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Trodelvy® (sacituzumab govitecan-hziy) Use in 1L PD-(L)1 Inhibitor-Ineligible mTNBC: Efficacy by Trop-2 Status

This document is in response to your request for information regarding Trodelvy® (sacituzumab govitecan-hziy [SG]) and its efficacy by trophoblast cell-surface antigen 2 (Trop-2) status in first-line (1L) treatment in 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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The full indication, important safety information, and boxed warnings for neutropenia and diarrhea are available at: www.gilead.com/-/media/files/pdfs/medicines/oncology/trodelvy/trodelvy_pi.

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.

SG is a Trop-2-directed antibody-drug conjugate. Sacituzumab is a humanized antibody that recognizes Trop-2. The small molecule, SN-38, is a topoisomerase I inhibitor, which is covalently attached to the antibody by a linker. Pharmacology data suggest that SG binds to Trop-2-expressing cancer cells and is internalized with the subsequent release of SN-38 via hydrolysis of the linker. SN-38 interacts with topoisomerase I and prevents re-ligation of topoisomerase I-induced single strand breaks. The resulting DNA damage leads to apoptosis and cell death.

Clinical Data on SG Efficacy by Trop-2 Status in 1L PD-(L)1 Inhibitor-Ineligible mTNBC

ASCENT-03, an ongoing, global, open-label, randomized, phase 3 study, compares the efficacy and safety of SG vs treatment of physicians' choice (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.[2] A prespecified exploratory analysis evaluated the impact of Trop-2 expression on progression-free survival (PFS) for SG vs TPC.[3]

- Median PFS (mPFS) results in the Trop-2 biomarker analysis set (BAS) were consistent with those in the ITT population.[2,3]
  - In the ITT population, mPFS (95% CI) for SG and TPC groups were as follows: 9.7 (8.1–11.1) mo and 6.9 (5.6–8.2) mo, respectively (hazard ratio [HR], 0.62; 95% CI: 0.5–0.77; *P*<0.001).
  - In the Trop-2 BAS, mPFS (95% CI) for SG and TPC groups were as follows: 9.7 (7.8–11.1) mo and 6.8 (5.4–8.1) mo, respectively (HR, 0.64; 95% CI: 0.51–0.8).

- mPFS was longer with SG than with TPC across Trop-2 histochemical score (H-score) quartile (Q) subgroups. mPFS (95% CI) in the SG and TPC Trop-2 subgroups were as follows[3]:
  - Q1 subgroup (H-score, 0–184), 8.5 (5.6–12.7) mo vs 5.5 (4.2–8.1) mo, respectively (HR, 0.54; 95% CI: 0.35–0.84);
  - Q2 subgroup (H-score, 185–239), 8.3 (5.6–12.4) mo vs 6.8 (4.2–9) mo (HR, 0.62; 95% CI: 0.4–0.97);
  - Q3 subgroup (H-score, 240–283), 9.7 (7.6–11.3) mo vs 7 (5.3–8.5) mo (HR, 0.84; 95% CI: 0.54–1.31);
  - Q4 subgroup (H-score, 284–300), 9.9 (6.9–not estimable [NE]) mo vs 8.1 (4.4–8.5) mo (HR, 0.6; 95% CI: 0.38–0.95).

Clinical Data on SG Efficacy by Trop-2 Status in 1L PD-(L)1 Inhibitor-Ineligible mTNBC

ASCENT-03 Study

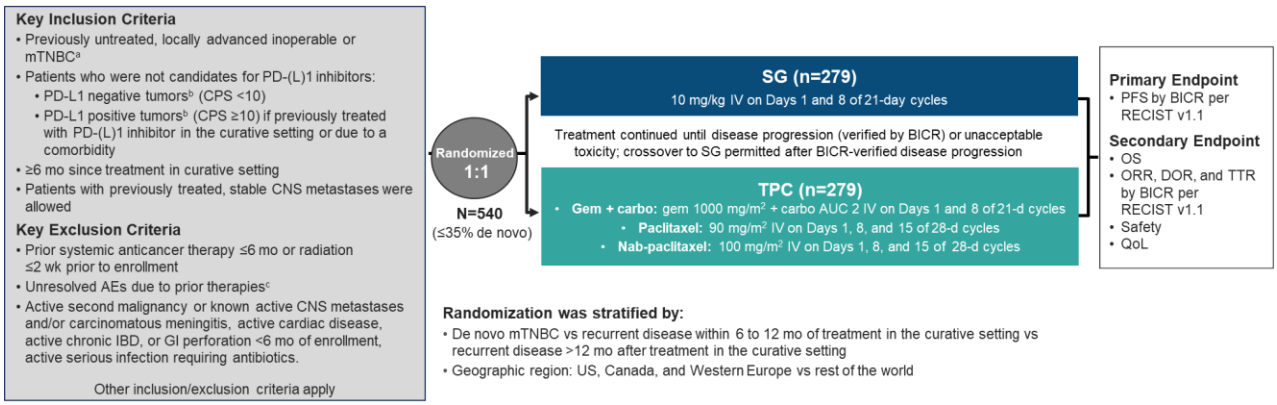
Study design and demographics

ASCENT-03, an ongoing, global, open-label, randomized, phase 3 study, compares 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, combined positive score [CPS] <10) and patients whose tumors 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 baseline 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 blinded independent central review (BICR) per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1.[2]

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



Abbreviations: AUC=area under the concentration-time curve; carbo=carboplatin; CNS=central nervous system; gem=gemcitabine; GI=gastrointestinal; IBD=inflammatory bowel disease; ORR=objective response rate; OS=overall survival; QOL=quality of life; TTR=time to onset of response.
[a]Centrally confirmed and determined according to American Society of Clinical Oncology-College of American Pathologists criteria.
[b]PD-L1 (immunohistochemistry [IHC] 22C3 assay) and triple-negative breast cancer status centrally confirmed.
[c]Any-grade neuropathy and alopecia were allowed.

Table 1. ASCENT-03: Baseline Demographics and Disease Characteristics[2]

Select Demographics and Characteristics		SG (n=279)	TPC (n=279)
Age, median (range), y		56 (28-84)	54 (23-86)
Age ≥65, n (%)		65 (23)	78 (28)
Sex, n (%)	Female	278 (>99)	277 (99)
Race or ethnic group,[a] n (%)	White/Asian/Black	178 (64)/66 (24)/10 (4)	178 (64)/65 (23)/7 (3)
	Other or not specified	25 (9)	29 (10)
Geographic region,[b] n (%)	US/Canada/Western Europe	89 (32)	89 (32)
	Rest of the world	190 (68)	190 (68)
ECOG PS, n (%)	0/1	183 (66)/96 (34)	187 (67)/92 (33)
PD-L1 negative status,[c] n (%)		277 (99)	278 (>99)
Disease status,[d] n (%)	Metastatic at initial diagnosis	87 (31)	88 (32)
	Recurrent within 6–12 mo[e]	58 (21)	57 (20)
	Recurrent >12 mo[e]	134 (48)	134 (48)
Metastatic sites, n (%)	Lymph node	179 (64)	180 (65)
	Lung	166 (59)	170 (61)
	Bone	95 (34)	87 (31)
	Liver	81 (29)	72 (26)
	Brain	15 (5)	14 (5)
	Other	98 (35)	84 (30)
Prior (neo)adjuvant therapies, n (%)	Taxane	162 (58)	162 (58)
	Platinum agents	51 (18)	49 (18)
	Capecitabine	50 (18)	57 (20)
	PD-(L)1 inhibitors	13 (5)	11 (4)

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Select Demographics and Characteristics	SG (n=279)	TPC (n=279)
Time since diagnosis of metastatic or LA unresectable disease to randomization, median (range), mo	1.9 (0.4–26.7)	1.9 (0.1–18.9)

