Pooled Safety Analysis of Sacituzumab Govitecan in Metastatic Breast Cancer, Including Data From Patients Treated in North America/Europe and Asia

FPN 345P

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Conclusions

- In this pooled safety analysis of 969 patients with metastatic breast cancer (mBC) treated with sacituzumab govitecan (SG), patients in North America/Europe (NA/EU) and Asia experienced comparable rates of any-grade and grade ≥ 3 treatment-emergent adverse events (TEAEs), as well as TEAEs leading to dose reduction, interruption, discontinuation, and death
- Patients in Asia experienced more neutropenia, anemia, leukopenia, increased aspartate and alanine aminotransferases, and hypoalbuminemia compared with those in NA/EU
- Patients in NA/EU had higher rates of diarrhea and fatigue than those in Asia
- Neutropenia, diarrhea, and nausea were manageable with supportive care per established guidelines
- This is the largest safety analysis of SG in mBC published to date, and provides further support for SG as an mBC treatment with a consistent and manageable safety profile across patient subgroups

Plain Language Summary

- Sacituzumab govitecan is a drug that is approved in multiple countries for some types of metastatic breast cancer (breast cancer that has spread to other parts of the body)
- Different adverse events (unwanted issues that occur during treatment) can occur in people depending on factors like their current health and geographic region
- This analysis grouped safety data from 6 clinical studies to understand the safety of sacituzumab govitecan in a large pool of participants with metastatic breast cancer
- While there were some differences in adverse events depending on whether participants lived in North America/Europe or Asia, neither of these groups had higher rates of treatment discontinuation or death, which shows that these adverse events can be managed by prompt intervention from healthcare professionals
- This analysis shows that adverse events from sacituzumab govitecan are similar across multiple clinical studies and multiple regions of the world, and these events are manageable with supportive care such as medications to reduce adverse events

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

Disclosures: **HSR** reports grants or contracts from Ambrx and Stemline Therapeutics; consulting and advisory roles from Bristol Myers Squibb, NAPO, PUMA, and Sanofi; and honoraria from AstraZeneca, Chugai, Daiichi Sankyo, F Hoffman La Roche, Gilead Sciences, Inc., Lilly, Merck, Mylan/Viatris, Novartis, OBI Pharma, and Pfizer.

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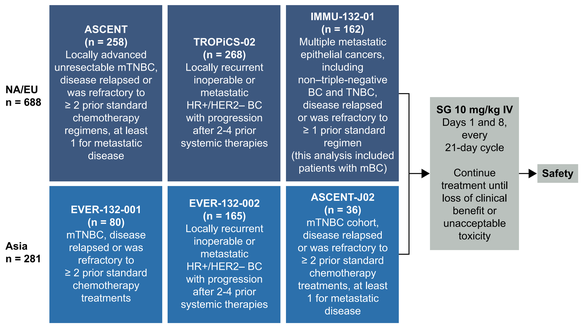
Introduction

- SG is a Trop-2–targeted antibody-drug conjugate (ADC) that has demonstrated significantly improved efficacy outcomes compared with standard-of-care treatment across multiple studies in patients with previously treated metastatic triple-negative breast cancer (mTNBC) and hormone receptor-positive/human epidermal growth factor receptor 2-negative (HR+/HER2–) mBC, with a manageable safety profile[1,2]
- Previous studies have indicated that the frequency of specific types of TEAEs in patients treated with ADCs may differ based on race or geographic region[3,4]
- We present an analysis of pooled safety data from patients with mBC who received SG during clinical studies

Methods

- Safety data for patients who received SG treatment (10 mg/kg, days 1 and 8 every 21-day cycle) were pooled from multiple clinical studies conducted in different regions (**Figure 1**)
  - NA/EU: ASCENT (NCT02574455), TROPiCS-02 (NCT03901339), IMMU-132-01 (NCT01631552)
  - Asia: EVER-132-001 (NCT04454437), EVER-132-002 (NCT04639986), ASCENT-J02 (NCT05101096)
- TEAEs were defined as any adverse events (AEs) that started on or after first dose date until ≤ 30 days after last dose date (or until initiation of subsequent anticancer therapy in studies in Asia)
- Safety data were analyzed by NA/EU vs Asia

Figure 1. Analyzed Clinical Studies



N values indicate number of SG-treated patients that met the specified criteria from each study.
BC, breast cancer; HER2–, human epidermal growth factor receptor-negative; HR+, hormone receptor-positive; IV, intravenous; mBC, metastatic breast cancer; mTNBC, metastatic triple-negative breast cancer; NA/EU, North America/Europe; SG, sacituzumab govitecan; TNBC, triple-negative breast cancer.

Results

- The analysis included a total of 969 patients (688 NA/EU, 281 Asia)
- Baseline characteristics were comparable between NA/EU and Asia, with the exception of race (**Table 1**)
- Rates of any-grade TEAEs and grade ≥ 3 TEAEs were consistent with previously reported rates and similar between patients in NA/EU and Asia; rates of TEAEs leading to dose reduction, dose interruption, discontinuation, and death were also comparable, although serious adverse events were slightly more common in NA/EU (**Table 2**)
- The most common TEAEs leading to discontinuation were:
  - NA/EU: neutropenia, diarrhea, fatigue, pneumonia (each < 1%)
  - Asia: neutropenia, leukopenia, fatigue, septic shock (each 1%)

Results

Table 1. Patient Characteristics

Characteristic	NA/EU (n = 688)	Asia (n = 281)
Median age (range), years	55 (27-86)	51 (23-72)
Sex, n (%)		
Male	4 (1)	0
Female	684 (99)	281 (100)
Race, n (%)		
White	517 (75)	0
Black	41 (6)	0
Asian	26 (4)	281 (100)
Other/unknown	104 (15)	0
Median BMI (range), kg/m²	25.2 (15.0-61.0)	23.5 (15.8-35.5)

BMI, body mass index; NA/EU, North America and Europe.

