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Trodelvy® (sacituzumab govitecan-hziy) ASCENT Study in mTNBC

This document is in response to your request for information regarding Trodelvy® (sacituzumab govitecan-hziy [SG]) and the phase 3 ASCENT trial in patients with metastatic triple-negative breast cancer (mTNBC).

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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 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.

ASCENT Study on SG in mTNBC

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

- SG prolonged the median PFS (primary endpoint; BMNeg population) in comparison with chemotherapy (5.6 vs 1.7 months; *P*<0.001).[2]
- The rates of OS were greater in the SG group than in the chemotherapy group (BMNeg population median OS: 12.1 vs 6.7 months; *P*<0.001).[2]
- The ORR (35% vs 5%) and the CR (4% vs 1%) and PR (31% vs 4%) rates were greater in the SG group than in the chemotherapy group in the BMNeg population.[2]
- A similar clinical benefit in PFS and OS was observed in the full study population of BMPos and BMNeg patients.[2]
- Updated results from the final database lock (February 25, 2021) demonstrated efficacy and safety results consistent with the previous analysis from the March 2020 data cut for the BMNeg population.[3]

ASCENT Study on SG in mTNBC

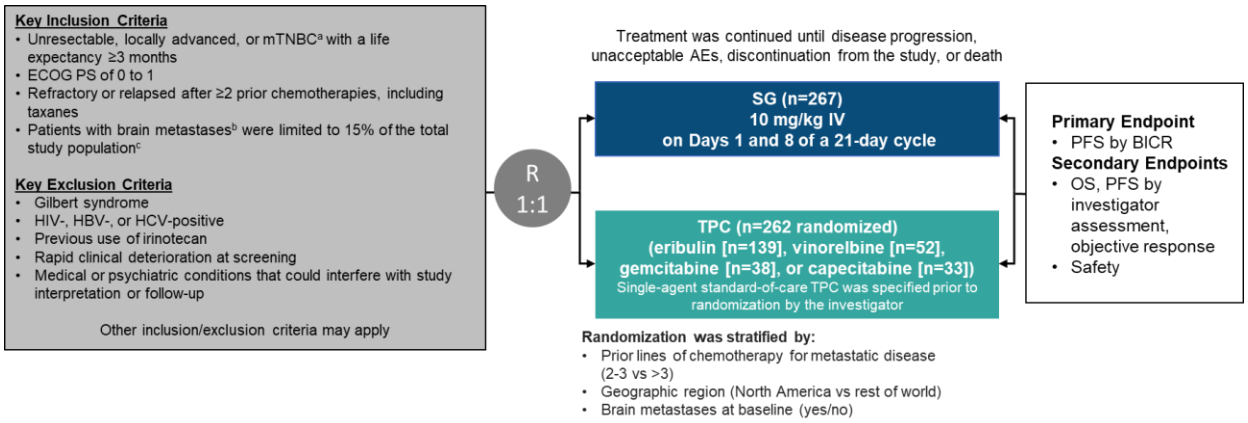
Study Design and Demographics[2]

ASCENT, a global, open-label, randomized, confirmatory, phase 3 study, was conducted to investigate 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 chemotherapy (n=262; eribulin, vinorelbine, capecitabine, or gemcitabine; Figure 1). The primary endpoint was PFS in BMNeg patients at baseline, as measured by a BICR. See Figure 1 for key secondary endpoints.

Figure 1. ASCENT Study Design[2]



Abbreviations: ASCO=American Society of Clinical Oncology; CAP=College of American Pathologists; ECOG PS=Eastern Cooperative Oncology Group Performance Status; R=randomized; TNBC=triple-negative breast cancer.

[a]TNBC diagnosis determined per ASCO/CAP guidelines. mTNBC was histologically or cytologically confirmed.

[b]Had stable central nervous system disease for ≥4 weeks and could use stable, low-dose corticosteroids (≤20 mg of prednisone/prednisolone or equivalent). Their data were not included in the primary endpoint analysis.

[c]MRIs to determine baseline brain metastases were required only for patients with known brain metastases, and imaging (MRI or CT scans) was conducted every 6 weeks for 36 weeks and every 9 weeks thereafter (until disease progression led to study treatment discontinuation); confirmatory imaging was performed 4 to 6 weeks later.

