

Trodelvy[®] (sacituzumab govitecan-hziy) Use in 1L Post-Endocrine Therapy in HR+/HER2- mBC

This document is in response to your request for information regarding Trodelvy[®] (sacituzumab govitecan-hizy [SG]) and its use as first line (1L) post-endocrine therapy (ET) in hormone receptor-positive/human epidermal growth factor receptor 2-negative (HR+/HER2-) metastatic breast cancer (mBC).

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Trodelvy is not indicated for use as 1L post-ET in HR+/HER2- mBC. 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

Clinical Data on SG Use in 1L Post-ET in HR+/HER2- mBC¹

The ASCENT-07 study is an ongoing, global, randomized, open-label, phase 3 study (N=690) that is investigating the efficacy and safety of SG vs chemotherapy treatment of physician's choice (capecitabine, paclitaxel, or nab-paclitaxel) in patients with HR+/HER2- (IHC 0, IHC 1+, IHC 2+/ISH-) LA, inoperable, or mBC.

- Eligible adults with HR+/HER2- mBC had previously received ET and were eligible for 1L chemotherapy in the advanced or metastatic setting.
- The study did not meet its primary endpoint of PFS by BICR according to RECIST v1.1; median PFS (95% CI) was 8.3 mo (8.1–10.3) for SG vs 8.3 mo (6.9–10) for TPC; HR (95% CI) 0.85 (0.69–1.05), $P=0.13$.
 - Median PFS (95% CI) per investigator assessment, a secondary endpoint, showed a numerical improvement with SG vs TPC: 8.4 mo (8.2–9.7) vs 6.4 mo (6–8.1), HR 0.78 (95% CI 0.64–0.93) nominal $P=0.008$.
- Formal statistical testing was not conducted for subsequent endpoints in the statistical hierarchy as PFS by BICR was not statistically significant, results of these endpoints are descriptive only.
 - Results for median OS were immature (27% maturity) at the time of the primary PFS analysis; an early trend favoring SG over TPC was observed: HR 0.72 (95% CI 0.54–0.97), nominal $P=0.029$.
 - ORR per BICR (95% CI) was similar between treatment arms: 37% (32–42) with SG vs 33% (27–39) with TPC, OR 1.2 (95% CI 0.86–1.69).
- The most common Grade ≥ 3 TEAEs for SG and TPC, respectively were neutropenia (56% vs 21%), leukopenia (14% vs 7%), and anemia (10% vs 5%).

- Rates of dose reduction were similar in both treatment arms (SG: 39%; TPC: 38%) and the treatment discontinuation rate was lower for SG (3% vs 7%).
- There were 6 TRAEs which led to death in the SG arm and 2 in the TPC arm.

