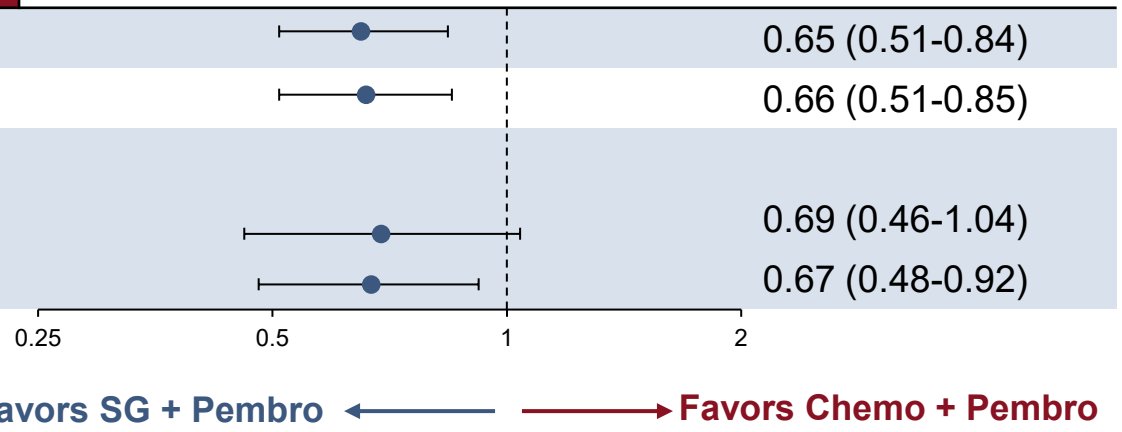
Mut, SG + pembro	39	36	33	28	21	16	11	10	8	6	2	1	1	0
Mut, Chemo + pembro	32	30	29	22	19	14	9	6	2	0	0	0	0	0

PFS improvement with SG + pembro vs chemo + pembro was observed across tBRCA subgroups

BICR, blinded independent central review; **chemo**, chemotherapy; **HR**, hazard ratio; mBC, metastatic breast cancer; **mo**, months; **mut**, mutant; **NE**, not estimable; **pembro**, pembrolizumab; **PFS**, progression-free survival; **SG**, sacituzumab govitecan; **tBRCA**, tumor BRCA; **WT**, wild-type.

PFS by HER2 Subgroups

Subgroup	SG + Pembro		Chemo + Pembro		HR (95% CI)
	n	mPFS, mo	n	mPFS, mo	
ITT Population[1,a]	221	11.2 (9.3-16.7)	222	7.8 (7.3-9.3)	0.65 (0.51-0.84)
HER2 BAS[b]	217	11.3 (9.3-16.7)	218	7.8 (7.3-9.3)	0.66 (0.51-0.85)
HER2 subgroup[b]					
HER2 IHC 0	84	16.6 (9.1-21.2)	82	9.0 (7.2-10.8)	0.69 (0.46-1.04)
HER2 low	133	11.2 (9.1-16.6)	136	7.7 (7.0-9.4)	0.67 (0.48-0.92)

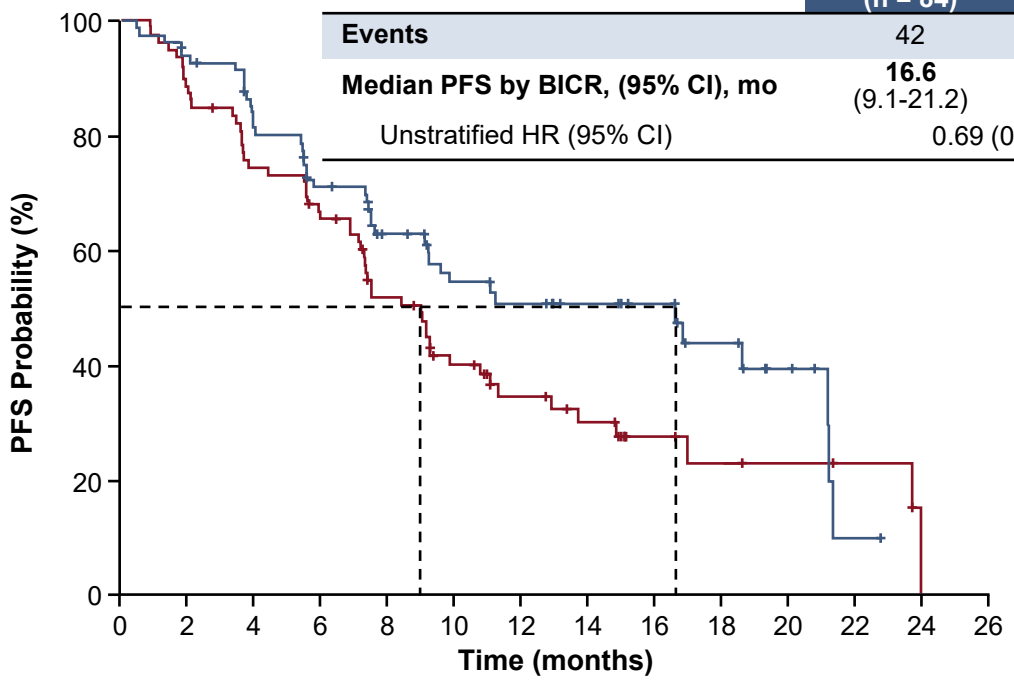


Median PFS was longer with SG + pembro vs chemo + pembro across both HER2 subgroups

[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; **pembro**, pembrolizumab; **PFS**, progression-free survival; **SG**, sacituzumab govitecan.
1. Tolaney SM, et al. *N Engl J Med.* 2026;394:354-66.

