Safety Analysis of ASCENT-03, a Phase 3 Study of Sacituzumab Govitecan vs Chemotherapy for Previously Untreated Advanced Triple-Negative Breast Cancer in Patients Who Are Not Candidates for PD-(L)1 Inhibitors

Sara Hurvitz[1], Aditya Bardia[2], Sara M Tolaney[3], Kevin Punie[4], Carlos Barrios[5], Andreas Schneeweiss[6], Roberto Hegg[7], Eriko Tokunaga[8], Joohyuk Sohn[9], Sung-Bae Kim[10], Seock-Ah Im[11], Yeon Hee Park[12], Bernardo Rapoport[13,14], Daniel Motola[15], Denise A Yardley[16], Florence Dalenc[17], Mafalda Oliveira[18], Barbara Pistilli[19], Gregory Vidal[20], Shani Paluch-Shimon[21], Binghe Xu[22], Theresa Valdez[23], Danjie Zhang[23], Sunita Padman[23], Javier Cortés[24-28]

[1]Department of Medicine, UW Medicine, Clinical Research Division, Fred Hutchinson Cancer Center, Seattle, WA, USA; [2]David Geffen School of Medicine, University of California and Jonsson Comprehensive Cancer Center, Los Angeles, CA, USA; [3]Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA; [4]Medical Oncology, Oncology Center Antwerp, Ziekenhuis aan de Stroom, Antwerp, Belgium; [5]Latin American Cooperative Oncology Group (LACOG), Porto Alegre, Brazil; [6]Heidelberg University Hospital and German Cancer Research Center, Heidelberg, Germany; [7]University of São Paulo, São Paulo, Brazil; [8]National Hospital Organization Kyushu Cancer Center, Fukuoka, Japan; [9]Yonsei Cancer Center, Seoul, Republic of Korea; [10]Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; [11]Seoul National University Hospital, Cancer Research Institute, Seoul National University College of Medicine, Seoul National University, Seoul, Republic of Korea; [12]Samsung Medical Center, Sunkyunkwan University School of Medicine, Seoul, Republic of Korea; [13]The Medical Oncology Centre of Rosebank, Clinical and Translational Research Unit (CTRU), Saxonworld, South Africa; [14]Department of Immunology, Faculty of Health Sciences, University of Pretoria, Pretoria, South Africa; [15]Cryptex Investigación Clínica, Mexico City, Mexico; [16]Sarah Cannon Research Institute, Nashville, TN, USA; [17]Oncopole Claudius Regaud, IUCT-Oncopole, Toulouse, France; [18]Vall d'Hebron University Hospital, Breast Cancer Group, Vall d'Hebron Institute of Oncology (VHIO), Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain; [19]Gustave Roussy and IHU-National PRecISion Medicine Center in Oncology, Villejuif, France; [20]West Cancer Center and Research Institute, Memphis, TN, USA; [21]Hadassah - Hebrew University Medical Center, Jerusalem District, Israel; [22]Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [23]Gilead Sciences, Inc., Foster City, CA, USA; [24]International Breast Cancer Center (IBCC), Pangaea Oncology, Quiron Group, Barcelona, Spain; [25]IOB Madrid, Institute of Oncology, Hospital Beata Maria Ana, Madrid, Spain; [26]Oncology Department, Hospital Universitario Torrejón, Ribera Group, Madrid, Spain; [27]Universidad Europea de Madrid, Faculty of Biomedical and Health Sciences, Department of Medicine, Madrid, Spain; [28]Medica Scientia Innovation Research (MEDSIR), Barcelona, Spain and Ridgewood, NJ, USA

