Subgroup Analyses From the Phase 3 EVER-132-002 Study of Asian Patients With HR+/HER2– Metastatic Breast Cancer

P2-09-25
EVER-132-002

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*At the time study was conducted.

San Antonio Breast Cancer Symposium®- December 10-13, 2024

Conclusions

- PFS and OS favored SG vs chemotherapy regardless of prior CDK4/6i treatment and regardless of HER2 status in Asian patients with pretreated HR+/HER2– mBC in the phase 3 EVER-132-002 study
- The safety profile of SG was similar across all subgroups analyzed
- Efficacy and safety in the prior CDK4/6i treatment and HER2 status subgroups were consistent with those observed in the intent-to-treat population
- The results of this analysis further support SG as an effective treatment option for patients with HR+/HER2– mBC, irrespective of prior CDK4/6i treatment or HER2 status

Plain Language Summary

- Sacituzumab govitecan (SG) is a drug that has been approved for the treatment of previously treated hormone-receptor-positive/ human epidermal growth factor receptor 2-negative (HR+/HER2–) metastatic breast cancer, which is the most common subtype of breast cancer
- Whether a person has received another type of cancer drug, called a cyclin-dependent kinase 4/6 inhibitor (CDK4/6i), may affect how likely it is that a later treatment will succeed
- Whether a person's tumor expresses HER2 may also affect the likelihood of treatment success
- This analysis used data from the EVER-132-002 study to show that patients treated with SG lived longer and had more time without their disease progressing than participants who were treated with chemotherapy, and these benefits were seen regardless of participants' prior CDK4/6i treatments or HER2 status
- These results support SG as an effective treatment for people with pretreated HR+/HER2– metastatic breast cancer, regardless of their tumor's HER2 status or whether they have received CDK4/6i

Introduction

- The most common subtype of breast cancer (BC; 70% of cases) is hormone receptor-positive/human epidermal growth factor receptor 2-negative (HR+/HER2– [HER2 immunohistochemistry (IHC) 0, 1+, or 2+/in situ hybridization-negative (ISH–)])[1]
- Sacituzumab govitecan (SG), an antibody-drug conjugate targeted to Trop-2,[2] is approved in multiple countries for HR+/HER2– metastatic BC (mBC) after endocrine therapy and at least 2 additional systemic chemotherapies[3]
- In the phase 3, randomized EVER-132-002 study (NCT04639986), SG demonstrated significantly improved progression-free survival (PFS; hazard ratio [HR], 0.67; 95% CI, 0.52-0.87; *P* = .0028) and overall survival (OS; HR, 0.64; 95% CI, 0.47-0.88; *P* = .0061) vs chemotherapy in Asian patients with pretreated HR+/HER2– mBC, with a safety profile consistent with other studies of SG[4]
- Treatment with cyclin-dependent kinase 4/6 inhibitors (CDK4/6is) is recommended in standardized guidelines for first-line treatment of HR+/HER2– mBC,[5] and the sequencing of CDK4/6i may affect efficacy of subsequent treatments[6]
- SG treatment has previously been shown to provide PFS and OS benefit vs chemotherapy across HER2 subgroups in metastatic triple-negative breast cancer and HR+/HER2– mBC[7,8]

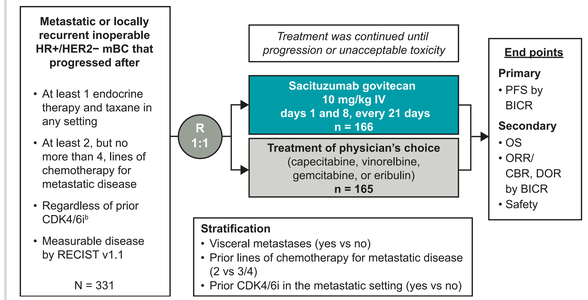
Objective

- To determine efficacy and safety of SG vs chemotherapy by prior treatment with CDK4/6is and by baseline HER2 status in patients with pretreated HR+/HER2– mBC from the EVER-132-002 study

Methods

- EVER-132-002 is a phase 3, open-label, randomized study of SG vs chemotherapy for Asian patients from mainland China, Republic of Korea, and Taiwan with pretreated HR+/HER2– mBC (**Figure 1**)
- The median follow-up at the data cutoff (April 30, 2023) was 13.4 months (range, 0.1-28.7)
- For the subgroup analysis, patients were grouped by prior CDK4/6i treatment in the metastatic setting (yes vs no) and by HER2 status (HER2 IHC 0 vs HER2-low [HER2 IHC 1+ or 2+/ISH–])

Figure 1. Study Design[a]



[a]ClinicalTrials.gov. NCT04639986. [b]Prior use of CDK4/6i was not mandatory in EVER-132-002.
BICR, blinded independent central review; CBR, clinical benefit rate; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; DOR, duration of response; HER2–, human epidermal growth factor receptor 2-negative; HR+, hormonal receptor positive; IV, intravenous; mBC, metastatic breast cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; R, randomized; RECIST, Response Evaluation Criteria in Solid Tumors.

