GILEAD | Medical Information

Trodelvy® (sacituzumab govitecan-hziy) Use in Patients With mTNBC in the 2L+ Setting

This document is in response to your request for information regarding Trodelvy® (sacituzumab govitecan-hziy [SG]) and its use in patients with metastatic triple-negative breast cancer (mTNBC) in the second-line and later (2L+) setting.

Some data may be outside of the US FDA-approved prescribing information. In providing this data, Gilead Sciences, Inc. is not making any representation as to its clinical relevance or to the use of any Gilead product(s). For information about the approved conditions of use of any Gilead drug product, please consult the FDA-approved prescribing information.

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 is indicated for the treatment of adult patients with unresectable locally advanced or mTNBC who have received ≥2 prior systemic therapies, ≥1 of them for metastatic disease.

Clinical Data on SG Use in Patients With mTNBC in the 2L+ Setting

The phase 3 ASCENT study evaluated the efficacy and safety of SG or single-agent chemotherapy TPC in BMNeg and BMPos patients (stable, previously treated) with locally advanced or mTNBC who relapsed after ≥2 prior chemotherapies.[2]

- The median PFS in the BMNeg population (primary endpoint) was prolonged with SG compared with TPC: 5.6 vs 1.7 mo, respectively (*P*<0.001).[2]
- The median OS in the BMNeg population was longer in the SG group than in the TPC group: 12.1 vs 6.7 mo, respectively (*P*<0.001).[2]
- In the BMNeg population, the following outcomes were greater with SG vs TPC: ORR, 35% vs 5%, respectively; CR, 4% vs 1%; and PR, 31% vs 4%.[2]
- In the full study population of BMPos and BMNeg patients, in the SG vs TPC groups, median PFS were 4.8 mo vs 1.7 mo (HR 0.43; 95% CI 0.35−0.54), respectively, and OS were 11.8 mo vs 6.9 mo (HR 0.51; 95% CI 0.41–0.62).[2]
- Updated results from the final database lock for the BMNeg population demonstrated efficacy and safety results consistent with the previous analysis from an earlier data cut for the BMNeg population.[3]
- The most common Grade ≥3 TRAEs in the SG and TPC groups included neutropenia, diarrhea, leukopenia, anemia, and febrile neutropenia. Dose reductions occurred in 22% of patients in the SG group and in 26% of patients in the TPC group. AEs that led to treatment discontinuation occurred in 5% of patients in each group.[2]

Clinical Data on SG Use in Patients With mTNBC in the 2L+ Setting

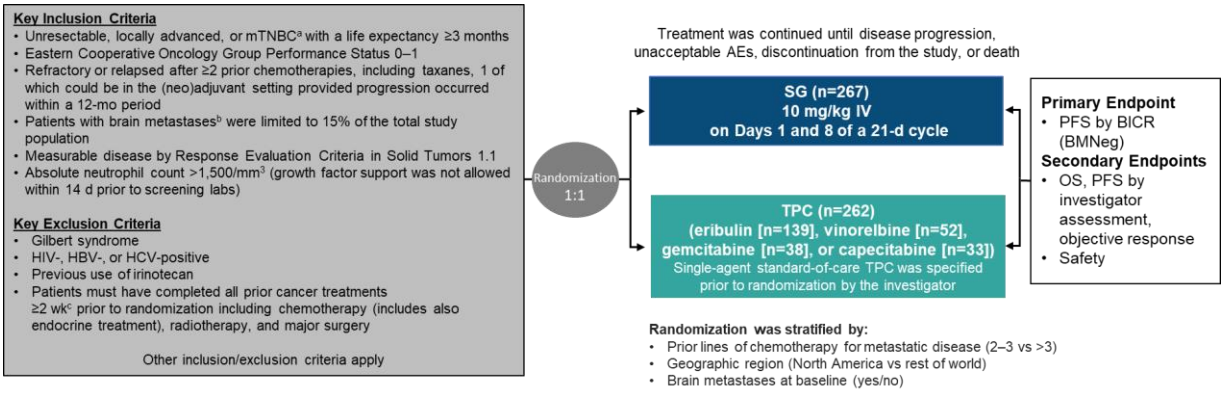
ASCENT Study

Study design and Demographics[2]

ASCENT, a global, open-label, randomized, confirmatory, phase 3 study, evaluated the efficacy and safety of SG vs TPC in patients with refractory or relapsed mTNBC who had received ≥2 prior chemotherapies for unresectable, locally advanced, or metastatic disease.

