



P2.170: Clinical impact of NY-ESO expression on the efficacy of immune checkpoint inhibitors in lung squamous cell carcinoma

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IASLC 2026 World
Conference on Lung Cancer

SEPTEMBER 12 - 15, 2026
SEOUL, REPUBLIC OF KOREA

INTRODUCTION

To improve clinical outcome of lung squamous cell carcinoma (LUSC) in the era of immune checkpoint inhibitors (ICIs), novel strategies targeting cancer antigens have been investigated. NY-ESO, a cancer-testis antigen, is selectively expressed in tumor cells, and novel agents targeting NY-ESO are under development. In this study, we retrospectively analyzed the tumor specimens from LUSC patients treated with ICIs to investigate the association between NY-ESO expression and the therapeutic efficacy of ICIs in LUSC to seek the subset who may benefit from NY-ESO targeting.

METHODS

Study design and participant selection: LUSC patients who received or were scheduled to receive ICIs-containing therapy at Wakayama Medical University Hospital were enrolled between December 2021 and March 2025.

Immunohistochemistry (IHC): IHC was conducted using Leica BOND staining platform with an anti-NY-ESO mouse monoclonal antibody (clone D8.38, Millipore, #MABC1151). NY-ESO expression was evaluated in tumor cytoplasm using the H-score, calculated using the following formula: H-score = 3 × (% of strong positive tumor cells) + 2 × (% of moderate positive tumor cells) + 1 × (% of weak positive tumor cells). Samples with H-score ≥10 were defined as NY-ESO-positive, and those with H-score <10 were defined as NY-ESO-negative.

Genotyping: Genomic DNA was extracted from LUSC patient derived peripheral blood using QIAamp DNA Blood Mini Kit according to manufacturer's instructions and was used for HLA genotyping. HLA-A allele information was obtained at the second-field, four-digit level using the Luminex method.

Statistical analysis: Progression-free survival (PFS) was analyzed using the Kaplan–Meier method and compared using the log-rank test.

RESULTS

Table. Characteristics

	Case (N=78)	Case (N=78)	Sample (N=208)
Age, median (range)	73 (41-90)		
Sex, N (%)		Stage, N (%)	
male	73 (93.6)	I-II	56 (26.9)
female	5 (6.4)	III	93 (44.7)
Genotype		IV	59 (28.4)
HLA-A*02:01 and/or 02:06	29 (37.2)	multiple stages	-
others	48 (61.5)	Sampling timepoint, N (%)	
NE	1 (1.3)	pre-ICI	150 (72.1)
ICI, N (%)		post-ICI	58 (27.9)
Pembrolizumab	42 (53.8)	paired	-
Nivolumab	11 (14.1)	Sample origin, N (%)	
Durvalumab	18 (23.1)	Lung	165 (79.3)
Atezolizumab	1 (1.3)	Lymph node	33 (15.9)
multiple ICIs	4 (5.1)	Pleura	3 (1.4)
no ICI	2 (2.6)	Liver	3 (1.4)
PD-L1 TPS, N (%)		Brain	2 (1.0)
< 1%	16 (20.5)	Bone	2 (1.0)
1% ≤ TPS < 50%	33 (42.3)		
50% ≥ TPS	28 (35.9)		
NE	1 (1.3)		

COI

Research funding: Daiichi Sankyo Co., Ltd.

