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Trodelvy® (sacituzumab govitecan-hziy) Efficacy and Safety by HER2 Status in Patients With mTNBC

This document is in response to your request for information about Trodelvy® (sacituzumab govitecan-hziy [SG]) and its efficacy and safety by human epidermal growth factor receptor 2 (HER2) status 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: HER2 Analysis in Patients with mTNBC

ASCENT, a phase 3 study, compared the efficacy and safety of SG compared with chemotherapy treatment of physicians' 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 showed consistent efficacy outcomes with SG vs TPC, regardless of HER2 status. Among those in the HER2 immunohistochemistry (IHC) 0 and HER2-low (IHC 1+ or IHC 2+/ in situ hybridization (ISH) negative) subgroups, the following outcomes were observed in the SG and TPC groups, respectively.

- Median progression-free survival (PFS) of 4.3 months vs 1.6 months, hazard ratio (HR) 0.38 (95% CI: 0.28–0.5) in the HER2 IHC 0 group, and median PFS of 6.2 months vs 2.9 months, HR 0.45 (95% CI: 0.27–0.73) in the HER2-low group.[3]
- Median overall survival (OS) of 11.7 months vs 5.9 months, HR 0.5 (95% CI: 0.39–0.65) in the HER2 IHC 0 group, and median OS of 13.4 months vs 8.7 months, HR 0.52 (95% CI: 0.34–0.78) in the HER2-low group.[3]
- The incidence of Grade ≥3 treatment-emergent adverse events (TEAEs) was 66% vs 52% in the HER2 IHC 0 group and 82% vs 69% in the HER2-low group.[3]

Results should be interpreted with caution due to the proportion of patients without available IHC expression data and lack of central assessment of HER2 expression in 22% of patients.[4]

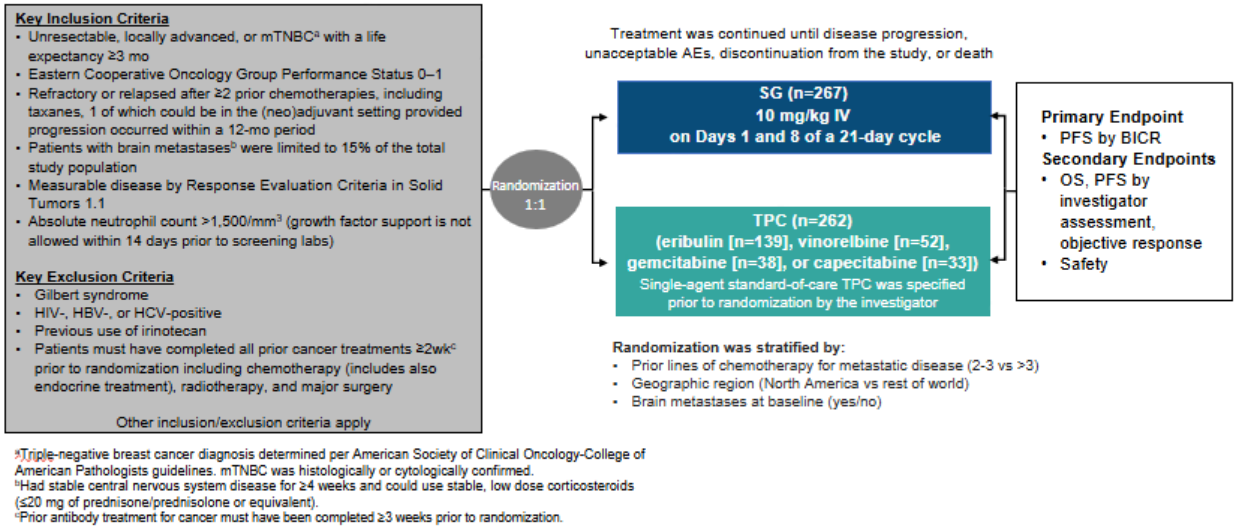
Efficacy and Safety by HER2 Status in Patients With mTNBC

ASCENT Study

Study design and demographics

ASCENT, a phase 3 study, compared efficacy and safety of SG compared with TPC in 529 patients with refractory or relapsed mTNBC who had received ≥2 prior chemotherapies for unresectable, locally advanced, or metastatic disease (Figure 1).[2]

Figure 1. ASCENT Study Design[2,5]



[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 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.

A retrospective, post hoc subgroup analysis of the ITT population evaluated efficacy and safety of SG vs TPC according to HER2 status by analyzing local IHC and ISH results. Of the 529 patients in the ITT population, 78% were HER2 evaluable by IHC and were included in this analysis. Seventy-one percent of patients were HER2 IHC 0, and 29% of patients were HER2-low. Key demographics and baseline characteristics were similar between the ITT and HER2-evaluable ITT populations (Table 1). Note that patients with HER2-positive breast cancer were excluded from the ASCENT study.[3]

Table 1. ASCENT: Demographics and Disease Characteristics in the ITT Population and According to HER2 Status[3]

Variable		ITT Population		HER2-Evaluable ITT Population	
		SG (n=267)	TPC (n=262)	SG (n=211)	TPC (n=204)
Age at study entry, median (range), y		54 (27-82)	53 (27-81)	54 (27-82)	53 (27-81)
Race, n (%)	White	215 (81)	203 (77)	169 (80)	163 (80)
	Black	28 (10)	34 (13)	24 (11)	25 (12)
	Asian	13 (5)	9 (3)	12 (6)	5 (2)
	Other	11 (4)	16 (6)	6 (3)	11 (5)
ECOG PS, n (%)	0	121 (45)	108 (41)	91 (43)	92 (45)
	1	146 (55)	154 (59)	120 (57)	112 (55)

Variable	ITT Population		HER2-Evaluable ITT Population	
	SG (n=267)	TPC (n=262)	SG (n=211)	TPC (n=204)
Previous chemotherapies, 2–3/>3, n (%)	184 (69)/83 (31)	181 (69)/81 (31)	145 (69)/66 (31)	139 (68)/65 (32)

Efficacy

SG showed consistent PFS and OS benefit vs TPC, regardless of HER2 status (Table 2). Objective response rates (ORRs) were greater among those who received SG than among those who received TPC in the HER2 IHC 0 and HER2-low populations and were similar to those observed in the ITT population. Additional efficacy outcomes according to HER2 status are presented in Table 2. Results should be interpreted with caution due to the proportion of patients without available IHC expression data and the lack of central assessment of HER2 expression in 22% of patients.[4]

Table 2. ASCENT: Efficacy in the ITT Population and According to HER2 Status[3]

Variable		ITT		HER2 IHC0		HER2-Low	
		SG (n=267)	TPC (n=262)	SG (n=149)	TPC (n=144)	SG (n=62)	TPC (n=60)
PFS, events, n		191	171	109	103	41	33
Median (95% CI), mo		4.8 (4.1–5.8)	1.7 (1.5–2.5)	4.3 (3–5.8)	1.6 (1.5–2.4)	6.2 (3.8–7.1)	2.9 (1.6–4.2)
HR (95% CI)		0.413 (0.33–0.517)		0.38 (0.28–0.5)		0.45 (0.27–0.73)	
OS, events, n		201	222	113	125	46	47
Median (95% CI), mo		11.8 (10.5–13.8)	6.9 (5.9–7.7)	11.7 (9.9–14)	5.9 (4.8–7.3)	13.4 (9.6–15.2)	8.7 (6.7–9.7)
HR (95% CI)		0.514 (0.422–0.625)		0.5 (0.39–0.65)		0.52 (0.34–0.78)	
ORR, n (%)		83 (31)	11 (4)	46 (31)	5 (4)	20 (32)	5 (8)
OR (95% CI); *P*-value		11 (5.7–21.4); <0.0001		12.4 (4.8–32.3); not reported		5.2 (1.8–15.1); not reported	
Best overall response, n (%)	CR	10 (4)	2 (1)	3 (2)	0	3 (5)	1 (2)
	PR	73 (27)	9 (3)	43 (29)	5 (3)	17 (27)	4 (7)
Clinical benefit rate, n (%)[a]		108 (40)	21 (8)	54 (36)	9 (6)	30 (48)	7 (12)
OR (95% CI); *P*-value		8.1 (4.8–13.5); <0.0001		8.5 (4–18.1); not reported		7.1 (2.8–18); not reported	
Duration of response, median (95% CI), mo[b]		6.3 (5.5–7.9)	3.6 (2.8–NE)	6.9 (5.4–9)	2.9 (2.8–NE)	5.6 (4.3–NE)	3.6 (2.9–NE)
Time to response, median (95% CI), mo[b]		1.5 (0.7–10.6)	1.5 (1.3–4.2	1.6 (1.4–2.8)	1.4 (1.3–NE)	1.5 (1.4–3.3)	1.4 (1.3–NE)

Abbreviations: CR=complete response; NE=not evaluable; OR=odds ratio; PR=partial response; SD=stable disease.

[a]Defined as the percentage of patients with a confirmed best overall response of CR, PR, and SD with a duration of ≥6 mo .

[b]Only patients achieving CR or PR were including in the duration of response and time to response analyses

Safety

Results of safety outcomes in the overall safety population and according to HER2 status are presented in Table 3.

Table 3. ASCENT: Safety in the Overall Safety Population and According to HER2 Status[4]

Variable	Overall Safety Population		HER2 IHC0		HER2-Low	
	SG (n=258)	TPC (n=224)	SG (n=143)	TPC (n=119)	SG (n=60)	TPC (n=52)
Grade ≥3	188 (73)	145 (65)	98 (66)	75 (52)	49 (82)	36 (69)
Led to dose reduction	57 (22)	59 (26)	30 (21)	27 (23)	15 (25)	19 (37)
Led to dose delay	162 (63)	87 (39)	88 (62)	43 (36)	39 (65)	20 (39)
Led to treatment discontinuation	12 (5)	12 (5)	4 (3)	6 (5)	5 (8)	2 (4)
Led to death	1 (<1)[a]	3 (1)	1 (<1)[a]	0	0	3 (6)

[a]Considered unlikely to be related to SG treatment.

References

1. TRODELVY® Gilead Sciences Inc. Trodelvy (sacituzumab govitecan-hziy) for injection, for intravenous use. U.S. Patient 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*. Apr 22 2021;384(16):1529-1541.
3. 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.
4. 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.
5. Bardia A, Hurvitz SA, Tolaney SM, et al. Sacituzumab govitecan in metastatic triple-negative breast cancer [Protocol]. *N Engl J Med*. Apr 22 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: www.gilead.com/-/media/files/pdfs/medicines/oncology/trodelvy/trodelvy_pi.

Follow-Up

For any additional questions, please contact Trodelvy Medical Information at:

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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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