Trop-2 Expression and Association With Efficacy in Patients Treated With Sacituzumab Govitecan + Pembrolizumab ± Carboplatin in the EVOKE-02 Study of Non–Small Cell Lung Cancer

LB399

Jyoti D Patel,[1] Marianna Zavodovskaya,[2] Byoung Chul Cho,[3] Martin Reck,[4] Jhanelle E Gray,[5] Noemí Reguart,[6] Enriqueta Felip,[7] Joel W Neal,[8] Kai-Wen Lin,[2] Juliane M Jürgensmeier,[2] Sabeen Mekan,[2] Farnoush Safavi,[2] Michael Chisamore,[9] Edward B Garon[10]

[1]Northwestern University Feinberg School of Medicine, Chicago, IL, USA; [2]Gilead Sciences, Inc, Foster City, CA, USA; [3]Division of Medical Oncology, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea; [4]Airway Research Center North, German Center for Lung Research (DZL), LungenClinic, Grosshansdorf, Germany; [5]H Lee Moffitt Cancer Center and Research Institute, University of South Florida, Tampa, FL, USA; [6]Hospital Clínic de Barcelona, Barcelona, Spain; [7]Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology, Barcelona, Spain; [8]Stanford Cancer Center, Stanford, CA, USA; [9]Merck & Co, Inc, Rahway, NJ, USA; [10]David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA, USA

Conclusions

- We conducted an exploratory analysis of Trop-2 expression in EVOKE-02 to identify potential prognostic or predictive value of this biomarker
  - Several Trop-2 intensity scores and exploratory cut points were investigated
  - The baseline characteristics and efficacy results for the BEP were comparable with those of the patients evaluable for response across all 4 cohorts
- Trop-2 was highly expressed in NSCLC tumor specimens from EVOKE-02
  - Trop-2 expression was comparable across squamous and nonsquamous histologies and PD-L1 subgroups
- Evaluation of Trop-2 expression did not identify a subgroup of patients that derived greater benefit (ORR or PFS) from treatment with SG + pembrolizumab
- These data are consistent with those of the Trop-2 biomarker evaluation from the EVOKE-01 randomized phase 3 study, in which SG monotherapy was compared with docetaxel in 2L NSCLC[2]

References: 1. Kuo P, et al. *PLoS One.* 2025. In press. **2.** Garassino MC, et al. Presented at AACR, April 25-30, 2025; Chicago, IL, USA, Poster LB260. **3.** Trodelvy. Package insert. Gilead Sciences, Inc; 2024. **4.** Patel JD, et al. Presented at ASCO, May 31-June 4, 2024; Chicago, IL, USA, Poster 8592. **5.** Gray JE, et al. Presented at WCLC, September 7-10, 2024; San Diego, CA, USA, Oral presentation OA08.07.

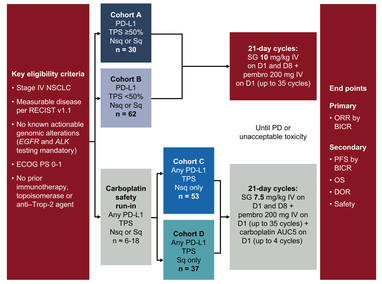
Acknowledgments: This study is in collaboration with Merck Sharp & Dohme LLC, a subsidiary of Merck & Co, Inc, Rahway, NJ, USA and was funded by Gilead Sciences, Inc, Foster City, CA, USA. Medical writing and editorial support were provided by Cara-Lesley Strauss, PhD, Mihaela Marina, PhD, and Frederique Evans, MBS, of Ashfield MedComms, an Inizio company, and funded by Gilead Sciences, Inc.

Disclosures: Dr Jyoti D Patel reports consulting or advisory for AstraZeneca, AbbVie, AnHeart, Blueprint, BMS, Genentech, Gilead, Guardant, Lilly, Regeneron, and Takeda.

