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Trodelvy® (sacituzumab govitecan-hziy) Patient-Reported Outcomes in 1L PD-(L)1 Inhibitor–Ineligible mTNBC

This document is in response to your request for information regarding Trodelvy® (sacituzumab govitecan-hziy [SG]) and patient-reported outcomes (PROs) in first-line (1L) treatment of patients with locally advanced unresectable or metastatic triple-negative breast cancer (mTNBC) who are ineligible for programmed death-(ligand) 1 (PD-[L]1) inhibitors.

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Summary

Relevant Product Labeling[1]

SG, as a single agent, is indicated for the 1L treatment of adult patients with unresectable locally advanced or mTNBC who are not candidates for PD-(L)1 inhibitor based therapy.

PROs With SG Use in 1L PD-(L)1 Inhibitor-Ineligible mTNBC

ASCENT-03, an ongoing, global, open-label, randomized, phase 3 study, is comparing the efficacy and safety of SG vs chemotherapy TPC (eg, gem + carbo, paclitaxel, or nab-paclitaxel) as 1L treatment in patients (N=558) with previously untreated, locally advanced, inoperable or mTNBC who are not candidates for PD-(L)1 inhibitor therapy.[2]

PRO outcomes of the EORTC QLQ-C30 questionnaire were compared between the SG and TPC arms.[3]

- At BL, PRO scores for EORTC QLQ-C30 domains were generally comparable between treatment arms and general population norms.
- Key secondary endpoints from the EORTC QLQ-C30 were as follows[3]:
  - LSM change from BL in physical functioning domain at Week 25 (key secondary endpoint) was 1.1 in the SG arm and -6.2 in the TPC arm (LSM difference, 6.89; 95% CI: 3.5–10.28).
  - Median (95% CI) TTDs for the fatigue domain (key secondary endpoint) were similar between treatment arms: SG, 1.4 (1.1–1.7); TPC, 1.6 (1.2–1.9); stratified HR, 0.98 (95% CI: 0.8–1.19).
- Exploratory endpoints from the EORTC QLQ-C30 were as follows[3]:
  - The LSM change from BL to Week 25 favored SG vs TPC in scores for several domains, including role functioning (-1.8 vs -10.12, respectively), GHS/QoL (-0.27 vs -4.67), pain (-5.93 vs 0.25), fatigue (4.29 vs 10.18), and dyspnea (2.32 vs 7.43),

and the change from BL to Week 25 for the diarrhea domain favored TPC vs SG (10.27 vs 4.75, respectively).

- The median TTD for the dyspnea domain favored SG vs TPC (HR, 0.69; 95% CI: 0.54–0.87) and the TTDs for nausea/vomiting (HR, 1.44; 95% CI: 1.16–1.78) and diarrhea (HR, 1.87; 95% CI: 1.58–2.48) domains favored TPC vs SG.
- Mean (95% CI) TTCDs for the fatigue domain were similar between treatment arms: SG, 1.5 (1.1–2.1); TPC, 1.9 (1.2–2.7); stratified HR, 0.96 (95% CI: 0.78–1.18).
- Among domains where >50% of patients were eligible for improvement, TTIs (HR; 95% CI) were shorter with SG than with TPC for the following domains, including physical functioning (1.7; 1.23–2.34); role functioning (1.47; 1.1–1.97); social functioning (1.3; 0.99–1.71); fatigue (1.43; 1.11–1.84); and insomnia (1.44; 1.12–1.85). These findings suggested that patients who had poor QoL at BL could experience a faster benefit with SG than with TPC.

