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Patient-Reported Outcomes With Sacituzumab Govitecan vs Chemotherapy in Patients With Previously Untreated Advanced Triple-Negative Breast Cancer Who Are Not Candidates for PD-(L)1 Inhibitors in the Phase 3 ASCENT-03 Study

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Disclosure Information

Kevin Punie, MD

I have the following relevant relationships to disclose:

Consultant for: AstraZeneca, Axiom, Eli Lilly, Exact Sciences, Focus Patient, Gilead Sciences, Inc., Hoffmann/La Roche, Medscape, MSD, Mundi Pharma, Need, Inc., NordicPharma, Novartis, Pfizer, Sanofi, Seagen

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Addressing the Unmet Need in 1L mTNBC

UNMET NEED in 1L mTNBC TREATMENT	• ~60% of patients with previously untreated mTNBC are not candidates for PD-(L)1 inhibitor therapy[1] • ~50% of patients who receive 1L treatment for mTNBC do not receive 2L+ treatment[2] • There is a substantial deterioration in QOL with each line of therapy[3]
CLINICAL IMPACT OF ASCENT-03	• 1L SG led to a statistically significant and clinically meaningful improvement in PFS vs chemotherapy (median, 9.7 vs 6.9 months; HR, 0.62; $P < 0.0001$) in participants with advanced TNBC who are not candidates for PD-(L)1 inhibitors[4] • The safety profile of SG was consistent with previous studies, and no new safety concerns were identified[4]

We report the impact of treatment on QOL, including symptom burden and functional status in the ASCENT-03 study

1L, first-line; **2L+**, second-line or later; **HR**, hazard ratio; **mTNBC**, metastatic TNBC; **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; **SG**, sacituzumab govitecan; **TNBC**, triple-negative breast cancer.

1. Cortés J, et al. *N Engl J Med*. 2022;387:217-26. 2. Punie K, et al. *Oncologist*. 2025;30:oyaf034. 3. Zhang Y, et al. *Value Health*. 2025;28:S359-60. 4. Cortés J, et al. *N Eng J Med*. 2025; doi: 10.1056/NEJMoa2511734.

ASCENT-03: Study Design

Participants 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

Treatment was continued until BICR-verified progression or unacceptable toxicity

N = 558

R 1:1

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

Chemotherapy
Paclitaxel 90 mg/m^2 OR
nab-Paclitaxel 100 mg/m^2
(days 1, 8, and 15 of 28-day cycles) OR
Gemcitabine 1000 mg/m^2 + 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 (EORTC QLQ-C30)

Exploratory
- Additional QOL (EORTC QLQ-C30)

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

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; **EORTC QLQ-C30**, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30; **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; **TNBC**, triple-negative breast cancer; **TTR**, time to response.

Patient-Reported Outcomes (EORTC QLQ-C30)

Key secondary end points

- Change from baseline in physical functioning at week 25
- Time to first deterioration[a] in fatigue

Exploratory end points

- Change from baseline at week 25 (excluding physical functioning)
- Time to first deterioration (excluding fatigue)[a]
- Time to confirmed deterioration[b]
- Time to first improvement[c]

PRO Assessment Schedule for EORTC QLQ-C30 (All Randomized Patients)

	Completion Rate (% of eligible patients)	
	SG (n = 279)	Chemo (n = 279)
Baseline	98	98
Week 13	86	88
Week 25	85	82

Baseline score

- Domain scores were similar between treatment groups and largely comparable to the general population norms
- Several domains tended to have worse scores (eg, physical functioning, role functioning, pain)

[a]TTD is defined as the time between randomization and the assessment at which a participant first experienced a worsening exceeding prespecified MWPC from baseline or death. [b]TTCD is defined as meaningful deterioration from baseline confirmed by a next scheduled visit or followed by missing PRO visit or death < 56 days after last PRO assessment or death < 56 days after randomization if baseline/post-baseline assessments were missing. [c]TTI is defined as the time between randomization and the assessment at which a participant first experienced an improvement exceeding prespecified MWPC from baseline. **Chemo**, chemotherapy; **EORTC QLQ-C30**, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30; **MWPC**, meaningful within patient change; **PRO**, patient-reported outcome; **SG**, sacituzumab govitecan; **TTCD**, time to confirmed deterioration; **TTD**, time to first deterioration; **TTI**, time to first improvement.

