Poster # PO1-06-10

Overall Survival Results From EVER-132-001, a Phase 2b Single-Arm Study of Sacituzumab Govitecan in Chinese Patients With Metastatic Triple-Negative Breast Cancer

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Key Findings

- **SG treatment resulted in clinically meaningful median OS in Chinese patients with pretreated mTNBC, and median OS was generally consistent across multiple prespecified subgroups**
- **Clinically meaningful ORR and median PFS results were maintained at this updated analysis**
- **No new safety signals were identified, and SG had a manageable safety profile with continued follow-up**

Conclusions

Continued benefit with SG in the EVER-132-001 trial supports the use of SG as a new standard of care for Chinese patients with pretreated mTNBC

Clinically meaningful efficacy with SG in Chinese patients with mTNBC was consistent with previous efficacy analyses of EVER-132-001[7] and consistent with the global phase 3 ASCENT trial of SG in mTNBC[6]

SG demonstrated efficacy across patient subgroups, and demonstrated safety consistent with previous studies of SG

References: **1.** Chen W, et al. *Chin J Cancer Res*. 2018;30:1-12. **2.** International Agency for Research on Cancer. China population fact sheet, Globocan 2020. https://gco.iarc.fr/today/data/factsheets/populations/160-china-fact-sheets.pdf. Accessed September 8, 2023. **3.** Ismail-Khan R, et al. *Cancer Control*. 2010;17:173-176. **4.** Foulkes WD, et al. *N Engl J Med*. 2010;363:1938-1948. **5.** Manjunath M, et al. *Oncol Lett*. 2021;22:512. **6.** Bardia A, et al. *N Engl J Med*. 2021;384:1529-1541. **7.** Xu B, et al. *Int J Cancer*. 2023;152:2134-2144. **8.** Rugo S, et al. *Lancet*. 2023;402:1423-1433. **9.** Rugo HS, et al. *NPJ Breast Cancer*. 2022;8:98.

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Introduction

- Breast cancer is the most frequently diagnosed cancer and the fifth most common cause of cancer-related death in Chinese women,[1] with over 416,000 new cases and over 117,000 deaths estimated in 2020[2]
- Triple-negative breast cancer (TNBC) accounts for 10% to 20% of breast cancer cases in women[3-5]
- In the phase 3 ASCENT study of primarily non-Asian patients with metastatic TNBC (mTNBC), second-line or later (2L+) sacituzumab govitecan (SG) demonstrated improved efficacy vs treatment of physician's choice (TPC), with a manageable safety profile[6]
  - Median progression-free survival (PFS) for SG vs TPC was 5.6 months vs 1.7 months, respectively (hazard ratio [HR], 0.41; 95% confidence interval [CI], 0.32-0.52)
  - Median overall survival (OS) for SG vs TPC was 12.1 vs 6.7 months, respectively (HR, 0.48; 95% CI, 0.38-0.59)
- The single-arm phase 2b EVER-132-001 study demonstrated substantial clinical activity and manageable safety of 2L+ SG in Chinese patients with mTNBC and no brain metastases,[7] consistent with data from the primary analysis population from ASCENT[6]
  - Objective response rate (ORR) was 39% (95% CI, 28-50), median PFS was 5.6 months (95% CI, 4.1-not estimable)
  - Grade ≥ 3 treatment-emergent adverse events (TEAEs) were seen in 78% of patients, with TEAEs leading to treatment discontinuation in 6% of patients

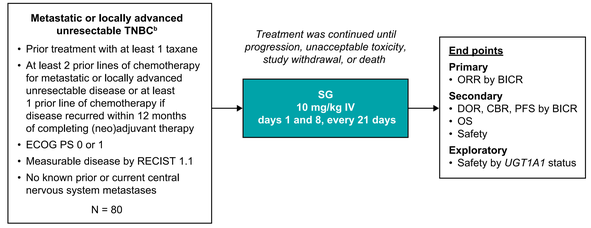
Objective

- To present updated results from EVER-132-001, including the first report of median OS

