Efficacy and Safety Analyses by Prior Lines of Chemotherapy From the Phase 3 TROPiCS-02 Study of Sacituzumab Govitecan Versus Treatment of Physician's Choice in Patients With HR+/HER2– Metastatic Breast Cancer

Poster #389P

Javier Cortés,[1] Frederik Marmé,[2] Peter Schmid,[3] Hope S. Rugo,[4] Sara M. Tolaney,[5] Wendy Verret,[6] Theresa Valdez,[7] Yanan Huo,[8] Aditya Bardia[9]

[1]Department of Medicine, Oncology Department, International Breast Cancer Center (IBCC), Pangaea Oncology, Quiron Group, Barcelona, Spain/Medica Scientia Innovation Research (MedSIR), Barcelona, Spain; [2]Department of Obstetrics and Gynaecology, Universitätsmedizin Mannheim, Heidelberg, Germany; [3]Medical Oncology, Barts Health NHS Trust, London, UK; [4]Department of Medicine, University of California San Francisco Helen Diller Family Comprehensive Cancer Center, San Francisco, CA, USA; [5]Department of Medical Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA; [6]Department of Clinical Development, Gilead Sciences, Inc., Foster City, CA, USA; [7]Department of Patient Safety, Gilead Sciences, Inc., Foster City, CA, USA; [8]Department of Biostatistics, Gilead Sciences, Inc., Foster City, CA, USA; [9]Medical Oncology, Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, MA, USA

Key Findings

- **OS and PFS benefit was observed in patients treated with SG vs TPC regardless of number of prior LoT in the metastatic setting**
- **SG demonstrated improved CBR regardless of number of prior LoT, and improved ORR during earlier LoT, compared with TPC**

Conclusions

SG exhibited efficacy benefit vs TPC regardless of number of prior LoT, with a manageable safety profile, in patients with pretreated, endocrine-resistant HR+/HER2– mBC

These results are consistent with results in the intent-to-treat population, suggesting that SG may provide therapeutic benefit in earlier LoT

SG is currently being evaluated in earlier LoT for patients with endocrine-resistant, chemotherapy-naive HR+/HER2– mBC (NCT05840211)

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 September 20, 2023. **2.** American Cancer Society. Female breast cancer subtypes. https://seer.cancer.gov/statfacts/html/breast-subtypes.html. Accessed September 20, 2023. **3.** Park IH, et al. *Clin Breast Cancer*. 2015;15:e55-e62. **4.** TRODELVY® (sacituzumab govitecan-hziy) [prescribing information]. Foster City, CA: Gilead Sciences, Inc.; June 2023. **5.** TRODELVY® (sacituzumab govitecan-hziy) [summary of product characteristics]. County Cork, Ireland: Gilead Sciences Ireland UC; August 2023. **6.** Rugo HS, et al. *J Clin Oncol*. 2022;40:3365-3376. **7.** Rugo HS, et al. *Lancet*. 2023. Published online August 23, 2023. doi: 10.1016/S0140-6736(23)01245-X.

Acknowledgments: We would like to thank the patients, their caregivers, and families for their participation and commitment to clinical research. Thank you to the clinical trial investigators and their team members, without whom this work would not have been possible. This study was sponsored by Gilead Sciences, Inc. Medical writing and editorial support was provided by Ben Labbe, PhD, of Parexel, and funded by Gilead Sciences, Inc.

Presenting author disclosures: Dr. Javier Cortés reports research funding from Ariad Pharmaceuticals, AstraZeneca, Baxalta GMBH/Servier Affaires, Bayer Healthcare, Eisai, Guardant Health, Merck Sharp & Dohme, Pfizer, Piqur Therapeutics, Puma B, Queen Mary University of London, and Roche; honoraria from Celgene, Daiichi Sankyo, Eisai, Eli Lilly, Merck Sharp & Dohme, Novartis, Pfizer, Roche, and Samsung Bioepis; advisory roles with AstraZeneca, Athenex, Bioasis, BioInvent, Boehringer Ingelheim, Celgene, Cellestia, Clovis Oncology, Daiichi Sankyo, Eli Lilly, Ellipses, Erytech, ExpreS2ion Biotechnologies, Gemoab, Gilead Sciences, Inc., GSK, Hibercell, LEUKO, Menarini, Merck Sharp & Dohme, Polyphor, Reveal Genomics, Roche, Seattle Genetics, and Zymeworks; stocks or shares in MedSIR; and travel accommodations/expenses from AstraZeneca, Daiichi Sankyo, Eisai, Gilead Sciences, Inc., Novartis, Pfizer, and Roche.