Poster #PS1-13-24

San Antonio Breast Cancer Symposium®-December 9-12, 2025

Conclusions

- In the ASCENT-03 study, the safety profile of sacituzumab govitecan (SG) was consistent with previous studies in breast cancer, and no new toxicities were identified, in participants with previously untreated metastatic triple-negative breast cancer (mTNBC) who were not candidates for programmed death (ligand) 1 (PD-[L]1) inhibitors
- After adjusting for longer duration of treatment with SG vs chemotherapy (chemo), rates of treatment-emergent adverse events (TEAEs) leading to dose reduction and treatment discontinuation and rates of anemia, thrombocytopenia, and peripheral neuropathy favored SG, while the rate of diarrhea favored chemo, consistent with the known safety profile of SG
- The majority of fatal events with SG were infections secondary to neutropenia. These participants had multiple risk factors for febrile neutropenia and did not receive primary prophylaxis with granulocyte-colony stimulating factor (G-CSF), reiterating the importance of proactive adverse events management with SG use, according to established guidelines
- Time to onset and duration of neutropenia and diarrhea were generally comparable between treatment groups, and both TEAEs were manageable with supportive care
  - Both neutropenia and diarrhea were most common early in the SG treatment period and should be managed proactively according to established guidelines
  - Primary prophylaxis with G-CSF was associated with lower rates of neutropenia and less severe neutropenia in the SG group

Plain Language Summary

In the ASCENT-03 clinical study, participants received either sacituzumab govitecan (SG) or chemotherapy (chemo) to see which treatment was more effective as the initial treatment for metastatic triple-negative breast cancer. Participants in ASCENT-03 were not candidates for treatment targeting PD-L1, a protein expressed on some tumors. Here, the researchers performed a more detailed analysis of safety in ASCENT-03. When the researchers accounted for the amount of drug that participants received over the study, those who received SG experienced fewer adverse events leading to dose reduction and treatment discontinuation compared with those who received chemo. Deaths with SG were mainly infections related to neutropenia. These participants had many risk factors for neutropenia and did not receive preventative treatment according to current management practices. Neutropenia and diarrhea, which are common adverse events during SG treatment, generally resolved quickly using standard management practices. These results support SG as an effective treatment that has adverse events that can be managed for people with metastatic triple-negative breast cancer who are not candidates for PD-L1–targeting treatment.

References: **1.** Goldenberg DM, et al. *Oncotarget*. 2015;6:22496-512. **2.** Bardia A, et al. *N Engl J Med*. 2021;384:1529-41. **3.** TRODELVY® (sacituzumab govitecan-hziy) [prescribing information]. Foster City, CA: Gilead Sciences, Inc.; 2025. **4.** TRODELVY® (sacituzumab govitecan-hziy) [summary of product characteristics]. County Cork, Ireland: Gilead Sciences Ireland UC; 2025. **5.** Cortés J, et al. *N Engl J Med*. 2025; online first. doi: 10.1056/NEJMoa2511734.

Acknowledgments: We extend our thanks to the patients, their families, and all participating investigators. This study was funded by Gilead Sciences, Inc. Medical writing and editorial support was provided by Ben Labbe, PhD, of Parexel, and funded by Gilead Sciences, Inc.

Disclosures: **SH** reports grants or contracts from Ambrx, Amgen, Arvinas, AstraZeneca, Bayer, Celcuity, Cytomx, Daiichi Sankyo, Dantari, Dignitana, Genentech/Roche, G1-Therapeutics, Gilead Sciences, Inc., Greenwich Life Sciences Inc, GSK, Immunomedics, Jazz Pharmaceuticals, Lilly, LOXO, Macrogenics, Novartis, OBI Pharma, Orinove, Orum, Pfizer, Phoenix Molecular Designs, Ltd., Pieris, PUMA, Radius, Samumed, Sanofi, Seattle Genetics/Seagen, Stemline/Menarini, and Zymeworks; royalties or licenses from Elsevier, McGraw Hill, Sage, and Wolters Kluwer; consulting fees from Arvinas/Pfizer, Beigene, Bristol Myers Squibb, Boehringer Ingelheim, Briacell, BridgeBio, Daiichi Sankyo, Jazz Pharmaceuticals/Zymeworks, Gilead Sciences Inc., Luminate, MedSir, Menarini, Mersana, Novartis, and Roche; participation on Data Safety Monitoring or Advisory Board with Alliance Foundation, InClin/Atossa, and QuantumLeap; and stock or stock options with RomTech.