Mean Change From Baseline to Week 25 in Physical Functioning Favored SG vs Chemotherapy

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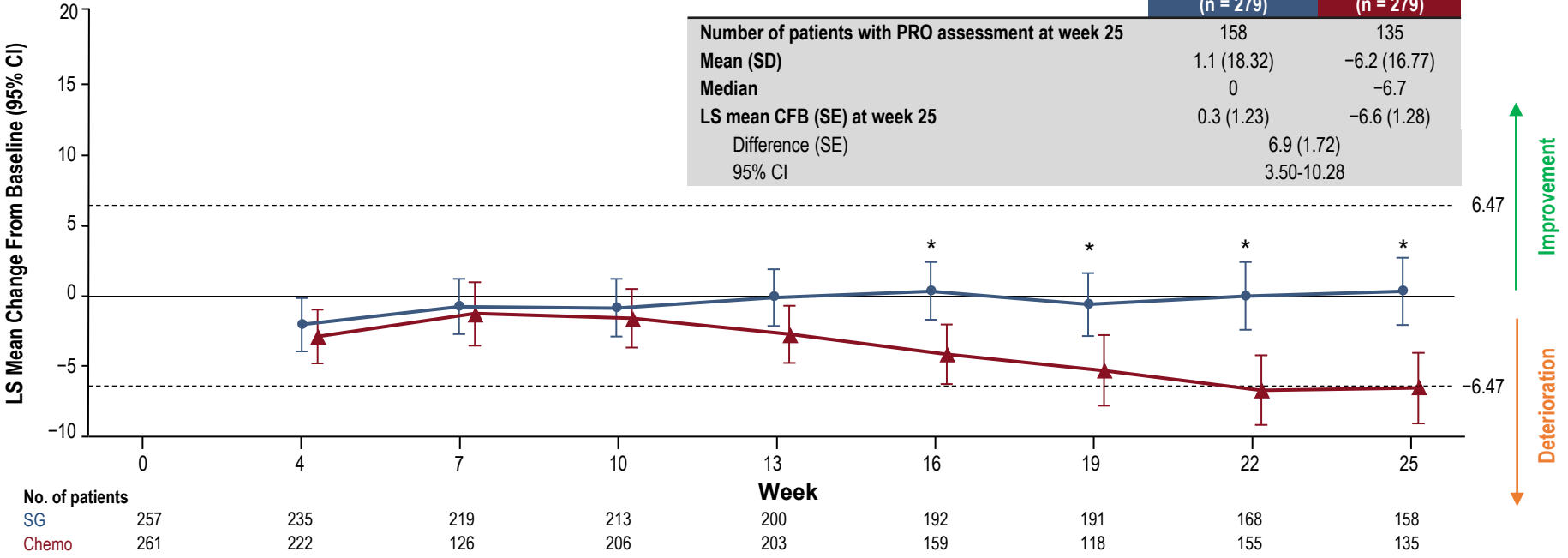
Physical functioning scores were maintained in the SG group; a gradual worsening was observed in the chemotherapy group over time

	SG (n = 279)	Chemo (n = 279)
Number of patients with PRO assessment at week 25	158	135
Mean (SD)	1.1 (18.32)	−6.2 (16.77)
Median	0	−6.7
LS mean CFB (SE) at week 25	0.3 (1.23)	−6.6 (1.28)
Difference (SE)	6.9 (1.72)	
95% CI	3.50-10.28	