Clinical Data on SG Use in 1L Post-ET HR+/HER2-mBC

ASCENT-07 Study

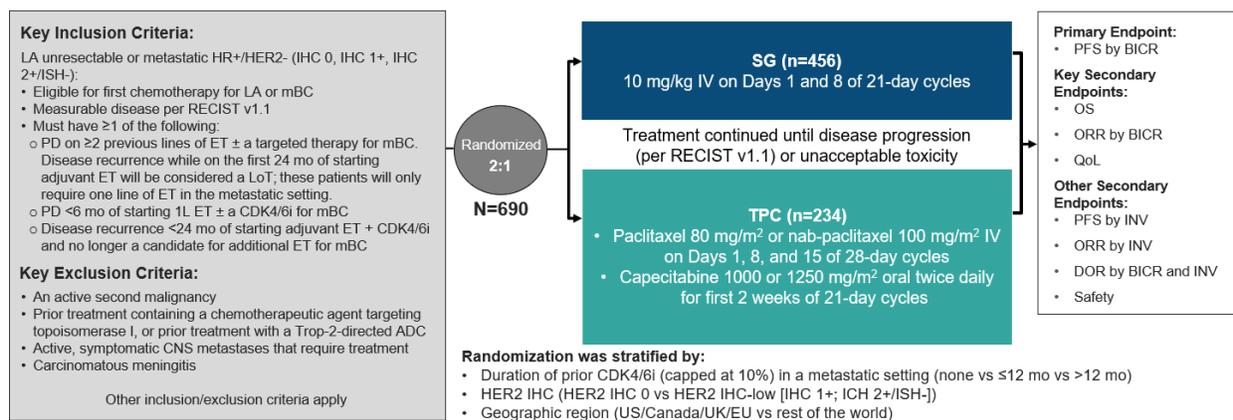
Study design and demographics

ASCENT-07, an ongoing, global, randomized, open-label, phase 3 study, is investigating the efficacy and safety of SG vs TPC (capecitabine, paclitaxel, or nab-paclitaxel) in 690 patients (99% female) with HR+/HER2- LA, inoperable, or mBC (Figure 1). Eligible adults with HR+/HER2- mBC had previously received ET and were eligible for 1L chemotherapy in the advanced or metastatic setting and met ≥ 1 of the following criteria¹:

- PD in the metastatic setting after ≥ 2 lines of ET \pm targeted therapy. Only one line of ET in the metastatic setting was required if disease recurrence occurred while on the first 24 mo after starting adjuvant ET
- PD < 6 mo of starting 1L ET \pm CDK4/6i for mBC
- Disease recurrence < 24 mo of starting adjuvant ET + CDK4/6i and not a candidate for further ET for mBC.

See Table 1 for baseline demographics and disease characteristics.

Figure 1. ASCENT-07 Study Design^{1,2}



Abbreviations: ADC=antibody drug conjugate; QoL=quality of life.

Table 1. ASCENT-07: Baseline Demographics and Disease Characteristics¹

Select Demographics and Characteristics		SG (n=456)	TPC (n=234)
Age, median (range), y		57 (29–88)	58 (27–80)
Age ≥ 65 , n (%)		106 (23)	74 (32)
Race or ethnic group, ^a n (%)	White/Asian/Black	227 (50)/ 176 (39)/ 10 (2)	106 (45)/ 95(41)/ 3 (1)
	Other or not specified	43 (9)	30 (13)
Geographic region, ^b n (%)	US/Canada/Europe	181 (40)	93 (40)
	Rest of the world	275 (60)	141 (60)

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Select Demographics and Characteristics		SG (n=456)	TPC (n=234)
ECOG PS, n (%)	0/1	269 (59)/ 187 (41)	145 (62)/ 89 (38)
ER/PR status, ^c n (%)	ER+ and PR+	286 (63)	165 (71)
	ER+ and PR-	164 (36)	66 (28)
	ER- and PR+	2 (<1)	2 (1)
HER2 expression, ^{c,d} n (%)	IHC0	192 (42)	100 (43)
	HER2 low (IHC 1+; IHC 2+/ISH-)	264 (58)	134 (57)
Primary endocrine resistance, ^e n (%)		143 (31)	62 (26)
Time since metastatic diagnosis to randomization, median (range), mo		23.9 (0.5–192)	26.2 (0.3–152.1)
De novo metastatic disease at diagnosis, n (%)		111 (24)	48 (21)
Visceral disease, n (%)		407 (89)	205 (88)
Metastatic sites, n (%)	Liver	320 (70)	156 (67)
	Brain	18 (4)	14 (6)
Bone disease, n (%)		18 (4)	11 (5)

^aPatient reported. Other/Not specified: American Indian or Alaska Native, other races, and not provided or collection not permitted.

^bEurope: Austria, Belgium, Czech Republic, France, Germany, Greece, Hungary, Italy, Poland, Portugal, and Spain. Rest of the world: Argentina, Australia, Brazil, Chile, China, Hong Kong, Israel, Japan, Malaysia, Mexico, Republic of Korea, Singapore, South Africa, and Taiwan.

^cPer local testing.

^dPer interactive response technology.

^eDefined as relapse that had occurred during the first 2 y of adjuvant ET or PD that had occurred during the first 6 mo of 1L ET for mBC.

