



Trodelvy[®] (sacituzumab govitecan-hziy)

Dose Modifications in mBC Studies

This document is in response to your request for information regarding Trodelvy[®] (sacituzumab govitecan-hziy [SG]) monotherapy and the rate and impact of dose modifications in metastatic breast cancer (mBC) studies.

Gilead continually assesses safety data from all sources for unidentified drug reactions and updates the product label information accordingly to reflect the safety profile of SG. Because case reports of potential adverse reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish causal relationship to drug exposure. For this reason, Gilead does not provide information from post-marketing spontaneous reports.

Some data may be outside of the US FDA-approved prescribing information. In providing this data, Gilead Sciences, Inc. is not making any representation as to its clinical relevance or to the use of any Gilead product(s). For information about the approved conditions of use of any Gilead drug product, please consult the FDA-approved prescribing information.

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 Labeling¹

Warning—Neutropenia and Diarrhea: SG can cause severe, life-threatening, or fatal neutropenia. Withhold SG for absolute neutrophil count $<1500/\text{mm}^3$ or neutropenic fever. Monitor blood cell counts periodically during treatment. Primary prophylaxis with G-CSF is recommended for all patients at increased risk of febrile neutropenia. Initiate anti-infective treatment in patients with febrile neutropenia without delay.

SG can cause severe diarrhea. Monitor patients with diarrhea and give fluid and electrolytes as needed. At the onset of diarrhea, evaluate for infectious causes and, if negative, promptly initiate loperamide. If severe diarrhea occurs, withhold SG until resolved to \leq Grade 1 and reduce subsequent doses.

Dosage and Administration: 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.

Monitor patients during the infusion and for at least 30 minutes after completion of infusion. Treatment interruption and/or dose reduction may be needed to manage adverse reactions.

Premedication: Prior to each dose of SG, premedication for prevention of infusion reactions and prevention of chemotherapy-induced nausea and vomiting is recommended. Premedicate with antipyretics, H1 and H2 blockers prior to infusion, and corticosteroids may be used for patients who had prior infusion reactions. Premedicate with a two or three drug

combination regimen (eg, dexamethasone with either a 5-HT₃ receptor antagonist or an NK₁ receptor antagonist, as well as other drugs as indicated).

Prophylaxis for Neutropenia: Primary prophylaxis with G-CSF is recommended starting in the first cycle for all patients at increased risk of febrile neutropenia.

Management of adverse reactions may require temporary interruption, dose reduction, or treatment discontinuation of SG as described in Tables 1 and 2 of the US FDA-approved Prescribing Information. Do not re-escalate the SG dose after a dose reduction for adverse reactions has been made.

Dose Modifications of SG in mBC Clinical Studies

A total of 1063 patients from four studies of multiple epithelial tumors (ASCENT,² TROPiCS-02,³ TROPY-U-01,⁴ and IMMU-132-01⁵) were included in this pooled safety analysis.⁶ These studies included patients with mTNBC treated in the 2L+ setting and pretreated HR+/HER2- mBC. The median treatment duration with SG was 4.1 (range: 0–63) mo.⁷

- Overall, dose reductions and interruptions due to any-grade TEAEs occurred in 31% and 58% of patients, respectively. Data related to dose reduction were not collected within IMMU-132-01; thus, they were excluded from the overall data.⁶

Another pooled safety analysis of SG examined safety outcomes in 969 patients from six mBC studies in NA/EU (ASCENT,² TROPiCS-02,³ and IMMU-132-01⁵) and Asia (EVER-132-001,⁸ EVER-132-002,⁹ and ASCENT-J02¹⁰).¹¹

- Dose reductions due to any-grade TEAEs occurred in 28% and 24% of patients in NA/EU and Asia, respectively; 61% and 63% of patients had TEAEs that led to dose interruptions. Data related to dose reduction were not collected in IMMU-132-01; thus, they were excluded from the overall data.¹¹

In ASCENT, a study in 2L+ mTNBC, 61% and 33% of patients in the SG and TPC groups, respectively, had a dose interruption. Dose reductions occurred in 26% and 22% of patients in the SG and TPC groups, respectively.¹²

- Patients in the SG group had improved ORR, CBR, and PFS vs patients in the TPC group, regardless of these dose modifications.¹²

In ASCENT-03, a study in patients treated with SG vs TPC in 1L mTNBC, TEAEs led to dose interruptions in 66% of patients who received SG vs 62% of patients who received TPC, and dose reductions were reported in 37% and 45% of patients, respectively.¹³

In TROPiCS-02, a study in patients with pretreated HR+/HER2- mBC, AEs that led to dose delays and dose reductions occurred in 66% and 33% of patients in the SG group vs 44% and 33% of patients in the TPC group, respectively.^{3,14}

- In the SG group, rates of PFS, OS, CR, and CBR declined with decreases in RDI.¹⁵

In ASCENT-07, a study in 1L post-ET HR+/HER2- breast cancer who have received prior ET, TEAEs led to dose interruption in 75% of patients who received SG vs 46% of patients who received TPC. TEAEs led to dose reduction in 39% and 38% with SG and TPC, respectively.¹⁶

