Pooled Safety Analysis of Sacituzumab Govitecan in Multiple Solid Tumor Types

Poster # 3029

ASCENT
TROPiCS-02
TROPHY-U-01
IMMU-132-01

Hope S Rugo[1], Sara M Tolaney[2], Aditya Bardia[3], Javier Cortés[4], Frederik Marmé[5], Peter Schmid[6], Lisa A Carey[7], Sibylle Loibl[8], Kevin Kalinsky[9], Joyce O'Shaughnessy[10], Sara A Hurvitz[11], Theresa Valdez[12], Ya Meng[12], Wendy Verret[12], Scott T Tagawa[13]

[1]University of California San Francisco Helen Diller Family Comprehensive Cancer Center, San Francisco, CA, USA; [2]Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA; [3]UCLA Health Jonsson Comprehensive Cancer Center, Los Angeles, CA, USA; [4]International Breast Cancer Center (IBCC), Pangaea Oncology, Quirónsalud Group, Barcelona, Spain & Universidad Europea de Madrid, Madrid, Spain; [5]Universitätsmedizin Mannheim, Heidelberg, Germany; [6]Bart's Cancer Institute, Queen Mary University of London, London, UK; [7]University of North Carolina Lineberger Comprehensive Cancer Center, Chapel Hill, NC, USA; [8]Hämatologisch-Onkologische Gemeinschaftspraxis am Bethanien-Krankenhaus, Frankfurt, Germany; [9]Winship Cancer Institute, Emory University, Atlanta, GA, USA; [10]Baylor University Medical Center, Texas Oncology, US Oncology, Dallas, TX, USA; [11]Fred Hutchinson Cancer Center and University of Washington Medicine, Seattle, WA, USA; [12]Gilead Sciences, Inc., Foster City, CA, USA; [13]Weill Cornell Medicine, New York, NY, USA

Conclusions

- This pooled safety analysis of 1063 patients treated with SG in clinical trials was consistent with previous reports, with neutropenia remaining the most common grade ≥ 3 TEAE
- Prophylaxis with G-CSF was associated with lower rates of neutropenia and longer time to onset of grade ≥ 3 neutropenia
- Of the 681 (64%) patients who experienced diarrhea, 477 (70%) received antidiarrheal treatment
- The *28/*28 *UGT1A1* genotype was associated with higher rates of grade ≥ 3 TEAEs, as previously observed
- The rate of TEAEs leading to discontinuation (7%) was low
- This is the largest SG safety analysis published to date, providing further support for SG as a well-tolerated treatment with a consistent and manageable safety profile regardless of *UGT1A1* status across multiple solid tumors

Plain Language Summary

- Sacituzumab govitecan is a drug that is approved in multiple countries to treat several types of metastatic cancer (a type of cancer that has spread to other parts of the body), including metastatic breast and bladder cancers, and has been shown to be well tolerated
- Some participants may have a form of the *UGT1A1* gene that can reduce the ability to clear sacituzumab govitecan from the body; these participants tended to have similar side effects as the general group of participants, but these side effects were more common
- This analysis grouped safety data from several clinical trials to understand sacituzumab govitecan safety across over 1000 participants
- The results were similar to what has been shown before in individual trials and found that low levels of neutrophils, a white blood cell involved in the protection against infection, is the most frequent severe medical event
- This analysis confirms that side effects from sacituzumab govitecan are similar across clinical trials and can be managed by health care professionals by following guidelines

References: **1.** Starodub AN, et al. *Clin Cancer Res*. 2015;21:3870-78. **2.** TRODELVY® (sacituzumab govitecan-hziy) [prescribing information] Foster City, CA: Gilead Sciences, Inc., February 2023. **3.** TRODELVY® (sacituzumab govitecan-hziy) [summary of product characteristics]. County Cork, Ireland: Gilead Sciences Ireland UC; August 2023. **4.** Bardia A, et al. *N Eng J Med*. 2021;384:1529-41. **5.** Rugo HS, et al. *J Clin Oncol*. 2022;40:3365-76. **6.** Loriot Y, et al. *Ann Oncol*. 2024;S0923-7534(24)00009-7. **7.** Bardia A, et al. *Ann Oncol*. 2021;32:746-56. **8.** Rugo HS, et al. *NPJ Breast Cancer*. 2022;8:98.

