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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

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Key Findings

- **PFS, OS, ORR, and CBR benefit were observed with SG vs TPC regardless of age subgroup in patients with pretreated endocrine-resistant HR+/HER2− mBC**
- **As expected, older patients had higher ECOG PS scores and more preexisting comorbidities**
- **Similar rates of TEAEs were observed regardless of age subgroup, and improved efficacy was observed at higher vs lower RDI in patients who were < 65 years**
- **TTD for fatigue was significantly longer for SG vs TPC in patients who were < 65 years**

Conclusions

Consistent with prior results in the intent-to-treat population, efficacy benefit was observed with SG vs TPC regardless of age subgroup, with manageable safety

SG demonstrated a favorable benefit/risk profile in older patients, supporting the use of SG vs TPC in this patient population, which is known to experience greater toxicity and lower efficacy with chemotherapy treatment

References: **1.** American Cancer Society. Key Statistics for Breast Cancer. https://www.cancer.org/cancer/breast-cancer/about/how-common-is-breast-cancer.html. Accessed June 28, 2023. **2.** American Cancer Society. Female Breast Cancer Subtypes. https://seer.cancer.gov/statfacts/html/breast-subtypes.html. Accessed June 28, 2023. **3.** TRODELVY® (sacituzumab govitecan-hziy) [prescribing information]. Foster City, CA: Gilead Sciences, Inc.; June 2023. **4.** TRODELVY® (sacituzumab govitecan-hziy) [summary of product characteristics]. County Cork, Ireland: Gilead Sciences Ireland UC; June 2023. **5.** Rugo HS, et al. *J Clin Oncol.* 2022;40:3365-3376. **6.** Rugo HS, et al. *Lancet.* 2023;402:1423-1433. **7.** Tesarova P, et al. *Rep Pract Oncol Radiother.* 2013;18:26-33.

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Introduction

- Breast cancer is the second most common cause of cancer-related death in women,[1] and the most common form, hormone receptor-positive (HR+)/human epidermal growth factor receptor 2-negative (HER2−; immunohistochemistry [IHC] 0, IHC1+, or IHC2+ and in situ hybridization-negative [ISH−]) breast cancer, represents approximately 70% of breast cancers[2]
- Sacituzumab govitecan (SG), an antibody-drug conjugate targeted to trophoblast cell-surface antigen 2 (Trop-2), has been approved in the United States[3] and European Union[4] for the treatment of pretreated HR+/HER2− metastatic breast cancer (mBC) and in multiple countries for the treatment of pretreated metastatic triple-negative breast cancer
- SG showed significantly improved progression-free survival (PFS) vs treatment of physician's choice (TPC; median 5.5 vs 4.0 months; HR, 0.66; *P* = .0003)[5] and significantly improved overall survival (OS; median 14.4 vs 11.2 months; HR, 0.79; *P* = .020)[6] with manageable safety in the phase 3 TROPiCS-02 study of patients with pretreated, endocrine-resistant HR+/HER2− mBC[5,6]
- The most important risk factor for breast cancer is age; advanced age is associated with a higher rate of comorbidities, and with worse efficacy and greater toxicity from chemotherapy[7]

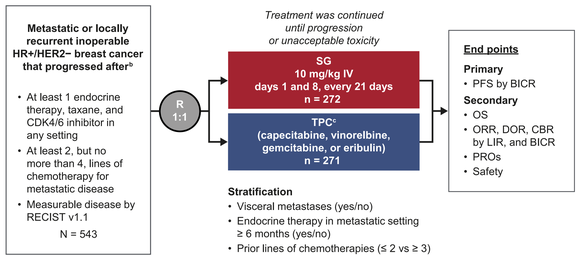
Objective

- We present a post hoc analysis of efficacy, safety, and quality of life (QoL) outcomes by age subgroup with SG vs TPC from TROPiCS-02

Methods

- TROPiCS-02 is a phase 3, randomized, open-label study of SG vs TPC for the treatment of patients with pretreated, endocrine-resistant HR+/HER2− mBC[5] **(Figure 1)**
- The data cutoff date was July 1, 2022, except for PFS, which was January 3, 2022

