GILEAD | Medical Information

Trodelvy® (sacituzumab govitecan-hziy) Use in Patients With 3L+ HR+/HER2- mBC

This document is in response to your request for information about Trodelvy® (sacituzumab govitecan-hziy [SG]) and its use in the third-line and later setting (3L+) patients with hormone receptor-positive (HR+)/human epidermal growth factor receptor 2-negative (HER2-) metastatic breast cancer (mBC).

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]

SG is indicated for the treatment of adult patients with unresectable locally advanced or metastatic HR+, HER2- (IHC 0, IHC 1+ or IHC 2+/ISH-) breast cancer who have received endocrine-based therapy and ≥2 additional systemic therapies in the metastatic setting.

Clinical Data on SG Use as 3L+ in HR+/HER2- mBC

TROPiCS-02, a phase 3 study, compared the safety and efficacy of SG 10 mg/kg IV on Days 1 and 8 of a 21-day cycle to chemotherapy TPC in 543 patients with HR+/HER2- mBC who were previously treated with ≥1 taxane, ≥1 endocrine therapy, and ≥1 CDK4/6i in any setting and who had received 2 to 4 prior chemotherapy regimens for metastatic disease.[2]

- SG prolonged median PFS (primary endpoint) vs TPC (5.5 vs 4 mo; *P*=0.0003), with a 34% risk reduction of disease progression or death and a higher proportion of patients alive and progression-free at all landmark timepoints.[2] The final exploratory PFS analysis at 12.8 mo (median follow-up) continued to demonstrate an SG improvement with a 35% risk reduction (nominal *P*=0.0001).[3]
- Following a numeric trend for OS improvement (key secondary endpoint) with SG vs TPC at the first planned interim analysis, the second planned interim analysis showed statistically longer median OS with SG (14.4 vs 11.2 mo; *P*=0.02), with a 21% risk reduction of death.[2,4] The 21% risk reduction was maintained at 12.8 mo for the final exploratory analysis (14.5 vs 11.2 mo; nominal *P*=0.0133).[3]
- Across the second and final analyses, the ORR (21% vs 14%), CBR (34% vs 22%), and median DoR (8.1 vs 5.6 mo) were improved with SG vs TPC, respectively.[3,4]
- At the final exploratory analysis, the most common Grade ≥3 TEAEs were neutropenia (52%), diarrhea (10%), and anemia (7%) with SG and neutropenia (39%) with TPC.[3] The SG safety profile was consistent with previous analyses; no new safety concerns were identified.[2-6]

- In a post hoc exploratory analysis, PFS, OS, and ORR showed a treatment benefit with SG vs TPC (BE population) in patients with DDR mutations vs those without.[7]
- In another exploratory analysis, regardless of treatment, a lower baseline ctDNA (assessed via mean VAF) was associated with longer PFS and OS. Patients with high baseline mean VAF values and <50% reductions in ctDNA from baseline to C2D1 had the worst outcomes.[8]

The efficacy of SG was compared to that of TPC in a meta-analysis of TROPiCS-02 and EVER-132-002 (a phase 3 study in 331 Asian patients with HR+/HER2- mBC who were previously treated with ≥1 taxane, ≥1 endocrine therapy, ± ≥1 CDK4/6i in any setting and had received 2 to 4 prior chemotherapy regimens for metastatic disease).[9,10]

- Combined individual patient data in the overall population and in patients previously treated with CDK4/6i therapies demonstrated that SG vs TPC prolonged both PFS (HR, 0.62 vs 0.65, respectively; *P*<0.001) and OS (HR, 0.66 vs 0.65, respectively; *P*<0.001).[9]