Correspondence: Javier.cortes@maj3.health

Introduction

- Breast cancer is the second most common cause of cancer-related death in women.[1] The most common form of breast cancer is hormone receptor-positive (HR+)/human epidermal growth factor receptor 2-negative (HER2−),[a] which represents approximately 70% of breast cancers[2]
- Resistance to chemotherapy increases with multiple lines of chemotherapy in the metastatic setting, leading to poor outcomes[3]
- Sacituzumab govitecan (SG) is an antibody-drug conjugate targeted to trophoblast cell-surface antigen 2 (Trop-2), which has been approved in multiple countries for the treatment of pretreated HR+/HER2− metastatic breast cancer (mBC) and for the treatment of metastatic triple-negative breast cancer after at least 1 prior therapy[4,5]
- In the phase 3 randomized TROPiCS-02 study, SG demonstrated significantly improved median progression-free survival (PFS; 5.5 vs 4.0 months; hazard ratio [HR], 0.66; $P = .0003$)[6] and median overall survival (OS; 14.4 vs 11.2 months; HR, 0.79; $P = .020$)[7] vs treatment of physician's choice (TPC), with a manageable safety profile, for patients with pretreated, endocrine-resistant HR+/HER2− mBC[6,7]

[a]Immunohistochemistry (IHC)0, IHC1+, or IHC2+ and in situ hybridization-negative (ISH−).

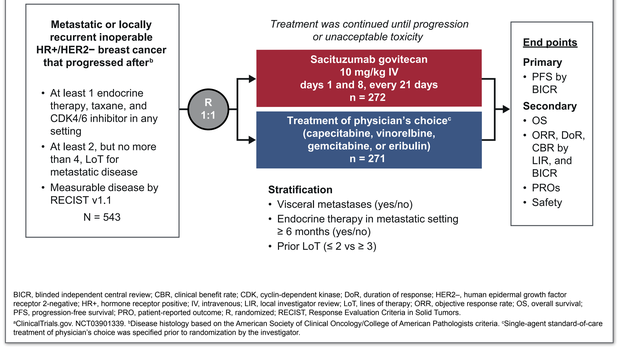
Objective

- We present a post hoc analysis of the efficacy and safety outcomes with SG vs TPC by number of prior lines of chemotherapy (LoT) in the metastatic setting from TROPiCS-02

Methods

- TROPiCS-02 is a phase 3, randomized, open-label study of SG vs TPC for pretreated, endocrine-resistant HR+/HER2− mBC **(Figure 1)**[4]
- Patients were stratified by number of prior LoT in the metastatic setting (≤ 2 vs ≥ 3)
- The data cutoff was July 1, 2022, except for PFS, which was January 3, 2022

Figure 1. TROPiCS-02: a phase 3 study of sacituzumab govitecan in HR+/HER2− mBC[a]



BICR, blinded independent central review; 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; LoT, lines of therapy; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PRO, patient-reported outcome; R, randomized; RECIST, Response Evaluation Criteria in Solid Tumors.
[a]ClinicalTrials.gov. NCT03901339. [b]Disease histology based on the American Society of Clinical Oncology/College of American Pathologists criteria. [c]Single-agent standard-of-care treatment of physician's choice was specified prior to randomization by the investigator.

Results

Baseline characteristics by prior LoT in the metastatic setting

- Baseline characteristics were generally consistent in patients with ≤ 2 and ≥ 3 prior LoT and across treatment groups **(Table 1)**

Table 1. Demographics and baseline characteristics

	≤ 2 Prior LoT[a]		≥ 3 Prior LoT[a]	
	SG (n = 113)	TPC (n = 120)	SG (n = 159)	TPC (n = 151)
Female, n (%)	111 (98)	118 (98)	159 (100)	150 (99)
Median age (range), years	56 (29-79)	55 (32-77)	58 (29-86)	56 (27-78)
Median baseline BMI (range), kg/m²	25 (17-61)	25 (16-45)	25 (16-45)	24 (16-41)
Race,[b] n (%)				
White	84 (74)	77 (64)	100 (63)	101 (67)
Non-White	6 (5)	13 (11)	13 (8)	10 (7)
ECOG PS, n (%)				
0	55 (49)	60 (50)	60 (38)	66 (44)
1	58 (51)	60 (50)	99 (62)	85 (56)
Prior CDK4/6 inhibitor use,[c] n (%)				
≤ 12 months	62 (55)	74 (62)	99 (62)	92 (61)
> 12 months	48 (42)	44 (37)	58 (36)	58 (38)

