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Trodelvy® (sacituzumab govitecan-hziy) Comparison With TPC by Agent in Patients With mTNBC

This document is in response to your request for information on Trodelvy® (sacituzumab govitecan-hziy [SG]) in patients with metastatic triple-negative breast cancer (mTNBC) in comparison with individual chemotherapy treatment of physician's choice (TPC) agents.

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The full indication, important safety information, and boxed warnings for neutropenia and diarrhea are available at: https://www.gilead.com/-/media/files/pdfs/medicines/oncology/trodelvy/trodelvy_pi.pdf

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.

Comparison With TPC by Agent in Patients With mTNBC

The ASCENT study investigated the efficacy and safety of SG in comparison with chemotherapy TPC in patients with refractory or relapsed mTNBC who relapsed after ≥2 prior chemotherapies. In the primary analysis, median PFS in the full population was 4.8 mo (95% CI: 4.1–5.8) vs 1.7 mo (95% CI: 1.5–2.5) in the SG and TPC groups, respectively. Median OS in the full population was 11.8 mo (95% CI: 10.5–13.8) and 6.9 mo (95% CI: 5.9–7.7) in the SG vs TPC groups, respectively.[2]

A post hoc subgroup analysis, in patients with or without brain metastases, evaluated outcomes among patients who received SG or individual TPC agent.[3]

- Median PFS was numerically longer with SG vs eribulin, vinorelbine, capecitabine, or gemcitabine (ITT population: 4.8 mo vs 2.1, 1.5, 1.6, and 2.4 mo, respectively).[3]
- Median OS was numerically longer with SG vs eribulin, vinorelbine, capecitabine, or gemcitabine (ITT population: 11.8 mo vs 7.2, 5.6, 5.2, and 8.4 mo, respectively).[3]
- The most commonly reported all grade TEAEs were diarrhea (65%), neutropenia (64%), and nausea (62%) with SG, neutropenia (39%), fatigue (39%), and nausea (35%) with eribulin, and neutropenia (49%), fatigue (40%), and anemia (30%) with vinorelbine, capecitabine, and gemcitabine.[3]
- Treatment discontinuation due to Grade ≥3 AEs occurred in 5%, 3%, 10%, 7% and 10% of patients receiving SG, eribulin, vinorelbine, capecitabine, or gemcitabine, respectively.[3]
- One treatment-emergent death occurred in the eribulin group; none were reported with SG or the other TPC groups.[3]

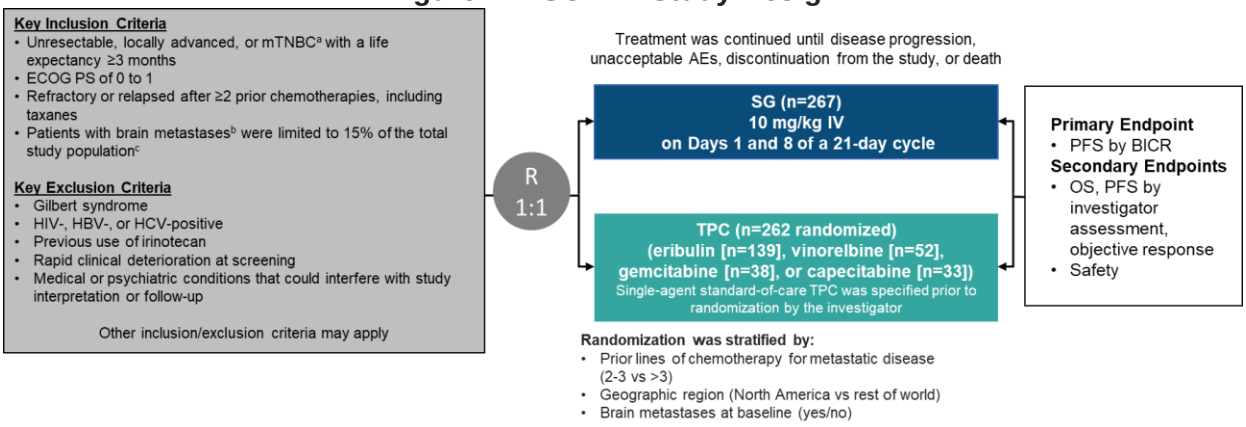
Comparison With TPC by Agent in Patients With mTNBC