Methods

- EVER-132-001 is a phase 2b study of SG in Chinese patients with pretreated mTNBC **(Figure 1)**
- The data cutoff date was September 19, 2022
- Median follow-up was 14.7 months (range, 1.2-25.3)

Figure 1. EVER-132-001 study design[a]



BICR, blinded independent central review; CBR, clinical benefit rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; IV, intravenously; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; SG, sacituzumab govitecan; TNBC, triple-negative breast cancer; *UGT1A1*, uridine diphosphate glucuronosyltransferase 1A1.
[a]ClinicalTrials.gov; NCT04454437. [b]Estrogen receptor- and progesterone receptor-negative (< 1% of cells expressing receptors by IHC), and HER2-negative (IHC0, IHC1, or IHC2+ and ISH ratio of HER2 gene:chromosome 17 < 2).

Results

Baseline characteristics

- Median age of patients was 48 years, 59% of patients had an Eastern Cooperative Oncology Group performance status (ECOG PS) of 1, and all patients had received previous chemotherapy in the metastatic setting **(Table 1)**

Results

Table 1. Demographics and baseline characteristics

	SG (N = 80)		
Female, %	100	**Median prior systemic regimens (range), n**	4 (2-8)
Median age (range), y	48 (24-70)	**Median time from initial metastatic diagnosis to study entry (range), y**	1.0 (< 0.1-3.6)
ECOG PS 0, %	41		
ECOG PS 1, %	59	**Types of prior systemic therapy in metastatic setting,[a] %**	
Site of metastases,[a] %		Chemotherapy	100
Lymph node	61	Endocrine therapy	14
Lung	53	Immunotherapy	35
Bone	34	Targeted therapy	48
Liver	30		
Other	48	***UGT1A1* genotype,[b,c] %**	
Prior systemic regimens in metastatic setting, %		*1/*1	48
1	15	*1/*28	16
2	35	*1/*6	29
≥ 3	50	*6/*6	4
		*1/*27	1

ECOG PS, Eastern Cooperative Oncology Group performance status; SG, sacituzumab govitecan; *UGT1A1*, uridine diphosphate glucuronosyltransferase 1A1; y, years.
[a]Patients could be included in more than 1 category. [b]Percentages do not add up to 100 due to rounding. [c]*UGT1A1* genotype missing, n = 2.

Efficacy

- SG treatment continued to result in clinical activity **(Table 2)**, consistent with a previous analysis[7] and the global ASCENT trial that demonstrated an ORR of 35%, clinical benefit rate of 45%, median duration of response of 6.3 months, and median time to response of 1.5 months for patients treated with SG[6]

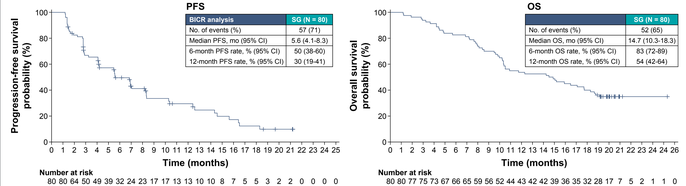
Table 2. Responses

BICR analysis[a]	SG (N = 80)		
ORR, n (%)	32 (40)	**Best overall response, n (%)**	
95% CI	29-52	CR	3 (4)
Clinical benefit rate, n (%)	37 (46)	PR	29 (36)
95% CI	35-58	SD	34 (43)
Median DOR,[b] mo	11.6	SD ≥ 6 mo	5 (6)
95% CI	7.0-13.8	PD	12 (15)
Median time to response,[b] mo (range)	1.6 (1.2-4.2)	NE/NA	2 (3)

BICR, blinded independent central review; CI, confidence interval; CR, complete response; DOR, duration of response; mo, months; NA, not available; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease; SG, sacituzumab govitecan.
[a]Confirmed responses. [b]Assessed in responders, n = 32.

