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Trodelvy® (sacituzumab govitecan-hziy) Analysis in Black Patients with mTNBC

This document is in response to your request for information about Trodelvy® (sacituzumab govitecan-hziy [SG]) in patients who self-identified as Black with relapsed or refractory metastatic triple-negative breast cancer (mTNBC).

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 two or more prior systemic therapies, at least one of them for metastatic disease.

Clinical Pharmacology

Pharmacogenomics

SN-38 is metabolized via UGT1A1. Genetic variants of the UGT1A1 gene such as the UGT1A1*28 allele lead to reduced UGT1A1 enzyme activity. Individuals who are homozygous or heterozygous for the UGT1A1*28 allele are at increased risk for neutropenia, febrile neutropenia, and anemia from SG compared to individuals who are wildtype (*1/*1). Approximately 20% of the Black or African American population, 10% of the White population, and 2% of the East Asian population are homozygous for the UGT1A1*28 allele (*28/*28). Approximately 40% of the Black or African American population, 50% of the White population, and 25% of the East Asian population are heterozygous for the UGT1A1*28 allele (*1/*28). Decreased function alleles other than UGT1A1*28 may be present in certain populations.

ASCENT Subanalysis: Outcomes in the Black Study Population

ASCENT is a phase 3, global, open-label, randomized, confirmatory study comparing the efficacy and safety of SG compared with treatment of physician's choice (TPC) in 529 patients with refractory or relapsed mTNBC who had received ≥2 prior chemotherapies for unresectable, locally advanced, or metastatic disease.[2]

A post hoc subgroup analysis, in patients with or without brain metastases (BMPos and BMNeg, respectively), evaluated outcomes among patients who self-identified as Black

(n=62) and received SG or TPC. The following outcomes were observe in the SG and TPC groups, respectively.[3]

- Median progression-free survival (PFS) of 5.4 months vs 2.2 months, hazard ratio (HR) 0.44 (95% CI: 0.24-0.8; *P*=0.008).[3]
- Median overall survival (OS) of 13.8 months vs 8.5 months, HR 0.64 (95% CI: 0.34-1.19; *P*=0.159).[3]
- Objective response rate (ORR) of 9 (32%) vs 2 (6%).[3]
- The safety profile of this subgroup was consistent with that observed in the overall ASCENT study.[3]

ASCENT Study

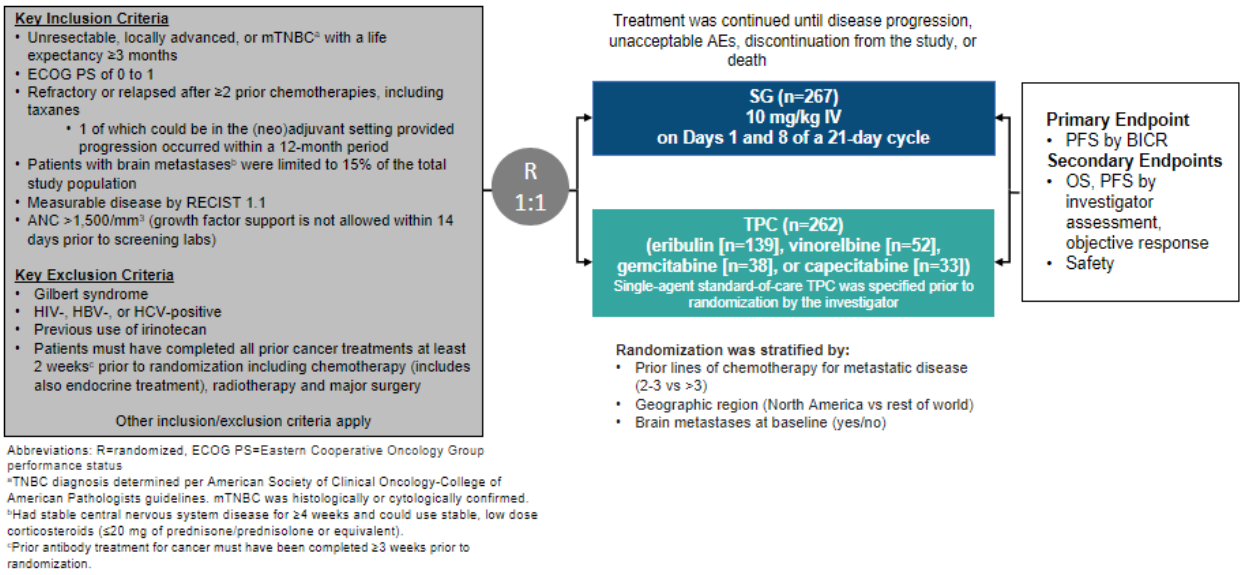
Overall Study Design[2]