PROs With SG Use in 1L PD-(L)1 Inhibitor-Ineligible mTNBC

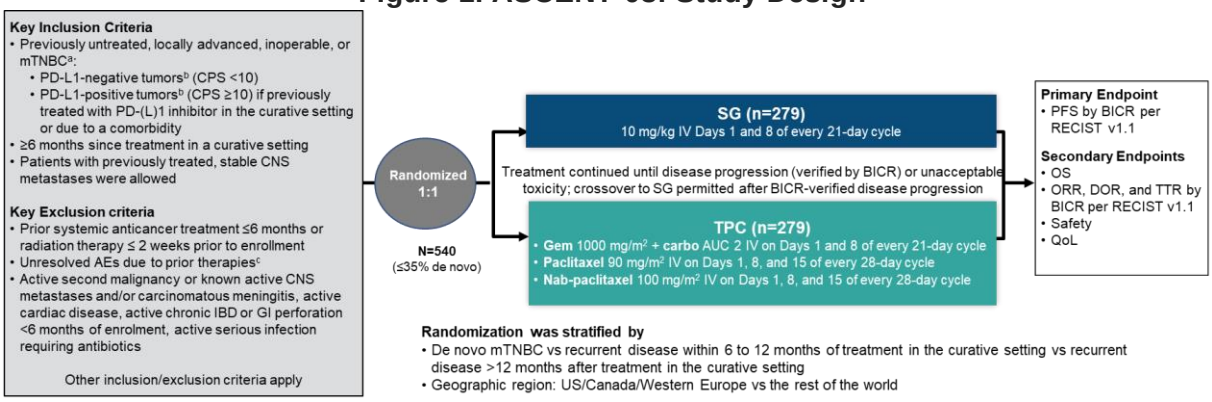
ASCENT-03 Study

Study design and demographics

ASCENT-03, an ongoing, global, open-label, randomized, phase 3 study, is comparing the efficacy and safety of SG vs TPC as 1L treatment in patients (N=558) with previously untreated, locally advanced, inoperable or mTNBC who were ineligible for PD-(L)1 inhibitor therapy (Figure 1).[2]

The study enrolled patients whose tumors did not express PD-L1 (PD-L1 negative tumors [CPS <10]) and patients who did express PD-L1 (PD-L1 positive tumors [CPS ≥10]) if they received prior PD-(L)1 inhibitor therapy in the (neo)adjuvant setting or had a comorbidity preventing treatment with a PD-(L)1 inhibitor (see Table 1 for further BL demographics and disease characteristics). Patients must have had ≥6 mo between the completion of curative intent systemic treatment in the (neo)adjuvant setting and first documented local or distant disease recurrence. The primary endpoint is PFS by BICR per RECIST v1.1.[2]

Figure 1. ASCENT-03: Study Design[2,4,5]



Abbreviations: AE=adverse event; CNS=central nervous system; DOR=duration of response; GI=gastrointestinal; IBD=inflammatory bowel disease; IHC=immunohistochemistry; TNBC=triple-negative breast cancer; TTR=time to response.

[a]Centrally confirmed and determined according to American Society of Clinical Oncology-College of American Pathologists criteria. [b]PD-L1 (IHC 22C3 assay) and TNBC status centrally confirmed. [c]Any-grade neuropathy and alopecia were allowed.

PRO outcomes

In the statistical testing hierarchy, OS will be formally tested for significance once PFS is statistically significant, followed by ORR, and QoL endpoints (once the prior endpoint in the hierarchy was significant).[4]

Specifically, key secondary PRO endpoints using the EORTC QLQ-C30 included the change from BL to Week 25 in the physical functioning domain and TTD in the fatigue domain. TTD was defined as the duration of time between treatment randomization and the study assessment at which the patient noted the first worsening that was exceeding prespecified MWPC from BL or death.[3]

Exploratory endpoints included the following[3]:

- Change from BL to Week 25 in EORTC QLQ-C30 domains other than physical functioning;
- TTD in domains except for fatigue;
- TTCD, which was defined as a meaningful deterioration from BL that was confirmed at the next study visit or was followed by a missing visit that assessed PROs or death that occurred <56 days after the last PRO assessment (or death that occurred <56 days post-randomization if the BL/post-BL assessments were missing);
- TTI, which was defined as the duration of time between treatment randomization and the first assessment at which the patient had an improvement that was exceeding prespecified MWPC from BL.

The assessment schedule for PROs was BL and Day 1 of all cycles until the end of treatment. At BL, PRO scores for EORTC QLQ-C30 domains were generally comparable between treatment arms and with general population norms; however, the physical functioning, role functioning, and pain domains generally had worse scores.[3]

EORTC QLQ-C30: physical functioning and fatigue domains (key secondary endpoints)[3]

Physical functioning domain scores were relatively stable through Week 25 for the SG arm (n=158; mean [SD] change from BL, 1.1 [18.32]) and tended to worsen in the TPC arm (n=135; mean [SD] change from BL, -6.2 [16.77]). The LSM changes from baseline to Week 25 by treatment arm were as follows: SG, 0.32; TPC, -6.58; LSM difference [SE], 6.89 [1.72] (95% CI: 3.5–10.28; Table 1). The MID for this domain was 6.47, with positive values indicating an improvement and negative values indicating a deterioration. The LSM changes from baseline were nominally different between groups beginning at Week 16 and continued through Week 25 (each, $P<0.05$).

