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Trodelvy® (sacituzumab govitecan-hziy) Impact of BMI on Safety and Efficacy

This document is in response to your request for information regarding the impact of BMI on the safety and efficacy of Trodelvy® (sacituzumab govitecan-hziy [SG]) in patients with metastatic triple-negative breast cancer (mTNBC).

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

Relevant Product Labeling[1]

The recommended dosage of SG is 10 mg/kg administered as an IV infusion once weekly on Days 1 and 8 of 21-day treatment cycles. Continue treatment until disease progression or unacceptable toxicity. Do not administer SG at doses >10 mg/kg.

Calculate the required dose (mg) of SG based on the patient's current body weight.

Clinical Data on the Impact of BMI on the Safety and Efficacy of SG

ASCENT Study

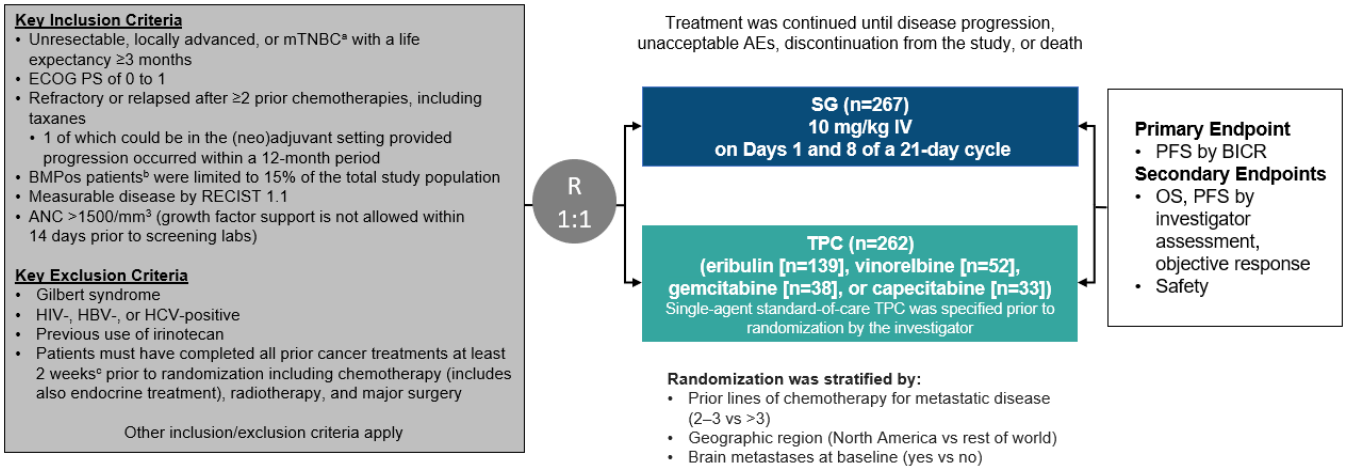
Study design[2]

ASCENT, a global, open-label, randomized, confirmatory, phase 3 study, was conducted to investigate the efficacy and safety of SG in comparison with treatment of physician's choice (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 enrolled and randomly assigned to receive SG (n=267) or TPC (n=262; Figure 1).

The primary endpoint was progression-free survival (PFS) in patients negative for brain metastases at baseline, as measured by a blinded independent central review (BICR). See Figure 1 for key secondary endpoints.

Figure 1. ASCENT Design[2]



Abbreviations: AE=adverse event; ANC=absolute neutrophil count; BMPos=positive for brain metastases; ECOG PS=Eastern Cooperative Oncology Group Performance Status; OS=overall survival; R=randomized; RECIST=Response Evaluation Criteria in Solid Tumors; TNBC=triple-negative breast cancer.
[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.

Ad hoc subgroup analysis[3]

An exploratory ad hoc subgroup analysis was conducted to assess the association of BMI with the efficacy and safety of SG vs chemotherapy in patients from the ITT population of ASCENT (N=509). Patients received either SG 10 mg/kg body weight or TPC; dosage was not capped for high BMI. BMI was assessed at baseline and was classified as underweight (<18.5 kg/m^2), normal (18.5 to <25 kg/m^2), overweight (25 to <30 kg/m^2), or obese (≥30 kg/m^2). Data from patients who were underweight (SG, n=8; TPC, n=11) were excluded from the analysis, as the number of patients was too small to draw meaningful conclusions. Overall, 222/509 patients (44%) had normal BMI values, 155/509 (30%) had overweight BMI, and 132/509 (26%) had obese BMI (Table 1).