Acknowledgments: We extend our thanks to the patients, their families, and all participating investigators. This study was funded by Gilead Sciences, Inc. All authors contributed to and approved the presentation; medical writing support was provided by Ben Labbe, PhD, CMPP, of Parexel, and was funded by Gilead Sciences, Inc.

Presenting Author Disclosures: **HSR** reports consulting and advisory roles for Daiichi Sankyo, Eisai, Mylan, Napo Pharmaceuticals, and Puma Biotechnology; and her institution received research funding from Astellas Pharma, AstraZeneca, Daiichi Sankyo, Genentech/Roche, Gilead Sciences, Inc., GlaxoSmithKline, Lilly, Merck, Novartis, OBI Pharma, Pfizer, Stemline Therapeutics, Taiho Oncology, and Veru.

Correspondence: Hope S. Rugo, Hope.Rugo@ucsf.edu.

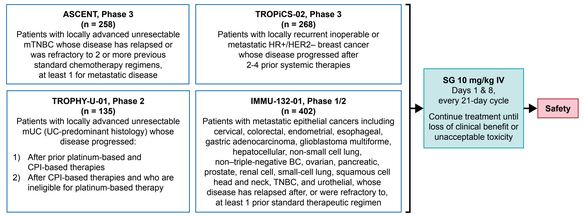
Introduction

- Sacituzumab govitecan (SG) is an antibody-drug conjugate targeted to Trop-2[1] that received approval for the treatment of patients with
  - Previously treated metastatic triple-negative breast cancer (mTNBC) and HR+/HER2– mBC[2,3]
  - Previously treated metastatic urothelial cancer (mUC) in the United States (accelerated approval)[2]
- In multiple clinical trials, SG has demonstrated significantly improved efficacy compared with standard-of-care therapies and a consistent, manageable safety profile with low treatment discontinuation rates from adverse events (AEs)[4-7]
- Patients who are homozygous for the *UGT1A1* *28 allele are at potentially increased risk for neutropenia, febrile neutropenia, diarrhea, and anemia when receiving SG treatment[8]
- We present an analysis of pooled safety data, including differences by *UGT1A1* polymorphisms, from patients treated with SG in clinical trials

Methods

- Safety data for patients treated with SG (10 mg/kg, days 1 and 8 every 21-day cycle) were pooled from 4 clinical trials of multiple solid tumors, including mTNBC, HR+/HER2– mBC, and mUC (Figure 1): ASCENT (NCT02574455), TROPiCS-02 (NCT03901339), TROPHY-U-01 (NCT03547973), and IMMU-132-01 (NCT01631552)[4-7]
- Treatment-emergent AEs (TEAEs) were defined as any AE that started on or after the first dose date until ≤ 30 days after the last dose date
- Safety data were also analyzed by *UGT1A1* genotypes

Figure 1. Pooled Clinical Trials



BC, breast cancer; CPI, checkpoint inhibitor therapies; HER2–, human epidermal growth factor receptor 2-negative; HR+, hormone receptor-positive; mTNBC, metastatic triple-negative breast cancer; mUC, metastatic urothelial cancer.

Results

- The pooled analysis included 1063 patients across multiple solid tumors whose characteristics are summarized in Table 1

Table 1. Patient Characteristics

Characteristic	All Patients (N = 1063)
Median age (range), years	59 (27-90)
Sex, n (%)	
Male	223 (21)
Female	840 (79)
Race, n (%)	
White	826 (78)
Black	55 (5)
Asian	38 (4)
Other/unknown	144 (14)
Median BMI (range), kg/m²	25.3 (14.8-61.0)
ECOG performance status, %	
0/1	36/64
Median time since metastatic disease diagnosis (range), months	28.7 (–0.1 to 412.6)
Median number of prior lines of systemic therapy, n (range)	5 (1-17)
Presence of visceral metastasis, n (%)	882 (83)
***UGT1A1* status, n (%)**	
*1/*1	416 (39)
*1/*28	420 (40)
*28/*28	112 (11)
Other	13 (1)
Unknown	102 (10)

BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; *UGT1A1*, UDP glucuronosyltransferase family 1 member A1.