In IMMU-132-01, AEs led to SG treatment interruption and dose reductions in 51.7% and 32.3% of patients with metastatic epithelial cancer, respectively.⁵

In an exposure-response analysis of patients with mTNBC in IMMU-132-01 and ASCENT (N=277), the risk of dose reductions, dose delays, any-grade AEs of vomiting, diarrhea, nausea, or neutropenia, and Grade ≥ 3 neutropenia increased as the CAVG_{SG} increased. The likelihood of continuing SG without requiring a dose reduction or delay was lower with an SG 10 mg/kg starting dose than with SG 8 mg/kg.¹⁷

Dose Modifications of SG in mBC Real-World Studies

A database study (N=433) found that patients who received an SG starting dose of 10 mg/kg had a median DoT of 136 d compared with 77 d for patients with a starting dose of 7.5 mg/kg or less ($P=0.012$). Additionally, dose reductions resulted in a DoT of 172 d compared with 89 d for those without dose reductions ($P<0.001$).¹⁸

A retrospective cohort study analyzed data from medical records of 83 patients with mTNBC in four oncology centers in Poland. Median OS was 8.43 mo for the 74 patients who received $>80\%$ of the initial SG dose vs 2.8 mo for the 9 patients who received $\leq 80\%$ of the initial SG dose (HR 4.826; 95% CI: 2.06–11.3; $P<0.001$). There was no significant impact on PFS between those who received $>80\%$ vs $\leq 80\%$ of the initial SG dose. Initial dose reduction did not significantly affect the toxicity profile (further dose reductions, Grade ≥ 2 or ≥ 3 AEs) or the need for G-CSF administration.¹⁹

A single-center, retrospective chart review of 128 patients with mTNBC and HR+/HER2-mBC was conducted to explore associations between patient/tumor characteristics and SG response. Data analyzed included SG dosage. Improved PFS ($P=0.018$) was demonstrated in patients who had dose reductions. Multivariate analysis supported improved PFS, which was observed in patients who had dose reductions (HR, 0.67; 95% CI: 0.46–0.99; $P=0.044$).²⁰

A single-center, retrospective cohort study compared outcomes of patients who received ≥ 1 cycle of SG 10 mg/kg vs those of patients who received 8 mg/kg. Overall, 12-month OS rates (95% CI) were 39.5% (22.9–68%) in patients who received a standard dose and 48.5% (31.8–74%) in those who received a reduced dose; 24-month OS rates were 13.1% (3.7–46.1%) and 36.9% (20.9–65.3%), respectively. Hospitalization due to SG toxicity was reported in 20.8% of patients who received the standard SG dose and in 4.2% of patients who received the reduced dose ($P=0.19$). Dose reduction was reported in approximately half of patients who received the standard dose and in 33% in the reduced dose group.²¹

Pooled SG Safety Analyses

Safety Analysis in Patients With Multiple Epithelial Tumors

A pooled safety analysis (Figure 1) examined exposure to SG in 1063 patients from four studies of multiple epithelial tumors (ASCENT,² TROPiCS-02,³ TROPY-U-01,⁴ and

IMMU-132-01⁵). These studies included patients with mTNBC treated in the 2L+ setting and pretreated HR+/HER2- mBC.⁶

The median treatment duration with SG in this population was 4.1 (range: 0–63) mo.⁷

Figure 1. Pooled Clinical Studies in Patients With Multiple Epithelial Tumors⁶

| | |
|--|---|
| ASCENT, Phase 3 (n=258) | TROPiCS-02, Phase 3 (n=268) |
| An open label, randomized, confirmatory study in patients with refractory or relapsed mTNBC who had received ≥2 prior chemotherapy regimens, ≥1 for metastatic disease | An open-label, randomized, multicenter study in patients with HR+/HER2- mBC who had received ≥1 taxane, ≥1 endocrine therapy, and ≥1 CDK4/6i in any setting and 2–4 prior chemotherapy regimens for metastatic disease. |
| SG 10 mg/kg IV on Days 1 and 8 of a 21-day cycle Continue treatment until loss of clinical benefit or unacceptable toxicity | |
| TROPHY-U-01, Phase 2 (n=135) | IMMU-132-01, Phase 1/2 (n=402) |
| A multi-cohort, open-label study in patients with unresectable locally advanced, or mUC whose disease progressed: Cohort 1: After prior PLT-based and CPI-based therapies Cohort 2: After CPI-based therapies and who were ineligible for PLT-based therapy. | A single-arm, open-label basket study in patients with metastatic epithelial cancers (including cervical, colorectal, endometrial, esophageal, gastric adenocarcinoma, glioblastoma multiforme, hepatocellular, non-small cell lung, non-TNBC, ovarian, pancreatic, prostate, renal cell, small-cell lung, squamous cell head and neck, TNBC, and urothelial) who had relapsed after or were refractory to ≥1 prior therapy for metastatic disease. |

Abbreviations: CDK4/6i=cyclin-dependent 4/6 inhibitor; PLT=platinum; TNBC=triple-negative breast cancer.

Dose reductions and interruptions⁶

SG dose reductions and interruptions due to any-grade TEAEs occurred in 31% and 58% of patients, respectively (Table 1); data related to dose reduction were not collected within IMMU-132-01, thus, they were excluded from the overall data. Of patients with available *UGT1A1* GTs, those with the *28/*28 GT had a numerically higher rate of dose reductions and interruptions than those with *1/*1 or *1/*28 GTs (Table 1).

Table 1. Pooled Safety in Multiple Epithelial Tumors: Dose Reductions and Interruptions⁶

| TEAEs, n (%) or n/N (%) | All Patients (N=1063) | <i>UGT1A1</i> GT ^a | | |
|------------------------------------|-----------------------|-------------------------------|----------------|-----------------|
| | | *1/*1 (n=416) | *1/*28 (n=420) | *28/*28 (n=112) |
| Led to dose reduction ^b | 205/661 (31) | 69/268 (26) | 89/270 (33) | 30/76 (39) |
| Led to dose interruption | 615 (58) | 243 (58) | 230 (55) | 78 (70) |

^aOther GTs, n=13; missing GTs/not done, n=102.

^bThese data were not collected in IMMU-132-01; those patients were not included in the total.

In an exploratory analysis of G-CSF use that evaluated its use from Day 1 of SG through 30 d after the last SG dose, 9% of those who received a first dose of G-CSF for neutropenia also necessitated a dose reduction.

Safety Analysis in Patients With mBC

Another pooled safety analysis examined exposure to SG 10 mg/kg IV on Days 1 and 8 of a 21-day treatment cycle in 969 patients with either mTNBC treated in the 2L+ setting or pretreated HR+/HER2- mBC from six studies¹¹: ASCENT (n=258), TROPiCS-02 (n=268), and IMMU-132-01 (n=162) in NA/EU; EVER-132-001 (n=80; mTNBC that was relapsed or refractory to ≥2 prior chemotherapy regimens),⁸ EVER-132-002 (n=165; locally recurrent inoperable or metastatic HR+/HER2- BC that progressed after 2–4 prior systemic therapies),⁹ and ASCENT-J02 (mTNBC cohort, n=36; mTNBC that was relapsed or

refractory to ≥ 2 prior chemotherapy regimens, ≥ 1 for metastatic disease)¹⁰ in Asia. Safety data were analyzed by region.¹¹

Dose reductions and interruptions¹¹

Rates of TEAEs that led to dose reductions and interruptions are presented in Table 2.

Table 2. Pooled Safety in mBC: Dose Reductions and Interruptions by Study Region¹¹

| TEAEs, n (%) or n/N (%) | NA/EU (n=688) | Asia (n=281) |
|------------------------------------|---------------|--------------|
| Led to dose reduction ^a | 147/526 (28) | 68 (24) |
| Led to dose interruption | 417 (61) | 177 (63) |

^aThese data were not collected in IMMU-132-01; those patients were not included in the total.

The analysis also evaluated whether certain AEs led to dose reduction. Nausea led to dose reduction in 2% of patients (7/318) in the NA/EU region and 1% (2/159) in the Asian region. Vomiting led to dose reduction in 3% (5/151) and 2% (2/116) of patients in the NA/EU and Asian regions, respectively.

Dose Modifications of SG in mBC Clinical Studies

Adverse reactions were managed with established supportive care measures and included dose modifications.^{3,5,22,23}

ASCENT Study in 2L+ mTNBC

In ASCENT, patients in the SG group (n=258) received a median (range) of 7 (1–33) treatment cycles, with a median (range) treatment duration of 4.4 (0.03–22.9) mo.²²

Efficacy¹²

The primary analysis assessed efficacy in patients who were BMNeg and who received ≥ 1 dose of SG or TPC. A post hoc analysis evaluated efficacy in patients who were BMNeg and who required dose interruption or dose reduction, compared with the overall BMNeg population. SG improved ORR, CBR, and PFS vs TPC, regardless of dose modifications. Additionally, patients in the SG group who had dose interruption(s) or reduction(s) experienced similar efficacy outcomes vs patients without dose modifications (Table 3).

Table 3. ASCENT: Efficacy Outcomes by Dose Reduction and Interruption (BMNeg Population)¹²

| | | ORR, ^a | CBR, ^a | Best Overall Response, n (%) | | PFS, ^a Median |
|--------------------------|-------------|-------------------|-------------------|------------------------------|------------------|--------------------------|
| | | n (%) | n (%) | CR | Partial Response | (95% CI), Mo |
| Overall BMNeg population | SG (n=235) | 82 (35) | 105 (45) | 10 (4) | 72 (31) | 5.6 (4.3–6.3) |
| | TPC (n=233) | 11 (5) | 20 (9) | 2 (1) | 9 (4) | 1.7 (1.5–2.6) |
| Dose reductions | SG (n=62) | 29 (47) | 37 (60) | 5 (8) | 24 (39) | 8.3 (5.4–10.3) |
| | TPC (n=52) | 7 (13) | 11 (21) | 1 (2) | 6 (12) | 2.9 (2.7–4.3) |
| No dose reductions | SG (n=173) | 53 (31) | 68 (39) | 5 (3) | 48 (28) | 4.6 (3.5–5.7) |
| | TPC (n=181) | 4 (2) | 9 (5) | 1 (1) | 3 (2) | 1.5 (1.4–1.7) |
| Dose interruptions | SG (n=144) | 56 (39) | 71 (49) | 7 (5) | 49 (34) | 5.7 (4.3–7) |
| | TPC (n=78) | 5 (6) | 12 (15) | 0 | 5 (6) | 2.7 (1.7–3) |
| No dose interruptions | SG (n=91) | 26 (29) | 34 (37) | 3 (3) | 23 (25) | 4.2 (2.9–6.8) |
| | TPC (n=155) | 6 (4) | 8 (5) | 2 (1) | 4 (3) | 1.6 (1.5–2.2) |