The median (95% CI) TTDs for the fatigue domain were similar between treatment arms: SG, 1.4 (1.1–1.7); TPC, 1.6 (1.2–1.9); stratified HR, 0.98 (95% CI: 0.8–1.19). The MWPC prespecified threshold was a worsening from BL by ≥10 points or death.

EORTC QLQ-C30: change from BL to Week 25 in all (exploratory endpoint)[3]

The LSM change from BL to Week 25 in scores for several domains, including role functioning, GHS/QoL, pain, fatigue, and dyspnea, favored SG vs TPC, and the change from BL to Week 25 for the diarrhea domain favored TPC vs SG (Table 1).

Table 1. ASCENT-03: Mean Change From BL in EORTC QLQ-C30 Scores at Week 25[3]

EORTC QLQ-C30 Domain	LSM Change From BL to Week 25		Difference (95% CI)	MID
	SG	TPC		
Functioning domains				
Physical functioning (secondary endpoint)	0.32	-6.58	**6.89 (3.5–10.28)[a,b]**	6.47
Role functioning	-1.8	-10.12	**8.33 (3.6–13.05)[a,b]**	8.24
Social functioning	-4.39	-8.33	3.94 (-0.7 to 8.58)	7.69
Emotional functioning	3.94	1.06	2.89 (-1.13 to 6.9)	7.01
Cognitive functioning	-3.08	-4.83	1.74 (-1.64 to 5.13)	5.83
GHS/QoL	-0.27	-4.67	4.41 (0.58–8.24)[a]	6.44
Symptom domain				
Pain	-5.93	0.25	-6.18 (-11.2 to -1.16)[a]	8.52
Fatigue	4.29	10.18	-5.89 (-10.43 to -1.35)[a]	7.12
Dyspnea	2.32	7.43	-5.11 (-9.83 to -0.39)[a]	7.24
Appetite loss	-0.29	3.73	-4.03 (-9.2 to 1.14)	7.83
Insomnia	-4.04	-0.79	-3.24 (-8.53 to 2.04)	9.03
Constipation	1.84	2.74	-0.9 (-5.72 to 3.92)	7.45
Financial difficulties	1.55	1.08	0.47 (-4.02 to 4.96)	8.85
Nausea/vomiting	4.52	2.15	2.38 (-1.36 to 6.11)	4.29
Diarrhea	10.27	4.75	5.52 (0.84–10.2)[c]	4.24

[a]Cells shaded in light blue denote those where SG treatment was favored vs TPC: if difference (95% CI) was >0 for GHS/QoL and functioning domains or if difference (95% CI) was <0 for symptom domains.
[b]Bolded cells indicate those whose LSM difference was >MID of 0.3 × SD.
[c]Cells shaded in light teal denote those where TPC treatment was favored vs SG: if difference (95% CI) was <0 for GHS/QoL and functioning domains or if difference (95% CI) was >0 for symptom domains.

EORTC QLQ-C30: TTD in all domains (exploratory endpoint)[3]

The TTDs for most domains were generally similar between treatment arms, including for the fatigue domain; however, the TTD for the dyspnea domain favored SG vs TPC, and the TTDs for the nausea/vomiting and diarrhea domains favored TPC vs SG (Table 2).

Table 2. ASCENT-03: TTD in EORTC QLQ-C30 Domains[3]

EORTC QLQ-C30 Domain	TTD,[a] Median (95% CI), Months		HR (95% CI)[b]
	SG (n=279)	TPC (n=279)	
Functioning domains			
GHS/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 (0.7–1.1)
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)	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 (2–4.1)	1.05 (0.85–1.3)
Fatigue (secondary endpoint)	1.4 (1.1–1.7)	1.6 (1.2–1.9)	0.98 (0.8–1.19)
Symptom domains			
Nausea/vomiting	2 (1.6–2.8)	4 (2.8–5.8)	1.44 (1.16–1.78)[c]
Pain	5.2 (3.2–6.5)	3 (2.6–4.4)	0.85 (0.68–1.07)
Dyspnea	10 (6.3–12.2)	4.8 (3.4–5.7)	0.69 (0.54–0.87)[d]
Insomnia	5.3 (4–7.6)	4.2 (3.4–5.6)	0.89 (0.7–1.12)
Appetite loss	4 (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)[c]
Financial difficulties	8.5 (6.9–NR)	7.7 (5–11.5)	0.96 (0.74–1.26)

[a]TTD was defined as the duration of time between treatment randomization and the study assessment at which the patient first had a worsening in the assessment that exceeded the prespecified MPWC of ≥10 points

(13.33 for the physical functioning domain, as this domain's scores increased in 6.67-point increments) from BL or death.
[b]The HR for the time to first meaningful deterioration for a domain or death, or without premature discontinuation due to a reason other than death, if it occurred <56 d from the last attended study visit.
[c]Cells shaded in light teal denote domains that favored TPC (HR >1 and log-rank nominal *P*<0.05).
[d]Cells shaded in light blue denote domains that favored SG (HR <1 and log-rank nominal *P*<0.05).

EORTC QLQ-C30: TTCD[3]

The median (95% CI) TTCDs for the fatigue domain were similar between treatment arms: SG, 1.5 (1.1–2.1); TPC, 1.9 (1.2–2.7); stratified HR, 0.96 (95% CI: 0.78–1.18).

EORTC QLQ-C30: TTI[3]

Several domains had TTIs that were shorter with SG than with TPC among domains where >50% of patients were eligible for improvement (defined as patients with BL scores ≤90 for functional domains and ≥10 for symptom domains), which suggested that patients who had poor QoL at BL could experience a faster benefit with SG than with TPC (Table 3).

Table 3. ASCENT-03: TTI in EORTC QLQ-C30 Domains With >50% of Patients Eligible for Improvement[3]

EORTC QLQ-C30 Domain	TTI,[a] Median (95% CI), Months		HR (95% CI)[b,c]
	SG (n=279)	TPC (n=279)	
GHS/QoL	5.7 (3–NR)	NR (6.3–NR)	1.25 (0.97–1.62)
Physical functioning	3.9 (2.5–9.9)	NR (19.6–NR)	1.7 (1.23–2.34)
Role functioning	1.7 (1.4–2.3)	2.1 (1.6–NR)	1.47 (1.1–1.97)
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 (1.5–3.7)	1.3 (0.9–1.71)
Fatigue	3 (1.8–5.3)	6.6 (3.1–NR)	1.43 (1.11–1.84)
Pain	1.4 (1–1.5)	1.1 (1–1.8)	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)

[a]Defined as the duration of time between treatment randomization and the time that a patient first had an improvement from BL that exceeded the prespecified MWPC by ≥10 points or death.
[b]HR >1 and Gray's test nominal P<0.05 favored SG vs TPC. Rows shaded in light blue denote domains favored SG vs TPC.
[c]Referred to the HR for the TTI in a domain prior to a premature discontinuation of treatment due to any cause.
Note: Eligible patients had BL scores ≤90 for functional domains and ≥10 for symptom domains.

References

1. TRODELVY® Gilead Sciences Inc. Trodelvy (sacituzumab govitecan-hziy) for injection, for intravenous use. U.S. Prescribing Information. Foster City, CA.
2. Cortés J, Punie K, Barrios C, et al. Sacituzumab govitecan in untreated, advanced triple-negative breast cancer. *N Engl J Med.* 2025;393(19):1912-1925.
3. Punie K, Tolaney S, Bardia A, et al. 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 [Oral RF6-05]. San Antonio Breast Cancer Symposium (SABCS); December 9-12, 2025; San Antonio, TX.
4. Cortés J, Punie K, Barrios C, et al. Sacituzumab govitecan in untreated, advanced triple-negative breast cancer [Supplementary Appendix]. *N Engl J Med.* 2025;393(19):1912-1925.
5. Cortés J, Bardia A, Punie K, et al. 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 [Oral LBA20]. Presented at: European Society For Medical Oncology (ESMO) Congress; 17-21 October, 2025; Berlin, Germany.

Abbreviations

1L=first line
BICR=blinded independent central review
BL=baseline
carbo=carboplatin
CPS=combined positive score
EORTC QLQ-C30=European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire-Core 30
gem=gemcitabine
GHS=Global Health Status
HR=hazard ratio
LSM=least squares mean
MID=minimum important difference
MWPC=meaningful within patient change
mTNBC=metastatic triple-negative breast cancer
NR=not reached
ORR=objective response rate
OS=overall survival
PD-(L)1=programmed death (ligand) 1
PFS=progression-free survival
QoL=quality of life
RECIST v1.1=Response Evaluation Criteria in Solid Tumors version 1.1
PRO=patient-reported outcome
SG=sacituzumab govitecan-hziy
TPC=treatment of physicians' choice
TTCD=time to confirmed deterioration
TTD=time to first deterioration
TTI=time to first improvement

Product Label

For the full indication, important safety information, and boxed warning(s), please refer to the Trodelvy US Prescribing Information available at: www.gilead.com/-/media/files/pdfs/medicines/oncology/trodelvy/trodelvy_pi.

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