Figure 1. Study design[a]



ASCO, American Society of Clinical Oncology; BICR, blinded independent central review; CAP, College of American Pathologists; CBR, clinical benefit rate; CDK, cyclin-dependent kinase; DOR, duration of response; HER2−, human epidermal growth factor receptor 2-negative; HR+, hormone receptor-positive; IV, intravenous; LIR, local investigator review; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PRO, patient-reported outcome; R, randomized; RECIST, Response Evaluation Criteria in Solid Tumors; SG, sacituzumab govitecan; TPC, treatment of physician's choice

[a]ClinicalTrials.gov: NCT03901339. [b]Disease histology based on the ASCO/CAP criteria. [c]Single-agent standard-of-care treatment of physician's choice was specified by the investigator prior to randomization.

Results

Baseline characteristics by age subgroup

- Baseline characteristics were generally consistent among patients across age subgroups and across treatment groups **(Table 1)**
- A total of 543 patients were randomized to receive SG (n = 272) or TPC (n = 271)
- In both age subgroups, a higher proportion of patients had Eastern Cooperative Oncology Group performance status (ECOG PS) of 1 than 0

Results

Table 1. Demographics and baseline characteristics

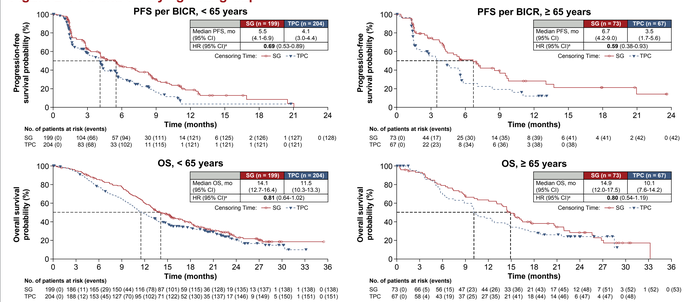
	< 65 years		≥ 65 years	
	SG (n = 199)	TPC (n = 204)	SG (n = 73)	TPC (n = 67)
Female, n (%)	197 (99)	202 (99)	73 (100)	66 (99)
Median age (range), y	53 (29-64)	52 (27-63)	71 (65-86)	69 (65-78)
Median baseline BMI (range), kg/m²	25 (17-61)	24 (16-45)	24 (16-36)	24 (16-38)
Race or ethnic group,[a,b] n (%)				
White	134 (67)	135 (66)	50 (68)	43 (64)
Other	18 (9)	18 (9)	1 (1)	5 (7)
ECOG PS 1, n (%)	107 (54)	100 (49)	50 (68)	45 (67)
Prior CDK4/6 inhibitor use,[c] n (%)				
≤ 12 months	121 (61)	129 (63)	40 (55)	37 (55)
> 12 months	74 (37)	72 (35)	32 (44)	30 (45)
No. pre-existing comorbidities, n (%)				
0	4 (2)	7 (3)	0	1 (1)
1-3	48 (24)	44 (22)	8 (11)	12 (18)
≥ 4	147 (74)	153 (75)	65 (89)	54 (81)

BMI, body mass index; CDK, cyclin-dependent kinase; ECOG PS, Eastern Cooperative Oncology Group performance status; SG, sacituzumab govitecan; TPC, treatment of physician's choice.
[a]Numbers may not add up to 100 because of rounding. [b]Other includes Asian (n = 14), Black (n = 19), native Hawaiian or other Pacific Islander (n = 1), and other races or ethnicities (n = 2) in < 65 years and Asian (n = 2), Black (n = 2), multiple (n = 1), and other races or ethnicities (n = 1) in ≥ 65 years. Race was not reported in 98 patients (SG, n = 47; TPC, n = 51) < 65 years and in 41 patients (SG, n = 22; TPC, n = 19) ≥ 65 years. [c]Prior CDK4/6 inhibitor use was unknown in 7 patients (SG, n = 4; TPC, n = 3) < 65 years and in 1 patient (SG, n = 1) ≥ 65 years.