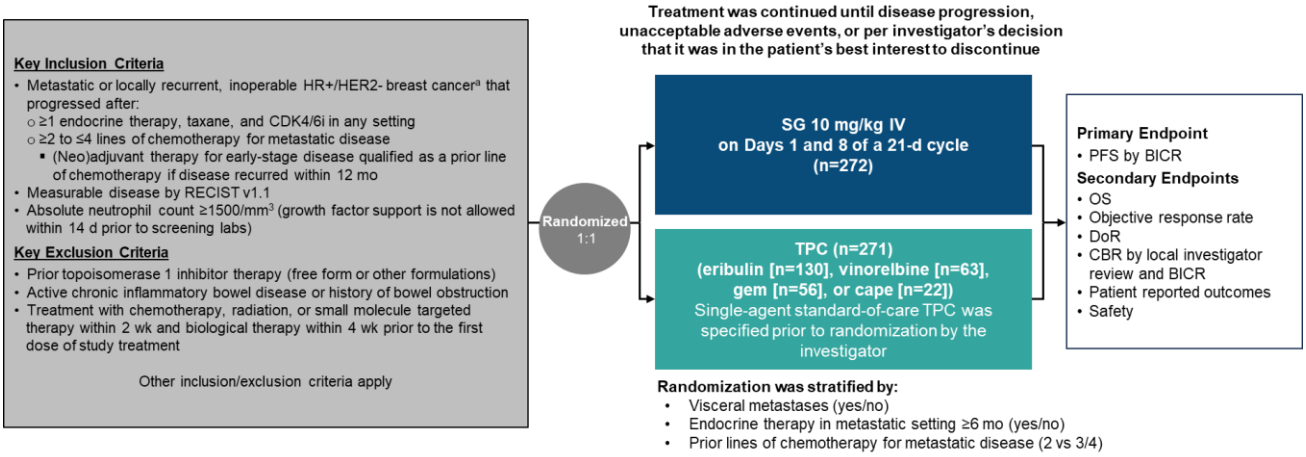
Clinical Data on SG Use as 3L+ in HR+/HER2- mBC

TROPiCS-02 Study

Study design and demographics

TROPiCS-02, an open-label, randomized, multicenter, phase 3 study, compared the safety and efficacy of SG with TPC in patients with HR+/HER2- mBC who were previously treated with ≥1 taxane, ≥1 endocrine therapy, and ≥1 CDK4/6i in any setting and who had received 2 to 4 prior chemotherapy regimens for metastatic disease (Figure 1).[2]

Figure 1. TROPiCS-02 Study Design[2,11]



[a]Disease histology based on American Society of Clinical Oncology/College of American Pathologists criteria.

In the statistical testing hierarchy, OS was formally tested for significance once PFS was statistically significant, followed by ORR, time to deterioration of Global Health Status/ quality of life, and fatigue (once the prior endpoint in the hierarchy was significant).[2,4]

Use of chemotherapy in the (neo)adjuvant settings was reported in 64% and 68% of the SG and TPC arms, respectively. The median (range) number of prior chemotherapy metastatic regimens was 3 (0–8) with SG and 3 (1–5) with TPC. Prior CDK4/6i use for ≤12 mo and

>12 mo was reported in 59% and 39% of patients in the SG arm, respectively, and 61% and 38% in the TPC arm, respectively. Prior endocrine therapy use for ≥6 mo in the metastatic setting was reported in 86% of patients in both treatment arms.[2,4] See Table 1 for patient characteristics.

Table 1. TROPiCS-02: Baseline Demographics and Disease Characteristics (ITT Population)[2,12]

Select Demographics and Characteristics		SG (n=272)	TPC (n=271)
Female, n (%)		270 (99)	268 (99)
Age, median (range), y		57 (29–86)	55 (27–78)
Race or ethnic group, n (%)	White/Black/Asian	184 (68)/8 (3)/11 (4)	178 (66)/13 (5)/5 (2)
	Other[a] or not reported[b]	69 (25)	75 (28)
ECOG PS, n (%)	0/1	116 (43)/156 (57)	126 (46)/145 (54)
Visceral metastases at baseline, n (%)		259 (95)	258 (95)
Liver metastases,[c] n (%)		229 (84)	237 (87)
De novo mBC, n (%)		78 (29)	60 (22)
Time since metastatic diagnosis to randomization, median (range), mo		48.5 (1.2–243.8)	46.6 (3–248.8)
Setting of prior anticancer regimens, n (%)	Neoadjuvant	67 (25)	62 (23)
	Adjuvant	186 (68)	206 (76)
	Advanced/metastatic	272 (100)	271 (100)
	Other/unknown	12 (4)	9 (3)
Most common prior anticancer therapy[d] in the metastatic setting, by class, n (%)	Endocrine therapy	268 (99)	269 (99)
	CDK4/6i	267 (98)	270 (>99)
	Targeted agent[e]	181 (67)	172 (63)
	Immunotherapy	21 (8)	15 (6)
	Chemotherapy	271 (>99)	271 (100)
	Cape	221 (81)	232 (86)
	Paclitaxel	174 (64)	147 (54)
	Eribulin	95 (35)	88 (33)

[a]American Indian or Alaska Native, Native Hawaiian, or other Pacific Islander.
[b]Local regulators did not allow collection of race or ethnicity information.
[c]Presence of baseline target/non-target liver metastases per RECIST v1.1 by local investigator review.
[d]Any breast cancer regimen in any setting (single or combination agent), including endocrine therapy and everolimus.
[e]Poly (adenosine diphosphate-ribose) polymerase, mammalian target of rapamycin, phosphatidylinositol 3-kinase, bromodomain and extra-terminal motif, protein kinase B, aurora A kinase, antibody drug conjugate, and other kinase inhibitors and targeted agents.

