GILEAD | Medical Information

# Trodelvy® (sacituzumab govitecan-hziy) Patient-Reported Outcomes in 2L+ 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) in a second-line and later setting (2L+) and patient-reported outcomes (PROs).

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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.

PROs in 2L+ mTNBC

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]

Health-related quality of life (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 also analyzed by clinical response: clinical responders (n=82 and n=11) and non-responders (n=154 and n=172) in the SG and TPC arms, respectively.[4]

- Time to first deterioration (TTD) was longer in SG clinical responders than in SG non-responders. In clinical responders, SG had longer TTD than TPC for HRQoL in all domains 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, except for nausea/vomiting and diarrhea.

An analysis was conducted among the ITT population using the Quality-adjusted Time Without Symptoms of disease progression or Toxicity of treatment (Q-TWiST) method. Survival time was assessed as three separate health states: toxicity (TOX), relapse (REL), and Time Without Symptoms of disease progression or Toxicity of treatment (TWiST).[5]

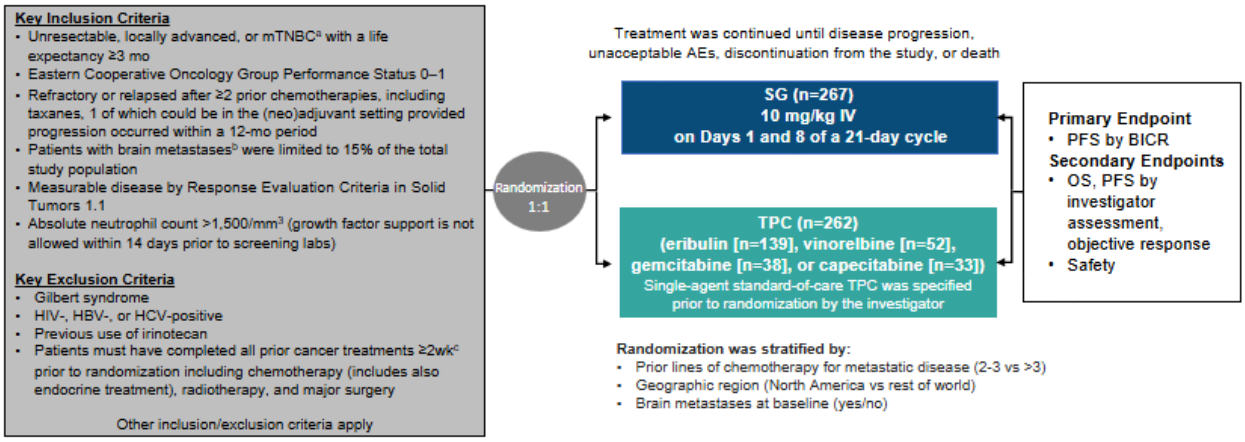
- At the maximum follow-up of 31 months, SG was associated with a statistically significant improvement in progression-free survival (PFS), overall survival (OS), TWiST, and Q-TWiST vs TPC (each, *P*<0.0001). There was a relative Q-TWiST gain of 39.5% with SG, which exceeded the ≥15% threshold for a clearly clinically important difference.

# PROs in 2L+ mTNBC

## ASCENT Study Design[2]

ASCENT, a global, open-label, randomized, confirmatory, phase 3 study, evaluated the efficacy and safety of SG vs 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[2,6]**




[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.

## ASCENT: 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. ASCENT: 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) |
| *BRCA* 1/2 mutational status, n (%) | Positive | 15 (6) | 14 (8) |
| | 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 (Table 2).

**Table 2. ASCENT: 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: Bold results indicate difference vs the general population norm greater than the MID. Underlined results indicate 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 (Table 3).

**Table 3. ASCENT: 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 |

| | LSM Change from Baseline (95% CI) | | | Non-Inferiority Margin |
|---|---|---|---|---|
| | SG (n=236) | TPC (n=183) | SG minus TPC | |
| **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 |
| 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: Bold results indicate SG was superior to TPC based on the MID and significance testing. Underlined results indicate SG was inferior to TPC (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 vs those who received TPC (Table 4). 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. ASCENT: Time to First Clinically Meaningful Deterioration in HRQoL[3]**

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

Note: Death was treated as an event.

