Progression-Free Survival After Next Line of Treatment (PFS2) and Subsequent Therapies in the ASCENT-03 Study of Participants With Previously Untreated Metastatic Triple-Negative Breast Cancer Treated With Sacituzumab Govitecan vs Chemotherapy

Sara Hurvitz[1], Javier Cortés[2-6], Sara M Tolaney[7], Kevin Punie[8], Andreas Schneeweiss[9], Joohyuk Sohn[10], Eriko Tokunaga[11], Adam Brufsky[12], Yeon Hee Park[13], Binghe Xu[14], Roberto Hegg[15], Mafalda Oliveira[16], Alessandra Fabi[17], Xinrui Zhang[18], Hao Wang[18], Anh Nguyen[18], Natalya Vaksman[18], Carlos Barrios[19]

[1]Department of Medicine, UW Medicine, Clinical Research Division, Fred Hutchinson Cancer Center, Seattle, WA, USA; [2]International Breast Cancer Center (IBCC), Pangaea Oncology, Quiron Group, Barcelona, Spain; [3]IOB Madrid, Institute of Oncology, Hospital Beata María Ana, Madrid, Spain; [4]Oncology Department, Hospital Universitario Torrejón, Ribera Group, Madrid, Spain; [5]Universidad Europea de Madrid, Faculty of Biomedical and Health Sciences, Department of Medicine, Madrid, Spain; [6]Medica Scientia Innovation Research (MEDSIR), Barcelona, Spain and Ridgewood, NJ, USA; [7]Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA; [8]Medical Oncology, Oncology Center Antwerp, Ziekenhuis aan de Stroom, Antwerp, Belgium; [9]Heidelberg University Hospital and German Cancer Research Center, Heidelberg, Germany; [10]Yonsei Cancer Center, Seoul, Republic of Korea; [11]National Hospital Organization Kyushu Cancer Center, Fukuoka, Japan; [12]Magee-Womens Hospital and the Hillman Cancer Center, University of Pittsburgh Medical Center, Pittsburgh, PA, USA; [13]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [14]Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [15]University of São Paulo, São Paulo, Brazil; [16]Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain; [17]Precision Medicine Unit in Senology, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Università Cattolica del Sacro Cuore, Rome, Italy; [18]Gilead Sciences, Inc., Foster City, CA, USA; [19]Latin American Cooperative Oncology Group (LACOG), Porto Alegre, Brazil

Key Takeaway Points: ASCENT-03 PFS2 and Subsequent Therapies

In the ASCENT-03 study, PFS2 was longer in the SG group compared with the chemo group, indicating sustained long-term benefit beyond first progression

Despite the high rate of crossover from the chemo group to SG, time to first and second subsequent therapies suggest that participants receiving 1L SG experience longer initial disease control and delayed need for subsequent therapy

These results support SG as a new 1L standard of care for patients with mTNBC who are not candidates for PD-(L)1 inhibitors

1L, first-line; **chemo**, chemotherapy; **mTNBC**, metastatic triple-negative breast cancer; **PD-(L)1**, programmed death (ligand) 1; **PFS2**, progression-free survival 2; **SG**, sacituzumab govitecan.

Background

- SG demonstrated significant improvement in PFS vs chemo in participants with previously untreated mTNBC who are not candidates for a PD-(L)1 inhibitor in ASCENT-03[1]

PFS by BICR

HR, 0.62; 95% CI, 0.50-0.77;
P < .0001

- OS data were immature at the primary analysis; no detriment was observed for participants receiving SG[1]

OS maturity rate, 37%
(as of Apr 2025)

- SG was provided on-study as crossover following PD on chemo and may have also been received commercially[1]

147 of 179 pts with subsq tx (**82%**) from the chemo group received SG in any subsq line

- PFS2 can be used to measure long-term clinical benefit in the absence of mature OS data and is particularly valuable when OS is confounded by a crossover design[2-4]