BMI, body mass index; CDK, cyclin-dependent kinase; ECOG PS, Eastern Cooperative Oncology Group performance status; LoT, lines of chemotherapy; SG, sacituzumab govitecan; TPC, treatment of physician's choice.
[a]Intent-to-treat population. [b]Race was not reported in 53 patients (SG, n = 23; TPC, n = 30) with ≤ 2 prior LoT and in 86 patients (SG, n = 46; TPC, n = 40) with ≥ 3 prior LoT. [c]Prior CDK4/6 inhibitor use was unknown in 5 patients (SG, n = 3; TPC, n = 2) with ≤ 2 prior LoT and in 3 patients (SG, n = 2; TPC, n = 1) with ≥ 3 prior LoT.

- Patients who received ≤ 2 and ≥ 3 prior LoT had received prior endocrine therapies, CDK4/6 inhibitors, targeted agents, and immunotherapies at similar rates **(Table 2)**

Table 2. Prior LoT

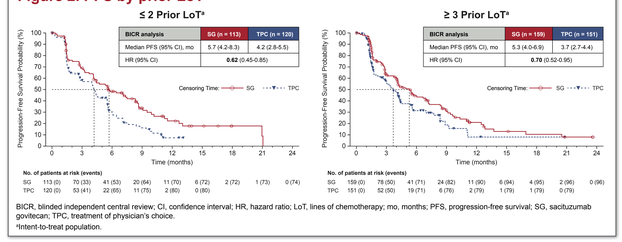
	≤ 2 Prior LoT[a]		≥ 3 Prior LoT[a]	
	SG (n = 113)	TPC (n = 120)	SG (n = 159)	TPC (n = 151)
Prior use of endocrine therapy, n (%)	111 (98)	119 (99)	157 (99)	150 (99)
Prior use of CDK4/6, n (%)	110 (97)	119 (99)	158 (99)	151 (100)
Prior use of targeted agent, n (%)	70 (62)	79 (66)	112 (70)	94 (62)
Prior use of immunotherapy, n (%)	12 (11)	8 (7)	12 (8)	12 (8)
Median no. of prior systemic LoT,[b] n (range)	2 (0-2)	2 (1-2)	3 (3-8)	3 (3-5)
Prior chemotherapy,[c] n (%)	112 (99)	120 (100)	159 (100)	151 (100)
Capecitabine	80 (71)	93 (78)	141 (89)	139 (92)
Paclitaxel	65 (58)	71 (59)	129 (81)	100 (66)
Eribulin	20 (18)	20 (17)	75 (47)	68 (45)
Cyclophosphamide	16 (14)	13 (11)	50 (31)	41 (27)
Doxorubicin	10 (9)	8 (7)	44 (28)	26 (17)
Gemcitabine	5 (4)	8 (7)	24 (15)	25 (17)

CDK, cyclin-dependent kinase; LoT, lines of chemotherapy.
[a]Intent-to-treat population. [b]Per protocol, patients with 2 to 4 prior LoT for metastatic disease were eligible. Patients with < 2 (n = 11) or > 4 (n = 8) prior LoT were included as protocol deviations. 8 patients who received SG and 2 patients who received TPC had 1 prior LoT. [c]Chemotherapy regimens used in ≥ 15% of patients in either treatment group and number of prior LoT.

Efficacy by prior LoT in the metastatic setting

- PFS favored SG over TPC regardless of number of prior LoT **(Figure 2)**

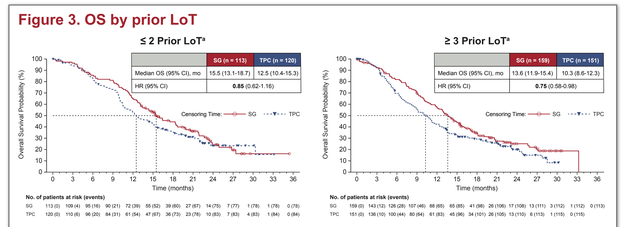
Figure 2. PFS by prior LoT



BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; LoT, lines of chemotherapy; mo, months; PFS, progression-free survival; SG, sacituzumab govitecan; TPC, treatment of physician's choice.
[a]Intent-to-treat population.