Table 1. ASCENT Subgroup Analysis: Baseline Demographics and Disease Characteristics by BMI Subgroup[3]

Key Demographics and Characteristics	Normal (18.5 to <25 kg/m^2)		Overweight (25 to <30 kg/m^2)		Obese (≥30 kg/m^2)	
	SG (n=119)	TPC (n=103)	SG (n=71)	TPC (n=84)	SG (n=68)	TPC (n=64)
Age, median (range), years	53 (29–82)	53 (277–81)	56 (27–80)	55 (30–80)	53 (31–74)	52 (34–80)
Female, n (%)	119 (100)	103 (100)	70 (99)	84 (100)	68 (100)	64 (100)
BMI, mean ± SD, kg/m^2	22.1±1.69	22.1±1.81	27.4±1.39	27.3±1.46	35.7±5.18	35.2±4.99
ECOG PS at screening, 0/1, n (%)	59 (50)/ 60 (50)	44 (43)/ 59 (57)	29 (41)/ 42 (59)	37 (44)/ 47 (56)	31 (46)/ 37 (54)	22 (34)/ 42 (66)
Prior systemic therapies, median (range), n	4 (2–11)	4 (2–14)	4 (2–17)	4 (2–14)	4 (2–11)	4 (2–11)

Results

Within the SG treatment group, higher BMI was associated with numerically improved ORR, PFS, and OS compared with normal BMI (Table 2 and Table 3).

Table 2. ASCENT Subgroup Analysis: PFS by Independent Review and OS Results by BMI Subgroup[3]

BMI Subgroup		SG	TPC	HR (95% CI)	*P*-Value
PFS, median (95% CI), months	Normal (n=222)	4.2 (2.9–5.6)	2.1 (1.5–2.8)	0.48 (0.34–0.67)	<0.0001
	Overweight (n=155)	4.6 (3.3–6.3)	1.5 (1.4–1.6)	0.31 (0.2–0.47)	<0.0001
	Obese (n=132)	5.9 (4.1–8.3)	2.6 (1.6–3)	0.34 (0.21–0.53)	<0.0001
OS, median (95% CI), months	Normal (n=222)	11.2 (9.4–13.5)	6.2 (4.7–7.1)	0.54 (0.4–0.72)	<0.0001
	Overweight (n=155)	10.8 (9–14.2)	6.7 (5.2–8.9)	0.51 (0.35–0.74)	0.0003
	Obese (n=132)	14.9 (11.2–16.8)	8.7 (6.7–9.8)	0.45 (0.3–0.67)	<0.0001

Abbreviation: HR=hazard ratio.

Table 3. ASCENT Subgroup Analysis: Response by Independent Review[3]

Response		Normal (18.5 to <25 kg/m^2)		Overweight (25 to <30 kg/m^2)		Obese (≥30 kg/m^2)	
		SG (n=119)	TPC (n=103)	SG (n=71)	TPC (n=84)	SG (n=68)	TPC (n=64)
ORR,[a] % (95% CI)		24 (17–33)	7 (3–14)	34 (23–46)	1 (0–7)	40 (28–52)	2 (0–8)
OR (95% CI)		4.42 (1.84–10.59)		42.38 (5.56–323.39)		41.49 (5.43–317.26)	
CBR,[b] % (95% CI)		34 (26–44)	10 (5–17)	41 (29–53)	5 (1–12)	50 (38–62)	6 (2–15)
OR (95% CI)		4.89 (2.3–10.39)		13.81 (4.55–41.91)		15 (4.9–45.89)	
BOR,[c] n (%)	CR	2 (2)	1 (1)	5 (7)	0	3 (4)	1 (2)
	PR	27 (23)	6 (6)	19 (27)	1 (1)	24 (35)	0
	SD	50 (42)	28 (27)	24 (34)	18 (21)	21 (31)	23 (36)
	SD ≥6 mo	12 (10)	3 (3)	5 (7)	3 (4)	7 (10)	3 (5)
	PD	31 (26)	37 (36)	17 (24)	38 (45)	14 (21)	20 (31)
	NE	9 (8)	31 (30)	6 (9)	27 (32)	6 (9)	20 (31)

Abbreviations: BOR=best overall response; CR=complete response; NE=not evaluable; OR=odds ratio; PD=progressive disease; PR=partial response; SD=stable disease.
[a]ORR defined as the best confirmed overall response (CR or PR).
[b]CBR defined as the best response of CR or PR or SD ≥6 months.
[c]BOR was based on independent review of tumor response at each tumor assessment per RECIST 1.1.

Safety

In the SG safety population (n=258), dose interruptions and serious adverse events (SAEs) occurred more frequently in the overweight and obese subgroups than in the normal weight subgroup (Table 4). The most common AEs (≥5%) that led to SG dose reductions were neutropenia in the normal weight and overweight subgroups and neutropenia, diarrhea, nausea, and febrile neutropenia in the obese subgroup. Rates of SG dose reductions were highest in the obese subgroup. Rates of treatment-emergent adverse events (TEAEs) that led to SG discontinuation or death were low and were similar between BMI subgroups.