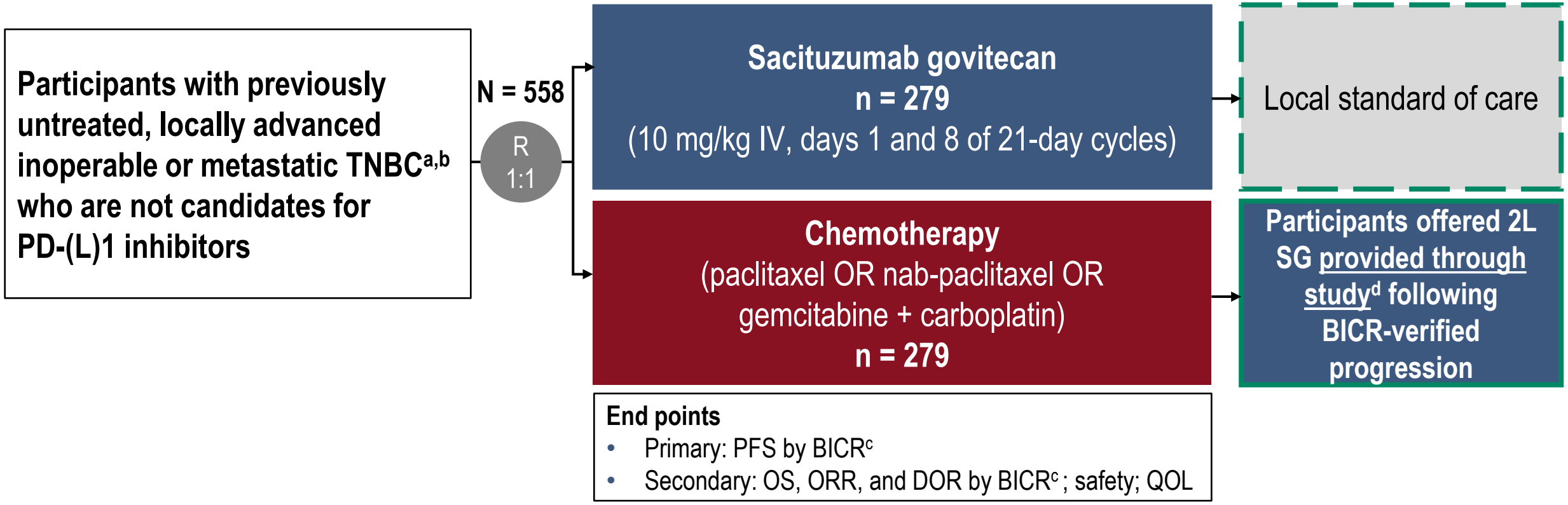
We report PFS2 and subsequent therapies from the ASCENT-03 study

BICR, blinded independent central review; **chemo**, chemotherapy; **HR**, hazard ratio; **mTNBC**, metastatic triple-negative breast cancer; **OS**, overall survival; **PD**, progressive disease; **PD-(L)1**, programmed death (ligand) 1; **PFS**, progression-free survival; **PFS2**, progression-free survival 2; **pts**, participants; **SG**, sacituzumab govitecan; **subsq**, subsequent; **tx**, treatment.

1. Cortés J, et al. *N Engl J Med*. 2025;393:1912-25. 2. Chowdhury S, et al. *Front Oncol*. 2020;10:1349. 3. Filis P, et al. *ESMO Open*. 2026;11:106062. 4. Woodford RG, et al. *Cancer*. 2022;128:1449-57.

