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

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

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

N = 558

R 1:1

Treatment was continued until BICR-verified progression or unacceptable toxicity

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

Chemotherapy
Paclitaxel 90 mg/m² OR nab-Paclitaxel 100 mg/m²
(days 1, 8, and 15 of 28-day cycles) OR
Gemcitabine 1000 mg/m² + Carboplatin AUC2
(days 1 and 8 of 21-day cycles)
n = 279

End points

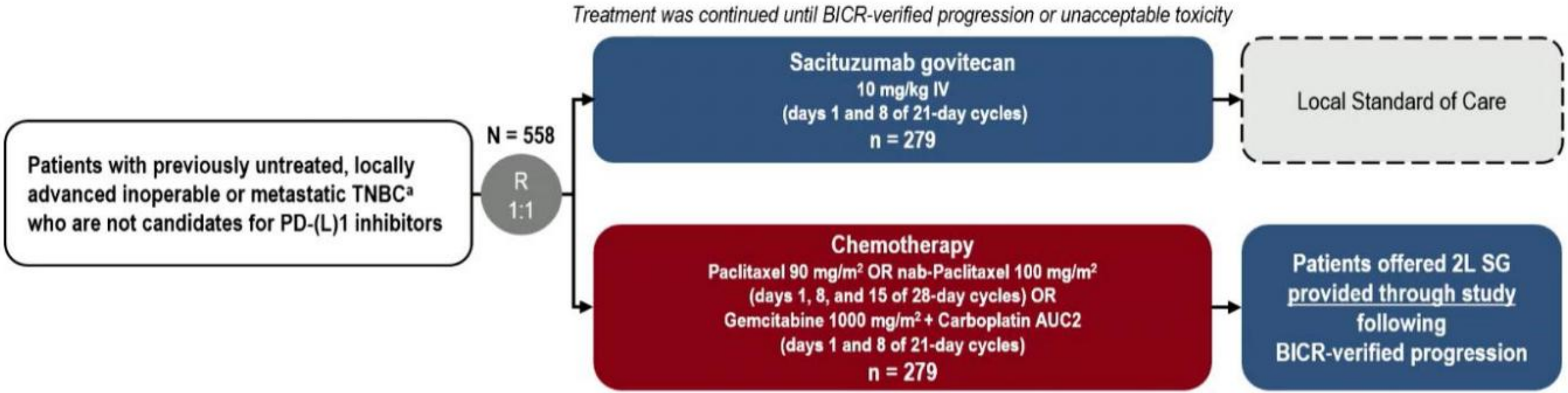
Primary
- PFS by BICR[d]