^aAssessed via BICR.

Safety

The safety population included all patients who received ≥ 1 dose of study treatment.^{2,12}

Dose reductions occurred in 26% and 22% of patients in the SG and TPC groups, respectively. Dose reductions due to treatment-related neutropenia or febrile neutropenia were observed in 11% and 19% of patients in the SG and TPC groups, respectively. Dose reductions due to treatment-related diarrhea occurred in 5% and $<1\%$ of patients in the SG and TPC groups, respectively.¹²

Dose interruptions occurred in 61% and 33% of patients in the SG and TPC groups, respectively. Dose interruptions due to treatment-related neutropenia or febrile neutropenia were observed in 46% and 21% of patients in the SG and TPC groups, respectively. No patients in the TPC group and 5% of patients in the SG group required dose interruption(s) due to treatment-related diarrhea.¹²

ASCENT-03 Study in 1L mTNBC

ASCENT-03, an ongoing, global, open-label, randomized, phase 3 study, compares the efficacy and safety of SG vs TPC (gem + carbo, paclitaxel, or nab-paclitaxel), as 1L treatment in patients (N=558) with previously untreated, locally advanced, inoperable or mTNBC who are not candidates for PD-(L)1 inhibitor therapy.²⁴ The median (range) duration of SG treatment at the final PFS analysis was 8.3 mo (<0.1 –28.7).^{13,24}

Neutropenia led to dose reduction in 54 patients (20%) in both treatment groups. Diarrhea led to dose reduction in 15 patients (5%) in the SG group and 3 patients (1%) in the TPC group. EAIRs, defined as the number of patients with ≥ 1 specified TEAE divided by total exposure time (patient years of exposure) in each treatment group, for dose interruption or dose reduction are presented in Table 4.¹³

Table 4. ASCENT-03: EAIRs for Dose Interruption or Dose Reduction¹³

| TEAEs | SG (n=275) | | TPC (n=276) | | EAIR Difference (95% CI) |
|--------------------------|---------------|-------------------|----------------|-------------------|-----------------------------|
| | n (%) | EAIR (95% CI) | n (%) | EAIR (95% CI) | |
| Led to dose interruption | 181 (66) | 2.05 (1.76, 2.37) | 171 (62) | 2.14 (1.83, 2.48) | -0.09 (-0.54, 0.36) |
| Led to dose reduction | 101 (37) | 0.68 (0.55, 0.82) | 124 (45) | 1.15 (0.96, 1.37) | -0.48 (-0.73, -0.23) |

TROPiCS-02 Study in Pretreated HR+/HER2- mBC

In the OSP (n=517), patients received a mean (range) of 8.2 (1–35) treatment cycles of SG over a median (range) duration of 4.1 (0.03–24.2) mo.³ Efficacy specific to patients who required dose interruption(s) or reduction(s), was not reported.^{3,25}

A post hoc subgroup analysis found that ORR, CBR, PFS, and OS results in the SG group decreased numerically as RDI decreased (Table 5).¹⁵

Table 5. TROPiCS-02: Efficacy Outcomes According to RDI in SG Group¹⁵

| Subgroup | | ORR, ^a n (%) | CBR, ^a n (%) | PFS, ^a Median (95% CI), Mo | OS, ^a Median (95% CI), Mo |
|------------------------|----------------|----------------------------|----------------------------|--|---|
| ITT population (n=272) | | 57 (21) | 92 (34) | 5.5 (4.2–7) | 14.4 (13–15.7) |
| RDI ^b | >90% (n=88) | 25 (28) | 37 (42) | 7.3 (4.4–8.9) | 16.5 (13.9–19.1) |
| | >74–90% (n=89) | 17 (19) | 29 (33) | 5.3 (4.1–7) | 15.2 (11.9–18.7) |
| | ≤74% (n=88) | 13 (15) | 24 (27) | 4.2 (2.8–5.7) | 13.1 (11.6–15.3) |

^aAssessed via BICR.

^bRDI accounted for dose reductions and delays; calculated as actual cumulative dose/total planned dose.