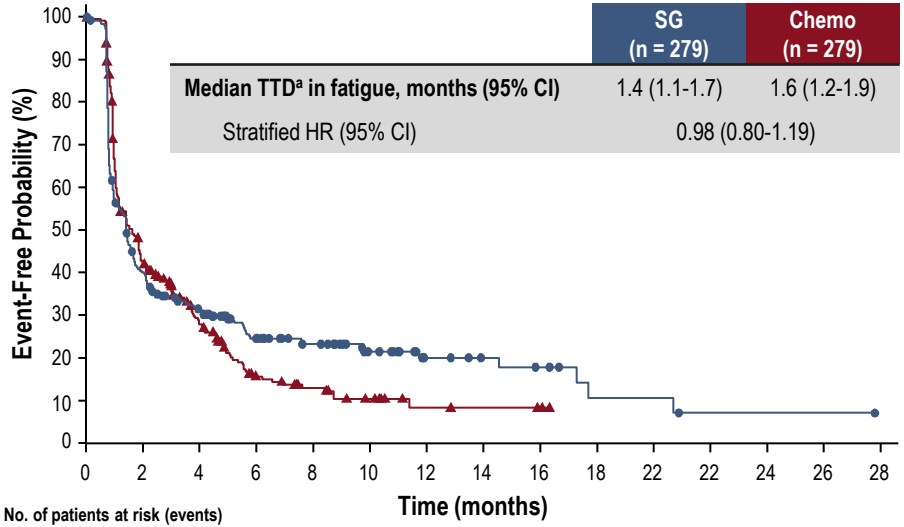
Comparison between treatment arms was analyzed using a mixed-effect model for repeated measure for CFB; an asterisk denote a nominal 2-sided *P*-value < 0.05. MID was defined as 0.3 × SD and corresponded to a change of ±6.47.
CFB, change from baseline; **chemo**, chemotherapy; **CI**, confidence interval; **LS**, least-squares; **MID**, minimum important difference; **MWPC**, meaningful within patient change; **PRO**, patient-reported outcome; **SD**, standard deviation; **SE**, standard error; **SG**, sacituzumab govitecan.

Time to Deterioration in Fatigue Was Similar Between SG and Chemotherapy

Similar results were observed between treatment groups and were consistent over 2 consecutive visits

Key Secondary End Point - TTD

	SG (n = 279)	Chemo (n = 279)
Median TTD[a] in fatigue, months (95% CI)	1.4 (1.1-1.7)	1.6 (1.2-1.9)
Stratified HR (95% CI)	0.98 (0.80-1.19)	

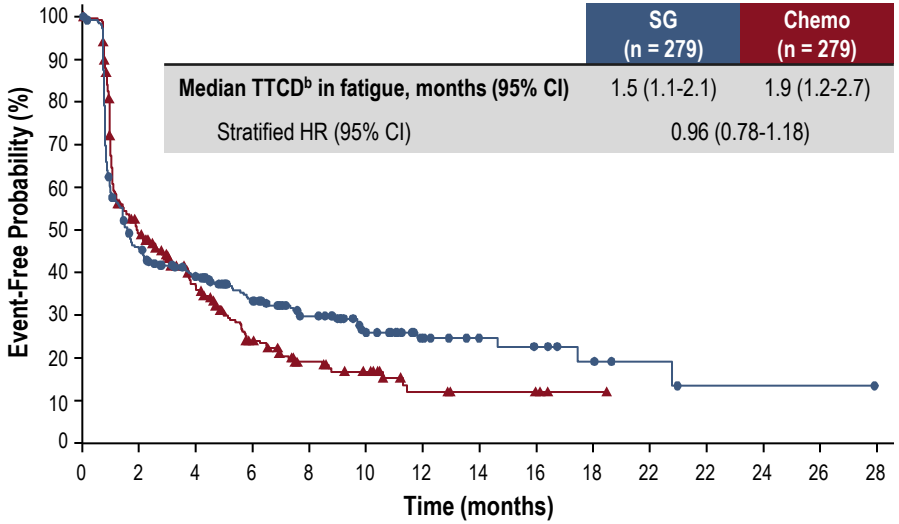


No. of patients at risk (events)