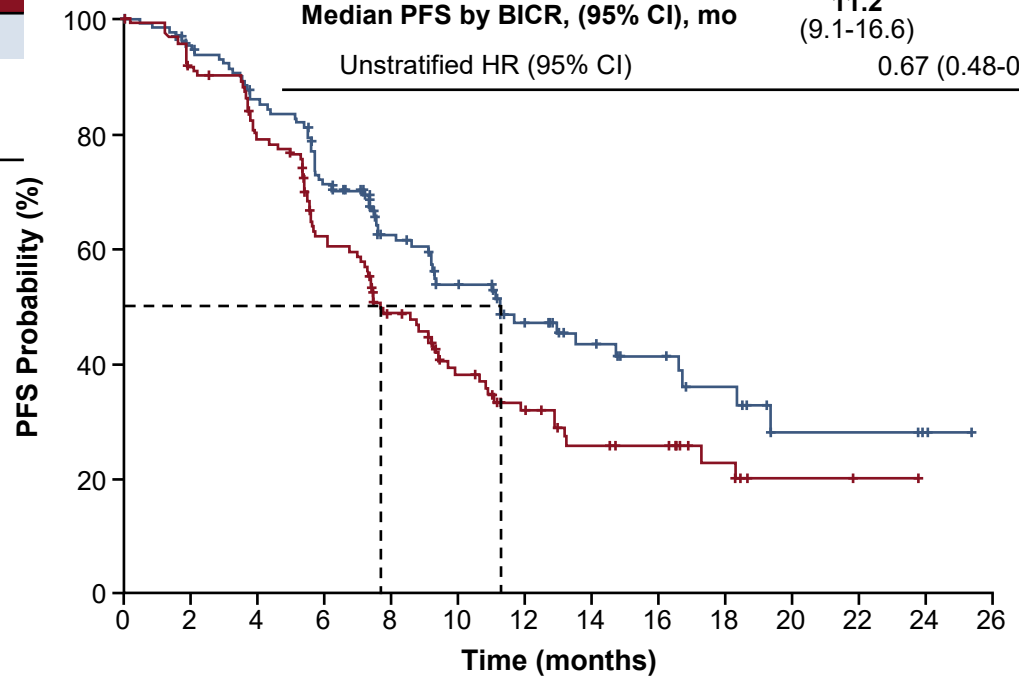
PFS by HER2 Subgroups

	HER2 IHC 0	
	SG + Pembro (n = 84)	Chemo + Pembro (n = 82)
Events	42	54
Median PFS by BICR, (95% CI), mo	**16.6** (9.1-21.2)	**9.0** (7.2-10.8)
Unstratified HR (95% CI)	0.69 (0.46-1.04)	



No. at risk														
HER2 IHC 0, SG + pembro	84	76	64	54	42	32	26	20	17	11	6	1	0	0
HER2 IHC 0, Chemo + pembro	82	70	58	50	37	25	17	13	7	5	4	3	1	0

	HER2 Low	
	SG + Pembro (n = 133)	Chemo + Pembro (n = 136)
Events	65	83
Median PFS by BICR, (95% CI), mo	**11.2** (9.1-16.6)	**7.7** (7.0-9.4)
Unstratified HR (95% CI)	0.67 (0.48-0.92)	



No. at risk														
HER2 Low, SG + pembro	133	122	106	84	60	46	32	22	17	11	5	5	2	0
HER2 Low, Chemo + pembro	136	118	98	71	50	33	23	16	14	8	3	1	0	0

PFS curves showed benefit with SG + pembro compared to chemo + pembro, regardless of HER2 expression status

BICR, blinded independent central review; **chemo**, chemotherapy; **HER2**, human epidermal growth factor receptor 2; **HR**, hazard ratio; **IHC**, immunohistochemistry; **KM**, Kaplan-Meier; **mo**, months; **pembro**, pembrolizumab; **PFS**, progression-free survival; **SG**, sacituzumab govitecan.

Conclusions

- Consistent with the results of the primary analysis of ASCENT-04, median PFS was longer across all key participant subgroups with SG + pembro vs chemo + pembro[1]
  - All Trop-2 expression quartiles
  - Participants with both tBRCA WT and tBRCA mut status
  - HER2 IHC 0 and HER 2 low expression subgroups
- The results of these analyses are consistent with results from the ASCENT study, in which participants with metastatic TNBC treated with SG had longer PFS versus chemotherapy across all Trop-2, BRCA, and HER2 categories[2,3]
- Sample sizes in many subgroups were small and the analyses were descriptive, so caution should be used in interpreting these results

The results of this analysis reinforce the significant, clinically meaningful benefit of SG + pembro as a first-line treatment option for patients with previously untreated advanced PD-L1–positive TNBC across key Trop-2, tBRCA, and HER2 biomarker subgroups

Chemo, chemotherapy; **HER2**, human epidermal growth factor receptor 2; **mut**, mutant; **PD-L1**, programmed cell death ligand 1; **pembro**, pembrolizumab; **PFS**, progression-free survival; **SG**, sacituzumab govitecan; **tBRCA**, tumor BRCA; **TNBC**, triple-negative breast cancer; **WT**, wild-type.

1. Tolaney SM, et al. *N Engl J Med.* 2026;394:354-66. 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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