Results

- Most patients (> 99%) experienced any-grade TEAEs, and 76% experienced grade ≥ 3 TEAEs (Table 2)
- Any-grade TEAEs led to SG dose reduction in 31% and SG treatment discontinuation in 7% of patients
- In patients with available *UGT1A1* genotypes, *28/*28 was associated with a higher rate of grade ≥ 3 TEAEs and TEAEs leading to dose reduction and interruption compared with *1/*1 and *1/*28; however, treatment discontinuation rates remained low across *UGT1A1* genotypes

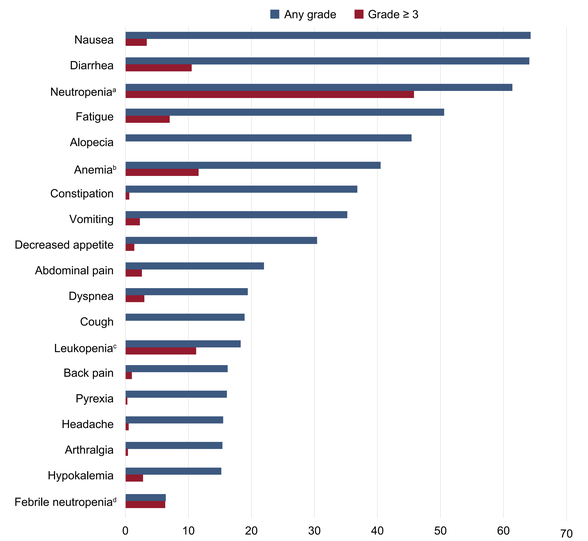
Table 2. Safety Summary

Safety, n (%)	All Patients (N = 1063)	*UGT1A1* Genotype[a]		
		*1/*1 (n = 416)	*1/*28 (n = 420)	*28/*28 (n = 112)
All TEAEs	1060 (> 99)	415 (> 99)	418 (> 99)	112 (100)
Grade ≥ 3	808 (76)	299 (72)	320 (76)	101 (90)
AEs leading to dose reduction[b]	205/661 (31)	69/268 (26)	89/270 (33)	30/76 (39)
AEs leading to interruption	615 (58)	243 (58)	230 (55)	78 (70)
AEs leading to discontinuation	78 (7)	27 (6)	27 (6)	8 (7)

[a]Other genotypes, n = 13; genotype missing/not done, n = 102. [b]AEs leading to dose reduction not collected in IMMU-132-01; these patients were excluded from total. AE, adverse events; TEAEs, treatment-emergent adverse events; *UGT1A1*, UDP glucuronosyltransferase family 1 member A1.

- The most common TEAEs are summarized in Figure 2
  - The most common grade ≥ 3 TEAEs were neutropenia (46%), anemia (12%), leukopenia (11%), and diarrhea (11%)
  - Febrile neutropenia occurred in 6% of patients
- The most common TEAEs that led to treatment discontinuation were neutropenia (1%), diarrhea (1%), pneumonia (1%), and fatigue (1%)
- When divided by *UGT1A1* status of *1/*1, *1/*28, and *28/*28, grade ≥ 3 neutropenia (43%, 49%, and 58%, respectively), diarrhea (8%, 12%, 15%), anemia (9%, 10%, 21%), and febrile neutropenia (6%, 5%, 14%) were more common in patients with *28/*28 genotypes than in those with other genotypes

Figure 2. Most Common TEAEs of Any Grade (≥ 15%) and Grade ≥ 3 (≥ 5%)



[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]Leukopenia includes preferred terms of leukopenia and white blood cell count decreased. [d]Febrile neutropenia is always grade ≥ 3 per Common Terminology Criteria for Adverse Events criteria. TEAEs, treatment-emergent adverse events.

- Neutropenia and diarrhea were treated according to recommended AE management strategies[2,3]
- An exploratory analysis of granulocyte-colony stimulating factor (G-CSF) use during SG clinical trials on or after the first dose date of SG and up to 30 days after the last dose date, and excluding incomplete G-CSF administration dates, showed:
  - Fewer patients experienced neutropenia after receiving either primary or secondary prophylaxis compared with those who did not receive prophylaxis (Table 3)
  - Primary and secondary prophylaxis were associated with longer time to onset of grade ≥ 3 neutropenia
  - Only 9% of patients who received G-CSF treatment for the first time also required a dose reduction due to the neutropenia being treated