SG	279 (0)	101 (154)	72 (175)	47 (189)	35 (191)	22 (193)	12 (194)	9 (194)	7 (195)	3 (197)	3 (197)	1 (198)	1 (198)	1 (198)	0 (198)
Chemo	279 (0)	104 (144)	60 (175)	26 (200)	17 (204)	10 (207)	4 (208)	3 (208)	2 (208)	0 (208)					

Exploratory End Point - TTCD

	SG (n = 279)	Chemo (n = 279)
Median TTCD[b] in fatigue, months (95% CI)	1.5 (1.1-2.1)	1.9 (1.2-2.7)
Stratified HR (95% CI)	0.96 (0.78-1.18)	



279 (0)	112 (134)	86 (159)	63 (171)	45 (177)	27 (182)	16 (183)	11 (183)	8 (184)	5 (185)	3 (185)	1 (186)	1 (186)	1 (186)	0 (186)
279 (0)	116 (131)	75 (159)	39 (184)	23 (192)	15 (195)	6 (198)	4 (198)	3 (198)	1 (198)	0 (198)				

Comparison between treatment arms was analyzed using the stratified Cox regression model. [a]TTD is defined as the time between randomization and the assessment at which a participant first experienced a worsening exceeding prespecified MWPC of ≥10 points from baseline or death. [b]TTCD is defined as meaningful deterioration from baseline confirmed by a next scheduled visit or followed by missing PRO visit or death < 56 days after last PRO assessment or death < 56 days after randomization if baseline/post-baseline assessments were missing. **Chemo**, chemotherapy; **CI**, confidence interval; **HR**, hazard ratio; **MWPC**, meaningful within patient change; **PRO**, patient-reported outcome; **SG**, sacituzumab govitecan; **TTCD**, time to confirmed deterioration; **TTD**, time to first deterioration.

Mean Change From Baseline in EORTC QLQ-C30 Scores at Week 25

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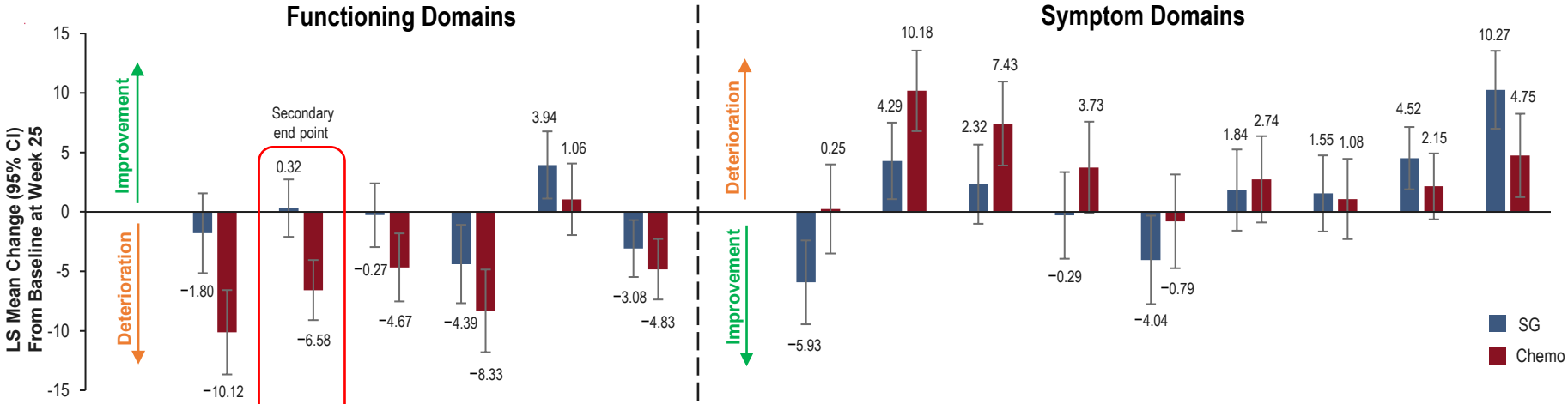
Change from baseline at week 25 favored SG for the secondary end point of physical functioning as well as for the exploratory end points of role functioning, global health status/QOL, fatigue, pain, and dyspnea; chemotherapy was favored for diarrhea