Prior to treatment, patients in the SG and TPC arms had a median of 2 lines of therapy in a metastatic setting; see Table 2 for additional details of prior therapies.¹

Table 2. ASCENT-07: Prior Therapies¹

		SG (n=456)	TPC (n=234)
Metastatic setting			
Number of lines, median (range)		2 (0–8)	2 (0–4)
Lines of ET, n (%)	None	8 (2)	1 (<1)
	1	122 (27)	63 (27)
	2	263 (58)	139 (59)
	≥3	63 (14)	31 (13)
Previous endocrine-based therapies, ^a n (%)	ET with CDK4/6i	416 (91)	216 (92)
	ET with CDK4/6i ≤6 mo ^b	74 (16)	35 (15)
	ET monotherapy	182 (40)	95 (41)
	ET with other targeted therapy ^c	160 (35)	74 (32)
(Neo)adjuvant setting^a, n (%)			
ET ^e		295 (65)	158 (68)
ET with CDK4/6i		17 (4)	8 (3)
Chemotherapy		260 (57)	140 (60)
Taxane		211 (46)	115 (49)
Anthracycline		217 (48)	118 (50)
Prior CDK4/6i use in metastatic setting, n (%)			
None		32 (7)	19 (8)
≤12 mo		197 (43)	98 (42)
>12 mo		227 (50)	117 (50)

^aTherapies reported are not mutually exclusive. ^bIn first line.

^cOther targeted therapies in the SG and TPC arms included everolimus (25% and 22%), alpelisib (5% and 3%), and olaparib (2% and 3%).

^dSome patients had unknown adjuvant therapy history. ^eET includes ET monotherapy and combination therapy.

Efficacy¹

Primary endpoint

The study did not meet statistical significance for the primary endpoint PFS per BICR with SG vs TPC (Table 3). Formal statistical testing was not conducted for subsequent endpoints in the statistical hierarchy as PFS by BICR was not statistically significant, results of these endpoints are, therefore, descriptive only.

Table 3. ASCENT-07: PFS per BICR at Primary Analysis¹

		SG (n=456)	TPC (n=234)
PFS, median (95% CI), mo		8.3 (8.1–10.3)	8.3 (6.9–10)
Stratified HR (95% CI), <i>P</i> -value ^a		0.85 (0.69–1.05), 0.13	
PFS rate, % (95% CI)	6-mo	71 (66–75)	64 (57–71)
	12-mo	40 (35–45)	37 (29–44)

^aTwo-sided *P*-value from stratified log-rank test.

Secondary endpoints

PFS per investigator assessment showed a numerical improvement with SG vs TPC (Table 4). Results for OS were immature (27% maturity rate) at the time of the primary PFS analysis and are descriptive only; an early trend favoring SG over TPC was observed. The study will continue to further assess OS.

Table 4. ASCENT-07: PFS per Investigator Assessment and OS at Primary Analysis¹

		SG (n=456)	TPC (n=234)
PFS, median (95% CI), mo		8.4 (8.2–9.7)	6.4 (6–8.1)
Stratified HR (95% CI), nominal <i>P</i> -value ^a		0.78 (0.64–0.93) 0.008	
PFS rate, % (95% CI)	6 mo	69 (64–73)	58 (51–64)
	12 mo	36 (32–41)	30 (24–36)
OS, median (95% CI), mo		NR (NR–NR)	NR (19.7–NR)
HR (95% CI), nominal <i>P</i> -value		0.72 (0.54–0.97), 0.029	

^aTwo-sided *P*-value from stratified log-rank test.

A total of 32% and 61% of patients in the SG and TPC arms, respectively, received an ADC following treatment discontinuation (Table 5). Other subsequent anticancer therapies are shown in Table 5.