## ASCENT: 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.

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 were evaluated. 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 (n=82) in the SG arm and 6% of patients (n=11) in the TPC arm were clinical responders (Table 5).

**Table 5. ASCENT: 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 or African American | 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 chemotherapy, 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, 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 from diagnosis to study entry, mean (SD), months | | 62.4 (62) | 60.5 (62.2) | 66.7 (92.9) | 65 (62.3) |

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

## ASCENT: Q-TWiST Analysis[5]

An analysis was conducted among the ITT population to assess the benefit-risk profile of SG vs TPC. Using the Q-TWiST method, survival time was assessed as three separate health states: TOX, or the time from a treatment emergent adverse event (TEAE) before disease progression to the point at which the TEAE resolved or disease progression, death, or end of follow-up occurred; REL, or the time from disease progression to either death or end of follow-up; and TWiST, or the time spent in the progression-free period without any Grade ≥3 TEAEs. The restricted mean survival time was calculated in TOX, REL, TWiST, PFS, and OS up to the last observed OS follow-up.

### Results

At the maximum follow-up of 31 months, SG was associated with a statistically significant improvement in PFS, OS, TWiST, and Q-TWiST vs TPC (each, *P*<0.0001; Table 7). There was a relative Q-TWiST gain of 39.5% with SG, which exceeded the ≥15% threshold for a clearly clinically important difference.

**Table 7. ASCENT: Q-TWiST Analysis at 31 months (ITT Population)[5]**

| Outcome (95% CI) | SG (n=267) | TPC (n=262) | Difference | *P*-Value |
|---|---|---|---|---|
| OS | 14.2 (13.1,15.4) | 9 (8.1, 9.9) | 5.3 (3.8, 6.6) | <0.0001 |
| PFS | 7.7 (6.5, 9) | 3.1 (2.7, 4.7) | 4.5 (2.8, 5.8) | <0.0001 |
| TOX | 0.7 (0.6, 0.9) [n=174] | 0.6 (0.5, 0.7) [n=115] | 0.2 (0, 0.4) | 0.078 |
| REL | 6.6 (5.4, 7.6) [n=248] | 5.8 (4.3, 6.6) [n=225] | 0.7 (-0.6, 2.7) | 0.39 |
| TWiST | 7 (5.8, 8.2) [n=267] | 2.6 (2.2, 4.1) [n=262] | 4.4 (2.6, 5.7) | <0.0001 |
| Q-TWiST | 8.3 (7.6, 9.1) | 4.8 (4.3, 5.4) | 3.5 (2.6, 4.4) | <0.0001 |

The duration of time spent in TOX, REL, and TWiST was numerically longer in the SG arm than the TPC arm in the base case analysis (Grade ≥3 TEAE); however, the between-group difference in time spent in TOX stabilized over time and was shown to be nonsignificant.

The benefit of SG vs TPC in the Q-TWiST analysis increased over time to Month 31. In the relative Q-TWiST gain analysis, the clinically important threshold (≥10%) was surpassed around 4.5 months, and the clearly clinically important threshold (≥15%) was surpassed around 6.5 months.

## 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. 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. doi:10.1016/j.ejca.2022.10.003. Epub ahead of print.

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 (SABCS); 07-10 December 2021; San Antonio, Texas.
5. Bardia A, Rugo HS, Sedrak MS, et al. Q-TWiST analysis to assess benefit-risk of sacituzumab govitecan in previously treated patients with metastatic triple-negative breast cancer. *JCO Oncol Pract*. 2025;OP2400806. doi:10.1200/OP-24-00806. Epub ahead of print.
6. 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: www.gilead.com/-/media/files/pdfs/medicines/oncology/trodelvy/trodelvy_pi.

# Follow-Up

For any additional questions, please contact Gilead 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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