Efficacy by age subgroup

- PFS and OS favored SG over TPC regardless of age < 65 or age ≥ 65 years **(Figure 2)**

Figure 2. PFS and OS by age subgroup



BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; mo, months; OS, overall survival; PFS, progression-free survival; SG, sacituzumab govitecan; TPC, treatment of physician's choice.
[a]Hazard ratio and 95% CI are based on unstratified Cox regression.

- SG demonstrated improved ORR, CBR, and DOR vs TPC in patients age < 65 and ≥ 65 **(Table 2)**

Table 2. Responses by age subgroup

	< 65 years			≥ 65 years		
BICR analysis	**SG (n = 199)**	**TPC (n = 204)**	**Odds ratio (95% CI)**	**SG (n = 73)**	**TPC (n = 67)**	**Odds ratio (95% CI)**
ORR, n (%)	42 (21)	28 (14)	1.68 (1.00-2.84)	15 (21)	10 (15)	1.47 (0.61-3.55)
CBR, n (%)	66 (33)	47 (23)	1.66 (1.07-2.57)	26 (36)	13 (19)	2.30 (1.06-4.97)
Median DOR,[a] mo (95% CI)	8.3 (6.5-9.7)	5.6 (3.8-7.9)	-	6.9 (5.8-NE)	4.3 (2.3-NE)	-

BICR, blinded independent central review; CBR, clinical benefit rate; CI, confidence interval; DOR, duration of response; mo, months; NE, not estimable; ORR, objective response rate; SG, sacituzumab govitecan; TPC, treatment of physician's choice.
[a]Number of responders: < 65 years, SG, n = 42, TPC, n = 28; ≥ 65 years, SG, n = 15, TPC, n = 10.

Safety by age subgroup

- Patients experienced more treatment-emergent adverse events (TEAEs) leading to dose reduction and treatment discontinuation with SG vs TPC in the ≥ 65 years subgroup, and TEAEs with SG leading to dose reduction and treatment discontinuation were more common in the ≥ 65 years subgroup vs < 65 years **(Table 3)**
- Grade ≥ 3 TEAEs and TEAEs leading to treatment interruptions occurred at higher rates in patients treated with SG vs TPC, and the rates of these TEAEs were similar across age subgroups **(Table 3)**

Table 3. TEAEs by age subgroup

	< 65 years				≥ 65 years			
	SG (n = 196)		TPC (n = 188)		SG (n = 72)		TPC (n = 61)	
All TEAEs,[a] n (%)	196 (100)		178 (95)		72 (100)		61 (100)	
Grade ≥ 3	144 (73)		113 (60)		54 (75)		37 (61)	
TEAEs leading to dose reduction	63 (32)		65 (35)		27 (38)		17 (28)	
TEAEs leading to treatment interruption	129 (66)		82 (44)		49 (68)		27 (44)	
TEAEs leading to treatment discontinuation	5 (3)		8 (4)		12 (17)		3 (5)	
Most common TEAEs,[a,b] n (%)	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3
Neutropenia	142 (72)	106 (54)	106 (56)	75 (40)	47 (65)	32 (44)	30 (49)	22 (36)
Nausea	117 (60)	2 (1)	69 (37)	6 (3)	40 (56)	1 (1)	18 (30)	1 (2)
Diarrhea	112 (57)	15 (8)	40 (21)	2 (1)	54 (75)	12 (17)	17 (28)	1 (2)
Alopecia	98 (50)	0	31 (16)	0	30 (42)	0	15 (25)	0
Fatigue	78 (40)	8 (4)	59 (31)	7 (4)	27 (38)	8 (11)	23 (38)	2 (3)
Constipation	72 (37)	1 (1)	45 (24)	0	21 (29)	0	16 (26)	0
Anemia	70 (36)	12 (6)	51 (27)	8 (4)	28 (39)	8 (11)	18 (30)	1 (2)

AE, adverse event; SG, sacituzumab govitecan; TEAE, treatment-emergent adverse event; TPC, treatment of physician's choice.
[a]TEAEs were defined as any AEs that started on or after the first dose date and up to 30 days after the last dose date. Severity grades were defined using Common Terminology Criteria for Adverse Events v5.0. [b]TEAEs occurring in ≥ 30% of patients in either treatment arm within either age subgroup.