ASCENT Study in mTNBC

Study Design

ASCENT, a global, open-label, randomized, confirmatory, phase 3 study, investigated the efficacy and safety of SG compared with 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 were randomly assigned to receive SG or single-agent TPC (Figure 1).[2]

Figure 1. ASCENT Study Design[2,4]



Abbreviations: ASCO=American Society of Clinical Oncology; CAP=College of American Pathologists; R=randomized; TNBC=triple-negative breast cancer.
[a]Diagnosis determined per ASCO/CAP 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 prednisone or 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 was conducted every 6 wk for 36 wk and every 9 wk thereafter (until disease progression led to treatment discontinuation); confirmatory imaging was performed 4–6 wk later.

A post hoc subanalysis compared outcomes between SG and individual TPC agent in the ITT population.[3]

Patient Disposition and Demographics

See Table 1 for baseline demographics, characteristics, and prior treatment history.

Table 1. ASCENT Subanalysis (ITT Population): Baseline Demographics and Disease Characteristics[3]

Demographics and Characteristics		SG (n=267)	TPC (n=262)			
			Eribulin (n=139)	Vinorelbine (n=52)	Capecitabine (n=33)	Gemcitabine (n=38)
Female, n (%)		265 (99)	139 (100)	52 (100)	33 (100)	38 (100)
Age, median (range), y		54 (27–82)	53 (27–80)	54 (30–74)	50 (31–81)	56 (36–81)
Race or ethnic group, n (%)[a]	White	215 (81)	109 (78)	36 (69)	27 (82)	31 (82)
	Black	28 (11)	18 (13)	12 (23)	2 (6)	2 (5)
	Asian	13 (5)	3 (2)	2 (4)	3 (9)	1 (3)
	Other	11 (4)	9 (7)	2 (4)	1 (3)	4 (11)
ECOG PS, n (%)	0	121 (45)	63 (45)	22 (42)	13 (39)	10 (26)
	1	146 (55)	76 (55)	30 (58)	20 (61)	28 (74)
Number of prior chemotherapies (n %)	2–3	99	57	4	18	13
	>3	168	82	48	15	25
Prior systemic regimens median (range)		4 (2–17)	4 (2–14)	5 (2–14)	3 (2–7)	5 (2–10)

[a]Race was self-reported. Other includes American Indian or Alaska Native, Native Hawaiian or other Pacific Islander. Other Race subgroup includes any patient who did not self-identify as Black race.

Efficacy[3]

The post hoc analysis demonstrated numerical improvements with SG vs each TPC agent for outcomes including PFS, OS, DOR, ORR, and CBR (Table 1).

Table 1. ASCENT Subanalysis (ITT Population): Efficacy Outcomes[3]

Efficacy Outcomes		SG (n=267)	TPC (n=262)			
			Eribulin (n=139)	Vinorelbine (n=52)	Capecitabine (n=33)	Gemcitabine (n=38)
PFS, median (95% CI), mo		4.8 (4.1–5.8)	2.1 (1.5–2.8)	1.5 (1.4–2.5)	1.6 (1.4–2.4)	2.4 (1.4–2.9)
OS, median (95% CI), mo		11.8 (10.5–13.8)	7.2 (6.2–8.2)	5.6 (3.5–6.7)	5.2 (3.5–8.6)	8.4 (5–9.4)
ORR, n (%)		83 (31)	6 (4)	2 (4)	2 (6)	1 (3)
Best overall response, n (%)	CR	10 (4)	2 (1)	0	0	0
	PR	73 (27)	4 (3)	2 (4)	2 (6)	1 (3)
	SD	96 (36)	39 (28)	10 (19)	8 (24)	14 (37)
	SD ≥6 mo	25 (9)	4 (3)	2 (4)	1 (3)	3 (8)
	PD	65 (24)	57 (41)	21 (40)	13 (39)	9 (24)
	NE[a]	23 (9)	37 (27)	19 (37)	10 (30)	14 (37)
CBR[b]		108 (40)	10 (7)	4 (8)	3 (9)	4 (11)
DOR, median (95% CI), mo		6 (6–8)	4 (3–NE)	3 (NE)	NA	3 (NE)
TTR, median (range), mo		2 (1–11)	1 (1–3)	1 (1–2)	3 (1–4)	2 (2–2)

Abbreviations: CR=complete response; NE=not estimable; PD=progressive disease; PR=partial response; SD=stable disease; TTR=time to response

[a]Response could not be evaluated for a variety of reasons, including a lack of postbaseline images or unreadable images.