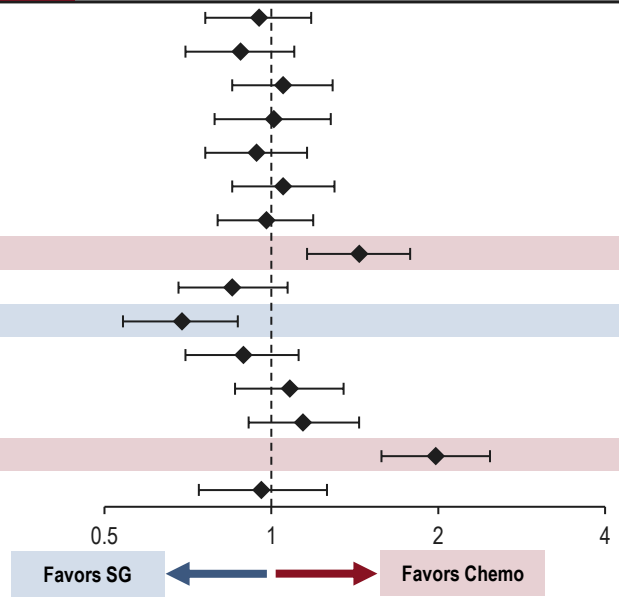
EORTC QLQ-C30 Domain	Role Functioning	Physical Functioning	GHS/QOL	Social Functioning	Emotional Functioning	Cognitive Functioning	Pain	Fatigue	Dyspnea	Appetite Loss	Insomnia	Constipation	Financial Difficulties	Nausea/ Vomiting	Diarrhea
Difference	**8.33***	**6.89***	**4.41**	3.94	2.89	1.74	**−6.18**	**−5.89**	**−5.11**	−4.03	−3.24	−0.90	0.47	2.38	**5.52**
95% CI	3.60 to 13.05	3.50 to 10.28	0.58 to 8.24	−0.70 to 8.58	−1.13 to 6.90	−1.64 to 5.13	−11.20 to −1.16	−10.43 to −1.35	−9.83 to −0.39	−9.20 to 1.14	−8.53 to 2.04	−5.72 to 3.92	−4.02 to 4.96	−1.36 to 6.11	0.84 to 10.20
MID	8.24	6.47	6.44	7.69	7.01	5.83	8.52	7.12	7.24	7.83	9.03	7.45	8.85	4.29	4.24

Comparison between treatment arms was analyzed using a mixed-effect model for repeated measure for changes from baseline. Favors SG if difference (95% CI) > 0 for GHS/QOL and functioning domains or difference (95% CI) < 0 for symptom domains (in bold and blue highlight). Favors chemotherapy if difference (95% CI) < 0 for GHS/QOL and functioning domains or difference (95% CI) > 0 for symptom domains (in bold and red highlight). An asterisk denotes a difference in LS mean exceeding the MID of 0.3 × SD. **Chemo**, chemotherapy; **CI**, confidence interval; **EORTC QLQ-C30**, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30; **GHS/QOL**, global health status/quality of life; **LS**, least-squares; **MID**, minimum important difference; **SD**, standard deviation; **SG**, sacituzumab govitecan.