Introduction

- SG is a Trop-2–directed antibody-drug conjugate[1] that has been approved in multiple countries for pretreated (≥ 2 prior systemic therapies, ≥ 1 for metastatic disease) mTNBC[2-4]
- In the phase 3, randomized ASCENT-03 study, SG demonstrated statistically significant and clinically meaningful improvement in progression-free survival (PFS) and longer duration of response (DOR) vs chemo in participants with previously untreated mTNBC who were not candidates for PD-(L)1 inhibitor treatment[5]
- We report the first in-depth safety analysis from ASCENT-03

Methods

- Participants had previously untreated, locally advanced unresectable or mTNBC and had tumors that were PD-L1 negative (combined positive score [CPS] < 10) or that were PD-L1 positive (CPS ≥ 10) with prior PD-(L)1 inhibitor treatment in the (neo)adjuvant setting or with a comorbidity preventing PD-(L)1 inhibitor treatment
- Participants were randomized to receive SG (10 mg/kg intravenously, days 1 and 8 of 21-day cycle) or chemo (paclitaxel, nab-paclitaxel, or gemcitabine + carboplatin) until disease progression or unacceptable toxicity as previously described[5]
- The primary end point was PFS by blinded independent central review (BICR); key secondary end points included overall survival, objective response rate and DOR by BICR, and safety
- EAIRs, defined as number of participants with ≥ 1 of the specified TEAE per patient-year of exposure (PYE), were determined as part of an exploratory analysis
  - EAIR was calculated as number of participants with a specific event divided by total PYE in each group; PYE was defined as the sum of each patient's time at risk (exposure duration) within the study
- The incidence, severity, time to onset, duration, and impact of adverse event management were assessed for select TEAEs of interest for SG

Results

- Participant demographics and baseline characteristics were well balanced between the treatment groups (Table 1)

Table 1. Baseline Characteristics in Safety Population

Characteristic	Category	SG (n = 275)	Chemo (n = 276)
Median age (range), years	—	56 (28–84)	55 (23–86)
Sex, n (%)	Female	274 (> 99)	274 (99)
Race or ethnicity,[a] n (%)	White	175 (64)	175 (63)
	Asian	66 (24)	65 (24)
	Black	9 (3)	7 (3)
	Other or not specified	25 (9)	29 (11)
Geographic region,[b] n (%)	North America	42 (15)	41 (15)
	Europe	95 (35)	105 (38)
	Asia/Pacific	83 (30)	73 (26)
	South America	48 (17)	51 (18)
	Rest of World	7 (3)	6 (2)
PD-L1 status,[c] n (%)	Negative	274 (> 99)	275 (> 99)
	Positive	1 (< 1)	1 (< 1)
ECOG PS, n (%)	0	181 (66)	185 (67)
	1	94 (34)	91 (33)

[a]As reported by participants. [b]Rest of World includes South Africa. [c]Assessed using PD-L1 IHC 22C3 assay (Dako, Agilent Technologies) at time of enrollment. Tumors with CPS ≥ 10 were considered positive. Chemo, chemotherapy; CPS, combined positive score; ECOG PS, Eastern Cooperative Oncology Group performance status; PD-L1, programmed cell death-ligand 1; SG, sacituzumab govitecan.

