Potential Prognostic/Predictive Biomarkers for Sacituzumab Govitecan in EVOKE-01

LB260

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Conclusions

- Exploratory biomarker analyses were conducted to identify potential biomarkers that are predictive for SG or prognostic for either treatment arm in EVOKE-01
- Trop-2 protein was highly expressed in NSCLC tumor specimens from EVOKE-01
  - Results were consistent in squamous and nonsquamous subgroups and with findings from other SG sudies[2,5]
- Trop-2 expression by multiple metrics and cut points was not predictive for better OS or PFS with SG vs docetaxel
- Trop-2 may be a negative prognostic biomarker in this NSCLC population, independent of treatment received in the study

References: **1.** Goldenberg DM, et al. *Oncotarget.* 2015;6:22496–22512. **2.** Kuo P, et al. *PLoS One*. 2025. In press. **3.** Trodelvy. Package insert. Gilead Sciences, Inc; 2024. **4.** Paz-Ares LG, et al. *J Clin Oncol.* 2024;42:2860-2872. **5.** Patel JD, et al. Presented at AACR, April 25-30, Chicago, IL, USA, Poster LB399.

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Introduction

- Trophoblast cell-surface antigen 2 (Trop-2) has become an attractive antibody-drug conjugate (ADC) target as it is expressed in multiple solid tumors, including non–small cell lung cancer (NSCLC)[1,2]
- Sacituzumab govitecan (SG), an ADC composed of a Trop-2–directed antibody coupled to SN-38 by a hydrolyzable linker, has demonstrated activity and is approved in metastatic triple-negative breast cancer and in metastatic hormone receptor–positive/human epidermal growth factor receptor 2-negative breast cancer[3]
- EVOKE-01 (NCT05089734) evaluated the efficacy and safety of SG vs docetaxel in patients with metastatic NSCLC that had progressed on or after platinum-based chemotherapy and anti–programmed cell death protein (ligand) 1 (PD-[L]1) treatment[4]
  - The study did not meet statistical significance for the primary end point of overall survival (OS) at final analysis; however, a numerical improvement in OS was seen with SG vs docetaxel
- Determining the prognostic value of biomarkers is key to predicting outcomes, guiding treatment choices, and improving patient care
  - To date, the biomarkers associated with the clinical efficacy of SG in NSCLC are not well characterized
- We performed a retrospective analysis of tumor samples from EVOKE-01 to evaluate Trop-2 expression as a predictive biomarker for SG treatment

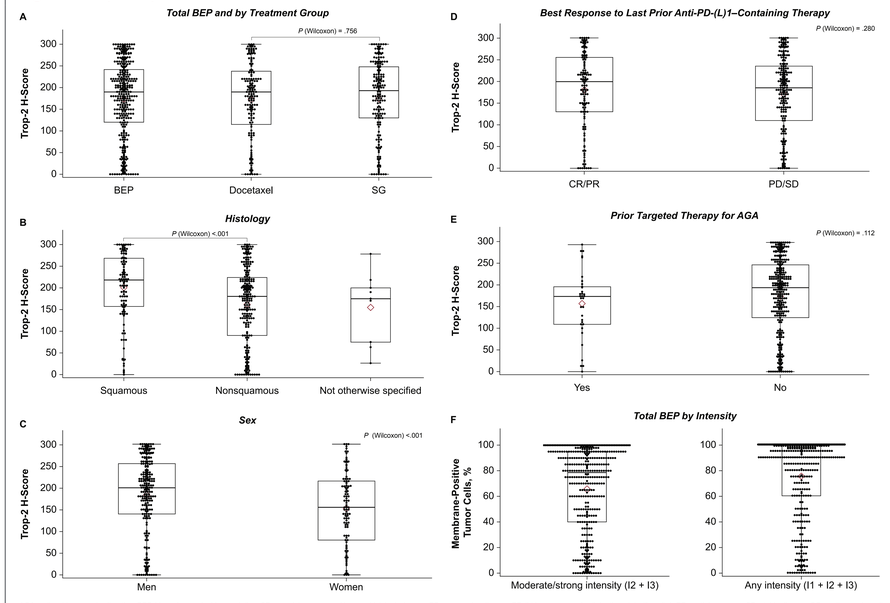
Methods

- Archival tumor samples were collected in this study; however, their collection was not mandated
- Exploratory biomarker analyses were conducted in the biomarker-evaluable population (BEP; n = 380), which represented 63% of the intent-to-treat (ITT) population
- Trop-2 membrane protein expression in archival tumor tissue was evaluated using the EPR20043 antibody for immunohistochemistry (Roche Tissue Diagnostics, Oro Valley, AZ, USA)
- Trop-2 expression was determined for BEP and used for subgroup analyses, including stratification factors
- Multiple Trop-2 expression metrics were explored for subgroup analysis
  - Histological scores (H-scores; I1 + 2 × I2 + 3 × I3), with subgroups defined using the overall median of 190 and tertiles
  - Intensity scores at any intensity (I1 + I2 + I3) and moderate/strong intensity (I2 + I3), with subgroups defined using 50% and 75% intensity scores
- Unstratified Cox regression models were used to determine interaction between Trop-2 expression and treatment outcomes
- Clinical data used in the biomarker analyses were from the study's final analysis (cutoff date: November 29, 2023)