ASCENT, a global, open-label, randomized, confirmatory, phase 3 study, was conducted to investigate the efficacy and safety of SG compared with TPC in patients with refractory or relapsed mTNBC who had received ≥2 prior chemotherapies (one of which could have been in the [neo]adjuvant setting if progression occurred within 12 months) for unresectable, locally advanced, or metastatic disease.

A total of 529 patients were enrolled and randomly assigned to receive SG (n=267) or TPC (n=262; eribulin, vinorelbine, capecitabine, or gemcitabine; Figure 1). The study protocol allowed a predefined maximum cap of 15% for patients with stable brain metastases (positive for brain metastasis).

The primary endpoint was PFS in BMNeg patients at baseline, as measured by a blinded independent central review (BICR). See Figure 1 for key secondary endpoints.

Figure 1. ASCENT Study Design[2,4]



Abbreviations: R=randomized, ECOG PS=Eastern Cooperative Oncology Group performance status
[a]TNBC 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 weeks 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 weeks prior to randomization.

ASCENT Subanalysis: Black Study Population[3]

A post hoc subgroup analysis was conducted, in BMPos and BMNeg patients, to evaluate outcomes among patients who self-identified as Black (n=62) who were randomly assigned to receive SG (n=28) or TPC (n=34). Baseline demographics were generally similar between patients who received SG and TPC (Table 1). The median length of treatment was 5.3 months in the SG group and 1.6 months in the TPC group.

Table 1. ASCENT Subanalysis: Demographics and Disease Characteristics[3]

Key Demographics and Characteristics	SG (n=28)	TPC (n=34)
Age, median (range), y	50 (35–69)	55 (32–75)
Female, n (%)	28 (100)	34 (100)
ECOG PS, n (%)		
0	12 (43)	14 (41)
1	16 (57)	20 (59)
BMPos at study entry, n (%)	0	6 (18)
Prior systemic regimens,[a] median (range), n	4 (2–8)	4 (2–10)
Number of prior chemotherapies, n (%)		
2–3	21 (75)	22 (65)
>3	7 (25)	12 (35)
Setting of prior systemic therapies, n (%)		
Metastatic	25 (89)	34 (100)
Adjuvant	16 (57)	17 (50)
Neoadjuvant	13 (46)	16 (47)
Locally advanced disease	2 (7)	0
BRCA1/2 mutational status, n (%)		
Negative	13 (46)	17 (50)
Positive	1 (4)	1 (3)
Unknown	14 (50)	16 (47)

BRCA=breast cancer gene
[a]Defined as regimens that had a start and end date of the regimen before the SG administration.

Efficacy[3]

Similar to the outcomes observed in the overall ASCENT population, the BICR analysis demonstrated that treatment with SG, in comparison with TPC, prolonged the median PFS. The median OS in the SG group was longer than in the TPC group. The ORR and clinical benefit rate (CBR) were greater with SG than with TPC, as is shown in Table 2.