Results

- Median duration of treatment was 8.3 months for SG and was 6.1 months for gemcitabine, 5.8 months for carboplatin, and 6.3 months for taxanes in the chemo group
- Any-grade TEAEs occurred in 273 (99%) participants who received SG and 269 (97%) who received chemo
  - Any-grade EAIR for SG was 40.21 (95% CI, 35.58, 45.27); for chemo, it was 21.66 (95% CI, 19.14, 24.40)
- Of 7 fatal TEAEs with SG, 6 were treatment-related and were due to infections; 5 infections were secondary to neutropenia in participants who had risk factors for febrile neutropenia but did not receive prophylaxis with G-CSF
- Additional EAIR data are shown in Figure 1

Figure 1. Exposure-Adjusted Incidence Rates

TEAEs	SG (n = 275) n (%)	SG (n = 275) EAIR (95% CI)	Chemo (n = 276) n (%)	Chemo (n = 276) EAIR (95% CI)	EAIR Difference (95% CI)
Grade ≥ 3	181 (66)	1.85 (1.59, 2.14)	171 (62)	2.02 (1.73, 2.35)	−0.18 (−0.59, 0.23)
Serious	71 (26)	0.40 (0.31, 0.51)	67 (24)	0.49 (0.38, 0.63)	−0.09 (−0.25, 0.06)
Led to any 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)
Led to treatment discontinuation	10 (4)	0.05 (0.02, 0.09)	33 (12)	0.22 (0.15, 0.30)	−0.17 (−0.26, −0.09)
Led to death	7 (3)	0.03 (0.01, 0.07)	1 (< 1)	0.01 (0.00, 0.04)	0.03 (−0.01, 0.07)
Neutropenia[a]	183 (67)	2.48 (2.13, 2.87)	157 (57)	2.01 (1.71, 2.35)	0.47 (−0.02, 0.96)
Febrile neutropenia	12 (4)	0.06 (0.03, 0.11)	3 (1)	0.02 (0.00, 0.06)	0.04 (0.00, 0.09)
Anemia[b]	107 (39)	0.77 (0.63, 0.93)	138 (50)	1.51 (1.27, 1.78)	−0.74 (−1.05, −0.45)
Thrombocytopenia[c]	12 (4)	0.06 (0.03, 0.11)	78 (28)	0.63 (0.50, 0.78)	−0.57 (−0.73, −0.43)
Diarrhea	148 (54)	1.42 (1.20, 1.67)	55 (20)	0.41 (0.31, 0.54)	1.01 (0.76, 1.28)
Fatigue[d]	130 (47)	1.15 (0.96, 1.37)	129 (47)	1.24 (1.03, 1.47)	−0.08 (−0.38, 0.21)
Peripheral neuropathy	12 (4)	0.06 (0.03, 0.11)	35 (13)	0.25 (0.17, 0.34)	−0.18 (−0.28, −0.10)

[a]Neutropenia includes preferred terms of neutropenia and neutrophil count decreased. [b]Anemia includes preferred terms of anemia, hemoglobin decreased, and red blood cell count decreased. [c]Thrombocytopenia includes preferred terms of thrombocytopenia and platelet count decreased. [d]Fatigue includes preferred terms of fatigue and asthenia. Chemo, chemotherapy; EAIR, exposure-adjusted incidence rate; SG, sacituzumab govitecan; TEAE, treatment-emergent adverse event.

- Median time to onset of diarrhea was shorter for participants treated with SG vs chemo, although the sample size was small and this result should be interpreted with caution (Table 2)
- Median duration of diarrhea and neutropenia was generally comparable between the treatment groups

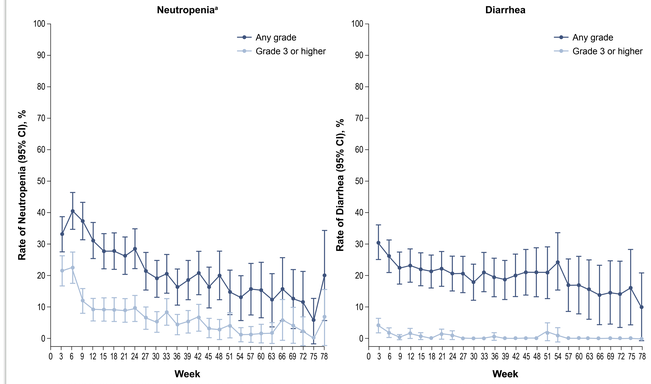
Table 2. Time to Onset and Duration of Neutropenia and Diarrhea

