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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 Labeling[1]

Dosage and Administration: Recommended Dosage

The recommended dosage of SG as a single agent or in combination with pembrolizumab is 10 mg/kg administered as an IV infusion on Days 1 and 8 of each 21-day cycle. Continue SG until disease progression or unacceptable toxicity. Do not administer SG at doses >10 mg/kg.

Dosage and Administration: Dosage Modifications for Adverse Reactions

Management of adverse reactions may require temporary interruption, dose reduction, or permanent 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.

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; see Tables 1 and 2 of the US FDA-approved Prescribing Information

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] TROPHY-U-01,[4] and IMMU-132-01[5]) were included in this pooled safety analysis. These studies included patients with mTNBC treated in the 2L+ setting and pretreated HR+/HER2- mBC.[6]

- 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-132-01[5]) and Asia (EVER-132-001,[7] EVER-132-002,[8] and ASCENT-J02[9]).[10]

- 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.[10]

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.[11]

- Patients in the SG group had improved ORR, CBR, and PFS vs patients in the TPC group, regardless of these dose modifications.[11]

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.[12]

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.[3,13]

- In the SG group, rates of PFS, OS, CR, and CBR declined with decreases in RDI.[14]

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.[15]

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.[16]

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).[17]

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 ≤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.[18]

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).[19]

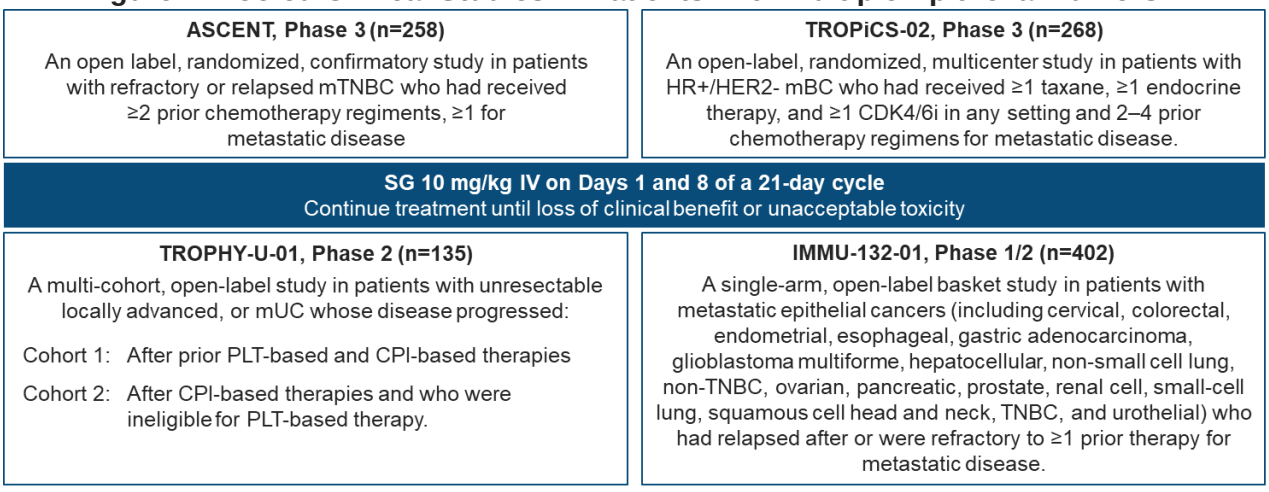
A single-center, retrospective cohort study compared outcomes of patients who received ≥1 cycle of SG 10 mg/kg vs those of patients who received 8 mg/kg. Overall, 12-month OS rates (95% CI) were 39.5% (22.9–68%) in patients who received a standard dose and 48.5% (31.8–74%) in those who received a reduced 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.[20]

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] TROPHY-U-01,[4] and IMMU-132-01[5]). These studies included patients with mTNBC treated in the 2L+ setting and pretreated HR+/HER2- mBC.[6]

Figure 1. Pooled Clinical Studies in Patients With Multiple Epithelial Tumors[6]