Introduction

- Trophoblast cell-surface antigen 2 (Trop-2) is highly expressed in both squamous and nonsquamous non–small cell lung cancer (NSCLC)[1,2]
- Sacituzumab govitecan (SG) is a first-in-class, Trop-2–directed antibody-drug conjugate with a hydrolysable linker coupled to a potent SN-38 payload[2]
- SG is approved in metastatic triple-negative breast cancer and in metastatic hormone receptor-positive/human epidermal growth factor receptor 2-negative breast cancer and is being investigated for the treatment of metastatic NSCLC (mNSCLC)[3]
- EVOKE-02 (NCT05186974; **Figure 1**) is an ongoing, open-label, global, multicohort, phase 2 study assessing first-line SG + pembrolizumab with or without chemotherapy in mNSCLC without actionable genomic alterations[4,5]
- Understanding the value of Trop-2 as a potential predictive/prognostic biomarker is important to optimize patient treatment; biomarkers associated with the efficacy of SG in NSCLC are currently not well understood
- We performed an exploratory analysis of tumors samples from patients enrolled in the EVOKE-02 study to evaluate Trop-2 as a potential prognostic/predictive biomarker

Figure 1. EVOKE-02 Study Design



ALK, anaplastic lymphoma kinase; AUC, area under the curve; BICR, blinded independent central review; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; *EGFR*, epidermal growth factor receptor; IV, intravenous; NSCLC, non–small cell lung cancer; nsq, nonsquamous; ORR, objective response rate; OS, overall survival; PD, progressive disease; PD-L1, programmed cell death ligand 1; pembro, pembrolizumab; PFS, progression-free survival; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SG, sacituzumab govitecan; sq, squamous; TPS, tumor proportion score; Trop-2, trophoblast cell-surface antigen 2.

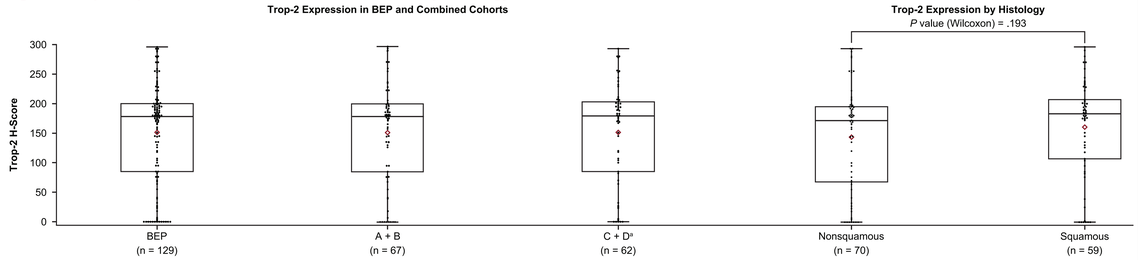
Methods

- Although not mandated by the study, archival tumor samples were collected from the biomarker-evaluable population (BEP), which consisted of 129 patients (70%) with Trop-2 data of the 184 patients evaluable for response across all 4 cohorts
- Tumor tissue samples were analyzed for Trop-2 membrane expression by histological scores (H-scores; scale 0-300) using EPR20043FLA immunohistochemistry (Roche Tissue Diagnostics, Oro Valley, AZ, USA)
  - H-scores (I1 + 2 × I2 + 3 × I3) with subgroups defined using the overall median (< or ≥ median H-score)
  - Intensity scores at any intensity (I1 + I2 + I3) and moderate/strong intensity (I2 + I3)
  - The median Trop-2 score was derived from the BEP and used for subgroup analyses
- Trop-2 expression was evaluated for association with clinical endpoints (objective response rate [ORR] and progression-free survival [PFS]) using clinical data from the June 3, 2024, cutoff date
- Correlation with efficacy in Trop-2 subgroups was performed for Cohorts A + B and C + D combined to boost the numbers of patients for subgroup analyses
- PD-L1 expression was assessed by immunohistochemistry using the 22C3 pharmDx assay (Agilent Technologies, Inc, Santa Clara, CA, USA) and tumor proportion score (TPS)

