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Trodelvy® (sacituzumab govitecan-hziy) Use in Combination With Pembrolizumab 1L in Patients With PD-L1+ mTNBC: Efficacy by *BRCA* Status

This document is in response to your request for information regarding Trodelvy® (sacituzumab govitecan-hziy [SG]) and its use in combination with pembrolizumab (pembro) as first-line (1L) treatment in patients with programmed death-ligand 1 positive (PD-L1+) metastatic triple-negative breast cancer (mTNBC) and efficacy by tumor *breast cancer gene* (t*BRCA*) status.

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Trodelvy is not indicated for use as 1L treatment in patients with PD-L1+ 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 + Pembro Efficacy by *BRCA* Status in 1L PD-L1+ mTNBC

ASCENT-04 is an ongoing, global, open-label, randomized, phase 3 study in SG + pembro (n=221) vs treatment of physician's choice (TPC) + pembro (n=222) as 1L treatment in patients with PD-L1+, inoperable, locally advanced or mTNBC. A prespecified retrospective exploratory analysis evaluated the impact of t*BRCA* on the efficacy of SG + pembro vs TPC + pembro.[1,2]

- Median progression-free survival (mPFS) results in the t*BRCA* 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: 11.2 (9.3–16.7) mo and 7.8 (7.3–9.3) mo, respectively (hazard ratio [HR], 0.65; 95% CI: 0.51–0.84; *P*<0.001).
  - In the t*BRCA* BAS, mPFS (95% CI) for SG and TPC groups were as follows: 11.1 (9.2–16.7) mo vs 7.8 (7.2–9.3) mo (HR, 0.69; 95% CI: 0.52–0.91).
- mPFS was longer with SG + pembro than with TPC + pembro in both t*BRCA* subgroups. mPFS (95% CI) in the SG and TPC t*BRCA* subgroups were as follows[2]:
  - Wild type (WT) t*BRCA* subgroup, 9.6 (7.6–16.7) mo vs 7.4 (6.9–9.2) mo, respectively (HR, 0.67; 95% CI: 0.49–0.91);
  - Mutation t*BRCA* subgroup, 16.6 (7.5–not estimable [NE]) mo vs 12.9 (7.1–NE) mo (HR, 0.88; 95% CI: 0.45–1.74).

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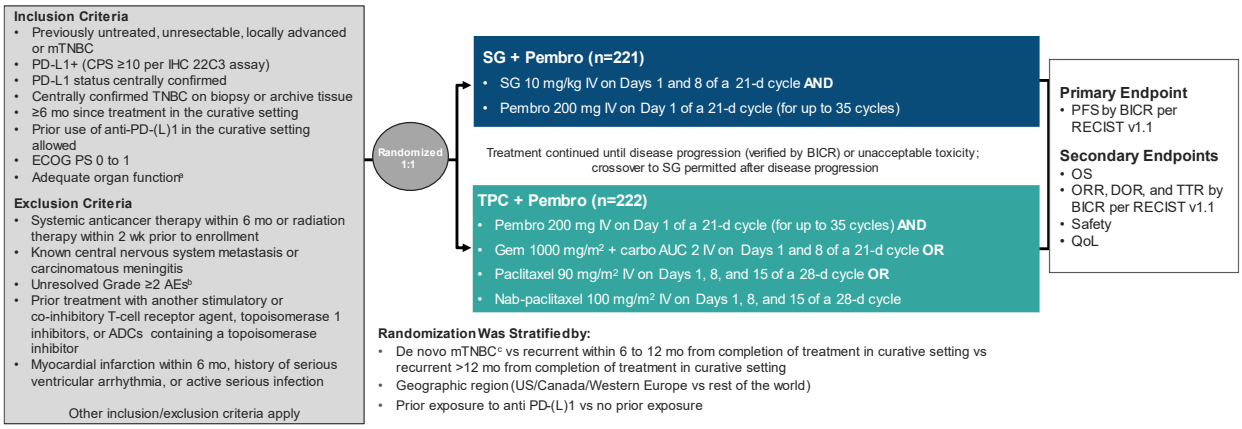
ASCENT-04 Study

Study design and demographics

ASCENT-04 is an ongoing, global, open-label, randomized, phase 3 study that is investigating the efficacy and safety of SG + pembro vs TPC + pembro as 1L treatment in patients with PD-L1+ (combined positive score [CPS]≥10) inoperable, locally advanced or mTNBC (Figure 1).[1]

A total of 443 female patients were enrolled. Patients who experienced disease progression during treatment with TPC + pembro (as verified by blinded independent central review [BICR]) could cross over to receive second-line SG monotherapy.[1]

Figure 1. ASCENT-04 Study Design[1,3]



Abbreviations: ADC=antibody drug conjugate; AE=adverse event; AUC=area under the concentration-time curve; DOR=duration of response; ECOG PS=Eastern Cooperative Oncology Performance Score; IHC=immunohistochemistry; TNBC=triple-negative breast cancer; ORR=objective response rate; OS=overall survival; PFS=progression-free survival; QoL=quality of life; RECIST=response evaluation criteria in solid tumors; ULN=upper limit of normal.

[a]Hgb ≥9 g/dL, absolute neutrophil count ≥1500/mm^3; platelets ≥100,000/mcL, bilirubin ≤1.5 × ULN, AST/ALT ≤2.5 × ULN or ≤5 × ULN with known liver metastases, serum albumin >3 g/dL, and CrCl ≥30 mL/min.

[b]Unresolved Grade ≤2 neuropathy, endocrine-related AEs, and any-grade alopecia were allowed.

[c]Up to 35% of patients with de novo mTNBC were eligible.