Abbreviations: ECOG PS=Eastern Cooperative Oncology Group Performance Status; LA=locally advanced.
[a]Patient reported.
[b]Western Europe: Austria, Belgium, France, Germany, Italy, Netherlands, Spain, Switzerland, and UK. Rest of the world: Argentina, Australia, Brazil, Chile, China, Czech Republic, Hong Kong, Hungary, Israel, Japan, Malaysia, Mexico, Poland, Romania, Slovakia, South Africa, South Korea, Taiwan, and Turkey.
[c]PD-L1 status assessed using the PD-L1 IHC 22C3 assay (Dako, Agilent Technologies) at the time of enrollment; 1 patient in each treatment arm was considered PD-L1 positive. One patient in the SG arm had a PD-L1 CPS missing.
[d]From completion of treatment in the curative setting.
[e]Corresponding numbers: SG: 86 de novo, 59 recurrent disease within 6 to 12 mo, 134 recurrent disease >12 mo; TPC: 83 de novo, 62 recurrent disease within 6 to 12 mo, 134 recurrent disease in >12 mo.

Efficacy by Trop-2 status

A prespecified exploratory analysis evaluated PFS (per BICR) by biomarker subgroups (via central testing) within the BAS (defined as patients who received ≥1 dose of study treatment and had ≥1 post-baseline biomarker assessment). Trop-2 expression was evaluated by H-score per IHC: 0, negative or no staining of tumor cells; 1, weak or faint staining; 2, moderate staining; 3, strong staining. Evaluation was performed according to Trop-2 expression quartile. At the primary data cutoff, the median (range) follow-up was 13.2 (<0.1–29.2) mo.[3]

In the ITT population, 349 PFS events were observed at the time of the primary analysis. SG significantly improved mPFS vs TPC, with a 38% reduction in the risk of disease progression or death (Table 2).[2]

PFS results in the Trop-2 BAS were consistent with those in the ITT population (Table 2). According to Trop-2 H-score subgroups, mPFS was longer with SG than with TPC. Higher Trop-2 levels were not associated with increased efficacy. Results should be interpreted with caution due to the small sample size and the descriptive nature of the analysis.[3]

Table 2. ASCENT-03 Subgroup Analysis: mPFS in ITT Population (Primary Endpoint; BICR) and in Trop-2 Overall BAS and by H-Score Subgroups[2,3]

Study Population		SG			TPC			HR (95% CI)
		n	Events	mPFS (95% CI), Mo	n	Events	mPFS (95% CI), Mo	
ITT population		279	161	9.7 (8.1–11.1)	279	188	6.9 (5.6–8.2)	0.62 (0.5–0.77)[a]; *P*<0.001
Trop-2 BAS		252	–	9.7 (7.8–11.1)	247	–	6.8 (5.4–8.1)	0.64 (0.51–0.8)
Trop-2 H-score subgroups	Q1 (0–184)	68	39	8.5 (5.6–12.7)	55	43	5.5 (4.2–8.1)	0.54 (0.35–0.84)
	Q2 (185–239)	60	37	8.3 (5.6–12.4)	62	43	6.8 (4.2–9)	0.62 (0.4–0.97)
	Q3 (240–283)	50	35	9.7 (7.6–11.3)	74	48	7 (5.3–8.5)	0.84 (0.54–1.31)
	Q4 (284–300)	74	35	9.9 (6.9–NE)	56	37	8.1 (4.4–8.5)	0.6 (0.38–0.95)

[a]Stratified HR.
Note: An HR <1 indicated treatment with SG was favorable to TPC.

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. Barrios C, Hurvitz S, Tolaney S, et al. ASCENT-03: efficacy by biomarker subgroup with sacituzumab govitecan vs chemotherapy in participants with previously untreated advanced triple-negative breast cancer who are not candidates for PD-(L)1 inhibitors [Oral Presentation]. Presented at: American Society of Clinical Oncology (ASCO) Annual Meeting; May 26-June 2, 2026; Chicago, IL.
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.

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.

Follow-Up

For any additional questions, please contact Trodelvy Medical Information at:

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