Results

- Baseline characteristics were generally consistent regardless of prior CDK4/6i treatment and HER2 status and were balanced across treatment groups (**Table 1**)
- Patients in all subgroups had received a median of 2 prior chemotherapy regimens in the metastatic setting (**Table 1**)

Table 1. Baseline Characteristics

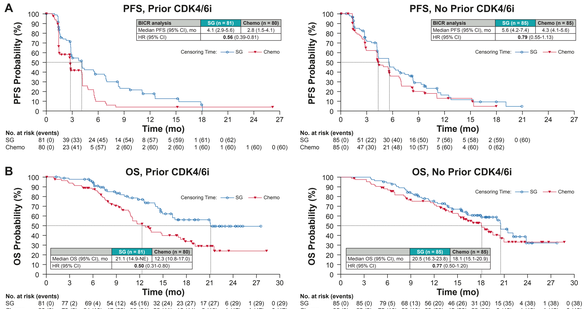
	Prior CDK4/6i				HER2 status			
	Yes		No		HER2 IHC 0		HER2 low[a]	
	SG (n = 81)	Chemo (n = 80)	SG (n = 85)	Chemo (n = 85)	SG (n = 53)	Chemo (n = 46)	SG (n = 113)	Chemo (n = 119)
Female, n (%)	81 (100)	79 (99)	85 (100)	84 (99)	53 (100)	46 (100)	113 (100)	117 (98)
Median age (range), years	51 (33-72)	50 (28-78)	55 (32-71)	53 (29-79)	52 (36-72)	52 (29-78)	53 (32-71)	51 (28-79)
Median BMI (range), kg/m²	23.4 (15.8-35.1)	22.6 (16.0-37.0)	24.5 (18.0-35.5)	24.3 (13.7-33.2)	23.6 (18.0-35.1)	23.4 (16.2-37.0)	23.9 (15.8-35.5)	23.5 (13.7-33.2)
ECOG PS, n (%)								
0	20 (25)	21 (26)	13 (15)	20 (24)	15 (28)	9 (20)	18 (16)	32 (27)
1	61 (75)	59 (74)	72 (85)	65 (76)	38 (72)	37 (80)	95 (84)	87 (73)
Visceral metastases, n (%)	71 (88)	71 (89)	75 (88)	76 (89)	46 (87)	41 (89)	100 (88)	106 (89)
Median number of prior systemic anticancer regimens (range)	6 (3-11)	6 (3-11)	6 (2-10)	5 (2-10)	6 (3-10)	6 (3-11)	6 (2-11)	6 (2-11)
Median number of prior lines of chemotherapy in metastatic setting (range)	2 (1-4)	2 (1-4)	2 (1-4)	2 (1-4)	2 (1-4)	2 (1-4)	2 (1-4)	2 (1-4)
Number of prior lines of chemotherapy in the metastatic setting, n (%)								
≤ 2	50 (62)	49 (61)	51 (60)	49 (58)	37 (70)	32 (70)	64 (57)	66 (55)
≥ 3	31 (38)	31 (39)	34 (40)	36 (42)	16 (30)	14 (30)	49 (43)	53 (45)

[a]HER2 low was defined as HER2 IHC 1+ or 2+/ISH–.
BMI, body mass index; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; Chemo, chemotherapy; ECOG PS, Eastern Cooperative Oncology Group performance status; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; SG, sacituzumab govitecan.

Efficacy by Prior CDK4/6i and HER2 Status

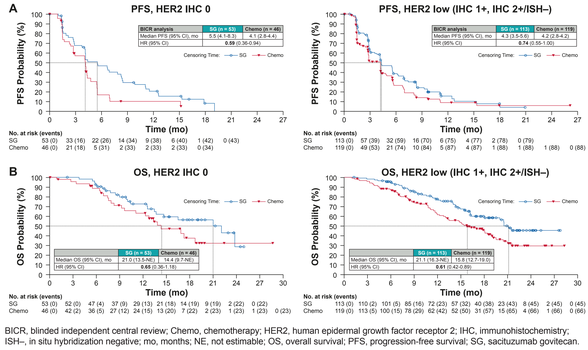
- PFS per blinded independent central review (BICR) (**Figure 2A**) and OS (**Figure 2B**) favored SG vs chemotherapy regardless of prior CDK4/6i treatment
- PFS per BICR (**Figure 3A**) and OS (**Figure 3B**) favored SG vs chemotherapy regardless of HER2 status

Figure 2. PFS and OS by Prior CDK4/6i Subgroup



BICR, blinded independent central review; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; Chemo, chemotherapy; mo, months; NE, not estimable; OS, overall survival; PFS, progression-free survival; SG, sacituzumab govitecan.

Figure 3. PFS and OS by HER2 Status



BICR, blinded independent central review; Chemo, chemotherapy; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH–, in situ hybridization negative; mo, months; NE, not estimable; OS, overall survival; PFS, progression-free survival; SG, sacituzumab govitecan.