Table 5. ASCENT-07: Subsequent Anticancer Therapy¹

n, (%)	SG (n=348)	TPC (n=203)
Patients without subsequent anticancer therapy ^a	66 (19)	43 (21)
Patients with any subsequent anticancer therapy ^b	282 (81)	160 (79)
ADC	91 (32)	97 (61)
Trastuzumab deruxtecan	83 (29)	66 (41)
SG	1 (0.4)	29 (18)
Datopotamab deruxtecan	0	3 (2)
Other ADC	8 (3)	7 (4)
Chemotherapy	238 (84)	106 (66)
Targeted therapy ^c	65 (23)	24 (15)
Endocrine therapy	42 (15)	24 (15)
Immunotherapy	10 (4)	3 (2)
Other	5 (2)	3 (2)

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^aDue to death or due to no subsequent treatment data available.

^bPatients could have received more than 1 treatment type across subsequent lines of treatment.

^cIncluded poly-adenosine diphosphate-ribose polymerase inhibitor, bevacizumab, mammalian target of rapamycin inhibitor, protein kinase B inhibitor, phosphatidylinositol 3-kinase inhibitor, CDK4/6i, other.

ORR per BICR was similar between treatment arms: 37% with SG vs 33% with TPC (OR 1.2), see Table 6. Numerical improvements in CBR were seen with SG vs TPC: 65% vs 53%, respectively, and median DOR was longer with SG: 12.1 vs 9.3 mo.

Table 6. ASCENT-07: Tumor Response and Duration of Response by BICR¹

Variable		SG (n=456)	TPC (n=234)
ORR, ^a % (95% CI)		37 (32–42)	33 (27–39)
Stratified OR (95% CI)		1.2 (0.86–1.69)	
Best Overall Response, n (%)	CR	4 (1)	0
	Partial response	164 (36)	77 (33)
	SD	202 (44)	112 (48)
	SD ≥6 mo	126 (28)	48 (21)
	PD	64 (14)	33 (14)
	Not evaluable ^b	22 (5)	12 (5)
CBR, ^c % (95% CI)		65 (60–69)	53 (47–60)
Responders		SG (n=168)	TPC (n=77)
Time To Response, ^d median (range), mo		2.3 (1.2–14.6)	2.3 (1.4–12.5)
DOR, median (95% CI), mo		12.1 (8.5–13.8)	9.3 (6.5–14.3)

^aDefined as the proportion of patients who achieved a best overall response of CR/partial response.

^bPatients without any evaluable post-baseline tumor assessment are included.

^cDefined as the proportion of patients who achieved best overall response of CR/PR or durable SD with duration ≥6 mo. The 95% CI is based on Clopper-Pearson method.

^dDate of first documented CR or PR - date of randomization + 1/30.4375.

Safety¹

The median duration (range) of treatment at the time of the primary PFS analysis with SG and TPC was 8.3 mo (0–22.1) and 6.1 mo (0.3–21.1), respectively.

In the SG and TPC arms, TEAEs which resulted in dose interruption, dose reduction, and those which lead to treatment discontinuation occurred in 75% vs 46%, 39% vs 38%, and 3% vs 7% of patients, respectively (Table 7).

TEAEs leading to death in the SG arm were respiratory failure (n=2), febrile neutropenia, intestinal ischemia, Klebsiella bacteremia, pneumonia, and septic shock (1 each), and in the TPC arm were septic shock, sepsis, diabetic ketoacidosis, and acute kidney injury (1 each), as well as 1 death of unknown cause. A total of 6 (1%) and 2 (1%) deaths in the SG and TPC arms, respectively, were deemed to be treatment-related.

Table 7. ASCENT-07: Safety Summary (Safety Population)¹

Safety Outcomes, n (%)	SG (n=449)	TPC (n=232)
Duration of treatment, median (range), mo	8.3 (0–22.1)	6.1 (0.3–21.1)
Relative dose intensity, ^a median (range), %	86.2 (33.1–135.5)	93 (43.2–108.4)
Any TEAE	448 (>99)	226 (97)
Treatment-related	447 (>99)	216 (93)
Grade ≥3 TEAEs	323 (72)	112 (48)
Treatment-related	305 (68)	86 (37)
Excluding neutropenia ^b	161 (36)	64 (28)
Treatment-emergent SAE	105 (23)	35 (15)

Safety Outcomes, n (%)	SG (n=449)	TPC (n=232)
Treatment-related	71 (16)	11 (5)
TEAEs that led to treatment discontinuation ^c	13 (3)	16 (7)
TEAEs that led to dose interruption	337 (75)	107 (46)
TEAEs that led to dose reduction	174 (39)	88 (38)
TEAEs that led to death	7 (2)	5 (2)
Treatment-related	6 (1)	2 (1)

TEAEs began on or after the first dose date of study drug up to 30 d after the last dose date of the study drug, if applicable, or the initiation of subsequent anticancer therapy, whichever occurred first.