- OS favored SG over TPC regardless of number of prior LoT **(Figure 3)**

Figure 3. OS by prior LoT



CI, confidence interval; HR, hazard ratio; mo, months; LoT, lines of chemotherapy; OS, overall survival; SG, sacituzumab govitecan; TPC, treatment of physician's choice.
[a]Intent-to-treat population.

- SG demonstrated improvement of objective response rate (ORR) in patients who received ≤ 2 LoT and improvement of clinical benefit rate (CBR) vs TPC regardless of prior LoT **(Table 3)**

Table 3. Responses by prior LoT

	≤ 2 Prior LoT[a]		≥ 3 Prior LoT[a]	
BICR analysis	**SG (n = 113)**	**TPC (n = 120)**	**SG (n = 159)**	**TPC (n = 151)**
ORR, n (%)	34 (30)	21 (18)	23 (15)	17 (11)
Odds ratio (95% CI)	2.03 (1.09-3.77)		1.33 (0.68-2.61)	
CBR, n (%)	47 (42)	31 (26)	45 (28)	29 (19)
Odds ratio (95% CI)	2.04 (1.18-3.56)		1.66 (0.98-2.83)	

BICR, blinded independent central review; CBR, clinical benefit rate; CI, confidence interval; LoT, lines of chemotherapy; ORR, objective response rate; SG, sacituzumab govitecan; TPC, treatment of physician's choice.
[a]Intent-to-treat population.

Safety by prior LoT in the metastatic setting

- Patients treated with SG experienced grade ≥ 3 treatment-emergent adverse events (TEAEs) and TEAEs leading to treatment interruptions at higher rates than those treated with TPC; rates were generally similar in patients with ≤ 2 and ≥ 3 prior LoT **(Table 4)**
- The most common grade ≥ 3 TEAEs in ≥ 10% of patients in either group were
  - ≤ 2 LoT: SG, neutropenia (54%), leukopenia (11%), and diarrhea (10%); TPC, neutropenia (31%)
  - ≥ 3 LoT: SG, neutropenia (49%) and diarrhea (10%); TPC, neutropenia (45%)

Table 4. TEAEs by prior LoT

	≤ 2 Prior LoT		≥ 3 Prior LoT	
	SG (n = 112)	TPC (n = 109)	SG (n = 156)	TPC (n = 140)
All TEAEs,[a] n (%)	112 (100)	106 (97)	156 (100)	133 (95)
Grade ≥ 3	83 (74)	58 (53)	115 (74)	92 (66)
TEAEs leading to dose reduction	37 (33)	33 (30)	53 (34)	49 (35)
TEAEs leading to treatment interruption	75 (67)	45 (41)	103 (66)	64 (46)
TEAEs leading to treatment discontinuation	6 (5)	2 (2)	11 (7)	9 (6)
Most common TEAEs,[a,b] n (%)				
Neutropenia[c]	86 (77)	50 (46)	103 (66)	86 (61)
Diarrhea	75 (67)	29 (27)	91 (58)	28 (20)
Nausea	70 (63)	38 (35)	87 (56)	49 (35)
Alopecia	61 (54)	27 (25)	67 (43)	19 (14)
Fatigue	43 (38)	37 (34)	62 (40)	45 (32)
Constipation	36 (32)	29 (27)	57 (37)	32 (23)
Anemia[d]	34 (30)	23 (21)	64 (41)	46 (33)
Vomiting	31 (28)	13 (12)	33 (21)	26 (19)

LoT, lines of chemotherapy; SG, sacituzumab govitecan; TEAE, treatment-emergent adverse event; TPC, treatment of physician's choice.
[a]Safety population. TEAEs were defined as any AEs that started on or after first dose date and up to 30 days after last dose date. Severity grades were defined using Common Terminology Criteria for Adverse Events 5.0. [b]Key any-grade TEAEs were defined as those occurring in ≥ 25% of patients in either treatment group. [c]Combined preferred terms of "neutropenia" and "neutrophil count decreased." [d]Combined preferred terms of "anemia," "hemoglobin decreased," and "red blood cell count decreased."