RESULTS

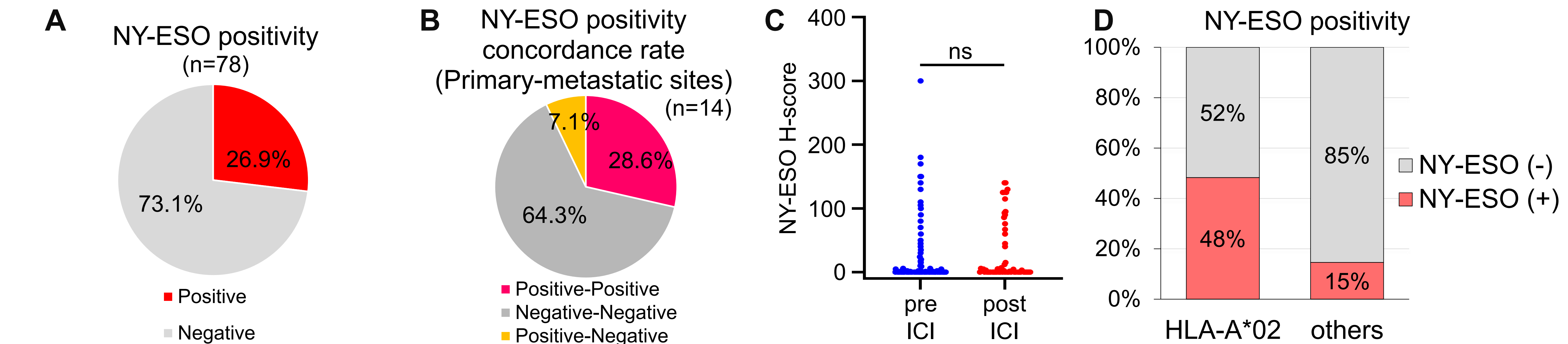


Fig. 1. (A) Twenty-one patients (26.9%) had at least one NY-ESO-positive specimen. (B) Among 14 patients with both primary and metastatic specimens, the concordance rate of NY-ESO positivity was 92.9%. (C) NY-ESO H-scores were not significantly different between pre- and post-ICIs specimens. (D) NY-ESO positivity was more frequently observed in patients with the HLA-A*02:01 and/or 02:06 genotype.

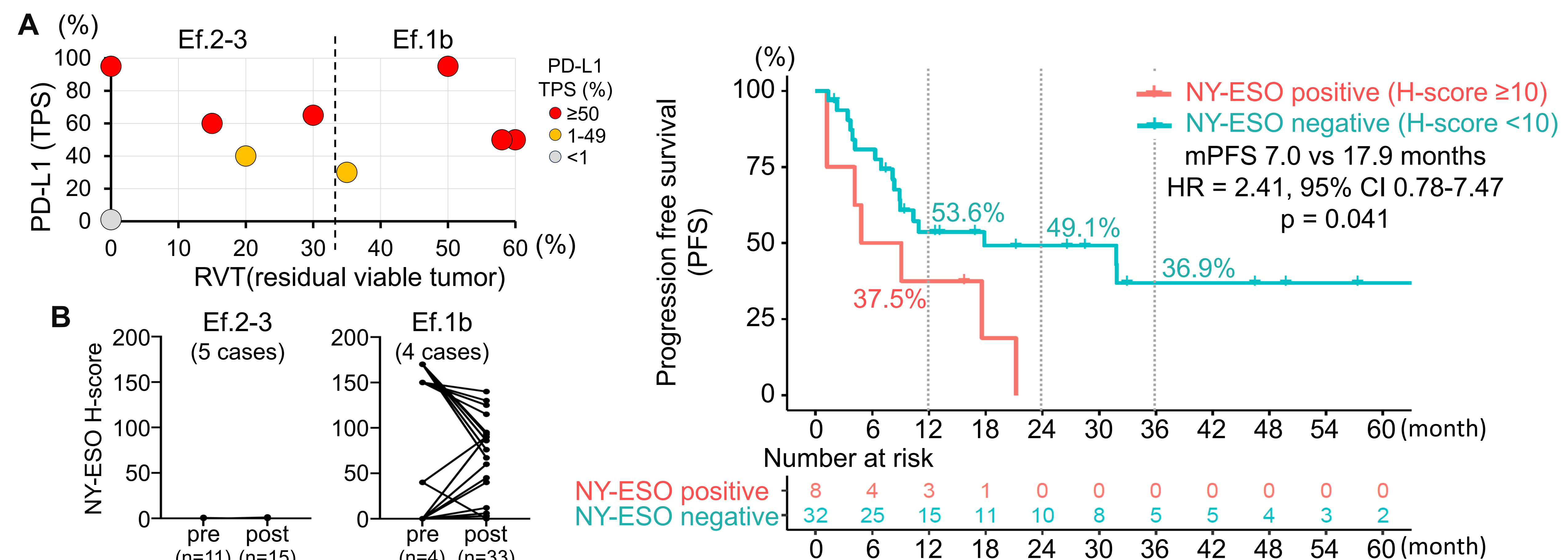


Fig. 2. PD-L1 expression and NY-ESO positivity in relation to response to neoadjuvant therapy in early-stage LUSC. (A) PD-L1 expression was not associated with response to neoadjuvant therapy. (B) NY-ESO-positive cases exhibited a poor response to neoadjuvant therapy (Ef.1b: RVT ≥1/3), whereas NY-ESO-negative cases showed a better therapeutic response (Ef.2–3: RVT <1/3). n, number of samples.

Fig. 3. