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Trodelvy® (sacituzumab govitecan-hziy) Health-Related Quality of Life in mTNBC

This document is in response to your request for information regarding Trodelvy® (sacituzumab govitecan-hziy [SG]) in patients with metastatic triple-negative breast cancer (mTNBC) and health-related quality of life (HRQoL).

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Summary

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.

HRQoL Subanalyses

The ASCENT study evaluated the efficacy and safety of SG vs chemotherapy treatment of physician's choice (TPC) in patients with refractory or relapsed mTNBC who relapsed after ≥2 prior chemotherapies [2]

HRQoL outcomes were analyzed in the SG (n=236) and TPC (n=183) study arms.[3]

- SG was non-inferior to TPC in all primary and secondary HRQoL domains except nausea/vomiting and diarrhea. Patients who received SG had statistically significant greater improvements in global health status/quality of life (QoL), physical functioning, pain, and fatigue.
- Patients who received SG had a significantly longer time to first clinically meaningful deterioration in physical functioning, role functioning, fatigue, and pain, as well as a significantly shorter time to first clinically meaningful improvement in physical functioning, pain, and dyspnea.

HRQoL outcomes were further analyzed by clinical response (n=82 and n=11) and non-response (n=154 and n=172) in the SG and TPC arms, respectively.[4]

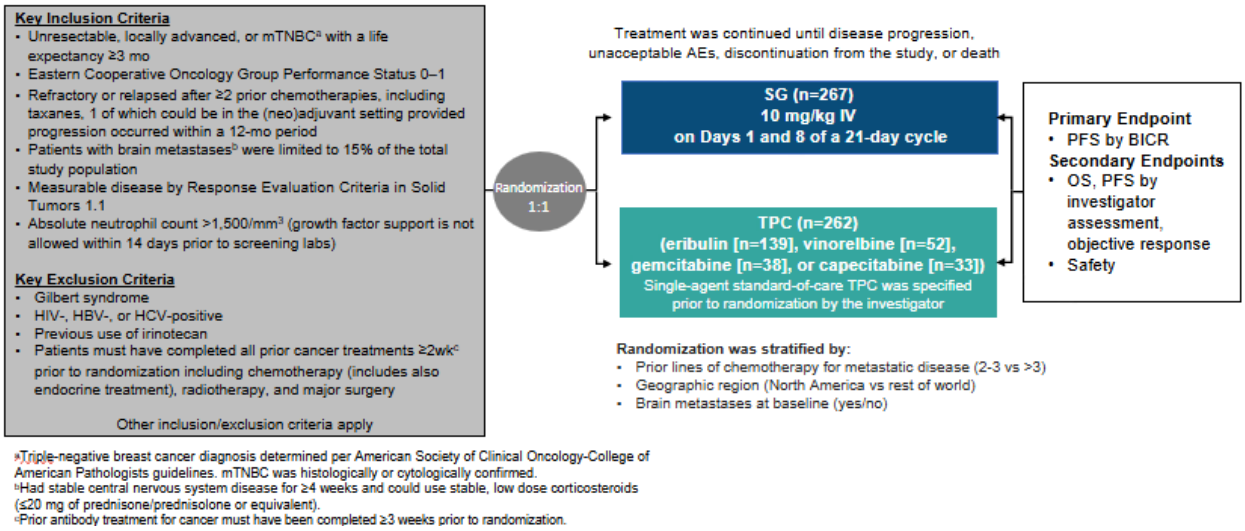
- The time to first deterioration (TTD) was longer among SG clinical responders than among SG non-responders. Across clinical responders, SG had longer TTD than TPC for HRQoL in each domain except fatigue.
- In most European Organization for Research and Treatment of Cancer Quality of Life Core 30 Questionnaire (EORTC QLQ-C30) domains, SG showed more favorable least-square mean (LSM) changes from baseline vs TPC regardless of clinical response status, with the exception of nausea/vomiting and diarrhea.

HRQoL Subanalyses

ASCENT Overall Study Design[2]

ASCENT, a global, open-label, randomized, confirmatory, phase 3 study, evaluated 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 (Figure 1).

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.

Subanalysis of HRQoL Outcomes[3]

A subanalysis compared HRQoL outcomes between SG and TPC over the course of treatment. HRQoL was assessed using EORTC QLQ-C30 within 28 days of initiation of Cycle 1, on Day 1 of each cycle, and 4 weeks after the last dose of study drug or at study discontinuation. The primary HRQoL domains assessed were global health status/HRQoL, physical functioning, role functioning, pain, and fatigue. Other EORTC QLQ-C30 domains were evaluated as secondary HRQoL domains.