Due to compelling evidence of efficacy with SG treatment, the ASCENT study was halted early in March 2020. The primary analysis population included 235 BMNeg patients in the SG group and 233 BMNeg patients in the TPC group (54% received eribulin, 20% received vinorelbine, 13% received capecitabine, and 12% received gemcitabine); 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.

At the final data cut (March 11, 2020), the median (range) duration of follow-up was 17.7 (5.8–28.1) months, 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) months; patients in the TPC group had a median of 3, 2, 2, and 2 cycles of eribulin, vinorelbine, gemcitabine, and capecitabine, respectively, for median treatment durations of 1.6, 1, 1.4, and 1.2 months (data from 6 patients who received capecitabine were unavailable).

Efficacy Results[2]

PFS

The BICR analysis demonstrated that treatment with SG, in comparison with TPC, significantly prolonged the median PFS (HR: 0.41; 95% CI: 0.32–0.52; *P*<0.001). The median PFS for BMNeg patients (primary endpoint) treated with SG was 5.6 months (95% CI: 4.3–6.3; 166 events), compared with 1.7 months (95% CI: 1.5–2.6; 150 events) for those treated with chemotherapy. The median PFS rates determined through central review were similar to those determined by investigator assessments: 5.5 months in the SG group and 1.7 months in the TPC group (HR: 0.35; 95% CI: 0.28–0.44). Within the BMNeg cohort, subgroup analyses of PFS were also evaluated.

Secondary endpoints

Table 1. ASCENT Study: Summary of Treatment Efficacy (per BICR)[2]

Variable	BMNeg		Full Population	
	SG (n=235)	TPC (n=233)	SG (n=267)	TPC (n=262)
PFS, 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 for disease progression or death (95% CI)	0.41 (0.32–0.52); *P*<0.001		0.43 (0.35−0.54)	
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 for death (95% CI)	0.48 (0.38–0.59); *P*<0.001		0.51 (0.41–0.62)	
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)
Response could not be evaluated,[c] n (%)	18 (8)	71 (30)	23 (9)	80 (31)
Time-to-response, 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: NE=not evaluable.
[a]The ORR was defined as a CR or PR.
[b]The CBR was defined as CR, PR, or SD with a duration of ≥6 months.
[c]Reasons include missing post-baseline images or having unreadable images.

Safety[2]

The most common Grade ≥3 TRAEs in the SG group and the TPC group included neutropenia (51% and 33%, respectively), diarrhea (10% and <1%), leukopenia (10% and 5%), anemia (8% and 5%), and febrile neutropenia (6% and 2%). 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 (none of the 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 2. ASCENT Study: TRAEs (Any-Grade AE in ≥10% of Patients ; Grade 3/4 AEs in ≥5% of Patients) in the Safety Population[2]

AEs, n (%)		SG (n=258)			TPC (n=224)		
		Any Grade	Grade 3	Grade 4	Any Grade	Grade 3	Grade 4
Any AE		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)
	Thrombocytopenia[d]	14 (5)	2 (1)	2 (1)	25 (11)	3 (1)	0
	Febrile neutropenia	15 (6)	12 (5)	3 (1)	5 (2)	4 (2)	1 (<1)
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
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 one Grade 3 rash in each of the SG and TPC groups.
[f]There were no Grade 3/4 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.

Updated Results From the Final Database Lock[3]

The final database lock date (February 25, 2021) included efficacy and safety data from an additional 17 patients after the final data cut.

Results of the follow-up analysis were consistent with those from the previous analysis from the March 2020 final data cut. In the BMNeg population, the median PFS was 5.6 months (95% CI: 4.3–6.3) in the SG group and 1.7 months (95% CI: 1.5–2.6) in the TPC group (HR: 0.39; *P*<0.0001). Since the previous analysis in the BMNeg population, 1 additional PFS event occurred in the SG group (number of events: SG group, n=167; TPC group, n=150). Results for OS, ORR, CBR, DOR, and time-to-response were similar to or

unchanged from those in the previous analysis. The 24-month OS rates in the BMNeg population were 22.4% (95% CI: 16.8–28.5) in the SG group and 5.2% (95% CI: 2.5–9.4) in the TPC group. The 24-month OS rates were similar in the overall ITT population: 20.5% (95% CI: 15.4–26.1) in the SG group and 5.5% (95% CI: 2.8–9.4) in the TPC group.

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.

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]. Paper presented at: American Society of Clinical Oncology (ASCO) Annual Meeting; 3-7 June, 2022; Chicago, IL & Online.

Abbreviations

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
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

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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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

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