Efficacy

Primary endpoint[2,4]

There was a statistically significant improvement in PFS with SG vs TPC, with a 34% reduction in the risk of disease progression or death and a higher proportion of patients alive and progression-free at all landmark timepoints (6, 9, and 12 mo; Table 2). The median duration of follow-up at the first planned interim analysis was 10.2 mo.

PFS results for SG vs TPC were maintained across most predefined subgroups, including subgroups of patients who received ≥3 prior chemotherapies for metastatic disease, those who had visceral metastases, and those aged ≥65 y.

Table 2. TROPiCS-02: PFS per RECIST v1.1 (ITT Population)[2]

BICR Analysis		SG (n=272)	TPC (n=271)
PFS, median (95% CI), mo		5.5 (4.2–7)	4.0 (3.1–4.4)
Stratified HR (95% CI); log-rank *P*-value		0.66 (0.53–0.83); 0.0003	
PFS rate, % (95% CI)	6 mo	46.1 (39.4–52.6)	30.3 (23.6–37.3)
	9 mo	32.5 (25.9–39.2)	17.3 (11.5–24.2)
	12 mo	21.3 (15.2–28.1)	7.1 (2.8–13.9)

Secondary endpoints: first and second planned interim analyses

Following a numeric trend of OS improvement with SG vs TPC at the first planned interim analysis of 272 events (13.9 vs 12.3 mo; 16% risk reduction of death; *P*=0.14),[2] the second planned interim analysis of 390 events demonstrated a statistically significant 21% risk reduction of death (Table 3). The median duration of follow-up at this analysis was 12.5 mo.[4]

OS for SG vs TPC was generally consistent across predefined subgroups at the first and second interim analyses.[2,4]

Table 3. TROPiCS-02: Second Planned Interim OS Analysis[4]

	SG (n=272)	TPC (n=271)
Number of events	191	199
OS, median (95% CI), mo	14.4 (13–15.7)	11.2 (10.1–12.7)
Stratified HR (95% CI); log-rank *P*-value	0.79 (0.65–0.96); 0.02	
12-mo OS rate, % (95% CI)	61 (55–66)	47 (41–53)

At the first interim analysis, the median (range) time to response with SG and TPC was 2.9 (1.2–11.3) mo and 2.7 (1.2–10.5) mo, respectively.[2]

SG showed a statistically significant improvement in ORR as well as prolonged median DoR vs TPC at the second interim analysis (Table 4).[4]

Table 4. TROPiCS-02 Second Planned Interim Analysis: Responses[4]

BICR Analysis		SG (n=272)	TPC (n=271)
ORR, n (%)		57 (21)	38 (14)
OR (95% CI); *P*-value		1.63 (1.03–2.56); 0.035	
BOR, n (%)	Complete response	2 (1)	0
	PR	55 (20)	38 (14)
	SD	142 (52)	106 (39)
	SD ≥6 mo	35 (13)	22 (8)
	PD	58 (21)	76 (28)
	Not evaluable	15 (6)	51 (19)
CBR,[a] n (%)		92 (34)	60 (22)
OR (95% CI); *P*-value		1.8 (1.23–2.63); 0.003	
DoR, median (95% CI), mo		8.1 (6.7–9.1)	5.6 (3.8–7.9)

[a]The percentage of patients with a confirmed BOR of complete response, PR, and SD ≥6 mo.

Primary and secondary endpoints: final exploratory analysis[3]

Since the second planned interim analysis, an additional 48 (9%) OS events occurred (23 [8%] and 25 [9%] in the SG and TPC arms, respectively) at a median follow-up of 12.8 mo. The total number of OS events at data cutoff was 438.

At the longer follow-up, PFS and OS with SG vs TPC were consistent with earlier analyses, with 35% (median 1.5 mo improvement) and 21% (median 3.3 mo improvement) risk reductions, respectively. A higher proportion of patients were alive at each timepoint

(Table 5). Across predefined subgroups, PFS and OS results for SG vs TPC were generally consistent. Results for ORR, BOR, CBR, and DoR were consistent with previous analyses.

