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Trodelvy® (sacituzumab govitecan-hziy) Use in 1L PD-(L)1 Inhibitor-Ineligible mTNBC: Efficacy by HER2 Status

This document is in response to your request for information regarding Trodelvy® (sacituzumab govitecan-hziy [SG]) and its efficacy by human epidermal growth factor receptor 2 (HER2) 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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Trodelvy is not indicated for use as 1L treatment in patients with PD-(L)1 inhibitor-ineligible mTNBC. 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

Clinical Data on SG Efficacy by HER2 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.[1] A prespecified exploratory analysis evaluated the impact of HER2 expression on progression-free survival (PFS) for SG vs TPC.[2]

- Median PFS (mPFS) results in the HER2 biomarker analysis set (BAS) were consistent with those in the ITT population.[1,2]
  - 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 HER2 BAS, mPFS (95% CI) for SG and TPC groups were as follows: 9.7 (8–11.1) mo and 6.9 (5.6–8.2) mo, respectively (HR, 0.67; 95% CI: 0.54–0.83).
- mPFS was longer with SG than with TPC across HER2 subgroups. mPFS (95% CI) in the SG and TPC HER2 subgroups were as follows:[2]
  - HER2 immunohistochemistry 0 (IHC 0) subgroup, 8.3 (6.9–10.3) mo vs 5.6 (4.3–7) mo, respectively (HR, 0.63; 95% CI: 0.46–0.85);
  - HER2-low subgroup, 9.8 (8.3–12.4) mo vs 8.3 (5.7–9.7) mo (HR, 0.74; 95% CI: 0.55–1.01).

Clinical Data on SG Efficacy by HER2 Status in 1L PD-(L)1 Inhibitor-Ineligible mTNBC

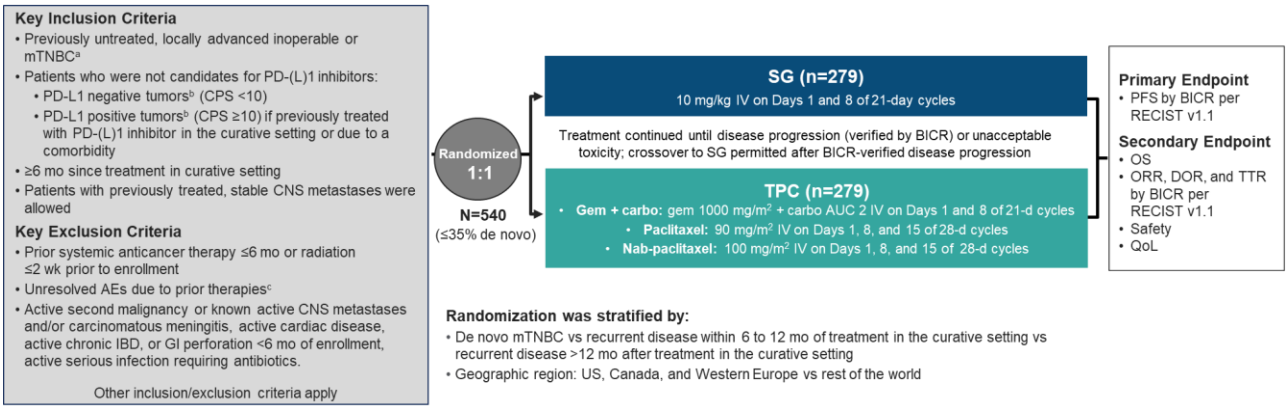
ASCENT-03 Study

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).[1]

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.[1]

Figure 1. ASCENT-03: Study Design[1,3,4]



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 (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[1]

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)

Select Demographics and Characteristics		SG (n=279)	TPC (n=279)
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 in >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)
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 missing PD-L1 CPS.
[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 HER2 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). HER2 expression was evaluated per in situ hybridization (ISH) and IHC; patients were categorized as HER2 IHC 0 or HER2-low, which included IHC 1+ or IHC 2+/ISH-. At the primary data cutoff, the median (range) follow-up was 13.2 (<0.1–29.2) mo.[2]

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).[1]

PFS results in the HER2 BAS were consistent with those in the ITT population (Table 2). Among the HER2 subgroups, mPFS was longer with SG than with TPC. Results should be interpreted with caution due to the small sample size and the descriptive nature of the analysis.[2]

Table 2. ASCENT-03 Subgroup Analysis: mPFS in the ITT Population (Primary Endpoint; BICR) and in the HER2 BAS Overall and by Subgroup[1,2]

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
HER2 BAS		274	–	9.7 (8–11.1)	277	–	6.9 (5.6–8.2)	0.67 (0.54–0.83)
HER2 subgroups	HER2 IHC 0	115	75	8.3 (6.9–10.3)	138	103	5.6 (4.3–7)	0.63 (0.46–0.85)
	HER2-low	159	85	9.8 (8.3–12.4)	139	83	8.3 (5.7–9.7)	0.74 (0.55–1.01)

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

References

1. 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.
2. 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.
3. 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.
4. 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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FDA MedWatch Program by ☎ 1-800-FDA-1088 or ✉MedWatch, FDA, 5600 Fishers Ln, Rockville, MD 20852 or 🖱 www.accessdata.fda.gov/scripts/medwatch

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