- PFS and OS **(Figure 2)** were consistent with the ASCENT trial[6]

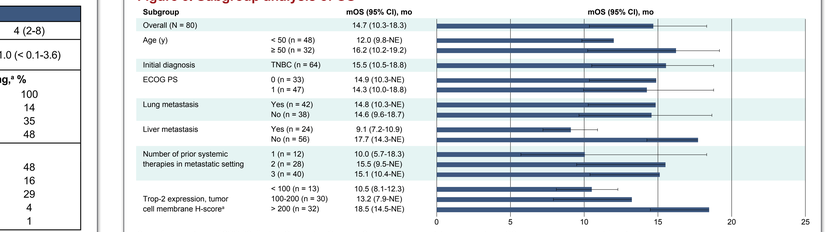
Figure 2. PFS and OS



BICR, blinded independent central review; CI, confidence interval; mo, months; OS, overall survival; PFS, progression-free survival; SG, sacituzumab govitecan.

- Median OS was generally similar across prespecified subgroups, although patients with liver metastases had a shorter median OS **(Figure 3)**

Figure 3. Subgroup analysis of OS



CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; mo, months; mOS, median overall survival; NE, not estimable; y, years.
[a]Data missing, n = 5.

Safety

- The most common grade ≥ 3 TEAEs were decreased neutrophil count, decreased white blood cell count, and anemia **(Table 3)**
- The safety profile of SG in this analysis was consistent with that of previous studies of SG[6-8]

Table 3. Safety summary

TEAEs, n (%)	SG (N = 80)	TEAEs, n (%)	SG (N = 80)	
			Any grade	Grade ≥3
Any TEAE	80 (100)	**Most common TEAEs[b]**		
Grade ≥ 3	63 (79)	Neutrophil count decreased	68 (85)	51 (64)
TEAEs leading to treatment discontinuation	6 (8)	Anemia	67 (84)	18 (23)
TEAEs leading to treatment interruption	38 (48)	White blood cell count decreased	66 (83)	40 (50)
TEAEs leading to dose reductions	16 (20)	Vomiting	51 (64)	1 (1)
Treatment-emergent SAEs	20 (25)	Nausea	41 (51)	0
TEAEs leading to death[a]	7 (9)	Alanine aminotransferase increased	39 (49)	2 (3)
Treatment-related	2 (3)	Diarrhea	33 (41)	2 (3)

SAE, serious adverse event; SG, sacituzumab govitecan; TEAE, treatment-emergent adverse event.
TEAEs were defined as any AEs that began or worsened on or after the start of study drug through 30 days after the last dose of study drug.
[a]Of 7 TEAEs leading to death, only 2 were considered by the investigator as treatment related (1 each of shock and septic shock). The other 5 were 1 each of disease progression, sudden cardiac death, circulatory collapse and respiratory failure, tumor ulceration, and death (unspecified). [b]TEAEs of any grade occurring in ≥ 40% of patients.

- Patients with *1/*1 and *1/*28 *UGT1A1* genotypes experienced lower rates of grade ≥ 3 TEAEs than those with *1/*6 and *6/*6 genotypes, although the low sample size limits interpretation **(Table 4)**

Table 4. TEAEs of special interest by *UGT1A1* genotype

TEAEs, n (%)	*UGT1A1* genotype[a]			
	*1/*1 (n = 38)	*1/*28 (n = 13)	*1/*6 (n = 23)	*6/*6 (n = 3)
Grade ≥ 3 TEAE[b]	29 (76)	10 (77)	19 (83)	3 (100)
Neutrophil count decreased	21 (55)	8 (62)	18 (78)	3 (100)
Anemia	5 (13)	5 (38)	5 (22)	2 (67)
Diarrhea	1 (3)	0	1 (4)	0
Febrile neutropenia	0	1 (8)	0	1 (33)

SG, sacituzumab govitecan; TEAE, treatment-emergent adverse event; *UGT1A1*, uridine diphosphate glucuronosyltransferase 1A1.
TEAEs were defined as any AEs that began or worsened on or after the start of study drug through 30 days after the last dose of study drug.
[a]1 patient had a genotype of *1/*27, and 2 patients had missing *UGT1A1* genotypes. [b]Selected TEAEs from known AEs from SG associated with *UGT1A1* polymorphisms.[9]