In the SG group, AEs that led to dose delays and dose reductions occurred in 178 and 89 patients, respectively. In the TPC group, AEs that led to dose delays and dose reductions occurred in 109 and 82 patients, respectively.²⁵

The absolute incidence rate for TEAEs that led to dose reduction(s) and dose delay(s), EAIRs, and EAIR difference with SG and TPC are presented in Table 6.¹⁴

Table 6. TROPiCS-02: Absolute Incidence, EAIRs,^a and EAIR Differences¹⁴

| | | SG (n=268) | TPC (n=249) |
|---|---------------------------------|-----------------------|------------------|
| TEAEs that led to dose reduction ^b | n (%) | 89 (33) | 82 (33) |
| | Patient-years of exposure | 85.8 | 50.1 |
| | EAIR (95% CI) | 1.04 (0.83–1.28) | 1.64 (1.3–2.03) |
| | EAIR difference vs TPC (95% CI) | -0.6 (-1.05 to -0.19) | |
| TEAEs that led to dose delay ^c | n (%) | 178 (66) | 109 (44) |
| | Patient-years of exposure | 57.1 | 44.6 |
| | EAIR (95% CI) | 3.12 (2.67–3.61) | 2.44 (2.01–2.95) |
| | EAIR difference vs TPC (95% CI) | 0.67 (0.002–1.33) | |

^aReported as patients with >1 event per 1 patient-year of exposure.

^bUpper bound of 95% CI <0 indicates statistically significant (nominally) lower EAIR in SG than TPC.

^cLower bound of 95% CI >0 indicates statistically significant (nominally) higher EAIR in SG than TPC.

A post hoc analysis of outcomes according to age (<65 y vs ≥65 y) was conducted among the SG and TPC groups (Table 7). The incidence of TEAEs that led to treatment interruptions was higher with SG than TPC and did not differ between age groups.¹⁵

Table 7. TROPiCS-02: TEAEs That Led to Dose Modifications According to Age Group¹⁵

| Outcome, n (%) | SG | | TPC | |
|--|---------------|--------------|---------------|--------------|
| | <65 Y (n=196) | ≥65 Y (n=72) | <65 Y (n=188) | ≥65 Y (n=61) |
| TEAEs that led to dose reduction | 63 (32) | 27 (38) | 65 (35) | 17 (28) |
| TEAEs that led to treatment interruption | 129 (66) | 49 (68) | 82 (44) | 27 (44) |

ASCENT-07 Study in 1L Post-ET in HR+/HER2- mBC¹⁶

ASCENT-07, an ongoing, global, open-label, randomized, phase 3 study (N=690), compares the efficacy and safety of SG vs TPC (capecitabine, paclitaxel, or nab-paclitaxel) in patients with HR+/HER2- (IHC 0, IHC 1+, IHC2+/ISH-) locally advanced, inoperable, or mBC who have received prior ET. The median (range) duration of SG treatment at the PFS analysis was 8.3 mo (0–22.1).

TEAEs led to dose interruption in 337 patients (75%) who received SG and in 107 patients (46%) who received TPC. TEAEs led to dose reduction in 174 patients (39%) and 88 patients (38%) who received SG and TPC, respectively.

IMMU-132-01 Study in Metastatic Epithelial Cancer

In IMMU-132-01, the median (range) treatment duration was 3.7 (0–55.2) mo,⁵ and *UGT1A1* testing was performed in all patients.⁵

Efficacy specific to patients who required dose interruption(s) or reduction(s) was not reported.⁵

All patients who received ≥ 1 dose of SG were included in the OSP (N=495). AEs that led to treatment interruption occurred in 51.7% of patients (n=256) and included neutropenia (21%), decreased neutrophil count (9.5%), and anemia (5.3%). Overall, ≥ 1 dose reductions were required in 160 patients (32.3%); 130 patients (26.3%) required a single dose reduction. The median (range) time to first dose reduction was 33 (7–609) d after the first dose of SG.⁵

Dose interruption(s) due to TEAEs were assessed in the safety subpopulation of patients with *UGT1A1* GT (n=403), excluding 92 patients with a status of “not done” and missing records. The dose interruptions were observed in 82 (46.3%), 87 (48.3%), and 33 (71.7%) patients with the **1/*1* (n=177), **1/*28* (n=180), and **28/*28* (n=46) GTs, respectively.²⁶

Exposure-Response Analyses of Efficacy and Safety in the IMMU-132-01 and ASCENT Studies¹⁷

The relationship between exposure to SG and outcomes was assessed in 277 patients with mTNBC from ASCENT and IMMU-132-01 who received SG starting doses 8 or 10 mg/kg. Of the 277 patients, 24 patients were from IMMU-132-01 (8 mg/kg, n=16; 10 mg/kg, n=5; 12 mg/kg, n=3) and 253 patients were from ASCENT (8 mg/kg, n=4; 10 mg/kg, n=249). Measures of exposure, such as CAVG (defined as the CAVG [eg, for SG, free SN-38, and total antibody] between the first SG dose and the time of event, and accounted for dose reductions and delays), were assessed. Models were used to predict response outcomes for SG 8 mg/kg and 10 mg/kg starting doses which included the following covariates: body weight, age, race, region, study (safety only), prior treatment, prior lines of treatment, ECOG PS status, *UGT1A1* GT, and use of *UGT1A1* inhibitors/inducers; lactate dehydrogenase and baseline trophoblast cell-surface antigen 2 (efficacy assessments only); and granulocyte colony stimulating factor (neutropenia assessment only).