The subanalysis included all patients in the ITT population who had evaluable assessments (≥1 of the 15 EORTC QLQ-C30 domains completed) on the EORTC QLQ-C30 at initiation of Cycle 1 and ≥1 post-baseline assessment (Table 1).

Table 1. HRQoL-Evaluable Population[3]

Key Demographics and Characteristics		SG (n=236)	TPC (n=183)
Age, mean (SD), years		53.8 (11.8)	55.5 (11.8)
Race or ethnic group, n (%)	White	195 (83)	139 (76)
	Black	22 (9)	27 (15)
	Asian	10 (4)	8 (4)
	Other	9 (4)	9 (5)
	Positive	15 (6)	14 (8)

BRCA 1/2 mutational status, n (%)	Negative	136 (58)	101 (55)
	Missing	85 (36)	68 (37)
Known brain metastases at study entry, n (%), Yes/No		27 (11)/ 209 (89)	18 (10)/ 165 (90)
Time from diagnosis to study entry, mean (SD), mo		61 (62)	65 (64)
Number of prior systemic therapies, mean (SD), n (%)	2 or 3	168 (71)	132 (72)
	>3	68 (29)	51 (28)

Abbreviation: *BRCA*=breast cancer gene.

Results[3]

Completion rate (number of valid HRQoL assessments divided by the number of ITT patients expected to provide an HRQoL assessment) was ≥90% up to Cycle 6 and was comparable between the 2 study arms. Mean baseline scores (range: 0–100) for the primary HRQoL domains were worse than those reported in the general population of similar age and gender but were comparable between the two arms (**Error! Reference source not found.**).

Table 2. Baseline Scores for the Primary HRQoL Domains[3]

Primary-focused Domains, mean (SD)	SG (n=236)	TPC (n=183)	General Population	MID Between Arms
Global health status/QoL[a]	63.2 (20.6)	**58.1** (21.9)	63.6	4
Physical functioning[b]	**74.9** (20.5)	**73** (20.3)	83.4	5
Role functioning[b]	**69.6** (29.5)	**67.9** (29.3)	83	6
Fatigue[c]	**38.3** (25.2)	**40.1** (25.2)	31.3	5
Pain[c]	**36.4** (30.1)	**40.3** (29.4)	26.7	6

Abbreviation: MID=minimal important difference
Note: Bolded text indicates difference compared with the general population norm greater than the MID. Underlined text indicates that TPC is worse than SG more than the MID. [a]Higher score=better HRQoL. [b]Higher score=better functioning. [c]Higher score=worse symptomatology.

SG was non-inferior to TPC for all primary and secondary HRQoL except nausea/vomiting and diarrhea. SG was superior vs TPC for global health status/QoL, physical functioning, fatigue, pain, emotional functioning, dyspnea, and insomnia (**Error! Reference source not found.**).

Table 3. Overall LSM Change from Baseline in Scores for Primary and Secondary HRQoL Domains[3]

	LSM Change from Baseline (95% CI)			Non-Inferiority Margin
	SG (n=236)	TPC (n=183)	SG minus TPC	
Primary HRQoL domains				
Global health status/ QoL[a]	0.66 (-2.21, 3.53)	-3.42 (-6.77, -0.08)	**4.08** (*0.82*, 7.35)[f]	-4
Physical functioning[b]	1.31 (-1.38, 3.99)	-4.39 (-7.52, -1.26)	**5.69** (*2.63*, 8.76)[g]	-5
Role functioning[b]	-2.24 (-6.13, 1.65)	-7.83 (-12.41, -3.25)	5.59 (*1.13*, 10.05)[f]	-6
Fatigue[c]	1.97 (-1.2, 5.13)	7.13 (3.4, 10.87)	**-5.17** (-8.81, *-1.52*)[g]	+5
Pain[c]	-8.93 (-12.57, -5.3)	-1.89 (-6.18, 2.4)	**-7.04** (-11.24, *-2.85*)[g]	+6
Secondary HRQoL domains				
Emotional functioning[b]	3.34 (0.46, 6.22)	-0.55 (-3.94, 2.84)	**3.89** (*0.56*, 7.22)[f]	-3[d]
Cognitive functioning[b]	-1.22 (-4, 1.56)	-1.98 (-5.21, 1.24)	0.76 (*-2.36*, 3.89)	-3
Social functioning[b]	-1.51 (-5.47, 2.45)	-5.41 (-10.04, -0.78)	3.9 (*-0.61*, 8.4)	-5