ASCENT-03: Study Design

Treatment was continued until BICR-verified progression or unacceptable toxicity

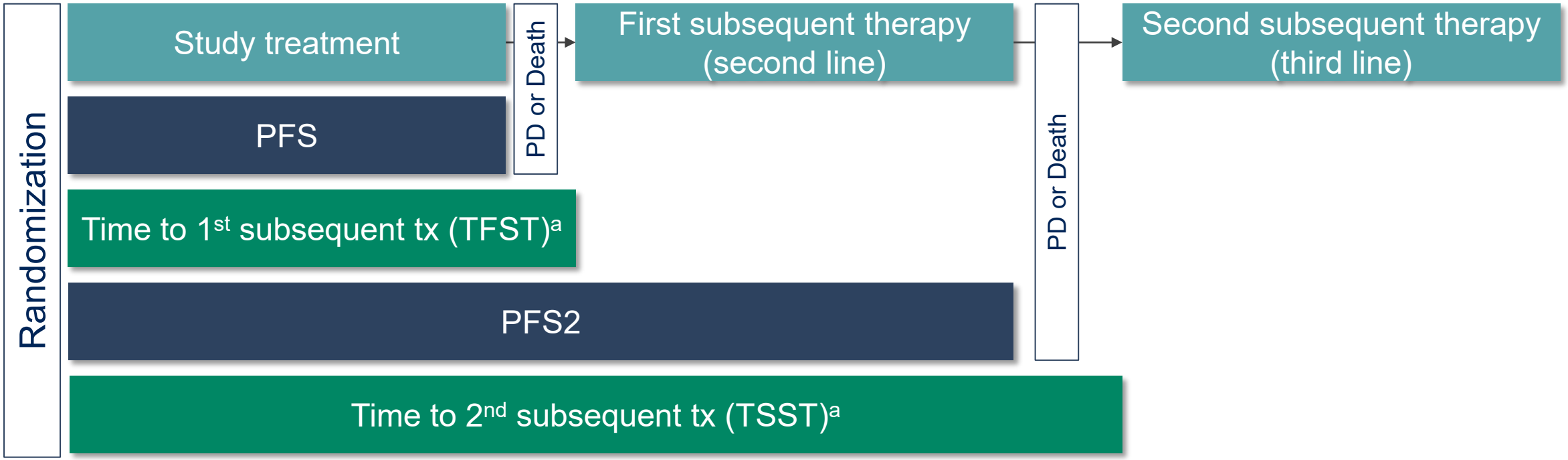


Exploratory end points included PFS2, TFST, and TSST

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. [c]Per Response Evaluation Criteria in Solid Tumors version 1.1. [d]Participants could have also received SG in any subsequent line commercially; other subsequent treatments per local practice were also permitted.

2L, second-line; **BICR**, blinded independent central review; **DOR**, duration of response; **IV**, intravenous; **mTNBC**, metastatic triple-negative breast cancer; **ORR**, objective response rate; **OS**, overall survival; **PD-(L)1**, programmed death (ligand) 1; **PFS**, progression-free survival; **PFS2**, progression-free survival 2; **QOL**, quality of life; **R**, randomized; **SG**, sacituzumab govitecan; **TFST**, time to first subsequent therapy; **TNBC**, triple-negative breast cancer; **TSST**, time to second subsequent therapy.

Methods



- ASCENT-03 *post hoc* analysis
  - The data cutoff date was April 2, 2025; at this time, the median follow-up was 13.2 months (range, <0.1-29.2)
  - Two-sided *P* value calculated using the stratified log-rank test and the hazard ratio with 95% CIs calculated using a Cox proportional hazards model adjusted for randomization stratification factors
  - PFS2 is defined as time from randomization to first documented progression on next-line therapy per investigator assessment, or death due to any cause, whichever occurred first

[a]Time to first or second subsequent therapy is defined as time from randomization to the start of the first or second subsequent treatment or death due to any cause, whichever occurred first.
PD, progressive disease**; PFS**, progression-free survival; **PFS2**, progression-free survival 2; **TFST**, time to first subsequent therapy; **TSST**, time to second subsequent therapy; **tx**, treatment.

Demographics and Baseline Characteristics

ITT Population	SG (n = 279)	Chemo (n = 279)
Female sex, n (%)	278 (> 99)	277 (99)
Median age (range), years	56 (28-84)	54 (23-86)
≥ 65 years, 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)

ITT Population	SG (n = 279)	Chemo (n = 279)
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 negative,[c] n (%)	277 (99)	278 (> 99)
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)

As previously reported, patient demographics were consistent between treatment groups

Data cutoff date: April 2, 2025. [a]As reported by the participants; 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 combined positive score missing. [d]Actual chemo received was consistent with what was selected prior to randomization; however, 3 participants were randomized but did not receive treatment.
Chemo, chemotherapy; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **ITT**, intent-to-treat; **PD-L1**, programmed death ligand 1; **SG**, sacituzumab govitecan.