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

Dose reductions and interruptions[6]

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 Interruptions[6]

TEAEs, n (%) or n/N (%)	All Patients (N=1063)	*UGT1A1* 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)

[a]Other GTs, n=13; missing GTs/not done, n=102.
[b]These 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 studies[10]: 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),[7] EVER-132-002 (n=165; locally recurrent inoperable or metastatic HR+/HER2- BC that progressed after 2–4 prior systemic therapies),[8] and ASCENT-J02 (mTNBC cohort, n=36; mTNBC that was relapsed or refractory to ≥2 prior chemotherapy regimens, ≥1 for metastatic disease)[9] in Asia. Safety data were analyzed by region.[10]

Dose reductions and interruptions[10]

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 Region[10]

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)

[a]These 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.[3,5,21,22]

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.[21]

Efficacy[11]

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)[11]

		ORR,[a] n (%)	CBR,[a] n (%)	Best Overall Response, n (%)		PFS,[a] Median (95% CI), Mo
				CR	Partial Response	
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)

[a]Assessed via BICR.

Safety

The safety population included all patients who received ≥1 dose of study treatment.[2,11]

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.[11]

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.[11]

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.[23] The median (range) duration of SG treatment at the final PFS analysis was 8.3 mo (<0.1–28.7). [12,23]

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.[12]

Table 4. ASCENT-03: EAIRs for Dose Interruption or Dose Reduction[12]

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.[3,24]

A post hoc subgroup analysis found that ORR, CBR, PFS, and OS results in the SG group decreased numerically as RDI decreased (Table 5).[14]

Table 5. TROPiCS-02: Efficacy Outcomes According to RDI in SG Group[14]

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)

[a]Assessed via BICR.
[b]RDI 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.[24]

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.[13]

Table 6. TROPiCS-02: Absolute Incidence, EAIRs,[a] and EAIR Differences[13]

		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)	

[a]Reported as patients with >1 event per 1 patient-year of exposure.
[b]Upper bound of 95% CI <0 indicates statistically significant (nominally) lower EAIR in SG than TPC.
[c]Lower 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.[14]

Table 7. TROPiCS-02: TEAEs That Led to Dose Modifications According to Age Group[14]

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- mBC[15]

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.[25]

Exposure-Response Analyses of Efficacy and Safety in the IMMU-132-01 and ASCENT Studies[16]

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 Dose[16]

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)

[a]Based 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 DoT[17]

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 mTNBC[18]

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 PFS[19]

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 Outcomes[20]

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

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Abbreviations

1L=first line
2L+=second line and later
5-HT3=5-hydroxytryptamine type 3
AE=adverse event
BICR=blinded independent central review
BMNeg=negative for brain metastasis
CAVG=average concentration
CBR=clinical benefit rate
CPI=checkpoint inhibitor
CR=complete response
DoT=duration of therapy
EAIR=exposure-adjusted incidence rate
ECOG PS=Eastern Cooperative Oncology Group Performance Status
ET=endocrine therapy
G-CSF=granulocyte colony-stimulating factor
GT=genotype
H1/2=histamine 1/2
HER2-=human epidermal growth factor receptor 2-negative
HR=hazard ratio
HR+=hormone receptor-positive
IHC=immunohistochemistry
ISH=in situ hybridization
mBC=metastatic breast cancer
mTNBC=metastatic triple-negative breast cancer
mUC=metastatic urothelial cancer
NA=North America
NK_1=neurokinin-1
OR=odds ratio
ORR=objective response rate
OS=overall survival
OSP=overall safety population
PD-(L)1=programmed death (ligand) 1
PFS=progression-free survival
RDI=relative dose intensity

SG=sacituzumab govitecan-hziy
SN-38=active metabolite of irinotecan
TEAE=treatment-emergent adverse event
TPC=treatment of physician's choice
UGT1A1=uridine diphosphate-glucuronosyl transferase 1A1

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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Gilead Pharmacovigilance and Epidemiology ☎ 1-800-445-3235, option 3 or 🖱 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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