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

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

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

ASCENT-03: Study Design

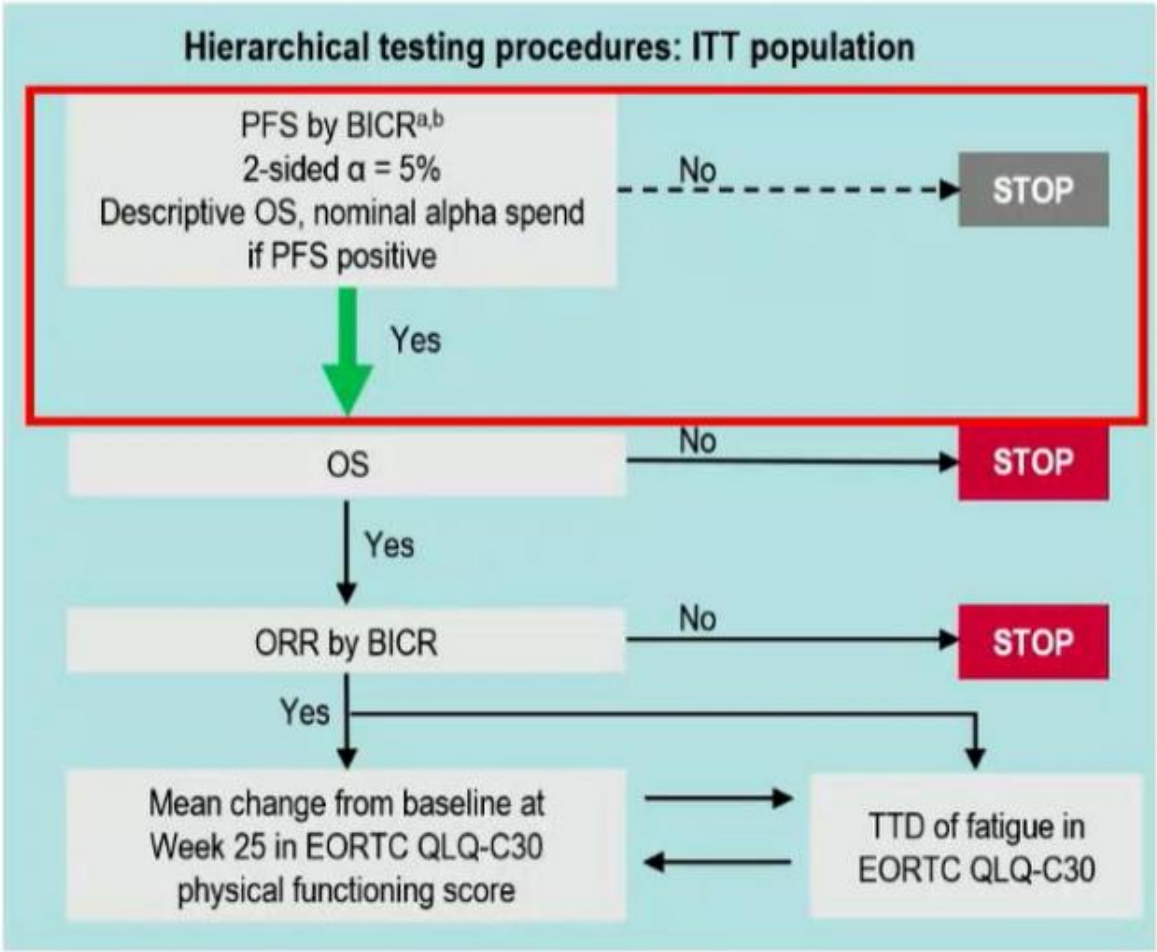


Stratification factors:

- 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

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

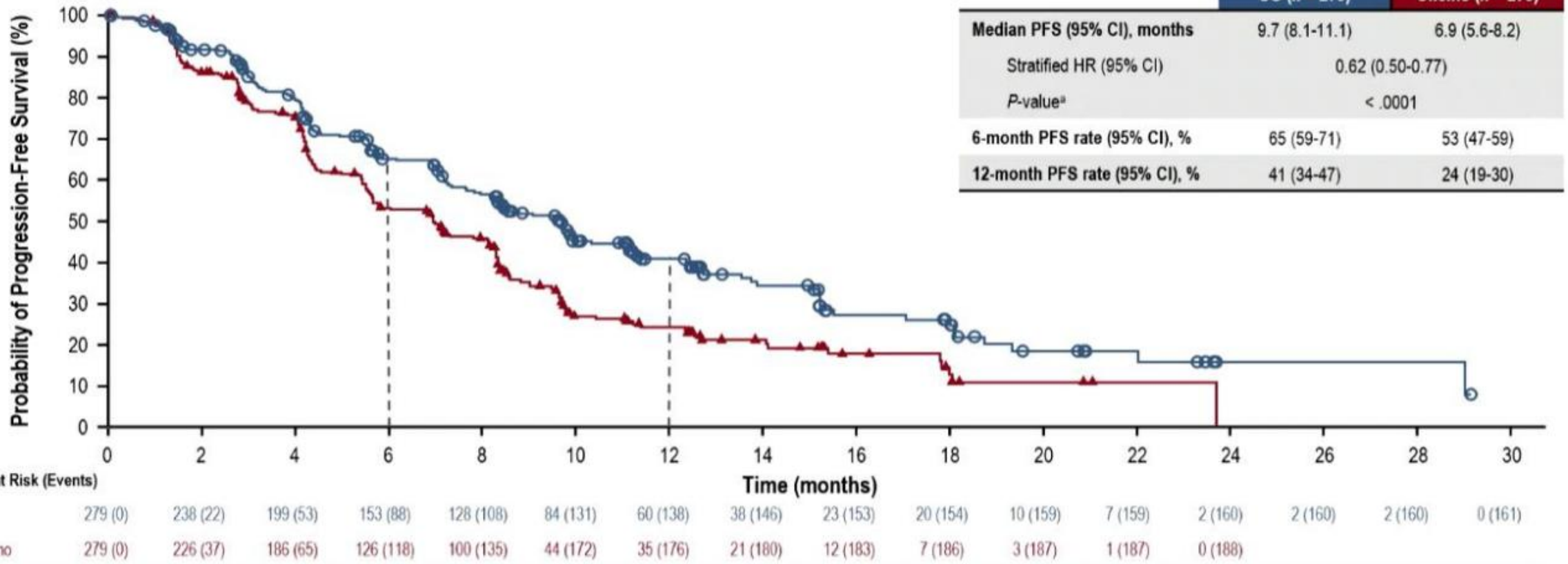


Demographics and Baseline Characteristics

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)