Participant Disposition and Subsequent Treatments

Participant Disposition, n (%)	SG (n = 279)	Chemo (n = 279)
Remaining on study treatment	75 (27)	39 (14)
Discontinued treatment[a]	204 (73)	240 (86)
Progressive disease[b]	161 (79)	195 (81)

Participants who discontinued first-line treatment,* n (%)	SG (n = 204)	Chemo (n = 240)
Received second-line and later therapy	126 (62)	179 (75)
Received any subsequent ADC[c]	19 (15)	153 (85)
Received any subsequent SG[c]	2 (2)	147 (82)
Received third-line therapy	31 (15)	55 (23)

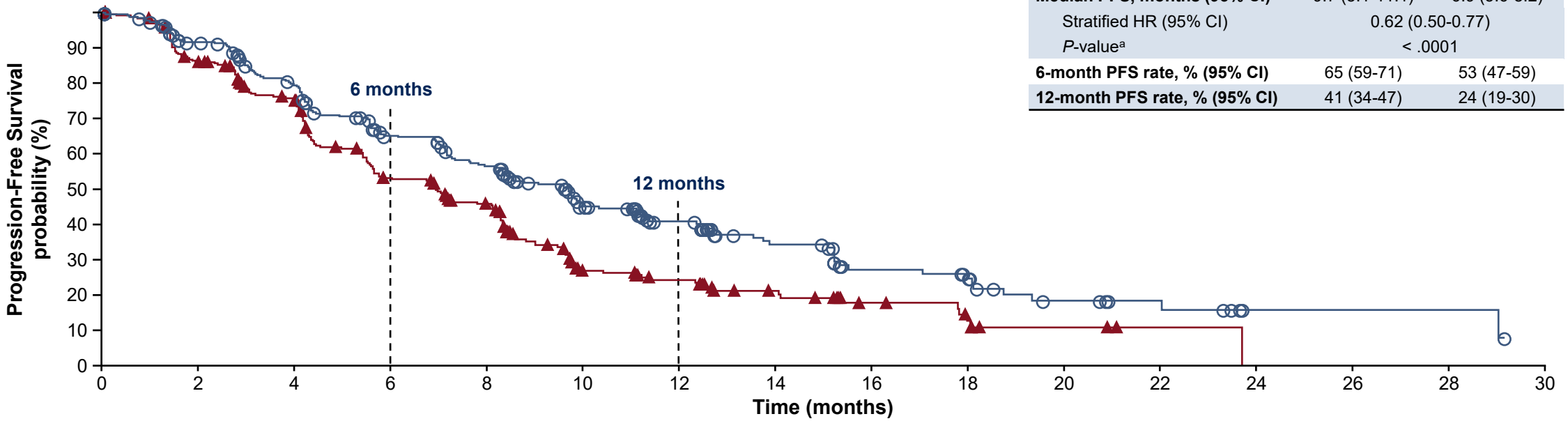
*Data are based on the primary analysis data-cut and follow-up is ongoing.

Almost twice as many participants in the SG group (27%) remained on study treatment compared with the chemo group (14%) at the time of data cutoff

[a]In the SG group, treatment discontinuation was also due to participant decision (n = 16); adverse events and investigator choice (n = 10 each); and death (n = 7); in the chemo group, treatment discontinuation was due to adverse events (n = 22); participant decision (n = 16); investigator choice (n = 5); and death (n = 2). [b]Percentages are calculated based on the number of participants who discontinued treatment. [c]Percentages are calculated based on the number of participants who received second-line or later therapy.
ADC, antibody-drug conjugate**; chemo,** chemotherapy; **SG**, sacituzumab govitecan.

Progression-Free Survival by BICR

	SG (n = 279)	Chemo (n = 279)
Median PFS, months (95% CI)	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. of Patients Still at Risk (Events)