Results

- Baseline characteristics were comparable between the BEP and ITT populations, with no statistically significant differences between treatment arms
- Trop-2 protein was highly expressed in NSCLC tumor samples with a median H-score of 190 (**Figure 1**)
  - Trop-2 expression was similar in both treatment arms (**Figure 1A**) but higher in patients with squamous histology (**Figure 1B**) and in men (**Figure 1C**)
  - Trop-2 expression was also similar regardless of best response (complete response/partial response vs progressive disease/stable disease) to last prior anti-PD-(L)1–containing therapy (**Figure 1D**) and in patients who received prior targeted therapy for actionable genomic alterations vs those who did not (**Figure 1E**)
- Overall, Trop-2 median score was 90% for any intensity (I1 + I2 + I3) and 79% for moderate/strong intensities (I2 + I3) (**Figure 1F**)

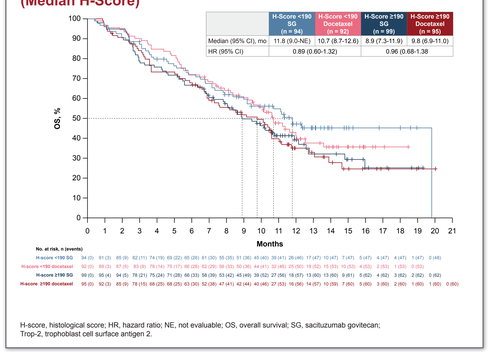
Figure 1. Trop-2 Expression Distribution



AGA, actionable genomic alteration; BEP, biomarker-evaluable population; CR, complete response; H-score, histological score; PD, progressive disease; PD-(L)1, programmed cell death protein (ligand) 1; PR, partial response; SD, stable disease; SG, sacituzumab govitecan; Trop-2, trophoblast cell surface antigen 2.

- In an initial analysis, OS with SG vs docetaxel was analyzed by Trop-2 expression assessed by H-score, moderate/strong intensity (I2 + I3), and any intensity (I1 + I2 + I3) as a continuous variable
- There was no evidence of an interaction between treatment and Trop-2 expression as a continuous variable on OS in this study. Interaction *P* values from unstratified Cox models (.6081 for Trop-2 H-score, .7255 for moderate/strong intensity, and .6080 for any intensity) were determined to be weak, indicating no clear evidence for dependency of treatment effect on OS outcome by baseline Trop-2 expression
- Therefore, exploratory subsequent analyses were performed using medians, tertiles, and predefined cut points
- Analyses did not identify any subgroup of patients that benefited more from SG than docetaxel
  - Median OS hazard ratio (HR; 95% CI) with SG vs docetaxel were 0.89 (0.60-1.32) and 0.96 (0.68-1.38) in the < median of 190 and ≥ median Trop-2 H-score subgroups, respectively
  - Median OS was shorter in patients with Trop-2 H-score ≥ median than in those with Trop-2 H-score < median with both SG (8.9 vs 11.8 months) and docetaxel (9.8 vs 10.7 months) (**Figure 2**)

Figure 2. OS by Treatment Arm and Trop-2 Subgroup (Median H-Score)



H-score, histological score; HR, hazard ratio; NE, not evaluable; OS, overall survival; SG, sacituzumab govitecan; Trop-2, trophoblast cell surface antigen 2.

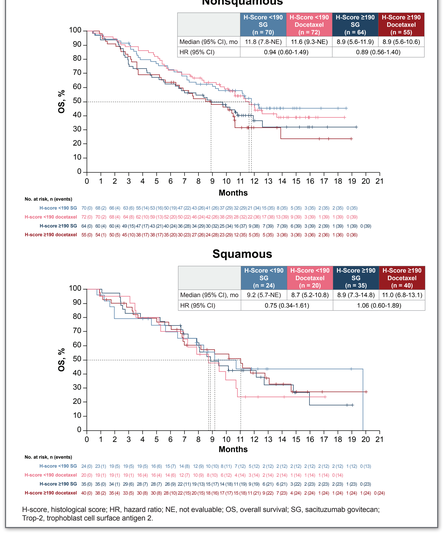
- No statistical differences in OS were observed between subgroups based on Trop-2 H-score tertiles (tertile 1, <150; tertile 2, 150 to ≤220; tertile 3, >220) for SG and docetaxel treatment arms, respectively (**Figure 3**)

Figure 3. OS by Trop-2 subgroup (H-Score Tertile)

H-score, histological score; HR, hazard ratio; NE, not evaluable; OS, overall survival; SG, sacituzumab govitecan; Trop-2, trophoblast cell surface antigen 2.