Table 5. TROPiCS-02: Final Exploratory Efficacy Analyses[3]

BICR Analysis		SG (n=272)	TPC (n=271)
PFS, median (95% CI), mo		5.5 (4.2–6.9)	4 (3–4.4)
Stratified HR (95% CI); nominal log-rank *P*-value		0.65 (0.53–0.81); 0.0001	
PFS rate, % (95% CI)	6-mo	45.6 (38.9–52)	29.4 (22.9–36.2)
	12-mo	21.7 (15.8–28.3)	8.4 (4.2–14.5)
	18-mo	14.4 (9.1–20.8)	4.7 (1.3–11.6)
OS, median (95% CI), mo		14.5 (13–16)	11.2 (10.2–12.6)
Stratified HR (95% CI); nominal log-rank *P*-value		0.79 (0.65–0.95); 0.0133	
OS rate, % (95% CI)	12-mo	60.9 (54.8–66.4)	47.1 (41–53)
	18-mo	39.2 (33.4–45)	31.7 (26.2–37.4)
	24-mo	25.7 (20.5–31.2)	21.1 (16.3–26.3)

Final safety analysis

In the SG and TPC arms, 74% and 60% of TEAEs were Grade ≥3, respectively; the most common were neutropenia, diarrhea, and anemia with SG and neutropenia, thrombocytopenia, fatigue, and dyspnea with TPC (Table 6). Treatment-emergent serious adverse events were reported by 28% and 19% of patients in the SG and TPC arms, respectively. Six TEAEs led to death in patients who received SG; none led to death with TPC. One death from septic shock due to neutropenic colitis was considered treatment related.[3]

Table 6. TROPiCS-02: Any-Grade (≥20%) and Grade ≥3 (≥10%) TEAEs[3]

TEAEs, n (%)		Any-Grade		Grade ≥3	
		SG (n=268)	TPC (n=249)	SG (n=268)	TPC (n=249)
Hematologic	Neutropenia[a]	189 (71)	136 (55)	140 (52)	97 (39)
	Anemia[b]	98 (37)	69 (28)	20 (7)	8 (3)
Gastrointestinal	Diarrhea	166 (62)	57 (23)	27 (10)	3 (1)
	Nausea	157 (59)	87 (35)	3 (1)	7 (3)
	Constipation	93 (35)	61 (24)	1 (<1)	0
	Vomiting	64 (24)	39 (16)	3 (1)	4 (2)
	Abdominal pain	53 (20)	34 (14)	10 (4)	2 (1)
Others	Alopecia	128 (48)	46 (18)	0	0
	Fatigue	105 (39)	82 (33)	16 (6)	9 (4)
	Asthenia	62 (23)	50 (20)	6 (2)	5 (2)
	Decreased appetite	57 (21)	52 (21)	4 (1)	2 (1)

[a]Combined preferred terms of neutropenia and neutrophil count decreased.
[b]Combined preferred terms of anemia, Hgb decreased, and RBC count decreased.

Treatment discontinuation due to TEAEs was reported in 6% and 4% of patients in the SG and TPC arms, respectively. TEAEs led to dose delay and reduction in 66% and 34% of patients in the SG arm and 44% and 33% of patients in the TPC arm, respectively. Overall, the safety profile for SG was consistent with prior studies.[2-6] No new safety signals were identified with the extended follow-up.[3]

Post hoc exploratory genomic analysis[7]

An exploratory post hoc analysis of DDR gene variant data evaluated the efficacy of SG vs TPC in patients with evaluable whole-exome sequencing biomarker data (BE population, n=195) and, within that cohort, those with and without DDR mutations.

Overall baseline demographics and disease characteristics in the BE population (SG and TPC arms: median age, 58 and 55 y, respectively; >2 lines of prior chemotherapy, 57% and 55%, respectively) were generally similar to those in the ITT population. More patients in the BE population than in the ITT population had an ECOG PS of 0 (SG, 48% vs 43%; TPC, 51% vs 46%, respectively) and received previous CDK4/6i for <12 mo (SG, 65% vs 60%; TPC, 67% vs 62%). A total of 58% (n=114) of the BE population had ≥1 DDR gene with a deleterious mutation. Demographics and characteristics were generally similar between those with and without DDR mutations in the BE population (Table 7).