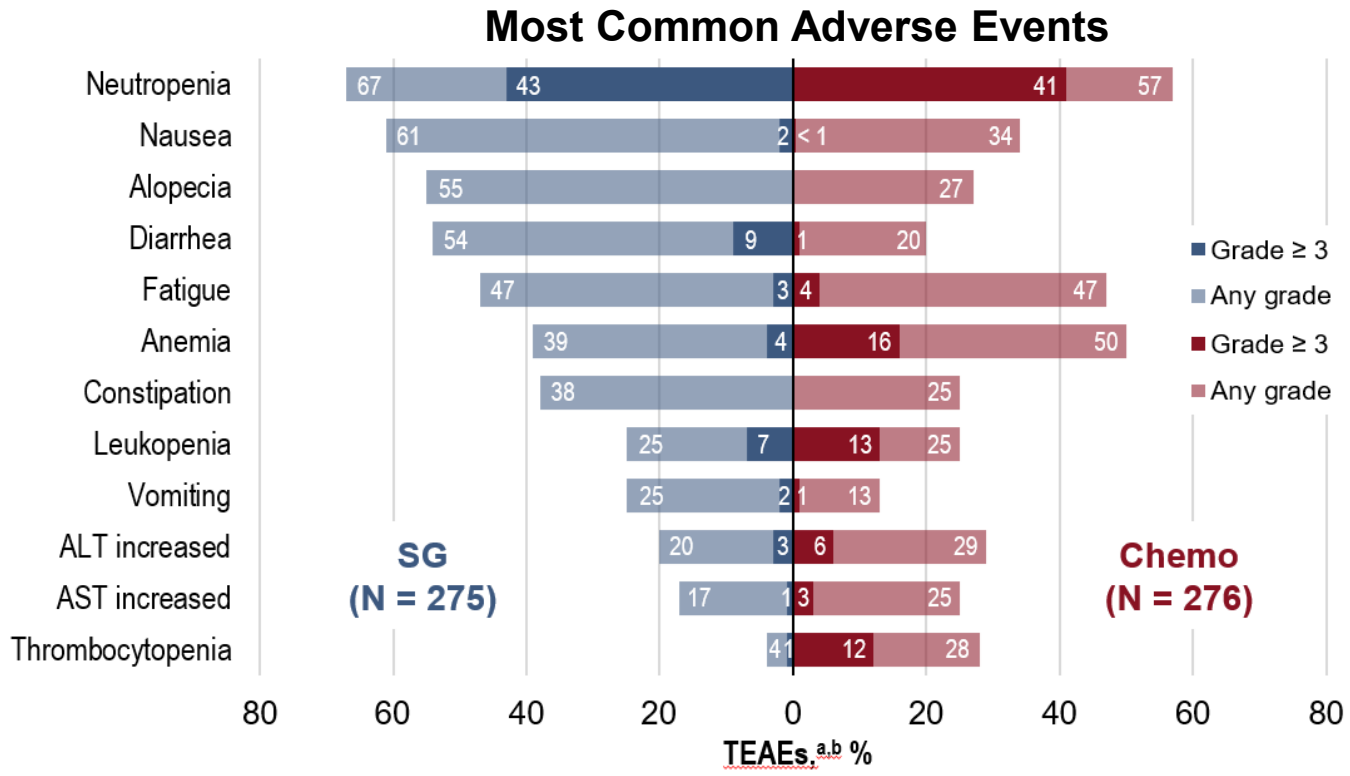
SG	279 (0)	238 (22)	199 (53)	153 (88)	128 (108)	84 (131)	60 (138)	38 (146)	23 (153)	20 (154)	10 (159)	7 (159)	2 (160)	2 (160)	2 (160)	0 (161)
Chemo	279 (0)	226 (37)	186 (65)	126 (118)	100 (135)	44 (172)	35 (176)	21 (180)	12 (183)	7 (186)	3 (187)	1 (187)	0 (188)			

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[1]

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.
1. Cortés J, et al. *N Engl J Med*. 2025;393:1912-25.

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)



The AEs observed were consistent with the known safety profile of SG, with no new safety concerns[1]