In this dataset, the median (range) age and body weight were 54 (27–82) y and 66.7 (37.2–132) kg, respectively; 99.3% were female, 80.5% were White, and 67.9% were from North America.

Exposure-safety analysis

As $CAVG_{SG}$ increased, the probability of any-grade AEs of vomiting, diarrhea, nausea, or neutropenia, and Grade ≥ 3 neutropenia were increased. Within the SG 10 mg/kg starting dose group, the model-predicted proportions of patients with any-grade AE vomiting, diarrhea, nausea, and neutropenia were 35.9%, 67.4%, 64.7%, and 67.1%, respectively; the model-predicted rate of Grade ≥ 3 neutropenia in this group was 54.3%.

$CAVG_{SG}$ was the most statistically significant exposure metric that correlated with the time to first dose reduction and time to first dose delay ($P < 0.001$); as $CAVG_{SG}$ increased, the risk of dose reductions and delays increased (Table 8).

None of the evaluated covariates had a significant effect on the time to first dose reduction, after adjusting for the effect of $CAVG_{SG}$. Patient body weight had a significant effect on the

probability of dose delays ($P<0.001$); patients with a higher body weight were estimated to have a lower risk of dose delays than those with a lower body weight. The likelihood of continuing SG without requiring a dose reduction or delay was lower with an SG 10 mg/kg dose than with SG 8 mg/kg.

Table 8. Exposure-Response Analysis for IMMU-132-01 and ASCENT: Model-Predicted Probability of Dose Modifications Over 12 Mo According to CAVG by Starting Dose¹⁷

| Endpoint | Probability at Mean 8 mg/kg CAVG _{SG} (95% CI) | Probability at Mean 10 mg/kg CAVG _{SG} (95% CI) |
|-------------------------|--|---|
| Dose reduction | 0.0674 (0.0356–0.0993) | 0.212 (0.148–0.276) |
| Dose delay ^a | 0.512 (0.43–0.594) | 0.886 (0.831–0.941) |

^aBased on a median body weight of 66.7 kg.

Dose Modifications of SG in mBC Real-World Studies

Impact of Starting Dose and Dose Reductions on DoT¹⁸

A real-world study utilizing the Integra Connect PrecisionQ database was conducted to evaluate how SG starting dose and rate of dose reduction impacted DoT in patients with ≥ 12 mo of follow-up (N=433). Patient average age was 59.6 y (median: 61 y). Patient diagnosis was not specified in the study.

Results

Three starting doses were evaluated: 10 mg/kg (358/433 [83%]), 7.5 mg/kg (57/433 [13%]), and ≤ 5 mg/kg (18/433 [4%]).

The overall dose reduction rate was 37% (159/433). The rate of dose reduction for patients who started on 10 mg/kg SG was 35% and was not significantly different compared to those who started SG at 7.5 mg/kg or less (43%; $P>0.05$). The dose reduction rate was also not significantly different for patients who started on 7.5 mg/kg SG (39%) compared to those who started SG at doses of ≤ 5 mg/kg (56%; $P>0.05$).

The median DoT overall was 116 d (n=336). Patients who started on 10 mg/kg SG (n=254) had a longer DoT compared to those who started on doses of ≤ 7.5 mg/kg (n=61): 136 d vs 77 d, respectively ($P=0.012$). Additionally, patients who had a dose reduction (n=125) had a longer DoT compared to those (n=190) who did not have a dose reduction: 172 d vs 89 d, respectively ($P<0.001$).

Efficacy and safety were not reported in this study.

Impact of Initial SG Dose Reduction on Efficacy and Safety in Patients With mTNBC¹⁹

A retrospective cohort study analyzed data from medical records of 83 patients with mTNBC in four oncology centers in Poland. The impact of initial SG dose reduction on clinical outcomes and tolerability was assessed. Median (IQR) age was 55 (30–86) y and median (IQR) follow-up was 7.5 (3.22–11.29) mo.

Results

In the full cohort of 83 patients (initial SG dose; >80% [n=74], ≤80% [n=9]), median (95% CI) PFS and OS were 3.9 (2.77–4.55) mo, and 8 (6.38–9.83) mo, respectively. Grade ≥2 and ≥3 AEs were observed in 69 (83.1%) and 47 (56.6%) of the 83 patients, respectively. G-CSF was administered in 70 cases (84.3%).

Median OS was 8.43 mo for the 74 patients who received >80% of the initial SG dose vs 2.8 mo for the 9 patients who received ≤80% of the initial SG dose (HR, 4.826; 95% CI: 2.06–11.3; $P<0.001$). There was no significant impact on PFS between those who received >80% vs ≤80% of the initial SG dose. Initial dose reduction did not significantly affect the toxicity profile (further dose reductions, Grade ≥2 or ≥3 AEs) or the need for G-CSF administration.