Time to First Deterioration in EORTC QLQ-C30 Domains

Time to first deterioration was comparable across most domains, including for the secondary end point of fatigue, but favored SG for exploratory end points of dyspnea and chemotherapy for nausea/vomiting and diarrhea

ITT Population	Median (95% CI) TTD,[a] Months SG (n = 279)	Median (95% CI) TTD,[a] Months Chemo (n = 279)	HR (95% CI)[b,c]
Global health status/QOL	3.9 (2.2-5.4)	3.7 (2.8-4.5)	0.95 (0.76-1.18)
Physical functioning	5.3 (3.9-7.2)	3.8 (3.2-4.9)	0.88 (0.70-1.10)
Role functioning	1.6 (1.4-2.2)	2.6 (1.9-3.1)	1.05 (0.85-1.29)
Emotional functioning	7.3 (4.9-9.7)	7.3 (5.6-9.0)	1.01 (0.79-1.28)
Cognitive functioning	3.5 (2.8-4.6)	3.5 (2.8-3.8)	0.94 (0.76-1.16)
Social functioning	2.2 (1.6-3.1)	3.1 (2.0-4.1)	1.05 (0.85-1.30)
Fatigue (secondary end point)	1.4 (1.1-1.7)	1.6 (1.2-1.9)	0.98 (0.80-1.19)
Nausea/vomiting	**2.0 (1.6-2.8)**	**4.0 (2.8-5.8)**	**1.44 (1.16-1.78)**
Pain	5.2 (3.2-6.5)	3.0 (2.6-4.4)	0.85 (0.68-1.07)
Dyspnea	**10.0 (6.3-12.2)**	**4.8 (3.4-5.7)**	**0.69 (0.54-0.87)**
Insomnia	5.3 (4.0-7.6)	4.2 (3.4-5.6)	0.89 (0.70-1.12)
Appetite loss	4.0 (2.4-5.2)	4.6 (3.1-5.6)	1.08 (0.86-1.35)
Constipation	2.8 (2.1-3.7)	3.8 (2.9-5.3)	1.14 (0.91-1.44)
Diarrhea	**1.7 (1.4-2.2)**	**5.7 (4.7-8.4)**	**1.98 (1.58-2.48)**
Financial difficulties	8.5 (6.9-NR)	7.7 (5.0-11.5)	0.96 (0.74-1.26)

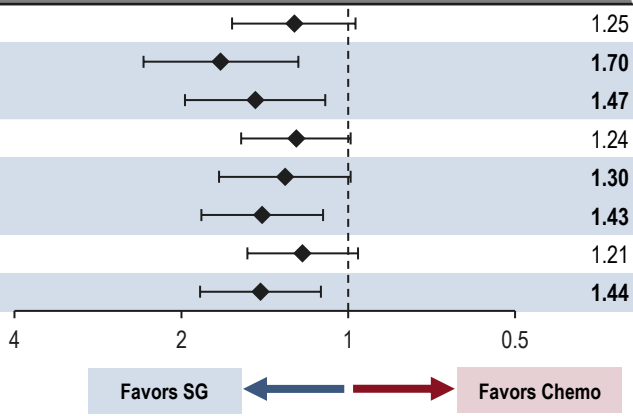


Comparison between treatment arms was analyzed using the stratified Cox regression model. [a]TTD is defined as the time between randomization and the assessment at which a participant first experienced a worsening exceeding the prespecified MWPC of ≥ 10 points (13.33 for physical functioning as scores change in 6.67 increments) from baseline or death. [b]Favors SG if HR < 1, and log-rank test nominal *P*-value < 0.05. Favors chemotherapy if HR > 1, and log-rank test nominal *P*-value < 0.05. [c]HR of the time to first meaningful deterioration in a given domain of the EORTC QLQ-C30 or death, or in the absence of premature treatment discontinuation due to any reason other than death, if occurring within 56 days of the last non-missing visit. **Chemo**, chemotherapy; **CI**, confidence interval; **EORTC QLQ-C30**, European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; **HR**, hazard ratio; **ITT**, intent-to-treat; **MWPC**, meaningful within patient change; **NR**, not reached; **QOL**, quality of life; **SG**, sacituzumab govitecan; **TTD**, time to first deterioration.