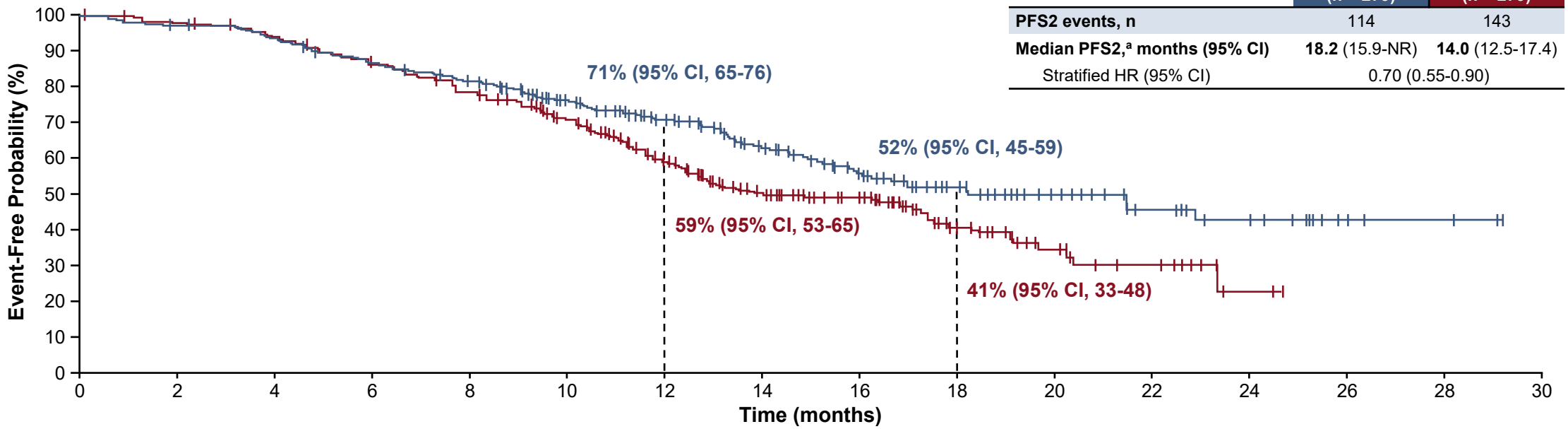
Data cutoff date: April 2, 2025. TEAEs were defined as any AEs that began or worsened on or after the first dose date of study drug up to 30 days after the last dose date of study drug or the initiation of subsequent anticancer therapy (including crossover treatment), whichever occurred first. [a]TEAEs 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; **SAE**, serious adverse event; **SG**, sacituzumab govitecan; **TEAE**, treatment-emergent adverse event.

1. Cortés J, et al. *N Engl J Med*. 2025;393:1912-25.

PFS After Next Line of Treatment (PFS2)

	SG (n = 279)	Chemo (n = 279)
PFS2 events, n	114	143
Median PFS2,[a] months (95% CI)	**18.2** (15.9-NR)	**14.0** (12.5-17.4)
Stratified HR (95% CI)	0.70 (0.55-0.90)	



No. of Patients Still at Risk (Events)

SG	279 (0)	270 (8)	259 (18)	238 (37)	221 (51)	189 (65)	156 (78)	107 (93)	79 (104)	54 (109)	33 (111)	20 (113)	13 (114)	4 (114)	3 (114)	0 (114)
Chemo	279 (0)	271 (6)	257 (18)	237 (36)	212 (59)	178 (79)	133 (106)	86 (126)	67 (127)	34 (136)	19 (140)	10 (142)	2 (143)	0 (143)		

PFS2 was longer in the SG group compared with the chemo group despite the high rate of crossover in the chemo group, with a 30% reduction in risk of a PFS2 event with SG

[a]PFS2 is defined as time from randomization to first documented progression on next-line therapy per investigator assessment, or death due to any cause, whichever occurred first.
Chemo, chemotherapy; **HR**, hazard ratio; **NR,** not reached; **PFS2**, progression-free survival 2; **SG**, sacituzumab govitecan.

Subsequent Therapy

Subsequent Therapies in the Second Line

	SG (n = 279)	Chemo (n = 279)
Any subsequent therapy, n	126	179
Any subsequent therapy in 2L,[a] n (%)	126 (100)	179 (100)
Platinum agents	43 (34)	4 (2)
Taxanes	32 (25)	5 (3)
Anthracyclines	14 (11)	3 (2)
ADC	13 (10)	149 (83)
Trastuzumab deruxtecan	12 (10)	7 (4)
Sacituzumab govitecan	1 (1)	142 (79)[b]
PD-(L)1 inhibitors	5 (4)	2 (1)
PARPi	2 (2)	1 (1)
Other[c]	85 (67)	25 (14)
Median TFST, months (95% CI)	11.2 (10.0-13.0)	7.9 (7.2-9.0)
Stratified HR (95% CI)	0.61 (0.50-0.75)	

Subsequent Therapies in the Third Line

	SG (n = 279)	Chemo (n = 279)
Any subsequent therapy, n	126	179
Any subsequent therapy in 3L,[a] n (%)	31 (25)	55 (31)
Taxanes	6 (5)	7 (4)
ADC	5 (4)	10 (6)
Trastuzumab deruxtecan	4 (3)	6 (3)
Sacituzumab govitecan	1 (1)	4 (2)[d]
Platinum agents	5 (4)	7 (4)
Anthracyclines	3 (2)	8 (4)
PD-(L)1 inhibitors	3 (2)	2 (1)
PARPi	2 (2)	2 (1)
Other[e]	16 (13)	36 (20)
Median TSST, months (95% CI)	17.3 (15.2-NR)	16.6 (13.6-18.5)
Stratified HR (95% CI)	0.82 (0.64-1.05)	