A total of 529 patients with mTNBC were enrolled and randomly assigned (1:1) to receive SG (n=267) or single-agent TPC (n=262; eribulin, vinorelbine, capecitabine, or gemcitabine; Figure 1). The primary endpoint was PFS in patients without brain metastases at baseline, as measured by a BICR. See Figure 1 for key secondary endpoints.

Figure 1. ASCENT: Study Design[2]



[a]Triple-negative breast cancer diagnosis determined per American Society of Clinical Oncology/College of American Pathologists guidelines. mTNBC was histologically or cytologically confirmed.
[b]Had stable central nervous system disease for ≥4 wk and could use stable, low-dose corticosteroids (≤20 mg of prednisone/prednisolone or equivalent).
[c]Prior antibody treatment for cancer must have been completed ≥3 wk prior to randomization.

Due to compelling evidence of efficacy with SG treatment, the ASCENT study was halted early. The primary analysis population included 235 BMNeg patients in the SG group and 233 BMNeg patients in the TPC group (eribulin, 54%; vinorelbine, 20%; capecitabine, 13%; and gemcitabine, 12%); 61 patients had stable, pretreated brain metastases at baseline and were not included in the primary analysis population. Seven patients in the SG group and 32 patients in the TPC group did not receive their assigned treatment or withdrew before treatment consent; their data were included in the efficacy analysis but not in the safety analysis.

The median (range) duration of follow-up was 17.7 (5.8–28.1) mo, and patients had received a median of 7 treatment cycles of SG, with a median treatment duration (range) of 4.4 (0.03–22.9) mo. For patients in the TPC group, the median number of cycles and treatment durations by TPC agent were as follows: eribulin, 3 cycles and 1.6 mo, respectively; vinorelbine, 2 cycles and 1 mo; gemcitabine, 2 cycles and 1.4 mo; and capecitabine, 2 cycles and 1.2 mo (data from 6 patients who received capecitabine were unavailable).

Efficacy results[2]

PFS

Per BICR analysis, SG significantly prolonged the median PFS in the BMNeg population relative to TPC (primary endpoint). Primary results are in Table 1. The median PFS rates of patients without brain metastases at baseline as determined through central review were similar to those determined by investigator assessments (secondary endpoint): SG, 5.5 mo; TPC, 1.7 mo (HR 0.35; 95% CI 0.28–0.44). PFS with SG vs TPC in the full study population of BMPos and BMNeg patients is shown in Table 1.

Table 1. ASCENT Study: PFS in BMNeg and Full Study Populations (Per BICR)[2,4]

Variable	BMNeg		Full Population	
	SG (n=235)	TPC (n=233)	SG (n=267)	TPC (n=262)
PFS, events	166	150	191	171
Median (95% CI), mo	5.6 (4.3–6.3)[a]	1.7 (1.5–2.6)[a]	4.8 (4.1–5.8)	1.7 (1.5–2.5)
HR (95% CI)	0.41 (0.32–0.52); *P*<0.001		0.43 (0.35−0.54)	

[a]Primary endpoint.

Within the BMNeg cohort, subgroup analyses of PFS were also evaluated (Table 2).

Table 2. ASCENT Study: PFS by Subgroups in BMNeg Population (Per BICR)[2]