	SG (n = 275)				Chemo (n = 276)			
	Any grade		Grade ≥ 3		Any grade		Grade ≥ 3	
	n	Days (range)	n	Days (range)	n	Days (range)	n	Days (range)
Median time to onset[a]								
Neutropenia	187	22 (6–274)	124	22 (7–720)	158	22 (6–406)	113	29 (7–295)
Diarrhea	148	13 (1–427)	25	67 (6–356)	55	26 (1–296)	2	210 (110–310)
Median duration[b]								
Neutropenia	183	9 (2–49)	122	8 (1–36)	155	14 (1–179)	112	8 (1–25)
Diarrhea	130	6 (1–273)	24	6 (1–18)	48	6 (1–370)	2	1 (1–1)

[a]Time to onset of first TEAE is defined as time from first dose date of study drug to onset date of first TEAE. [b]Duration of TEAE is median duration among multiple preferred terms; within each preferred term, duration is median duration among multiple episodes (end date of TEAE – onset date of TEAE + 1 day for each episode). Chemo, chemotherapy; SG, sacituzumab govitecan; TEAE, treatment-emergent adverse event.

- The frequencies of neutropenia and diarrhea with SG were highest early in treatment (Figure 2)

Figure 2. Neutropenia and Diarrhea Over Time With SG



Rate of neutropenia and diarrhea was calculated for every 3-week interval and defined as the number of participants who experienced the event in the interval divided by the number of participants at risk in the interval. [a]Neutropenia includes preferred terms of neutrophil count decreased, neutropenia, and febrile neutropenia. SG, sacituzumab govitecan.

- The use of G-CSF as primary prophylaxis was associated with less frequent and less severe neutropenia in the SG group (Table 3)
  - Neutropenia led to dose reduction in 54 (20%) participants in both groups and treatment discontinuation in 1 (< 1%) and 3 (1%) participants in the SG and chemo groups, respectively
- Most cases of diarrhea in both the SG and chemo groups were grade 1 to 2 (45% vs 19% incidence, respectively)
- In the SG group, 137 (50%) participants received antidiarrheals, as did 35 (13%) in the chemo group; loperamide was the most common in both treatment groups (SG group: 90% vs chemo group: 77%); multi-antidiarrheal regimens were used in 20% of participants that received any antidiarrheal treatment in both treatment groups
  - Diarrhea led to dose reduction in 15 (5%) participants and to treatment discontinuation in 1 (< 1%) participant in the SG group; 3 (1%) cases led to dose reduction, and no cases led to treatment discontinuation in the chemo group

Table 3. Management of Neutropenia

Neutropenia, n (%)	SG (n = 275)		Chemo (n = 276)	
Primary G-CSF prophylaxis	**Yes (n = 54)**	**No (n = 221)**	**Yes (n = 28)**	**No (n = 248)**
Any grade	28 (52)	159 (72)	21 (75)	137 (55)
Grade ≥ 3	15 (28)	109 (49)	14 (50)	99 (40)
Secondary G-CSF prophylaxis[a]	**Yes (n = 81)**	**No (n = 75)**	**Yes (n = 51)**	**No (n = 85)**
Any grade	46 (57)	52 (69)	38 (75)	50 (59)
Grade ≥ 3	30 (37)	20 (27)	29 (57)	39 (46)

[a]Excludes participants who received primary G-CSF prophylaxis. Chemo, chemotherapy; G-CSF, granulocyte-colony stimulating factor; SG, sacituzumab govitecan.