Table 2. ASCENT Subanalysis: Efficacy Outcomes[3]

Efficacy Outcomes	SG (n=28)	TPC (n=34)
PFS (BICR analysis)		
Events, n	20	26
Median (95% CI), mo	5.4 (2.8–7.4)	2.2 (1.5–2.9)
HR (95% CI); *P*-value	0.44 (0.24–0.8); *P*=0.008	
OS		
Events, n	17	26
Median (95% CI), mo	13.8 (9.4–18)	8.5 (4.8–12.4)
HR (95% CI), mo; *P*-value	0.64 (0.34–1.19); *P*=0.159	
ORR, n (%)	9 (32)	2 (6)
Best overall response, n (%)		
Complete response	1 (4)	1 (3)

Efficacy Outcomes	SG (n=28)	TPC (n=34)
Partial response	8 (29)	1 (3)
Stable disease	11 (39)	12 (35)
Stable disease for >6 months	3 (11)	3 (9)
Progressive disease	4 (14)	14 (41)
NE	4 (14)	6 (18)
CBR,[a] n (%)	12 (43)	5 (15)
Duration of response, median (95% CI), mo	9.2 (3.2–NE)	NE (2.9–NE)

NE=not evaluable.
[a]CBR was defined as the combined rate of patients who achieved partial response and stable disease for ≥6 months.

Safety[3]

Safety outcomes were similar to those observed in the overall ASCENT study population. The most common (≥40% in either group) all grade treatment-related adverse events (TRAEs) in the SG and TPC groups included neutropenia (64% vs 61%), diarrhea (64% vs 13%), fatigue (52% vs 39%), nausea (44% vs 36%), and anemia (40% vs 29%). The rates of key Grade 3/4 TRAEs (neutropenia, leukopenia, diarrhea, anemia, and fatigue) are provided in Table 3. Fewer patients in the SG group than in the TPC group required dose reductions due to treatment-emergent AEs (28% vs 35%). No patients in the SG group discontinued treatment due to TRAEs compared with 3% of patients in the TPC group. No treatment-related deaths were reported in either group.

Table 3. ASCENT Subanalysis : All Grade and Grade ≥3 TRAEs[3]*

TRAEs, n (%)	SG (n=25)			TPC (n=31)		
	All Grade	Grade 3	Grade 4	All Grade	Grade 3	Grade 4
Hematologic						
Neutropenia[a]	16(64)	9(36)	3(12)	19(61)	9(29)	4(13)
Anemia[b]	10(40)	3(12)	0	9(29)	2(7)	0
Leukopenia[c]	6(24)	2(8)	0	10(32)	4(13)	1(3)
Febrile neutropenia	2(8)	2(8)	0	1(3)	0	1(3)
Gastrointestinal						
Diarrhea	16(64)	1(4)	0	4(13)	0	0
Nausea	11(44)	0	1(4)	11(36)	0	0
Vomiting	9(36)	0	1(4)	8(26)	0	0
Constipation	2(8)	0	0	9(29)	0	0
Other						
Fatigue	13(52)	0	0	12(39)	3(10)	0
Alopecia	9(36)	0	0	3(10)	0	0

*Included all grades of TRAEs that occurred in ≥20% of patients, and Grade 3 and 4 TRAEs that occurred in ≥5% of patients. Treatment-related AEs included those that had a start date on or after the date of the first study dose and those reported ≤30 days of the last study dose.
[a]Combined preferred terms of 'neutropenia' and 'neutrophil count decreased'. [b]Combined preferred terms of 'anemia', 'hemoglobin decreased', and 'red blood cell count decreased'. [c]Combined preferred terms of 'leukopenia' and 'white blood cell count decreased'.

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. Carey LA, Zelnak A, Rugo HS, et al. Assessment of Sacituzumab Govitecan in Black Patients From the Phase 3 ASCENT Study in Metastatic Triple-Negative Breast Cancer [Poster P5-16-07]. Paper presented at: San Antonio Breast Cancer Symposium; 07-10 December, 2021; San Antonio, Texas.
4. Bardia A, Hurvitz SA, Tolaney SM, et al. Sacituzumab Govitecan in Metastatic Triple-Negative Breast Cancer [Protocol]. *N Engl J Med.* 2021;384(16):1529-1541.

Product Label

For the full indication, important safety information, and Boxed Warning(s), please refer to the Trodelvy US Prescribing Information available at: https://www.gilead.com/-/media/files/pdfs/medicines/oncology/trodelvy/trodelvy_pi.pdf

Follow Up

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☎1-866-MEDI-GSI (1-866-633-4474) or 🖱 www.askgileadmedical.com

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🖱 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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