- In the nonsquamous subgroup median OS HR (95% CI) with SG vs docetaxel were 0.94 (0.60-1.49) and 0.89 (0.56-1.40) in the < median and ≥ median Trop-2 H-score subgroups, respectively (**Figure 4**)
- In the squamous subgroups, there was a trend towards improved OS with SG vs docetaxel in the < median Trop-2 H-score subgroup, albeit the sample size was small (**Figure 4**)

Figure 4. OS by Histology and Trop-2 Subgroup (Median H-Score)



H-score, histological score; HR, hazard ratio; NE, not evaluable; OS, overall survival; SG, sacituzumab govitecan; Trop-2, trophoblast cell surface antigen 2.

- Defining patient subgroups by moderate/strong intensity and any intensity Trop-2 expression using 50% and 75% cut points also did not identify any subgroups that benefited more from SG vs docetaxel (**Table 1**)
- Findings were consistent with the analyses performed using H-scores

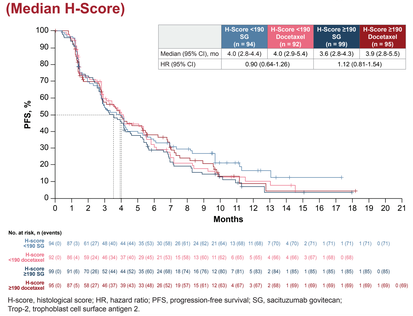
Table 1. OS by Treatment Arm and Trop-2 Intensity Subgroups

Intensity	Cut Point	Treatment	Patients (events), n	OS, Median (95% CI), mo	HR (95% CI)
Moderate/strong intensity	≥50%	SG	138 (79)	10.2 (8.4-12.2)	0.98
		Docetaxel	132 (79)	10.4 (8.2-11.4)	(0.71-1.33)
	<50%	SG	55 (31)	11.2 (7.2-NE)	0.85
		Docetaxel	55 (34)	10.2 (6.9-12.0)	(0.52-1.38)
	≥75%	SG	107 (63)	10.2 (8.0-12.6)	0.90
		Docetaxel	106 (66)	9.8 (7.0-11.0)	(0.63-1.27)
	<75%	SG	86 (47)	11.2 (7.3-NE)	0.99
		Docetaxel	81 (47)	10.6 (8.7-12.6)	(0.66-1.48)
Any intensity	≥50%	SG	154 (90)	9.7 (8.1-11.9)	1.0
		Docetaxel	146 (87)	10.4 (8.2-11.6)	(0.74-1.34)
	<50%	SG	39 (20)	12.3 (7.2-NE)	0.72
		Docetaxel	41 (26)	10.2 (6.9-12.0)	(0.40-1.30)
	≥75%	SG	133 (78)	10.0 (8.1-12.2)	0.96
		Docetaxel	132 (80)	10.2 (7.6-11.6)	(0.70-1.31)
	<75%	SG	60 (32)	11.8 (7.2-NE)	0.86
		Docetaxel	55 (33)	10.6 (7.6-12.0)	(0.53-1.41)

H-score, histological score; HR, hazard ratio; NE, not evaluable; OS, overall survival; SG, sacituzumab govitecan; Trop-2, trophoblast cell surface antigen 2.

- Median PFS was similar with SG and docetaxel treatment in both median Trop-2 H-score subgroups (**Figure 5**)
- No statistically significant differences in ORR were observed between arms when evaluating subgroups defined by Trop-2 expression (**Table 2**)
- Consistent PFS and ORR results were seen by moderate/strong intensity Trop-2 expression

Figure 5. PFS by Treatment Arm and Trop-2 Subgroup (Median H-Score)



H-score, histological score; HR, hazard ratio; PFS, progression-free survival; SG, sacituzumab govitecan; Trop-2, trophoblast cell surface antigen 2.

Table 2. ORR by Treatment Arm and Trop-2 Subgroup (Median H-Score)

Subgroup	Patients, n	ORR (95% CI), %
H-score <190		
SG	94	14.9 (8.4-23.7)
Docetaxel	92	20.7 (12.9-30.4)
H-score ≥190		
SG	99	11.1 (5.7-19.0)
Docetaxel	95	16.8 (9.9-25.9)

H-score, histological score; ORR, objective response rate; SG, sacituzumab govitecan; Trop-2, trophoblast cell surface antigen 2.