Table 7. TROPiCS-02 Post Hoc Exploratory DDR Analysis: Baseline Demographics and Disease Characteristics in Patients With and Without DDR Mutations (BE Population)[7]

Select Demographics and Characteristics		SG (n=100)		TPC[a] (n=95)	
		WT (n=41)	DDR Mutation (n=59)	WT (n=40)	DDR Mutation (n=55)
Age, median (IQR), y		59 (53–70)	56 (49–62)	57 (47–65)	55 (48–61)
Race, %	White/other[b]/not reported	63/10/27	66/5/29	83/0/17	60/16/24
ECOG PS, %	0/1	49/51	47/53	55/45	47/53
Visceral metastasis at baseline, %		95	93	88	95
Prior CDK4/6i for ≤12 mo, %		66	65	54	76
Endocrine therapy in metastatic setting for ≥6 mo, %		88	92	93	87
Number of prior chemotherapy regimens in the metastatic setting, %	2/3–4	46/54	41/59	42/58	47/53

[a]TPC agents in the WT and DDR mutation subgroups: eribulin, 38% vs 44%, respectively; vinorelbine, 25% vs 31%; gem, 20% vs 24%; and cape, 17% vs 2%. [b]Other races were not specified.

Results

In the ITT and BE populations, PFS and OS were similar, and response rates were numerically improved with SG vs TPC (Table 8). Patients with DDR mutations showed numerically greater treatment outcomes with SG vs TPC than did those without DDR mutations (Table 8).

Table 8. TROPiCS-02 Post Hoc Exploratory DDR Analysis: Outcomes in ITT and BE Study Populations and in Patients With and Without DDR Mutations (BE Population)[7]

Outcomes by Treatment: ITT and BE Populations		ITT Population		BE Population	
		SG	TPC	SG	TPC
PFS	Events, n/N	170/272	159/271	60/100	53/95
	Median (95% CI), mo	5.5 (4.2–7)	4 (3.1–4.4)	7.2 (4.1–8.5)	3.7 (1.8–5.6)
	HR (95% CI)	0.661 (0.53–0.824)		0.667 (0.458–0.971)	
OS	Events, n/N	191/272	199/271	73/100	71/95
	Median (95% CI), mo	14.4 (13–15.7)	11.2 (10.1–12.7)	15.3 (13.1–18.1)	10.8 (9.5–13.1)
	HR (95% CI)	0.8 (0.656–0.976)		0.738 (0.531–1.025)	

Outcomes in BE Population: With or Without DDR Mutations		WT		DDR Mutation	
		SG	TPC	SG	TPC
PFS	Events, n/N	22/41	19/40	38/59	34/55
	Median (95% CI), mo	7.3 (2.9–9.5)	5.6 (1.7–7.6)	7.2 (2.9–8.6)	2.9 (1.4–4.3)
	HR (95% CI)	0.762 (0.409–1.421)		0.609 (0.378–0.981)	
OS	Events, n/N	29/41	28/40	44/59	43/55
	Median (95% CI), mo	14.4 (11.1–23.7)	10.4 (6.5–17.2)	15.4 (12.8–18.4)	11.5 (9.5–13.1)
	HR (95% CI)	0.824 (0.488–1.383)		0.684 (0.449–1.043)	
ORR	n/N (%)	9/41 (22)	6/40 (15)	11/59 (19)	3/55 (5)
	OR (95% CI)	1.6 (0.5–5)		4 (1–15.1)	

Note: HRs were evaluated via a Cox regression model, and the ORR OR was evaluated via the Cochran-Mantel-Haenszel method.

Within the full interaction model, of the 87 genes, 39 and 47 mutated genes were predictive of the PFS and OS benefits, respectively, observed with SG vs TPC. Outcomes among patients with and without those DDR-predictive genes are shown in Table 9.

Table 9. TROPiCS-02 Post Hoc DDR Exploratory Analysis: Outcomes in Patients With and Without DDR-Predictive Contributing Gene Mutations (BE Population)[7]

Outcomes in BE Population		WT		DDR-Predictive Contributing Mutations	
		SG	TPC	SG	TPC
PFS	Events, n/N	41/66	26/54	19/34	27/41
	Median (95% CI), mo	5.5 (3.3–8.4)	6.5 (4.1–7.7)	11 (2.8–12.7)	1.5 (1.4–2.9)
	HR (95% CI)	1.08 (0.66–1.768)		0.333 (0.172–0.642)	
OS	Events, n/N	53/66	34/53	20/34	37/42
	Median (95% CI), mo	13.1 (11.1–15.4)	12.2 (9.2–21.3)	18.7 (15.7–21.9)	10.4 (7.6–12.3)
	HR (95% CI)	1.155 (0.749–1.781)		0.337 (0.193–0.588)	

Study limitations included the following: 87 of the 142 DDR genes were noted to have mutations, 114 of the 195 patients had those DDR mutations, most DDR genes were present in <5 patients, and co-mutations were not evaluated. Further validation of the predictive effect of the treatment benefit with SG vs TPC is needed.