Table 4. ASCENT Subgroup Analysis: SG Exposure and Safety Outcomes by BMI Subgroup (Safety Population)[3]

Safety Outcome	All SG (n=258)	Normal (18.5 to <25 kg/m^2) (n=117)	Overweight (25 to <30 kg/m^2) (n=67)	Obese (≥30 kg/m^2) (n=66)
Time to first dose reduction, median (range), months	1.8 (0.5–18.7)	1.7 (0.7–7.5)	1.8 (0.5–9.7)	1.8 (0.7–18.7)
Patients with dose reductions, n (%)	66 (26)	17 (15)	18 (27)	29 (44)
1 dose reduction/ 2 dose reductions	52 (20)/ 14 (5)	15 (13)/2 (2)	14 (21)/4 (6)	21 (32)/ 8 (12)
Any TEAE,[a] n (%)	257 (100)	117 (100)	66 (99)	66 (100)
Grade ≥3	188 (73)	79 (68)	52 (78)	51 (77)
Treatment-emergent SAEs, n (%)	69 (27)	21 (18)	23 (34)	22 (33)
TEAEs that led to SG interruption, n (%)	162 (63)	68 (58)	43 (64)	47 (71)
TEAEs that led to SG dose reduction, n (%)	57 (22)	12 (10)	16 (24)	27 (41)
TEAEs that led to SG discontinuation, n (%)	12 (5)	5 (4)	2 (3)	5 (8)
TEAEs that led to death, n (%)	1 (<1)	1 (<1)	0	0

[a]A TEAE was defined as an AE with a start date on or after the date of the first dose of SG and ≤30 days after the date of the last dose of SG.

The rates of the most common (≥10%) Grade ≥3 TEAEs were higher in the obese subgroup than in the normal weight subgroup, and the most common Grade ≥3 TEAE experienced by patients treated with SG in all evaluated BMI subgroups was neutropenia (Table 5). In the obese subgroup, diarrhea and infection led to SG discontinuation in 1 patient each; no patients in the obese subgroup discontinued SG due to neutropenia, leukopenia, anemia, or febrile neutropenia.

Table 5. ASCENT Subgroup Analysis: Most Common (≥10%) Grade ≥3 TEAEs in All SG-Treated Patients and by BMI Subgroups (Safety Population)[3]

TEAE,[a] n (%)	All SG (n=258)	Normal (18 to <25 kg/m^2) (n=117)	Overweight (25 to <30 kg/m^2) (n=67)	Obese (≥30 kg/m^2) (n=66)
Neutropenia	135 (52)	61 (52)	33 (49)	38 (58)
Diarrhea	30 (12)	6 (5)	9 (13)	13 (20)
Leukopenia	27 (10)	10 (9)	6 (9)	11 (17)
Infections and infestations[b]	25 (10)	7 (6)	9 (13)	8 (12)
Anemia	24 (9)	6 (5)	8 (12)	10 (15)
Febrile neutropenia	15 (6)	2 (2)	5 (7)	8 (12)

[a]A TEAE was defined as an AE with a start date on or after the date of the first dose of SG and ≤30 days after the date of the last dose of SG.
[b]Includes all preferred terms within the system organ class infections and infestations.

Retrospective Study in Poland[4]

A retrospective cohort study assessed the effects of BMI and weight changes on efficacy and safety outcomes in a Polish cohort that received SG for unresectable locally advanced or mTNBC (N=83). At baseline, 3.6% of patients were underweight (BMI <18.5 kg/m^2), 49.4% had normal weight (18.5–24.9 kg/m^2), 22.9% were overweight (25–29.9 kg/m^2), and 24.1% were obese (≥30 kg/m^2).

Median PFS and OS were 4.07 months and 8.01 months, respectively. There were no significant correlations between baseline weight, BMI, or weight changes and efficacy outcomes (Table 6).

Table 6. Correlations Between Baseline Weight, BMI, or Weight Changes and PFS or OS (Pieniazek et al)[4]

Subgroup	HR (95% CI); *P*-Value	
	PFS	OS
Baseline weight	0.99 (0.956–1.026); *P*=0.595	0.975 (0.933–1.018); *P*=0.252
Weight change[a]	1.017 (0.953–1.085); *P*=0.618	0.963 (0.904–1.027); *P*=0.249
Normal weight (18.5–24.9 kg/m^2)	0.768 (0.388–1.518); *P*=0.447	0.67 (0.307–1.46); *P*=0.313
Obese (≥30 kg/m^2)	0.916 (0.362–2.317); *P*=0.854	0.782 (0.263–2.325); *P*=0.658

[a]Defined as the difference between weight at SG initiation and weight at the last SG cycle.
Note: Multivariate Cox regression analyses were conducted for PFS and OS.

There was no significant correlation between weight stability or weight gain/loss and the incidence or severity of AEs (*P*>0.05). Neutropenia (63.9%) was the most common Grade ≥2 AE and was not associated with any BMI subcategory or weight change.

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. Garcia-Estevez L, Bardia A, Rugo HS, et al. The association of high body mass index with the safety and efficacy of sacituzumab govitecan in patients with metastatic triple-negative breast cancer from the ASCENT study. *ESMO Open.* 2025;10(6).
4. Pieniazek M, Polakiewicz-Gilowska A, Las-Jankowska M, et al. Assessment of weight change and BMI as prognostic markers of survival outcomes in sacituzumab govitecan therapy for mTNBC in a Polish female cohort (abstract). American Society of Clinical Oncology (ASCO); May 30 - June 3, 2025; Chicago, IL.

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

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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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