Results

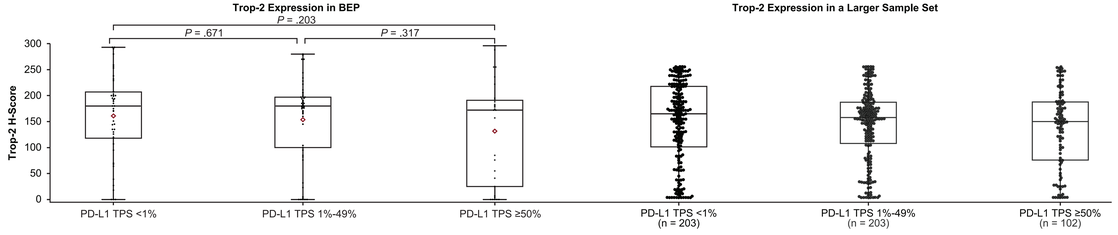
- Baseline characteristics and clinical outcomes for ORR/PFS for the BEP were comparable with those of the patients evaluable for response
- High Trop-2 expression was observed in NSCLC samples, with a median H-score of 178 (**Figure 2**)
  - Trop-2 expression at moderate or strong intensity (I2 + I3): median score, 79%
  - Trop-2 expression at any level of intensity (I1 + I2 + I3): median score, 90%
- Trop-2 expression was comparable in tumors with squamous or nonsquamous histology (**Figure 2**)
- Additionally, Trop-2 expression did not correlate with PD-L1 expression (TPS, <1%, 1%-49%, ≥50%) subgroups in samples from EVOKE-02 or a larger sample set that included samples from EVOKE-02 (**Figure 3**)

Figure 2. Trop-2 Expression in BEP, Combined Cohorts, and by Histology



[a]Biomarker data for safety run-in patients treated with SG + pembrolizumab and carboplatin were added to Cohorts C + D.
BEP, biomarker-evaluable population; H-score, histological score; Trop-2, trophoblast cell-surface antigen 2.

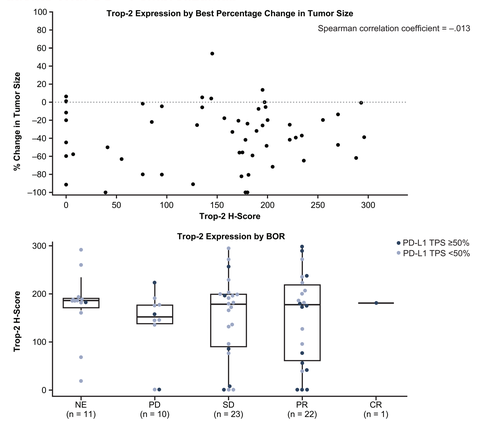
Figure 3. Trop-2 Expression Across PD-L1 TPS Subgroups in EVOKE-02 and in a Larger Tumor Sample Set



BEP, biomarker-evaluable population; H-score, histological score; PD-L1, programmed cell death ligand 1; Trop-2, trophoblast cell-surface antigen 2; TPS, tumor proportion score.

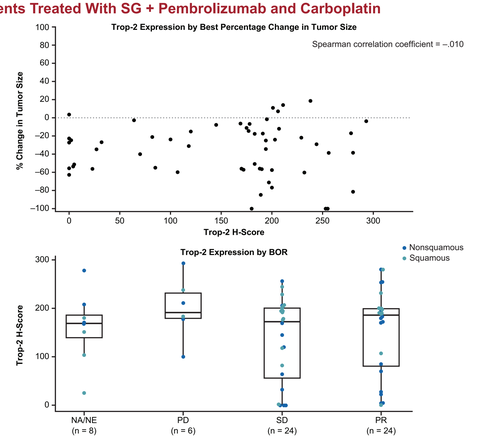
- No correlation was observed between Trop-2 expression and best percentage change in tumor size or best overall response (BOR) in patients treated with SG + pembrolizumab (**Figure 4**)
- Similarly, no correlation was observed between Trop-2 expression and best percentage change in tumor size or BOR for patients treated with SG + pembrolizumab and carboplatin (**Figure 5**)