^aCalculated as (total amount of study drug administered/total amount of actual study drug planned by protocol)*100.

^bCombined preferred terms includes neutrophil count decreased.

^cThe most common were pneumonia (<1%) in the SG arm and peripheral neuropathy (2%) and infusion-related reaction (<1%) in the TPC arm.

Across both treatment arms, the most common Grade ≥3 adverse events were neutropenia, leukopenia, and anemia (Table 8).¹

Table 8. ASCENT-07: Any-Grade TEAEs (≥20%) and Grade ≥3 TEAEs¹

TEAEs, ^a n (%)	SG (n=449)		TPC (n=232)	
	Any-Grade	Grade ≥3	Any-Grade	Grade ≥3
Neutropenia	76	56	39	21
Alopecia	61	0	36	0
Nausea	57	2	32	0
Diarrhea	54	7	31	2
Fatigue	54	5	41	3
Anemia	51	10	38	5
Constipation	40	0	20	0
Leukopenia	32	14	25	7
ALT increased	22	2	19	1
Vomiting	21	1	10	1
AST increased	21	2	23	2
Decreased appetite	21	1	10	0
Hand-foot syndrome	0	1	25	5

TEAEs began on or after the first dose date of study drug up to 30 days after the last dose date of the study drug or the day before initiation of subsequent anticancer therapy, whichever occurred first. Adverse events were coded using Medical Dictionary for Regulatory Activities. Any-grade hypersensitivity was 14% with SG and 9% with TPC; Grade ≥3 was <1% in both arms. Any-grade febrile neutropenia was 8% with SG and 1% with TPC.

^aCombined preferred terms of neutropenia includes neutrophil count decreased, fatigue includes asthenia, anemia includes hemoglobin decreased and RBC count decreased, and leukopenia includes WBC count decreased.

Use of primary and secondary G-CSF prophylaxis for neutropenia is presented in Table 9.

Table 9. ASCENT-07: Primary and Secondary G-CSF Prophylaxis

G-CSF prophylaxis, n (%)	SG (n=449)	TPC (n=232)
Primary prophylaxis	89 (20)	11 (5)
Secondary prophylaxis	192 (43)	24 (10)

References

1. 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.
2. Rugo HS, Cortes J, Curigliano G, et al. ASCENT-07: a phase 3, randomized, open-label study of sacituzumab govitecan versus treatment of physician's choice in patients with HR+/HER2-inoperable, locally advanced, or metastatic breast cancer post-endocrine therapy [Poster P01-05-09]. Paper presented at: San Antonio Breast Cancer Symposium (SABCS); December 5-9, 2023; San Antonio, TX.

Abbreviations

ADC=antibody drug conjugate

BICR=blinded independent central review

CBR=clinical benefit rate

CR=complete response

CDK4/6i =cyclin-dependent kinase 4/6 inhibitors

DOR=duration of response

ECOG PS= Eastern

Cooperative Oncology Group performance status

ER=estrogen receptor

TPC=Treatment of physician's choice

IHC=immunohistochemistry
ISH-=in situ hybridization negative

LA=locally advanced

OR=odds ratio

ORR=objective response rate

OS=overall survival

PD=progressive disease

PFS=progression-free survival

PR=progesterone receptor

RECIST=Response Evaluation Criteria in Solid Tumors

SD=stable disease

TEAE=treatment-emergent adverse event

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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Please report all adverse events to:

Gilead Global Patient Safety  1-800-445-3235, option 3 or

 <https://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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