Progression-Free Survival by BICR

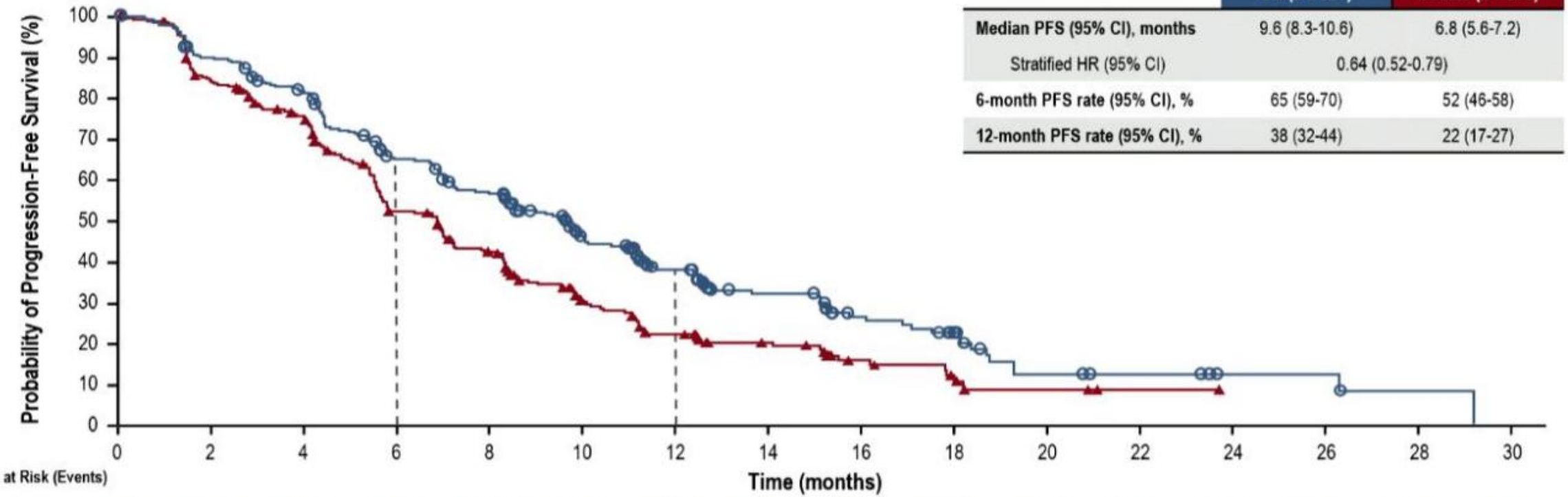


	SG (n = 279)	Chemo (n = 279)
Median PFS (95% CI), months	9.7 (8.1-11.1)	6.9 (5.6-8.2)
Stratified HR (95% CI)	0.62 (0.50-0.77)	
P-value[a]	< .0001	
6-month PFS rate (95% CI), %	65 (59-71)	53 (47-59)
12-month PFS rate (95% CI), %	41 (34-47)	24 (19-30)

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

Progression-Free Survival by Investigator Assessment[a]

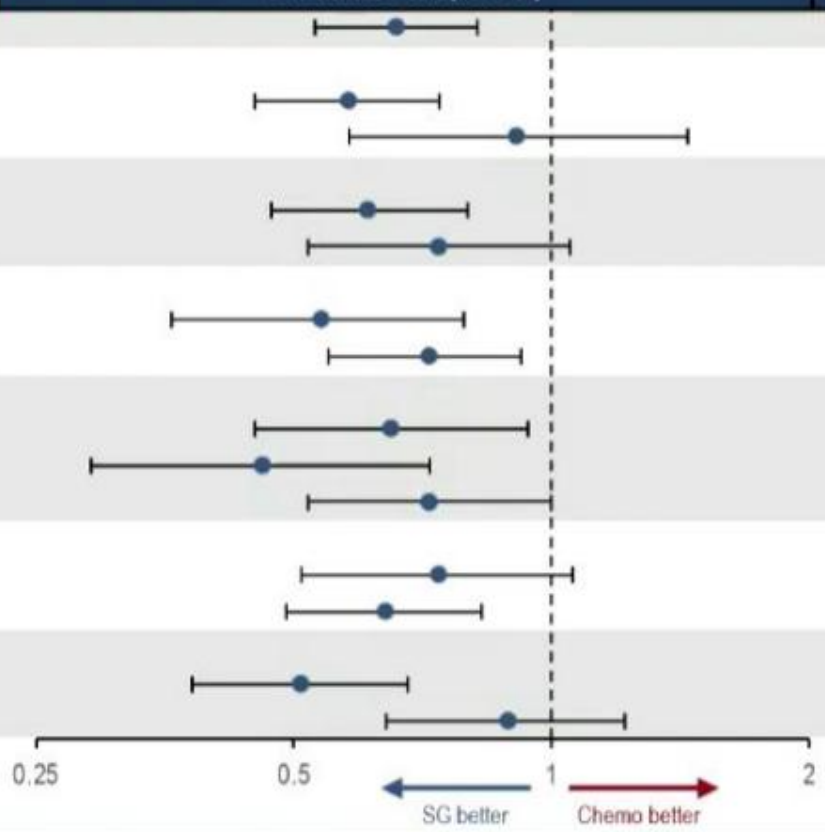
	SG (n = 279)	Chemo (n = 279)
Median PFS (95% CI), months	9.6 (8.3-10.6)	6.8 (5.6-7.2)
Stratified HR (95% CI)	0.64 (0.52-0.79)	
6-month PFS rate (95% CI), %	65 (59-70)	52 (46-58)
12-month PFS rate (95% CI), %	38 (32-44)	22 (17-27)