Impact of SG Dosage on PFS²⁰

A single-center, retrospective chart review of patients (N=128) with mTNBC (74.2%) and HR+/HER2- mBC explored associations between patient/tumor characteristics and SG response. Data analyzed included SG dosage. Patients received SG as median fourth-line therapy (range 1–13). Improved PFS ($P=0.018$) was demonstrated in patients who had dose reductions. Multivariate analysis supported improved PFS, which was observed in patients who had dose reductions (HR, 0.67; 95% CI: 0.46-0.99; $P=0.044$). Safety data specific to patients who had dose reductions was not reported.

Impact of Standard SG Dose vs Reduced Dose on Outcomes²¹

A single-center, retrospective cohort study of patients with mTNBC and ER+/HER2- mBC (N=48) compared outcomes of patients who received ≥1 cycle of SG standard dose (10 mg/kg; n=24) with those of patients who received a reduced dose (8 mg/kg; n=24). The median treatment duration for patients receiving the standard dose and the reduced dose were 98 days and 107 days, respectively ($P=0.71$). Overall, 12-month OS rates (95% CI) were 39.5% (22.9–68%) in patients who received a standard dose and 48.5% (31.8–74%) in those who received a reduced dose; 24-month OS rates were 13.1% (3.7–46.1%) and 36.9% (20.9–65.3%), respectively. Hospitalization due to SG toxicity was reported in 20.8% of patients who received the standard SG dose and in 4.2% of patients who received the reduced dose ($P=0.19$). Dose reduction was reported in approximately half of patients who received the standard dose and in 33% in the reduced dose group. The median time to dose reduction was 51 days with the standard dose and 29 days with the reduced dose.

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. Rugo HS, Bardia A, Marme F, et al. Sacituzumab govitecan in hormone receptor-positive/human epidermal growth factor receptor 2-negative metastatic breast cancer. *J Clin Oncol*. 2022;40(29):3365-3376.
4. Loriot Y, Petrylak DP, Kalebasty AR, et al. TROPHY-U-01, a phase II open-label study of sacituzumab govitecan in patients with metastatic urothelial carcinoma progressing after

- platinum-based chemotherapy and checkpoint inhibitors: updated safety and efficacy outcomes. *Ann Oncol.* 2024;35(4):392-401.
5. Bardia A, Messersmith WA, Kio EA, et al. Sacituzumab govitecan, a Trop-2-directed antibody-drug conjugate, for patients with epithelial cancer: final safety and efficacy results from the phase I/II IMMU-132-01 basket trial. *Ann Oncol.* 2021;32(6):746-756.
 6. Rugo HS, Tolaney SM, Bardia A, et al. Pooled safety analysis of sacituzumab govitecan in multiple solid tumor types [Poster 3029]. Presented at: American Society of Clinical Oncology (ASCO); May 31-June 4, 2024; Chicago, IL.
 7. TRODELVY® Gilead Sciences Inc. Trodelvy (sacituzumab govitecan-hziy) for injection, for intravenous use. U.S. Prescribing Information. Foster City, CA.
 8. Ma F, Wang S, Tong Z, et al. Overall survival results from EVER-132-001, a phase 2b single-arm study of sacituzumab govitecan in Chinese patients with metastatic triple-negative breast cancer [Poster PO1-06-10]. Presented at: San Antonio Breast Cancer Symposium (SABCS); December 5-9, 2023; San Antonio, TX.
 9. Xu B, Wang S, Yan M, et al. Sacituzumab govitecan in HR+/HER2- metastatic breast cancer: the randomized phase 3 EVER-132-002 trial. *Nat Med.* 2024;30(12):3709-3716.
 10. Naito Y, Nakamura S, Kawaguchi-Sakita N, et al. Preliminary results from ASCENT-J02: a phase 1/2 study of sacituzumab govitecan in Japanese patients with advanced solid tumors. *Int J Clin Oncol.* 2024;29(11):1684-1695.
 11. Rugo HS, Tolaney SM, Cortés J, et al. Sacituzumab govitecan in patients with metastatic breast cancer: pooled safety analysis of data from patients in North America, Europe, and Asia. *ESMO Open.* 2026;11(4).
 12. Rugo HS, Tolaney SM, Loirat D, et al. Safety analyses from the phase 3 ASCENT trial of sacituzumab govitecan in metastatic triple-negative breast cancer. *NPJ Breast Cancer.* 2022;98(8).
 13. Hurvitz S, Bardia A, Tolaney SM, et al. Safety analysis of ASCENT-03, a phase 3 study of sacituzumab govitecan vs chemotherapy for previously untreated advanced triple-negative breast cancer in patients who are not candidates for PD-(L)1 inhibitors [Poster PS1-13-24]. Presented at: San Antonio Breast Cancer Symposium (SABCS); December 9-12, 2025; San Antonio, TX.
 14. Tolaney SM, Schmid P, Bardia A, et al. Exposure-adjusted incidence rates of adverse events from the phase 3 TROPiCS-02 study of sacituzumab govitecan vs treatment of physician's choice in HR+/- HER2- metastatic breast cancer. Paper presented at: San Antonio Breast Cancer Symposium; December 6-10, 2022; San Antonio, Texas.
 15. Bardia A, Schmid P, Tolaney SM, et al. Clinical outcomes by age subgroups in the phase 3 TROPiCS-02 study of sacituzumab govitecan vs treatment of physician's choice in HR+/HER2- metastatic breast cancer. Paper presented at: Florida Society of Clinical Oncology Business of Oncology Summit & Spring Session; May 4-5, 2024; Kissimmee, FL.
 16. Jhaveri K, Park YH, Barrios C, et al. Sacituzumab govitecan vs chemotherapy as first therapy after endocrine therapy in HR+/HER2- (IHC 0, 1+, 2+/ISH-) metastatic breast cancer: primary results from ASCENT-07. Presented at: San Antonio Breast Cancer Symposium (SABCS); December 9-12, 2025; San Antonio, TX.
 17. Sathe AG, Diderichsen PM, Fauchet F, Phan SC, Girish S, Othman AA. Exposure-response analyses of sacituzumab govitecan efficacy and safety in patients with metastatic triple-negative breast cancer. *Clin Pharmacol Ther.* 2025;117(2):570-578.
 18. Gorantla V, Erin A, Mike G, et al. Assessment of initial dosing and dose management of Sacituzumab Govitecan-hziy (SG) and How Dosing Practices Impact duration of therapy (DOT) [Poster P02-18-01]. Paper presented at: San Antonio Breast Cancer Symposium (SABCS); December 5-9, 2023; San Antonio, Texas.
 19. Puskulluoglu M, Polakiewicz-Gilowska A, Las-Jankowska M, et al. Sacituzumab govitecan initial dose reduction in Polish patients with metastatic triple-negative breast cancer: Impact on efficacy and safety (abstract e13136). Presented at American Society of Clinical Oncology (ASCO); May 30-June 3, 2025; Chicago, IL.
 20. Wong M, LeVee A, Ruel N, McArthur H, Mortimer JE. Characteristics associated with sacituzumab govitecan response in the real-world setting [Abstract P1-09-30]. Presented at: San Antonio Breast Cancer Symposium (SABCS); December 10-14, 2024; San Antonio, TX.