Exploratory ctDNA analysis[8]

An exploratory analysis evaluated whether ctDNA data were predictive of efficacy outcomes. Patients with plasma samples at baseline and at C2D1 were analyzed (ctDNA population, n=210). Overall, demographics and characteristics were generally similar between the ctDNA and ITT populations (Table 10 and Table 1).

Table 10. TROPiCS-02 Exploratory ctDNA Analysis: Baseline Demographics and Disease Characteristics (ctDNA Population)[8]

Select Demographics and Characteristics		SG (n=113)	TPC (n=97)
Female, n (%)		112 (99)	95 (98)
Age, median (IQR), y		58 (50–65)	56 (48–65)
Race,[a] n (%)	White/Asian/Black or African American[a]	71 (63)/5 (4)/3 (3)	55 (57)/1 (1)/7 (7)
ECOG PS, n (%)	0/1	48 (42)/65 (58)	45 (46)/52 (54)
Duration of prior CDK4/6i, n (%)	≤12 mo/>12 mo[b]	62 (55)/51 (45)	63 (65)/33 (34)
Prior chemotherapy regimens in the metastatic setting, n (%)	2/3–4	47 (42)/66 (58)	45 (46)/52 (54)

[a]Not reported: SG, n=34; TPC, n=32. Other races were not specified: SG, n=0; TPC, n=2.
[b]Missing data: SG, n=0; TPC, n=1.

Results

Within the ITT (Table 2 and Table 3) and ctDNA populations (Table 11), PFS and OS were similar between SG and TPC. Within the mean VAF analysis subgroups, lower mean VAF values at baseline were associated with longer PFS and OS for SG and TPC (Table 11).

Table 11. TROPiCS-02 Exploratory ctDNA Analysis: Efficacy Outcomes Overall and by VAF Subgroups (ctDNA Population)[8]

Outcomes by Treatment		SG		TPC	
PFS, median (95% CI), mo		5.3 (4.1–6.9)		4.1 (2.8–5.6)	
OS, median (95% CI), mo		14.5 (11.9–17.5)		12.1 (10.1–13.6)	
BOR, PR/SD/PD, n		21/68/24		18/44/34	
Outcomes by Treatment and VAF Subgroup		**SG**		**TPC**	
		Mean VAF ≥5.4%	**Mean VAF <5.4%**	**Mean VAF ≥5.4%**	**Mean VAF <5.4%**
PFS	Patients/events	56/37	57/36	48/36	49/35
	Median (95% CI), mo	4.3 (2.8–6.4)	5.3 (4.1–8.3)	3.4 (1.7–5.5)	4.4 (2.7–7.1)
	HR (95% CI)	0.741 (0.466–1.178)		0.848 (0.53–1.354)	
OS	Patients/events	56/41	57/40	48/42	49/33
	Median (95% CI), mo	12.1 (10.3–16.3)	15.5 (13.3–21.9)	10.1 (6.9–12.3)	13.7 (11.2–21.6)
	HR (95% CI)	0.786 (0.508–1.216)		0.564 (0.356–0.891)	

Most patients had decreases in mean VAF from baseline to C2D1 with SG and TPC; patients with PR and PD had the largest and smallest decreases, respectively. The percent reduction in mean VAF with SG was greater in patients who achieved a PR than in those who had SD (P=0.049) or PD (P=0.02). The percent reduction in mean VAF with TPC was greater in patients who achieved a PR than in those who had PD (P=0.00016) and in patients with SD than in those with PD (P=0.00093).

Higher PFS and OS were observed in both arms in patients who had ≥50% reductions in mean VAF at C2D1 vs those who had <50% reductions (Table 12). PFS was lowest among patients with who had high mean VAF at baseline and <50% decreases from baseline to C2D1 in mean VAF (Table 12); similar results were observed for OS (data not presented).