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

Subgroup Analysis of Progression-free Survival by BICR

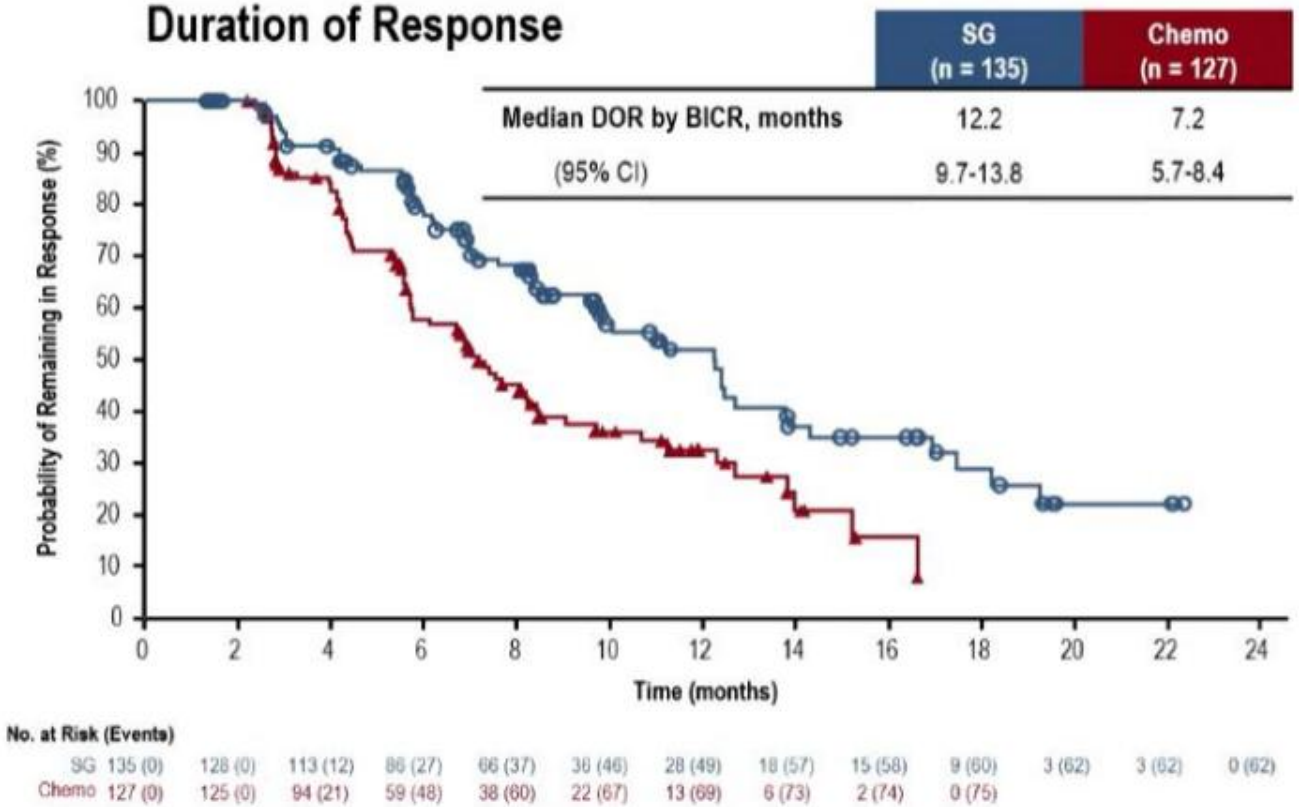
	SG		Chemo		Unstratified HR (95% CI)	Unstratified HR (95% CI)
	n	Median PFS, mo (95% CI)	n	Median PFS, mo (95% CI)		
ITT population	279	9.7 (8.1-11.1)	279	6.9 (5.6-8.2)		0.66 (0.53-0.82)
Age group						
< 65 years	214	9.6 (7.6-10.3)	201	5.7 (4.4-7.0)		0.58 (0.45-0.74)
≥ 65 years	65	11.1 (7.3-13.9)	78	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

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)