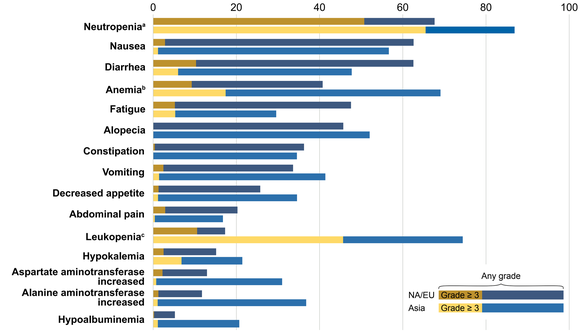
Table 2. Pooled Safety Summary

Safety, n (%)	NA/EU (n = 688)	Asia (n = 281)
All TEAEs	687 (> 99)	281 (100)
Grade ≥ 3	506 (74)	220 (78)
SAEs	195 (28)	62 (22)
Led to dose reduction	147/526 (28)[a]	68 (24)
Led to dose interruption	417 (61)	177 (63)
Led to discontinuation	36 (5)	11 (4)
Led to death	8 (1)	8 (3)

[a]Adverse events leading to dose reduction not collected in IMMU-132-01.
NA/EU, North America and Europe; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

- Any-grade and grade ≥ 3 neutropenia, anemia, and leukopenia occurred at higher rates in Asia than in NA/EU; any-grade increased aspartate aminotransferase, increased alanine aminotransferase, and hypoalbuminemia also occurred at higher rates in Asia (**Figure 2**)
- NA/EU had higher rates of any-grade and grade ≥ 3 diarrhea and any-grade fatigue compared with Asia

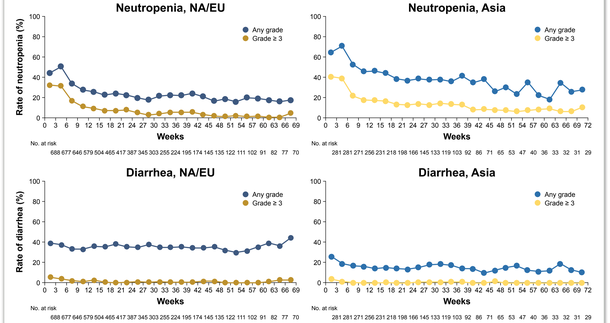
Figure 2. Most Common TEAEs by Region



Any-grade TEAEs that occurred in ≥ 20% of patients and grade ≥ 3 TEAEs that occurred in ≥ 10% of patients in either region are included. [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. NA/EU, North America/Europe; TEAE, treatment-emergent adverse event.

- Neutropenia was most common early in the treatment period, and the rate of neutropenia fell over time (**Figure 3**)
- The rate at which patients developed diarrhea remained fairly stable over time

Figure 3. Neutropenia and Diarrhea Over Time



NA/EU, North America/Europe.

- Neutropenia, diarrhea, and nausea were treated according to recommended AE management guidelines[5,6] (**Table 3**)

Table 3. TEAEs Management Summary

Patients, n (%)	Total Patients (N = 969)			
	Primary G-CSF Prophylaxis			
	NA/EU (n = 688)		Asia (n = 281)	
	Received (n = 65)	Did Not Receive (n = 623)	Received (n = 36)	Did Not Receive (n = 245)
Any-grade neutropenia	26 (40)	450 (72)	21 (58)	223 (91)
Grade ≥ 3 neutropenia	19 (29)	347 (56)	17 (47)	170 (69)
	Patients Who Received an Antidiarrheal During SG Treatment		Patients Who Experienced Diarrhea and Received an Antidiarrheal During SG Treatment	
	NA/EU (n = 343)	Asia (n = 120)	NA/EU (n = 298)	Asia (n = 88)
Any loperamide	304 (89)	59 (49)	271 (91)	56 (64)
Any atropine	67 (20)	6 (5)	58 (19)	5 (6)
Other antidiarrheal	80 (23)	87 (73)	76 (26)	58 (66)
	Nausea and Vomiting			
	NA/EU (n = 688)		Asia (n = 281)	
Any nausea	431 (63)		159 (57)	
Nausea leading to dose reduction	7/318 (2)[a]		2/159 (1)	
Any vomiting	231 (34)		116 (41)	
Vomiting leading to dose reduction	5/151 (3)[a]		2/116 (2)	
Any antinauseant/antiemetic for prophylaxis of nausea/vomiting[b]	518 (75)		268 (95)	
1 agent	289/518 (56)		123/268 (46)	
2 concurrently	199/518 (38)		211/268 (79)	
3 concurrently	193/518 (37)		104/268 (39)	
≥ 4 concurrently	96/518 (19)		24/268 (9)	

[a]AEs leading to dose reduction not collected in IMMU-132-01. [b]Includes patients who received the stated number of concurrent antinauseants/antiemetics between events of nausea/vomiting. Patients could be included in more than 1 group as they may have received different combinations of antinauseants/antiemetics between different events of nausea/vomiting.
AE, adverse event; G-CSF, granulocyte colony-stimulating factor; NA/EU, North America/Europe; SG, sacituzumab govitecan; TEAE, treatment-emergent adverse event.