Safety by Prior CDK4/6i and HER2 Status

- More grade ≥ 3 treatment-emergent adverse events (TEAEs) and TEAEs leading to treatment interruption were observed in patients treated with SG than in patients treated with chemotherapy across prior CDK4/6i and HER2 status subgroups (**Table 2**)
- Rates of TEAEs leading to treatment discontinuation were low and were comparable between treatment groups across all subgroups

Table 2. Safety Summary

	Prior CDK4/6i				HER2 status			
	Yes		No		HER2 IHC 0		HER2 low[a]	
Safety, n (%)	SG (n = 81)	Chemo (n = 78)	SG (n = 84)	Chemo (n = 86)	SG (n = 52)	Chemo (n = 45)	SG (n = 113)	Chemo (n = 119)
Any TEAE	81 (100)	78 (100)	84 (100)	86 (100)	52 (100)	45 (100)	113 (100)	119 (100)
Grade ≥ 3	65 (80)	52 (67)	70 (83)	62 (72)	40 (77)	32 (71)	95 (84)	82 (69)
TEAEs leading to dose reduction	17 (21)	28 (36)	25 (30)	25 (29)	16 (31)	17 (38)	26 (23)	36 (30)
TEAEs leading to interruption	54 (67)	30 (38)	58 (69)	36 (42)	36 (69)	20 (44)	76 (67)	46 (39)
TEAEs leading to discontinuation[b]	1 (1)	3 (4)	4 (5)	3 (3)	0	2 (4)	5 (4)	4 (3)
SAEs	15 (19)	18 (23)	23 (27)	14 (16)	12 (23)	11 (24)	26 (23)	21 (18)
TEAEs leading to death	1 (1)	1 (1)	0	0	0	1 (2)	1 (1)	0
TRAEs leading to death	0	0	0	0	0	0	0	0
Select grade ≥ 3 TEAEs[c]								
Neutropenia	55 (68)	45 (58)	59 (70)	56 (65)	34 (65)	28 (62)	80 (71)	73 (61)
Leukopenia	31 (38)	21 (27)	38 (45)	39 (45)	19 (37)	18 (40)	50 (44)	42 (35)
Anemia	15 (19)	3 (4)	15 (18)	7 (8)	12 (23)	3 (7)	18 (16)	7 (6)
Diarrhea	2 (2)	0	9 (11)	0	3 (6)	0	8 (7)	0
Hypokalemia	4 (5)	3 (4)	12 (14)	2 (2)	4 (8)	1 (2)	12 (11)	4 (3)
Febrile neutropenia	4 (5)	3 (4)	5 (6)	4 (5)	4 (8)	2 (4)	5 (4)	4 (3)
Thrombocytopenia	4 (5)	1 (1)	3 (4)	7 (8)	2 (4)	3 (7)	5 (4)	5 (4)
Lymphopenia	5 (6)	1 (1)	5 (6)	3 (3)	4 (8)	1 (2)	6 (5)	3 (3)
Fatigue	6 (7)	2 (3)	6 (7)	1 (1)	2 (4)	0	10 (9)	3 (3)
Gamma-glutamyltransferase increased	0	5 (6)	1 (1)	5 (6)	0	3 (7)	1 (1)	7 (6)

TEAEs are defined as any adverse events that started on or after first dose date and up to 30 days after last dose date.
[a]HER2 low was defined as HER2 IHC 1+ or 2+/ISH–. [b]TEAEs leading to discontinuation: prior CDK4/6i, SG - septic shock (n = 1), chemo - 1 each of pancreatitis, peripheral sensory neuropathy, and asphyxia; no prior CDK4/6i, SG - fatigue (n = 2) and 1 each of anemia and interstitial lung disease, chemo - 1 each of fatigue, pneumonia, and muscular weakness; HER2 IHC 0, SG - none, chemo - 1 each of peripheral sensory neuropathy and asphyxia; HER2 low, SG - fatigue (n = 2), 1 each of anemia, septic shock, and interstitial lung disease, chemo - 1 each of pancreatitis, fatigue, pneumonia, and muscular weakness. [c]Includes any grade ≥ 3 TEAEs that occurred in ≥ 5% of patients in any subgroup and treatment arm. CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; Chemo, chemotherapy; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; SAE, serious adverse event; SG, sacituzumab govitecan; TEAE, treatment-emergent adverse event; TRAEs, treatment-related adverse events.

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Acknowledgments: We thank the patients, their caregivers and families, and the clinical trial investigators. This study was sponsored by Gilead Sciences, Inc. All authors contributed to and approved the presentation; medical writing support was provided by Ben Labbe, PhD, of Parexel, and was funded by Gilead Sciences, Inc.

Disclosures: **JS** reports grants or contracts from AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, Celcuity, Daiichi Sankyo, Dragonfly, Eikon, Gilead Sciences, Inc., GSK, Hanmi, HLB Life Science, Ildong, Lilly, MSD, Novartis, Olema, Pfizer, Qurien, Roche, Samyang, Sanofi, Seagen, and Sermonix, and stock in Daiichi Sankyo.