Quality of life by age subgroup

- SG was favored (ie, had significantly longer time to deterioration [TTD]) over TPC for fatigue (*P* = .021) in the < 65 years subgroup **(Table 4)**
- SG was also numerically favored over TPC for global health status/QoL in both age subgroups and for pain score in the ≥ 65 years subgroup **(Table 4)**

Table 4. TTD by age subgroup

		< 65 years			≥ 65 years		
EORTC QLQ C-30 domain		**SG**	**TPC**	**HR (95% CI) *P* value**	**SG**	**TPC**	**HR (95% CI) *P* value**
Global health status/QoL	Median TTD, mo (95% CI)	4.4 (3.2-6.4)	3.0 (2.2-4.4)	0.81 (0.64-1.02) *P* = .066	3.4 (2.1-5.7)	2.9 (1.4-4.9)	0.71 (0.47-1.06) *P* = .094
Fatigue	Median TTD, mo (95% CI)	2.0 (1.5-2.8)	1.1 (1.0-1.8)	0.76 (0.61-0.96) *P* = .021	2.2 (1.2-4.4)	2.3 (1.3-3.7)	0.82 (0.55-1.22) *P* = .32
Pain	Median TTD, mo (95% CI)	3.7 (2.8-5.2)	4.6 (3.1-6.3)	1.00 (0.79-1.27) *P* = .97	4.4 (1.5-5.3)	2.6 (1.7-3.6)	0.73 (0.49-1.09) *P* = .12

CI, confidence interval; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; HR, hazard ratio; QoL, quality of life; SG, sacituzumab govitecan; TPC, treatment of physician's choice; TTD, time to deterioration.
A clinically meaningful deterioration using the predefined EORTC QLQ C-30 scales was defined as at least a 10-point worsening from baseline. Death is considered as an event.
HR and *P* values were estimated using a Cox proportional hazards regression analysis with treatment arm (SG vs TPC) as a covariate in the model for each subgroup level. Subjects with baseline score > 90 for QLQ C-30 fatigue and pain domains and baseline score < 10 for global health status/QoL were excluded from the QoL analysis.

Efficacy by relative dose intensity

- Patients with relative dose intensity (RDI) > 90% in the < 65 years subgroup experienced numerically higher median PFS, median OS, ORR, and CBR than patients with lower RDI **(Table 5)**
  - Patients in the ≥ 65-year subgroup also experienced PFS benefit in RDI > 90% vs lower RDI

Table 5. Efficacy by relative dose intensity

	< 65 years			≥ 65 years		
	RDI ≤ 74% (n = 60)	**RDI > 74% and ≤ 90% (n = 73)**	**RDI > 90% (n = 61)**	**RDI ≤ 74% (n = 28)**	**RDI > 74% and ≤ 90% (n = 16)**	**RDI > 90% (n = 27)**
Median PFS (95% CI),[a] mo	2.9 (1.6-5.6)	4.7 (3.3-6.9)	8.5 (4.4-9.4)	5.5 (2.7-21.0)	5.5 (3.8-NE)	6.7 (2.4-9.0)
Median OS (95% CI), mo	13.0 (11.4-15.3)	13.6 (11.7-18.4)	18.1 (12.8-19.8)	13.9 (8.1-20.6)	25.6 (5.3-NE)	15.4 (8.5-21.9)
ORR,[a] n (%)	8 (13)	14 (19)	19 (31)	5 (18)	3 (19)	6 (22)
CBR,[a] n (%)	15 (25)	23 (32)	27 (44)	9 (32)	6 (38)	10 (37)

CBR, clinical benefit rate; CI, confidence interval; mo, months; NE, not estimable; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; RDI, relative dose intensity; SG, sacituzumab govitecan. RDI for SG is defined as actual cumulative dose divided by total planned dose.
[a]Per blinded independent central review.