Figure 4. Trop-2 Expression by Percentage Change in Tumor Size and BOR in Patients With SG + Pembrolizumab



BOR, best objective response; CR, complete response; H-score, histological score; NE, not evaluable; PD, progressive disease; PD-L1, programmed cell death ligand 1; PR, partial response SD, stable disease; SG, sacituzumab govitecan;TPS, tumor proportion score; Trop-2, trophoblast cell-surface antigen 2.

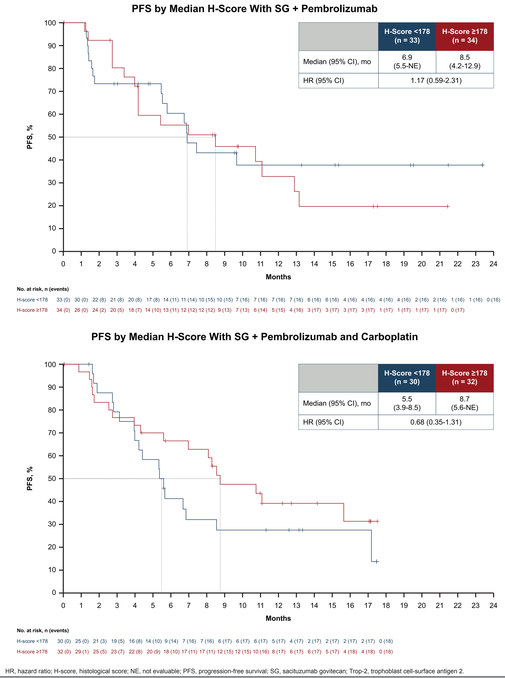
Figure 5. Trop-2 Expression by Percentage Change in Tumor Size and BOR in Patients Treated With SG + Pembrolizumab and Carboplatin



BOR, best overall response; CR, complete response; H-score, histological score; NA, not assessed; NE, not evaluable; PD, progressive disease; PD-L1, programmed death ligand 1; PR, partial response; SD, stable disease; SG, sacituzumab govitecan; TPS, tumor proportion score; Trop-2, trophoblast cell-surface antigen 2.

- Trop-2 expression ≥ median H-score did not result in improved PFS in patients treated with SG + pembrolizumab (**Figure 6**)
- In patients treated with SG + pembrolizumab and carboplatin, Trop-2 expression ≥ median H-score resulted in a numerically higher PFS that was not statistically significant, with the hazard ratio CI crossing 1 (**Figure 6**)
- Findings were consistent for additional metrics including Trop-2 intensity scores

Figure 6. PFS by Treatment With SG + Pembrolizumab ± Carboplatin and Trop-2 Subgroup (Median H-Score)



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

- Trop-2 expression ≥ median H-score did not result in a higher ORR in patients treated with SG + pembrolizumab (**Table 1**)
- In patients treated with SG + pembrolizumab and carboplatin, Trop-2 expression ≥ median H-score resulted in a numerically higher ORR that was not statistically different with overlapping 95% CI (**Table 1**)
- Conclusions were consistent for additional metrics including Trop-2 intensity scores with multiple predefined cuts

Table 1. ORR by Treatment With SG + Pembrolizumab ± Carboplatin and Trop-2 Subgroup (Median H-Score)

Treatment Group	Trop-2 H-Score	ORR, n/n (%)	95% CI
SG + pembrolizumab	<178	11/33 (33.3)	18.0-51.8
	≥178	12/34 (35.3)	19.7-53.5
SG + pembrolizumab + carboplatin	<178	10/30 (33.3)	17.3-52.8
	≥178	14/32 (43.8)	26.4-62.3

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