	LSM Change from Baseline (95% CI)			Non-Inferiority Margin
	SG (n=236)	TPC (n=183)	SG minus TPC	
Nausea/vomiting[c]	4.3 (1.92, 6.68)	2.5 (-0.23, 5.22)	1.81 (-0.83, 4.44)	+3
Dyspnea[c]	-3.79 (-7.52, -0.06)	3.95 (-0.51, 8.4)	**-7.74** (-12.13, *-3.35*)[g]	+4
Insomnia[c]	-4.69 (-8.92, -0.46)	0.34 (-4.64, 5.32)	**-5.03** (-9.89, *-0.16*)[f]	+4
Appetite loss[c]	3.52 (-0.47, 7.51)	7 (2.31, 11.68)	-3.47 (-8.05, *1.11*)	+5
Constipation[c]	2.16 (-1.76, 6.08)	2.69 (-1.89, 7.27)	-0.53 (-4.97, *3.91*)	+5
Diarrhea[c]	14.07 (9.94, 18.2)	-1.27 (-6.08, 3.54)	15.34 (10.65, 20.03)[g]	+3
Financial difficulties[c]	-2.87 (-6.39, 0.65)	0.68 (-3.5, 4.86)	-3.55 (-7.69, *0.59*)	+3
EORTC QLQ-C30 summary score[a]	-0.67 (-2.73, 1.39)	-3.15 (-5.54, -0.75)	2.48 (0.14, 4.81)[f]	-5[e]

Note: Bolded text indicates SG was superior to TPC based on the MID and significance testing. Underlined text indicates SG was inferior to TPC (the upper bound of the 95% CI was greater than the non-inferiority margin. [a]Higher score=better HRQoL.[b]Higher score=better functioning.[c]Higher score=worse symptomology.[d]The between-group MID could not be estimated, so a within-group MID based on a previously published threshold was used instead.[e]The MID was derived as 0.3 x SD for the overall sample (16.8).[f]*P*<0.05.[g]*P*<0.01

The Kaplan-Meier product limit method was used to analyze time to first clinically meaningful improvement or deterioration of HRQoL (above a pre-specified threshold of 10 points). Patients who received SG had a significantly longer time to first clinically meaningful deterioration in physical functioning, role functioning, fatigue, and pain than those who received TPC (**Error! Reference source not found.**). In addition, patients who received SG had a significantly shorter time to first clinically meaningful improvement in physical functioning (HR: 1.66, *P*=0.01) and pain (HR: 1.41, *P*=0.01).

Table 4. Time to First Clinically Meaningful Deterioration in HRQoL[3]

HRQoL Domain, median, wk	SG (n=236)	TPC (n=183)
Global health status/QoL	14.1	15.1
HR (95% CI)	0.87 (0.7, 1.07) *P*=0.18	
Physical functioning	22.1	12.1
HR (95% CI)	0.61 (0.49, 0.75); *P*<0.001	
Role functioning	11.4	7.1
HR (95% CI)	0.7 (0.56, 0.86); *P*<0.001	
Fatigue	7.7	6
HR (95% CI)	0.82 (0.66, 1); *P*<0.05	
Pain	21.6	9.9
HR (95% CI)	0.6 (0.48, 0.74); *P*<0.001	

Note: Death was treated as an event.

Subanalysis of HRQoL Outcomes According to Clinical Response[4]

HRQoL outcomes between clinical responders and non-responders to SG and TPC over the course of treatment were assessed with EORTC QLQ-C30 using the same schedule that was summarized in the previous subanalysis. Primary HRQoL domains assessed were global health status/QoL, physical functioning, role functioning, pain, and fatigue.

This subanalysis evaluated all patients who underwent randomization and had evaluable assessments (≥1 of the 15 EORTC QLQ-C30 domains completed) on the EORTC QLQ-C30 at baseline and ≥1 post-baseline assessment. Study investigators calculated completion rates (the denominator was the number of participants expected to have an HRQoL

assessment) and available data rates (the denominator was the number of participants in the ITT population). HRQoL outcomes were evaluated according to the best response achieved by patients in each treatment arm: clinical responders were those who had a best overall clinical response of partial response or complete response; non-responders had a best overall response of stable disease, progressive disease, or not evaluable. The TTD in HRQoL was defined as the time between treatment randomization and the time that a participant had a worsening from baseline of ≥10 points. Death was considered an event.

HRQoL assessments were completed by ≥90% of patients in each arm and were comparable between the 2 arms at visits up to Cycle 10. However, completion rates decreased over the study period; assessments were completed by more patients in the SG arm than in the TPC arm. Of those considered HRQoL-evaluable, 35% of patients (82/236) in the SG arm and 6% of patients (11/183) in the TPC arm were clinical responders (Table 5).