Time to First Improvement in EORTC QLQ-C30 Domains

Domains with >50% of patients eligible for improvement, time to first improvement was shorter with SG vs chemotherapy, suggesting patients starting with poor QOL can experience faster benefit with SG

ITT Population	Median (95% CI) TTI,[a] Months SG (n = 279)	Median (95% CI) TTI,[a] Months Chemo (n = 279)	HR (95% CI)[b,c]
Global health status/QOL	5.7 (3.0-NR)	NR (6.3-NR)	1.25 (0.97-1.62)
Physical functioning	**3.9 (2.5-9.9)**	**NR (19.6-NR)**	**1.70 (1.23-2.34)**
Role functioning	**1.7 (1.4-2.3)**	**2.1 (1.6-NR)**	**1.47 (1.10-1.97)**
Emotional functioning	1.5 (1.2-1.9)	2.1 (1.6-2.8)	1.24 (0.99-1.56)
Social functioning	**1.5 (1.4-2.1)**	**2.0 (1.5-3.7)**	**1.30 (0.99-1.71)**
Fatigue	**3.0 (1.8-5.3)**	**6.6 (3.1-NR)**	**1.43 (1.11-1.84)**
Pain	1.4 (1.0-1.5)	1.1 (1.0-1.8)	1.21 (0.96-1.52)
Insomnia	**1.4 (1.1-1.8)**	**1.9 (1.5-2.7)**	**1.44 (1.12-1.85)**



Patients eligible for improvement have baseline scores ≤ 90 for functional domains and ≥ 10 for symptom domains. Comparison between treatment arms was analyzed using the Fine-Gray subdistribution hazard regression model. [a]TTI is defined as the time between randomization and the assessment at which a participant first experienced an improvement exceeding the prespecified MWPC from baseline or death of ≥ 10 points. [b]Favors SG if HR > 1, and Gray's test nominal *P* value < 0.05. [c]HR of the time to first meaningful improvement in a given domain of the EORTC QLQ-C30 prior to premature treatment discontinuation due to any cause. **Chemo**, chemotherapy; **CI**, confidence interval; **EORTC QLQ-C30**, European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; **HR**, hazard ratio; **ITT**, intent-to-treat; **MWPC**, meaningful within patient change; **NR**, not reached; **QOL**, quality of life; **SG**, sacituzumab govitecan; **TTI**, time to first improvement.

Conclusion

In ASCENT-03, SG provided meaningful and sustained benefits in QOL vs chemotherapy; increased GI side effects with SG vs chemotherapy did not impact overall QOL. These data complement the clinically meaningful PFS to support SG as a potential new standard of care for patients with previously untreated advanced TNBC who are not candidates for PD-(L)1 inhibitors

- For key secondary end points, mean change from baseline in physical functioning favored SG vs chemotherapy; time to first deterioration in fatigue was similar between treatment groups

Physical Functioning

Scores were maintained in the SG group and deteriorated in the chemo group

- Exploratory analyses favored SG across multiple domains, including:
  - Change from baseline in global health status/QOL, role functioning, fatigue, pain, and dyspnea
  - TTD in dyspnea
  - TTI in physical, role, and social functioning, as well as fatigue and insomnia

Other Domains

Change from baseline and TTI in multiple domains favored SG

- Change from baseline and TTD in diarrhea and nausea/vomiting favored chemotherapy
- The gastrointestinal side effects of SG were consistent with the known safety profile of SG and can be managed by following established guidelines

GI Side Effects

Symptoms of diarrhea and nausea/vomiting were worse with SG vs chemo

Chemo, chemotherapy; **GI**, gastrointestinal; **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; **SG**, sacituzumab govitecan; **TNBC**, triple-negative breast cancer; **TTD**, time to first deterioration; **TTI,** time to first improvement.

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