Subgroup		Patients, n	PFS, Median (95% CI), Mo		HR (95% CI)
			SG	TPC	
Age group	<65 y	378	4.6 (3.7–5.7)	1.7 (1.5–2.5)	0.46 (0.35–0.59)
	≥65 y	90	7.1 (5.8–8.9)	2.4 (1.4–2.9)	0.22 (0.12–0.4)
Race	White	369	5.7 (4.3–6.8)	1.7 (1.5–2.6)	0.39 (0.3–0.51)
	Black	56	5.4 (2.8–7.4)	2.2 (1.5–2.9)	0.45 (0.24–0.86)
	Asian	18	NE (1.3–NE)	1.5 (1.2–NE)	0.4 (0.08–2.08)
Previous therapies	2–3	330	5.8 (4.2–7.1)	1.6 (1.5–2.5)	0.39 (0.29–0.52)
	>3	138	5.6 (3–6.5)	2.5 (1.5–2.8)	0.48 (0.32–0.72)
Geographic region	North America	298	4.9 (4–6.3)	2 (1.5–2.6)	0.44 (0.33–0.6)
	Rest of the world	170	5.9 (4.2–6.9)	1.6 (1.4–2.7)	0.36 (0.24–0.53)
Use of previous PD-(L)1 inhibitor	Yes	127	4.2 (3.2–5.6)	1.6 (1.4–2.3)	0.37 (0.24–0.57)
	No	341	6.2 (4.9–7.1)	2.1 (1.5–2.7)	0.42 (0.32–0.56)
Liver metastasis	Yes	199	4.2 (2.8–5.8)	1.5 (1.4–2.4)	0.48 (0.34–0.67)
	No	269	6.8 (4.6–8)	2.3 (1.6–2.7)	0.36 (0.26–0.5)
Initial diagnosis of TNBC	Yes	322	5.7 (4.3–6.9)	1.6 (1.5–2.6)	0.38 (0.29–0.51)
	No	146	4.6 (3.7–6.9)	2.3 (1.5–2.8)	0.48 (0.32–0.72)

Abbreviations: PD-(L)1=programmed death (ligand)-1; TNBC=triple-negative breast cancer.

Additional secondary endpoints

Additional outcomes, including OS, in the BMNeg and full study populations are shown below in Table 3.[2]

Table 3. ASCENT Study: Summary of Treatment Efficacy–Secondary Endpoints (Per BICR)[2]

Variable	BMNeg		Full Population	
	SG (n=235)	TPC (n=233)	SG (n=267)	TPC (n=262)
OS, median (95% CI), mo	12.1 (10.7–14)	6.7 (5.8–7.7)	11.8 (10.5–13.8)	6.9 (5.9–7.7)
HR (95% CI)	0.48 (0.38–0.59); *P*<0.001		0.51 (0.41–0.62)	

Variable	BMNeg		Full Population	
	SG (n=235)	TPC (n=233)	SG (n=267)	TPC (n=262)
ORR,[a] n (%)	82 (35)	11 (5)	83 (31)	11 (4)
CR, n (%)	10 (4)	2 (1)	10 (4)	2 (1)
PR, n (%)	72 (31)	9 (4)	73 (27)	9 (3)
CBR,[b] n (%)	105 (45)	20 (9)	108 (40)	21 (8)
SD, n (%)	81 (34)	62 (27)	96 (36)	71 (27)
SD for ≥6 mo, n (%)	23 (10)	9 (4)	25 (9)	10 (4)
Progressive disease, n (%)	54 (23)	89 (38)	65 (24)	100 (38)
NE,[c] n (%)	18 (8)	71 (30)	23 (9)	80 (31)
TTR, median (95% CI), mo	1.5 (0.7–10.6)	1.5 (1.3–4.2)	1.5 (0.7–10.6)	1.5 (1.3–4.2)
DOR, median (95% CI), mo	6.3 (5.5–9)	3.6 (2.8–NE)	6.3 (5.5–9)	3.6 (2.8–NE)
HR (95% CI)	0.39 (0.14–1.07)		–	

Abbreviation: SD=stable disease.
[a]ORR was defined as a CR or PR. [b]CBR was defined as CR, PR, or SD with a duration of ≥6 mo.
[c]Reasons include missing post-baseline images or having unreadable images.

Safety[2]

The most common Grade ≥3 TRAEs in the SG and TPC groups included neutropenia, diarrhea, leukopenia, anemia, and febrile neutropenia. Dose reductions occurred in 22% of patients in the SG group and in 26% of patients in the TPC group. AEs that led to treatment discontinuation occurred in 5% of patients in each group. Serious TRAEs occurred in 39 patients (15%) in the SG group and in 19 patients (8%) in the TPC group.