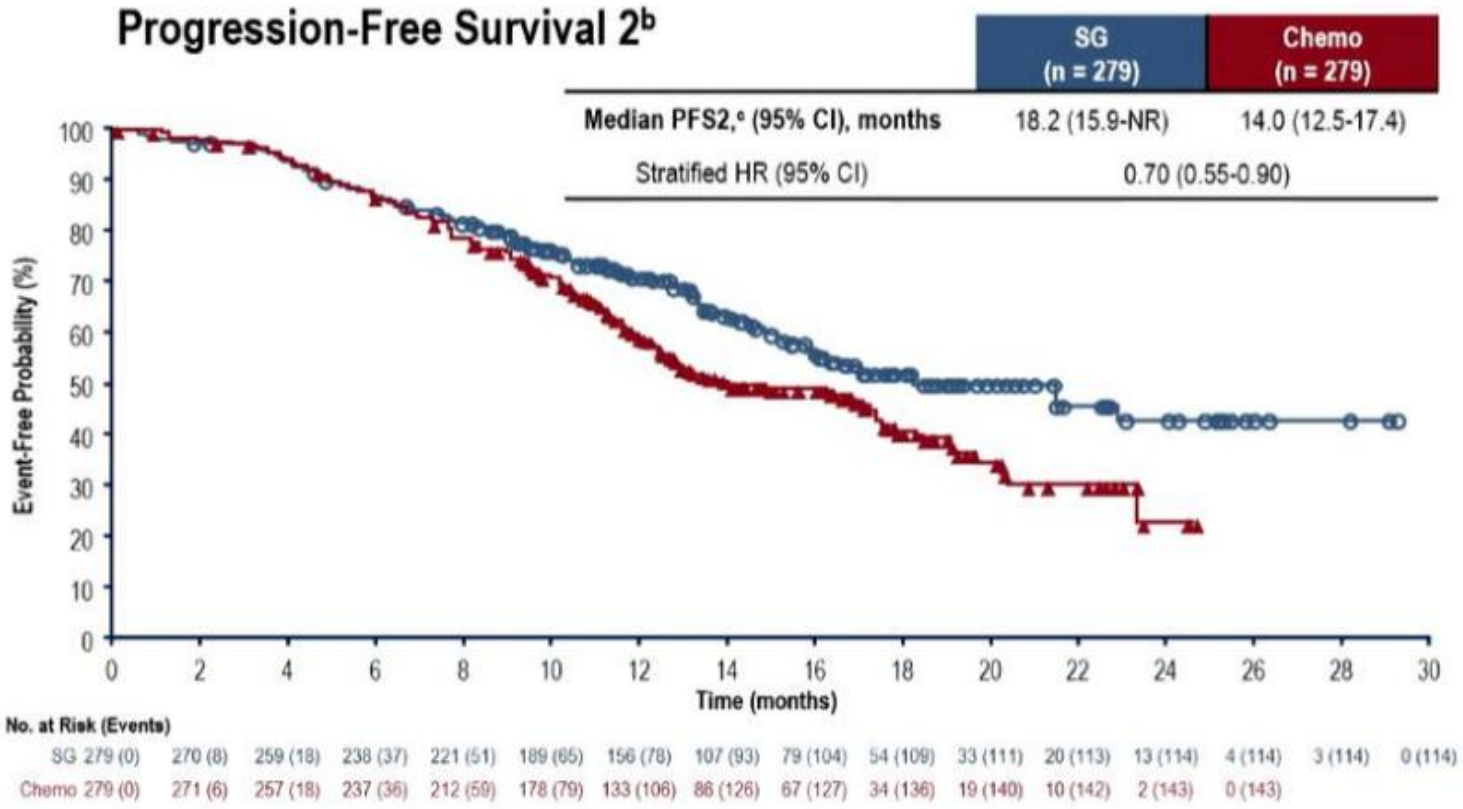


Objective response rates were similar in both treatment groups;
however, duration of response was substantially longer with SG vs chemo

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)