Table 12. TROPiCS-02 Exploratory ctDNA Analysis: Outcomes by Degree of Mean VAF Reduction From Baseline to C2D1 (ctDNA Population)[8]

Outcomes by Treatment and Mean VAF Reduction		SG		TPC	
		Reduction in VAF by ≥50%	**Reduction in VAF by <50%**	**Reduction in VAF by ≥50%**	**Reduction in VAF by <50%**
PFS	Patients/events	72/46	41/27	51/33	46/38
	Median (95% CI), mo	6.4 (5.3–7.5)	4 (2–4.2)	5.8 (4.3–8.3)	1.6 (1.4–2.8)
	HR (95% CI)	0.548 (0.336–0.893)		0.328 (0.201–0.535)	
OS	Patients/events	72/49	41/32	51/37	46/38
	Median (95% CI), mo	16.3 (13.9–22)	11.7 (9.6–14.1)	13.5 (10.6–20.1)	9.9 (6.3–12.4)
	HR (95% CI)	0.559 (0.355–0.881)		0.528 (0.33–0.846)	
PFS by Treatment		**SG**		**TPC**	
Baseline Mean VAF	**VAF Reduction**	**Patients/Events**	**PFS (95% CI)**	**Patients/Events**	**PFS (95% CI)**
Low	≥50%	33/21	7 (4.1–10.3)	22/14	8.3 (4–9.4)
Low	<50%	24/15	4.2 (2.7–9.5)	27/21	1.6 (1.4–4.2)
High	≥50%	39/25	6.4 (4.3–7.4)	29/19	5.5 (4–7.6)
High	<50%	17/12	1.5 (1.4–4)	19/17	1.5 (1.3–1.9)

Meta-Analysis of EVER-132-002 and TROPiCS-02

EVER-132-002, a phase 3 study, evaluated SG 10 mg/kg IV vs TPC in 331 Asian patients with HR+/HER2- mBC who were previously treated with ≥1 taxane, ≥1 endocrine therapy, and ≥1 CDK4/6i (not mandatory) in any setting and had received 2 to 4 prior chemotherapy regimens for metastatic disease.[10]

A meta-analysis of EVER-132-002 and TROPiCS-02 evaluated SG efficacy in the overall study population (ie, patients who had/had not received prior CDK4/6i therapies) and in patients who had received prior CDK4/6i therapies. To adjust for cross-study differences, two analytic models were used to estimate pooled treatment effects: a one-stage model (pooled individual patient-level data from each study) and a fixed-effect model (pooled study-level HRs from each study). Baseline population characteristics were similar (low heterogeneity, I^2=0%–9.6%) between the two studies, except for geography and prior CDK4/6i use. Results demonstrated that SG significantly improved PFS and OS vs TPC in the overall population and in patients previously treated with CDK4/6i (Table 13).[9]

Table 13. Meta-Analysis of EVER-132-002 and TROPiCS-02: Efficacy Analysis (One-Stage Approach and Fixed-Effect Model)[9]

Pooled Treatment Effect		Overall Population (N=874)	Prior CDK4/6i Treated (n=704)
Individual patient data (one-stage approach)	PFS, HR (95% CI); *P*-value	0.62 (0.5–0.77); <0.001	0.65 (0.52–0.81); <0.001
	OS, HR (95% CI); *P*-value	0.66 (0.55–0.8); <0.001	0.65 (0.53–0.8); <0.001
Study-level data (fixed-effect model)	PFS, HR (95% CI); *P*-value	0.67 (0.55–0.83); <0.001[a]	0.66 (0.52–0.84); 0.001[b]
	OS, HR (95% CI); *P*-value	0.7 (0.58–0.86); <0.001[c]	0.68 (0.55–0.84); <0.001[d]

[a] I^2 statistic=0% (no); Q (χ^2=0.38, *P*=0.54).
[b] I^2 statistic=0% (no); Q (χ^2=0.89, *P*=0.35).
[c] I^2 statistic=9.6% (no/low); Q (χ^2=1.11, *P*=0.29).
[d] I^2 statistic=73.8% (moderate); Q (χ^2=3.82, *P*=0.05).

References

1. TRODELVY® Gilead Sciences Inc. Trodelvy (sacituzumab govitecan-hziy) for injection, for intravenous use. U.S. Prescribing Information. Foster City, CA.
2. 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.
3. Tolaney SM, Bardia A, Marmé F, et al. Final overall survival analysis from the phase 3 TROPiCS-02 study of sacituzumab govitecan in patients with hormone receptor positive/HER2-negative metastatic breast cancer [Oral Presentation 1003]. Presented at: American Society of Clinical Oncology Annual Meeting; June 2-6, 2023; Chicago, IL.
4. Rugo HS, Bardia A, Marmé F, et al. Overall survival with sacituzumab govitecan in hormone receptor-positive and human epidermal growth factor receptor 2-negative metastatic breast cancer (TROPiCS-02): a randomised, open-label, multicentre, phase 3 trial. *The Lancet.* 2023;402(10411):1423-1433.
5. Kalinsky K, Diamond JR, Vahdat LT, et al. Sacituzumab govitecan in previously treated hormone receptor-positive/HER2-negative metastatic breast cancer: final results from a phase I/II, single-arm, basket trial. *Ann Oncol.* 2020;31(12):1709-1718.
6. 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.
7. Bardia A, Zhang Y, Marme F, et al. Genomic alterations in DNA damage response genes in HR+/HER2- metastatic breast cancer and impact on clinical efficacy with sacituzumab govitecan: biomarker results from TROPiCS-02 Study [Poster #1075]. Presented at: American Society of Clinical Oncology (ASCO) Annual Meeting; May 31-June 4, 2024; Chicago, IL.