Among those who received SG, ocular toxicity occurred in 5% of patients (all events were Grade 1), and no Grade >2 neuropathy was observed. One patient in the SG group developed Grade 3 pneumonitis, and no Grade 1 or 2 events of interstitial lung disease were observed. Three non–treatment-related deaths occurred in the SG group: respiratory failure, n=2; post-obstructive pneumonia, n=1. Three deaths also occurred in the TPC group; of these, 1 treatment-related death due to neutropenic sepsis was reported.

Table 4. ASCENT Study: Any-Grade TRAEs in ≥10% of Patients and Grade 3 or 4 AEs in ≥5% of Patients in the Safety Population[2]

TRAEs, n (%)		SG (n=258)			TPC (n=224)		
		Any Grade	Grade 3	Grade 4	Any Grade	Grade 3	Grade 4
Any TRAE		252 (98)	117 (45)	48 (19)	192 (86)	71 (32)	33 (15)
Hematologic	Neutropenia[a]	163 (63)	88 (34)	44 (17)	96 (43)	45 (20)	29 (13)
	Anemia[b]	89 (34)	20 (8)	0	54 (24)	11 (5)	0
	Leukopenia[c]	41 (16)	23 (9)	3 (1)	25 (11)	10 (4)	2 (1)
	Febrile neutropenia	15 (6)	12 (5)	3 (1)	5 (2)	4 (2)	1 (<1)
	Thrombocytopenia[d]	14 (5)	2 (1)	2 (1)	25 (11)	3 (1)	0
Gastrointestinal	Diarrhea	153 (59)	27 (10)	0	27 (12)	1 (<1)	0
	Nausea	147 (57)	6 (2)	1 (<1)	59 (26)	1 (<1)	0
	Vomiting	75 (29)	2 (1)	1 (<1)	23 (10)	1 (<1)	0
	Constipation	44 (17)	0	0	32 (14)	0	0
	Abdominal pain	29 (11)	3 (1)	0	9 (4)	1 (<1)	0
General disorders and administration site conditions	Fatigue	115 (45)	8 (3)	0	68 (30)	12 (5)	0
	Asthenia	31 (12)	2 (1)	0	23 (10)	3 (1)	0
Skin and subcutaneous disorders[e]	Alopecia	119 (46)	0	0	35 (16)	0	0

TRAEs, n (%)		SG (n=258)			TPC (n=224)		
		Any Grade	Grade 3	Grade 4	Any Grade	Grade 3	Grade 4
Metabolism and nutrition disorders	Decreased appetite	51 (20)	4 (2)	0	32 (14)	1 (<1)	0
Nervous system disorders[f,g]		64 (25)	1 (<1)	0	53 (24)	5 (2)	0
Respiratory, thoracic, and mediastinal disorders[g]		41 (16)	5 (2)	0	17 (8)	1 (<1)	0
Musculoskeletal and connective disorders[g]		32 (12)	0	0	28 (12)	3 (1)	0
Infections and infestations[g,h]		30 (12)	6 (2)	1 (<1)	22 (10)	4 (2)	3 (1)

[a]Included neutropenia and decreased neutrophil count.
[b]Included anemia, Hgb decreased, and decreased RBC count.
[c]Included leukopenia and decreased WBC count.
[d]Included thrombocytopenia and decreased platelet count.
[e]There was 1 Grade 3 rash in each of the SG and TPC groups.
[f]There were no Grade 3 or 4 neuropathy events with SG. In the TPC group, there were Grade 3 AEs of peripheral neuropathy (n=2) and peripheral sensory neuropathy (n=2).
[g]For this category, the overall any-grade AE rate was ≥10%, but the rate of all individual any-grade AEs was ≤5%.
[h]There was 1 case of Grade 3 pneumonitis in the SG group and none in the TPC group.