Table 3. Treatment of Neutropenia

Patients, n (%)	Primary Prophylaxis[a]		Secondary Prophylaxis[b]	
	Received Primary Prophylaxis (n = 54)	Did Not Receive Primary Prophylaxis (n = 1009)	Received Secondary Prophylaxis (n = 116)	Did Not Receive Secondary Prophylaxis (n = 893)
Any-grade neutropenia[c]	17 (31)	658 (65)	48 (41)	542 (61)
Grade ≥ 3 neutropenia[c]	14 (26)	504 (50)	29 (25)	408 (46)
Median time to onset of first grade ≥ 3 neutropenia, days	29	14	78	14

[a]Primary prophylactic G-CSF use is defined as G-CSF use on or after cycle 1 day 1 and prior to onset of first occurrence of neutropenia, regardless of grade, or G-CSF use when there is no event of neutropenia. For patients who received primary prophylaxis, neutropenia is subsequent to primary prophylaxis. For patients who did not receive primary prophylaxis, neutropenia is first occurrence since cycle 1 day 1. [b]Secondary prophylactic G-CSF use is defined as G-CSF use after resolution of grade ≥ 2 neutropenia (to grade ≤ 1) or occurrence of grade ≥ 1 neutropenia, and prior to onset of any subsequent grade ≥ 2 neutropenia or no occurrence of subsequent grade ≥ 2 neutropenia. For patients who received secondary prophylaxis, neutropenia is subsequent to secondary prophylaxis. For patients who did not receive secondary prophylaxis, neutropenia is the first occurrence since cycle 1 day 1. Patients who received primary prophylactic G-CSF were excluded from the secondary prophylactic G-CSF use analysis. [c]Neutropenia includes preferred terms of neutropenia, neutrophil count decreased, and febrile neutropenia. G-CSF, granulocyte colony stimulating factor.

- 681 (64%) of patients experienced any-grade diarrhea. Of these, 477 (70%) were treated with an antidiarrheal (Table 4)
- 90% of patients treated with an antidiarrheal received loperamide either alone or in combination with other antidiarrheals

Table 4. Treatment of Diarrhea

Patients, n (%)	Patients With Diarrhea Who Received Any Antidiarrheal (N = 477)
Any loperamide	428 (90)
Any atropine	97 (20)
Loperamide alone	277 (58)
Atropine alone	9 (2)
Other antidiarrheal alone	22 (5)
Multi-antidiarrheal regimen[a]	162 (34)

[a]Antidiarrheals that had the same start date or overlapping treatment dates were considered to be administered as an antidiarrheal regimen.

- TEAEs of interest (any grade) developed within a median of 7 weeks from start of treatment, and resolved in a median of less than 3 weeks (Table 5)
- Among TEAEs of interest (grade ≥ 3), neutropenia, febrile neutropenia, and diarrhea developed within a median of fewer than 3 weeks from start of treatment and resolved in a median of less than 2 weeks
- Grade ≥ 3 hypersensitivity and infections generally developed later than neutropenia, febrile neutropenia, and diarrhea, but median time to resolution was similar

Table 5. Time to Onset and Resolution for AEs of Interest

Time to onset/resolution (range), weeks	All Patients (N = 1063)			
	Time to Onset		Time to Resolution	
	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3
Infection[a]	6.9 (0.1-104.1)	6.1 (0.7-104.0)	1.6 (0.1-24.1)	1.1 (0.1-7.6)
Hypersensitivity[b]	4.1 (0.1-122.0)	9.9 (0.1-45.3)	2.1 (0.1-47.6)	1.3 (1.0-12.0)
Neutropenia	2.3 (0.1-62.1)	2.3 (0.3-86.1)	1.1 (0.1-89.1)	1.1 (0.1-89.1)
Febrile neutropenia	2.1 (1.0-67.3)	2.1 (1.0-67.3)	0.9 (0.1-3.3)	0.9 (1.0-2.3)
Diarrhea	1.9 (0.1-90.0)	2.1 (0.1-78.6)	1.1 (0.1-50.0)	1.0 (0.1-7.9)

[a]Any-grade infections of any kind occurred in 495 (47%) patients, and grade ≥ 3 infections of any kind occurred in 129 (12%) patients. Infection was defined as any event in the infections and infestations system organ class. [b]Any-grade hypersensitivity occurred in 369 (35%) patients, and grade ≥ 3 hypersensitivity occurred in 17 (2%) patients. Hypersensitivity was defined as hypersensitivity or anaphylactic reaction standardized MedDRA query events (narrow or broad scope) with onset dates on the day of or 1 day after study drug administration. AE, adverse events; MedDRA, Medical Dictionary for Regulatory Activities.