21. Stabellini N, Bennett A, Mallatt N, et al. Real world data with standard and reduced dose sacituzumab-govitecan in metastatic triple negative and ER+/HER2- metastatic breast cancer [Poster P3-12-14]. Paper presented at: Presented at: San Antonio Breast Cancer Symposium (SABCS); December 10-14, 2024; San Antonio, TX.
22. Bardia A, Hurvitz SA, Tolaney SM, et al. Sacituzumab govitecan in metastatic triple-negative breast cancer [Supplementary Appendix]. *N Engl J Med.* 2021;384(16):1529-1541.
23. Cortés J, Punie K, Barrios C, et al. Sacituzumab govitecan in untreated, advanced triple-negative breast cancer [Protocol]. *N Engl J Med.* 2025;393(19):1912-1925.
24. Cortés J, Punie K, Barrios C, et al. Sacituzumab govitecan in untreated, advanced triple-negative breast cancer. *N Engl J Med.* 2025;393(19):1912-1925.
25. Rugo HS, Bardia A, Marme F, et al. Sacituzumab Govitecan in Hormone Receptor-Positive/Human Epidermal Growth Factor Receptor 2-Negative Metastatic Breast Cancer [Supplementary Appendix] *J Clin Oncol.* 2022;40(29):3365-3376.
26. Bardia A, Messersmith WA, Kio EA, et al. Sacituzumab govitecan, a Trop-2-directed antibody-drug conjugate, for patients with epithelial cancer: final safety and efficacy results from the phase I/II IMMU-132-01 basket trial [Supplementary Appendix]. *Ann Oncol.* 2021;32(6):746-756.

Abbreviations

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| 1L=first line | G-CSF=granulocyte colony-stimulating factor | OS=overall survival |
| 2L+=second line and later | GT=genotype | OSP=overall safety population |
| 5-HT3=5-hydroxytryptamine type 3 | H1/2=histamine 1/2 | PD-(L)1=programmed death (ligand) 1 |
| AE=adverse event | HER2-=human epidermal growth factor receptor 2-negative | PFS=progression-free survival |
| BICR=blinded independent central review | HR=hazard ratio | RDI=relative dose intensity |
| BMNeg=negative for brain metastasis | HR+=hormone receptor-positive | SG=sacituzumab govitecan-hziy |
| CAVG=average concentration | IHC=immunohistochemistry | SN-38=active metabolite of irinotecan |
| CBR=clinical benefit rate | ISH=in situ hybridization | TEAE=treatment-emergent adverse event |
| CPI=checkpoint inhibitor | mBC=metastatic breast cancer | TPC=treatment of physician's choice |
| CR=complete response | mTNBC=metastatic triple-negative breast cancer | UGT1A1=uridine diphosphate-glucuronosyl transferase 1A1 |
| DoT=duration of therapy | mUC=metastatic urothelial cancer | |
| EAIR=exposure-adjusted incidence rate | NA=North America | |
| ECOG PS=Eastern Cooperative Oncology Group Performance Status | NK ₁ =neurokinin-1 | |
| ET=endocrine therapy | OR=odds ratio | |
| | ORR=objective response rate | |

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