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

Exposure and Safety Summary

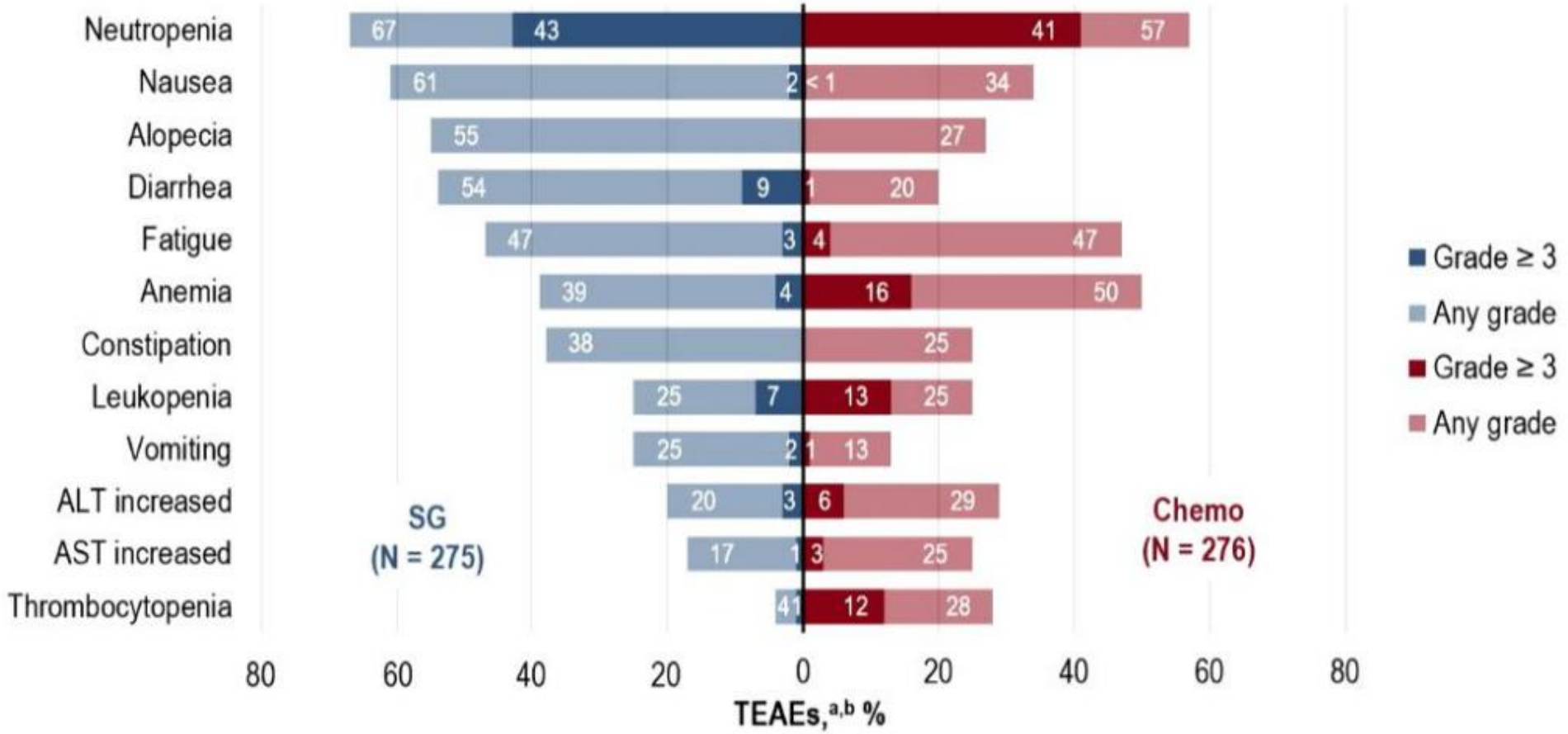
Safety population	SG (n = 275)	Chemo (n = 276)	
Treatment component	SG	Taxane	Gemcitabine/ Carboplatin
All treated patients, n	275	154	122
Median duration of treatment, months (range)	8.3 (< 0.1-28.7)	6.3 (< 0.1-24.2)	5.8 (< 0.1-23.1)

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

Safety Summary: Most Common Adverse Events



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

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