Table 1. ASCENT-04: Baseline Demographics and Disease Characteristics[1]

Select Demographics and Characteristics		SG + Pembro (n=221)	TPC + Pembro (n=222)
Age, median (range), y		54 (23–88)	55 (27–82)
≥65 y, n (%)		58 (26)	57 (26)
Race or ethnic group,[a] n (%)	White/Black/Asian	139 (63)/13 (6)/43 (19)	118 (53)/11 (5)/63 (28)
	Other or not specified	26 (12)	30 (14)
Geography, n (%)	US/Canada/Western Europe	85 (38)	85 (38)
	Rest of the world[b]	136 (62)	137 (62)
ECOG PS,[c] n (%)	0/1	156 (71)/65 (29)	154 (69)/67 (30)

Select Demographics and Characteristics		SG + Pembro (n=221)	TPC + Pembro (n=222)
Curative treatment-free interval, n (%)	De novo	75 (34)	75 (34)
	Recurrent within 6–12 mo	40 (18)	40 (18)
	Recurrent in >12 mo	106 (48)	107 (48)
Metastatic sites, n (%)	Lymph node	159 (72)	154 (69)
	Lung	111 (50)	95 (43)
	Bone	61 (28)	45 (20)
	Liver	55 (25)	57 (26)
	Brain	8 (4)	6 (3)
	Other[d]	81 (37)	71 (32)
Chemo selected prior to randomization,[e] n (%)	Taxane	116 (52)	114 (51)
	Gemcitabine/carboplatin	105 (48)	108 (49)
Prior anti-PD-(L)1 therapy,[f] n (%)		9 (4)	11 (5)

[a]As reported by patients; "other" included American Indian or Alaska Native and not permitted.
[b]Included Argentina, Australia, Brazil, Chile, Czech Republic, Hong Kong, Hungary, Israel, Japan, Malaysia, Mexico, Poland, Singapore, South Africa, South Korea, Taiwan, and Turkey.
[c]One patient in the TPC + pembro arm had an ECOG PS ≥2.
[d]Other metastatic sites included pleura, pleural effusion, skin, soft tissue, chest wall, and muscle.
[e]Actual chemotherapy received was consistent with what was selected prior to randomization; however, 2 patients were randomized but did not receive treatment.
[f]While 20 patients were included in the stratified subgroup of prior exposure to anti-PD-(L)1 therapy (yes) per the interactive response technology system, only 6 patients received prior treatment with anti-PD-(L)1 agents per the clinical database.

Efficacy by *BRCA* status

A prespecified retrospective exploratory analysis evaluated the impact of *BRCA* expression on the efficacy of SG + pembro vs TPC + pembro. Biomarker status was analyzed descriptively for association with PFS by BICR; patients who had received ≥1 dose of study treatment and had ≥1 evaluable post-baseline biomarker measurement were included in the BAS. In the ITT population, 18% of patients in the SG + pembro arm and 14% in the TPC + pembro arm had t*BRCA* mutation tumors. *Patients'* t*BRCA* status was measured by whole exome sequencing, and patients were grouped by t*BRCA* WT or mutation (*BRCA1*, *BRCA2*, or both) status.[2]

At the primary data cutoff, the median (range) follow-up was 14 (0.1–28.6) mo. mPFS results in the t*BRCA* BAS were consistent with those in the ITT population (Table 2). mPFS was longer with SG + pembro than with TPC + pembro in both t*BRCA* subgroups (Table 2). Results should be interpreted with caution due to the small sample size and the descriptive nature of the analysis.[2]

Table 2. ASCENT-04 Subgroup Analysis: Efficacy in ITT Population and by t*BRCA* Status[1,2]

Subgroup		SG + Pembro			TPC + Pembro			HR (95% CI)
		n	Events	mPFS (95% CI), Mo	n	Events	mPFS (95% CI), Mo	
ITT population		221	109	11.2 (9.3–16.7)	222	140	7.8 (7.3–9.3)	0.65 (0.51–0.84)[a]; *P*<0.001
t*BRCA* BAS		169	–	11.1 (9.2–16.7)	163	–	7.8 (7.2–9.3)	0.69 (0.52–0.91)
t*BRCA* subgroup	WT	130	69	9.6 (7.6–16.7)	131	90	7.4 (6.9–9.2)	0.67 (0.49–0.91)
	Mutation	39	18	16.6 (7.5–NE)	32	16	12.9 (7.1–NE)	0.88 (0.45–1.74)

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

References

1. Tolaney S, De Azambuja E, Kalinsky K, et al. Sacituzumab govitecan plus pembrolizumab for advanced triple-negative breast cancer. *N Engl J Med.* 2026;394:354-366.
2. Tolaney SM, Schmid P, de Azambuja E, et al. ASCENT-04: analysis of efficacy by biomarker subgroups with sacituzumab govitecan plus pembrolizumab vs chemotherapy plus pembrolizumab in participantts with previously untreated PD-L1 positive metastatic triple-negative breast cancer [Oral 1013]. Presented at: American Society of Clinical Oncology (ASCO); May 29-June 2, 2026; Chicago, IL.
3. Tolaney S, De Azambuja E, Emens LA, et al. ASCENT-04/KEYNOTE-D19: phase 3 study of sacituzumab govitecan plus pembrolizumab vs treatment of physician's choice plus pembro in first-line programmed death-ligand 1-positive metastatic triple-negative breast cancer [Poster 276TiP]. Presented at: European Society for Medical Oncology (ESMO) Congress; 9-13 September, 2022; Paris, France.

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:

☎1-888-983-4668 or 🖱 www.askgileadmedical.com

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Gilead Global Patient Safety ☎ 1-800-445-3235, option 3 or 🖱 https://www.gilead.com/utility/contact/report-an-adverse-event

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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