Final efficacy and safety results

The final database lock included efficacy and safety data from an additional 17 patients after the final data cut.[3]

Results of the follow-up analysis were consistent with those from the previous analysis. Since the previous analysis in the BMNeg population, 1 additional PFS event occurred in the SG group (Table 5). Results for OS, ORR, CBR, DOR, and TTR were similar to or unchanged from those in the previous analysis.[3] The 24-mo OS rates in the BMNeg population were similar to rates in the overall ITT population (Table 5).[4]

Table 5. ASCENT Study: Summary of Treatment Efficacy at Final Database Lock[3,4]

Variable	BMNeg		ITT Population	
	SG (n=235)	TPC (n=233)	SG (n=267)	TPC (n=262)
PFS, events	167	150	191	171
Median (95% CI), mo	5.6 (4.3–6.3)	1.7 (1.5–2.6)	4.8 (4.1–5.8)	1.7 (1.5–2.5)
HR (95% CI)	0.39 (0.31–0.49); *P*<0.0001		0.41 (0.33–0.52)[a]	
OS, events	173	199	201	222
Median (95% CI), mo	12.1 (10.7–14)	6.7 (5.8–7.7)	11.8 (10.5–13.8)	6.9 (5.9–7.7)
HR (95% CI)	0.48 (0.39–0.59); *P*<0.0001		0.51 (0.42–0.63)[a]	
24-mo rate (95% CI), %	22.4 (16.8–28.5)	5.2 (2.5–9.4)	20.5 (15.4–26.1)	5.5 (2.8–9.4)

[a]HR was stratified by number of prior chemotherapies and region.

AEs led to treatment discontinuation in 6 patients (3%) in the SG group and 7 patients (3%) in the TPC group. No additional treatment-related deaths occurred, and the incidence of TRAEs was consistent with that in the previous analysis.[3]

References

1. TRODELVY® Gilead Sciences Inc. Trodelvy (sacituzumab govitecan-hziy) for injection, for intravenous use. U.S. Prescribing Information. Foster City, CA.
2. Bardia A, Hurvitz SA, Tolaney SM, et al. Sacituzumab govitecan in metastatic triple-negative breast cancer. *N Engl J Med*. 2021;384(16):1529-1541.
3. Bardia A, Tolaney SM, Loirat D, et al. Sacituzumab govitecan versus treatment of physician's choice in patients with previously treated metastatic triple-negative breast cancer: final data from

the phase 3 ASCENT study [Poster 1071]. Presented at: American Society of Clinical Oncology (ASCO) Annual Meeting; 3-7 June 2022; Chicago, IL & Online.
4. Bardia A, Rugo HS, Tolaney SM, et al. Final results from the randomized phase III ASCENT clinical trial in metastatic triple-negative breast cancer and association of outcomes by human epidermal growth factor receptor 2 and trophoblast cell surface antigen 2 expression. *J Clin Oncol*. 2024;42(15):1738-1744.

Abbreviations

2L+=second-line and later
AE=adverse event
BICR=blinded independent central review
BMNeg=negative for brain metastasis
BMPos=positive for brain metastasis
CBR=clinical benefit rate
CR=complete response
DOR=duration of response
HR=hazard ratio
mTNBC=metastatic triple-negative breast cancer
NE=not evaluable
ORR=objective response rate
OS=overall survival
PFS=progression-free survival
PR=partial response
SD=stable disease
SG=sacituzumab govitecan-hziy
TPC=treatment of physician's choice
TRAE=treatment-related adverse event
TTR=time-to-response

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

Adverse Event Reporting

Please report all adverse events to:

Gilead Global Patient Safety ☎ 1-800-445-3235, option 3 or 🖱 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

Data Privacy

The Medical Information service at Gilead Sciences may collect, store, and use your personal information to provide a response to your medical request. We may share your information with other Gilead Sciences colleagues to ensure that your request is addressed appropriately. If you report an adverse event or concern about the quality of a Gilead or Kite

product, we will need to use the information you have given us in order to meet our regulatory requirements in relation to the safety of our medicines.

It may be necessary for us to share your information with Gilead's affiliates, business partners, service providers, and regulatory authorities located in countries other than your own. Gilead Sciences has implemented measures to protect the personal information you provide. Please see the Gilead Privacy Statement (www.gilead.com/privacy-statements) for more information about how Gilead handles your personal information and your rights. If you have any further questions about the use of your personal information, please contact gilead.privacy@gilead.com.