[b]The percentage of patients with a confirmed overall response of CR or PR and SD ≥6 mo.

Safety[3]

The safety population consisted of patients who received ≥1 dose of study treatment regardless of the presence of baseline brain metastasis. The individual safety profiles of the TPC agents were consistent with those observed in the overall TPC group. Treatment-related safety outcomes were compared between SG and eribulin and between SG and the combined vinorelbine, capecitabine, and gemcitabine group (Table 3).

Treatment-emergent safety outcomes between SG and individual TPC are reported in Tables 3 and 4.

Table 3. ASCENT Subanalysis (Safety Population): All Grade and Grade 3/4 TEAEs[3]

TEAEs,[a] %		SG (n=258)		TPC (n=224)			
				Eribulin (n=122)		Vinorelbine, Capecitabine, Gemcitabine (n=102)	
		TEAE Grade					
		All	3/4	All	3/4	All	3/4
Hematologic	Neutropenia[b]	64	52	39	31	49	37
	Anemia[c]	40	9	25	3	30	11
	Leukopenia[d]	NA	11	NA	5	NA	7
	Febrile neutropenia	NA	6	NA	3	NA	3
Gastrointestinal	Diarrhea	65	12	15	1	20	1
	Nausea	62	NA	35	NA	25	NA
	Vomiting	33	NA	18	NA	14	NA
	Abdominal pain	21	NA	6	NA	11	NA
	Constipation	37	NA	23	NA	24	NA
Other	Fatigue	52	4	39	7	40	11
	Decreased appetite	28	NA	19	NA	23	NA
	Cough	24	NA	19	NA	17	NA
	Dyspnea	17	4	22	6	20	5
	Alopecia	47	NA	26	NA	4	NA

[a]All grade TEAEs that occurred in ≥20% of patients, and worst grades ≥3 TEAEs that occurred in ≥5% of patients in the SG arm; TEAE is defined as an AE with start date on or after the date of first dose of study treatment and up to 30 days after date of last dose of study treatment. Patients may report ≥1 per system organ class or preferred term. At each level of summarization, a patient is counted once if he/she reported ≥1 AE.
[b]Included the combined terms: neutropenia and neutrophil count decreased.
[c]Included the combined terms: anemia and decreased Hgb and red blood cell count decreased.
[d]Included the combined terms: leukopenia and decreased WBC.

Table 4. ASCENT Subanalysis (Safety Population): Safety Summary[3]

Safety Outcomes, n (%)	SG (n=258)	TPC (n=224)			
		Eribulin (n=122)	Vinorelbine (n=43)	Capecitabine (n=28)	Gemcitabine (n=31)
Any TEAE	257 (99)	119 (98)	42 (98)	27 (96)	31 (100)
Grade ≥3					
Leading to dose reduction	57 (22)	27 (22)	17 (40)	3 (11)	12 (40)
Leading to dose interruption	162 (63)	37 (30)	27 (63)	7 (25)	16 (52)
Leading to discontinuation	12 (5)	3 (3)	4 (10)	2 (7)	3 (10)
Leading to death	0	1 (1)	0	0	0
Any SAE	69 (27)	32 (26)	15 (35)	8 (27)	9 (29)

Abbreviations: SAE=serious adverse event

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. Hurvitz SA, Bardia A, Punie K, et al. Subgroup analyses from the phase 3 ASCENT study of sacituzumab govitecan in metastatic triple-negative breast cancer. *NPJ Breast Cancer.* 2024;10(1):33.
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.

Abbreviations

AE=adverse event
BICR=blinded independent central review
CBR=clinical benefit rate
DOR=duration of response
ECOG PS=Eastern Cooperative Oncology Group performance score
mTNBC=metastatic triple-negative breast cancer
ORR=objective response rate
OS=overall survival
PFS=progression-free survival
SG=sacituzumab govitecan-hziy
TPC=treatment of physician's choice
TEAE=treatment-emergent 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: https://www.gilead.com/-/media/files/pdfs/medicines/oncology/trodelvy/trodelvy_pi.pdf.

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 🖱 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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