Table 5. HRQoL-Evaluable Population[4]

Key Demographics and Characteristics		SG		TPC	
		Clinical Responders (n=82)	Non-Responders (n=154)	Clinical Responders (n=11)	Non-Responders (n=172)
Age, mean (SD), years		56.4 (11.5)	52.4 (11.7)	52.8 (7.6)	55.6 (12)
Race, n (%)	White	69 (84.1)	126 (81.8)	8 (72.7)	131 (76.2)
	Black[a]	8 (9.8)	14 (9.1)	2 (18.2)	25 (14.5)
	Asian	3 (3.7)	7 (4.5)	0	8 (4.7)
	Other	2 (2.4)	7 (4.5)	1 (9.1)	8 (4.7)
Prior systemic therapies, mean (SD)		4 (1.6)	4.7 (2.1)	4.9 (2.5)	4.4 (2.1)
Prior lines of chemotherapies, n (%)	2–3	66 (80.5)	102 (66.2)	7 (63.6)	125 (72.7)
	>3	16 (19.5)	52 (33.8)	4 (36.4)	47 (27.3)
Known brain metastases[b], n (%)		1 (1.2)	26 (16.9)	0	18 (10.5)
BRCA 1/2 mutational status, n (%)	Negative	45 (54.9)	91 (59.1)	7 (63.6)	94 (54.7)
	Positive	3 (3.7)	12 (7.8)	1 (9.1)	13 (7.6)
	Missing	34 (41.5)	51 (33.1)	3 (27.3)	65 (37.8)
Time, diagnosis to study entry[b], mean (SD)		62.4 (62)	60.5 (62.2)	66.7 (92.9)	65 (62.3)

[a]Black or African American, [b]Months

Results[4]

TTD was longer among SG clinical responders than SG non-responders for all primary focused domains (Table 6). Across clinical responder groups, SG had longer TTD than TPC for HRQoL in each domain except fatigue which was similar (HR=1.03, 95% CI: 0.61-1.72). SG showed more favorable LSM changes in HRQoL scores from baseline vs TPC regardless of clinical response status, with the exception of nausea/vomiting and diarrhea.

Table 6. LSM Changes in HRQoL Scores for Primary Focused Domains[4]

HRQoL Domains	LSM Changes from Baseline (95% CI)			
	SG		TPC	
	Clinical Responders (n=82)	Non- Responders (n=154)	Clinical Responders (n=11)	Non-Responders (n=172)
Global health status/QoL[a]	2.46 (-1.52, 6.43)	-0.57 (-3.68, 2.54)	-1.64 (-10.22, 6.95)	-2.29 (-5.63, 1.05)
Functioning[b]				
Physical	2.93 (-0.92, 6.79)	0.22 (-2.71, 3.15)	-3.47 (-11.93, 4.99)	-3.75 (-6.87, -0.63)
Role	-0.35 (-5.74, 5.04)	-3.23 (-7.45, 0.99)	-8.4 (-19.93, 3.13)	-7.33 (-11.88, -2.78)
Symptoms[c]				
Fatigue	0.9 (-3.49, 5.28)	2.84 (-0.6, 6.29)	4.15 (-5.34, 13.65)	6.65 (2.93, 10.38)
Pain	-11.4 (-16.43, -6.36)	-8.57 (-12.48, -4.66)	-11.99 (-22.85, -1.13)	-0.24 (-4.47, 3.99)
Nausea/vomiting	4.68 (1.42, 7.95)	4.03 (1.42, 6.64)	1.38 (-5.53, 8.29)	2.62 (-0.21, 5.45)
Diarrhea	16.03 (10.32, 21.74)	13.65 (9.19, 18.11)	2.46 (-9.88, 14.80)	-1.53 (-6.34, 4.64)

Note: Data collected through Cycle 6, Day 1 (n≥25 in both arms) included in analysis. Between-group inferential statistical testing not performed due to the small n of TPC clinical responders. [a]Higher score=higher QoL. [b]Higher score=higher level of functioning. [c]Higher score=higher level of symptomology.

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*. Apr 22 2021;384(16):1529-1541.
3. Loibl S, Loirat D, Tolaney SM, et al. Health-related quality of life in the phase III ASCENT trial of sacituzumab govitecan versus standard chemotherapy in metastatic triple-negative breast cancer. *Eur J Cancer*. Jan 2023;178:23-33.
4. Loibl S, Tolaney SM, Punie K, et al. Assessment of health-related quality of life by clinical response from the phase 3 ASCENT study in metastatic triple-negative breast cancer (mTNBC) [Poster P5-16-01]. Presented at: San Antonio Breast Cancer Symposium; 07-10 December 2021; San Antonio, Texas.
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

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