8. Rugo HS, Zhang Y, Marmé F, et al. Exploratory circulating tumor DNA analysis in HR+/HER2- metastatic breast cancer and impact on clinical efficacy with sacituzumab govitecan in TROPiCS-02 [Poster 412P]. Presented at: European Society for Medical Oncology; September 13-17, 2024; Barcelona.
9. Gluz O, Xu B, Nanda R, et al. Efficacy of sacituzumab govitecan versus treatment of physician's choice in previously treated hormone receptor-positive/HER2-negative metastatic breast cancer: A meta-analysis of TROPiCS-02 and EVER-132-002 trials [Oral Presentation]. Presented at: Europen Society for Medical Oncology Breast Cancer (ESMO BC) Annual Congress; 15-17 May, 2024; Berlin, Germany.
10. Xu B, Ma F, Wang S, et al. Sacituzumab govitecan vs treatment of physician's choice in Asian patients with hormone receptor-positive and HER2-negative metastatic breast cancer: results from the phase 3 EVER-132-002 study [Presentation LBA4]. Presented at: Europen Society for Medical Oncology (ESMO) Asia Congress; 1-3 December, 2023; Singapore.
11. Rugo HS, Bardia A, Marme F, et al. Sacituzumab govitecan in hormone receptor-positive/human epidermal growth factor receptor 2-negative metastatic breast cancer [Protocol]. *J Clin Oncol.* 2022;40(29):3365-3376.
12. Rugo HS, Bardia A, Marme F, et al. Primary results from TROPiCS-02: a randomized phase 3 study of sacituzumab govitecan vs treatment of physician's choice in patients with hormone receptor-positive/HER2-negative advanced breast cancer [Oral Presentation]. Presented at: American Society of Clinical Oncology (ASCO) Annual Meeting; 03-07 June, 2022; Chicago, IL & Online.

Abbreviations

BE=biomarker evaluable
BICR=blinded independent central review
BOR=best overall response
C2D1=Cycle 2, Dose 1
cape=capecitabine
CBR=clinical benefit rate
CDK4/6i=cyclin-dependent 4/6 inhibitor
ctDNA=circulating tumor DNA
DDR=DNA damage response
DoR=duration of response
ECOG PS=Eastern Cooperative Oncology Group Performance Status
gem=gemcitabine
HR=hazard ratio
HR+/HER2-=hormone receptor-positive/human epidermal growth factor receptor 2-negative
IHC=immunohistochemistry
ISH=in situ hybridization
LA=locally advanced
mBC=metastatic breast cancer
OR=odds ratio
ORR=objective response rate
OS=overall survival
PD=progressive disease
PFS=progression-free survival
PR=partial response
RECIST=Response Evaluation Criteria in Solid Tumors
SD=stable disease
SG=sacituzumab govitecan-hziy
TEAE=treatment-emergent adverse event
TPC=treatment of physicians' choice
VAF=variant allele fraction
WT=wild type

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:

☎ 1-888-983-4668 or www.askgileadmedical.com

Adverse Event Reporting

Please report all adverse events to:

Gilead Global Patient Safety ☎ 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

Data Privacy

The Medical Information service at Gilead Sciences may collect, store, and use your personal information to provide a response to your medical request. We may share your information with other Gilead Sciences colleagues to ensure that your request is addressed appropriately. If you report an adverse event or concern about the quality of a Gilead or Kite product, we will need to use the information you have given us in order to meet our regulatory requirements in relation to the safety of our medicines.

It may be necessary for us to share your information with Gilead's affiliates, business partners, service providers, and regulatory authorities located in countries besides your own. Gilead Sciences has implemented measures to protect the personal information you provide. Please see the Gilead Privacy Statement (www.gilead.com/privacy-statements) for more information about how Gilead handles your personal information and your rights. If you have any further questions about the use of your personal information, please contact privacy@gilead.com.