The majority of participants in the chemo group received 2L SG and most in the SG group received 2L chemo

[a]Percentages are calculated based on the number of participants who received any subsequent therapy. [b]Includes both commercial use of SG in 2L (n = 28) and crossover to SG on study (n = 114). [c]Includes gemcitabine (n = 23); capecitabine (n = 18); cyclophosphamide and eribulin (n = 13 each); bevacizumab (n = 5); gemcitabine hypochloride, fluorouracil, and trastuzumab (n = 3 each); eribulin mesylate, pertuzumab, and zoledronic acid monohydrate (n = 2 each); and vinorelbine tartrate, dexmedetomidine, gimeracil-oteracil potassium-tegafur; nadunolimab, natural killer cells, Abbv 400, Azd 9574, Cln 619, investigational drug, other therapeutic products, and all other therapeutic products (n = 1 each) in the SG group and capecitabine (n = 16); cyclophosphamide, gemcitabine hypochloride, and vinorelbine tartrate (n = 2 each); gemcitabine, eribulin, eribulin mesylate, and larotrectinib (n = 1 each) in the chemo group. [d]One patient in the chemo group received SG beyond 3L. [e]Includes eribulin mesylate (n = 5); gemcitabine hypochloride (n = 4); eribulin (n = 3); bevacizumab (n = 2); and capecitabine and gemcitabine (n = 1 each) in the SG group and capecitabine (n = 10); cyclophosphamide (n = 6); eribulin (n = 5); gemcitabine and eribulin mesylate (n = 3 each); gemcitabine hypochloride and bevacizumab (n = 2 each); and bortezomib, gimeracil/oteracil potassium/tegafur, repotrectinib, and investigational drug (n = 1 each) in the chemo group. **2L**, second-line; **3L**, third-line; **ADC**, antibody-drug conjugate; **chemo,** chemotherapy; **HR,** hazard ratio; **NR,** not reached; **PARPi**, poly ADP-ribose polymerase inhibitor; **PD-(L)1**; programmed death (ligand) 1; **SG**, sacituzumab govitecan; **TFST**, time to first subsequent therapy; **TSST**, time to second subsequent therapy.

Conclusions

- PFS2 was longer in the SG group compared with the chemo group despite the high rate of crossover, indicating sustained long-term benefit beyond first progression

Median PFS2

18.2 vs 14.0 months
HR, 0.70 (95% CI, 0.55-0.90)

- The most frequent 2L+ subsequent therapy was chemo in the SG group and SG in the chemo group

Subsequent therapy in any line

Chemo group: SG (82%)
SG group: chemo (85%)

- Despite the high rate of crossover from the chemo group to SG, time to first and second subsequent therapies suggest that participants receiving 1L SG experience longer initial disease control and delayed need for subsequent therapy

Median TFST & TSST

TFST: 11.2 vs 7.9 months
TSST: 17.3 vs 16.6 months

These results from the ASCENT-03 study further support 1L SG use for patients with mTNBC who are not candidates for PD-(L)1 inhibitors

1L, first-line; **2L+,** second-line and later; **chemo**, chemotherapy; **HR**, hazard ratio; **mTNBC**, metastatic triple-negative breast cancer; **PD-(L)1**, programmed death (ligand) 1; **PFS2**, progression-free survival 2; **SG**, sacituzumab govitecan; **TFST**, time to first subsequent therapy; **TSST**, time to second subsequent therapy; **tx**, treatment.

Acknowledgments

- We thank the participants and their caregivers for their participation and commitment to clinical research
- Thank you to the clinical trial investigators and their devoted team members for contributing to the ASCENT-03 trial
- This study is sponsored by Gilead Sciences, Inc. Medical writing and editorial support was provided by Sonal S Joshi, PhD, of Parexel, and funded by Gilead Sciences, Inc.

- Correspondence: Sara Tolaney, Sara_Tolaney@DFCI.HARVARD.EDU

A **plain language summary** of this presentation is available via QR code* on this slide.

*Copies of this slide deck obtained through Quick Response (QR) Code are for personal use only and may not be reproduced without permission from ASCO® or the author of these slides.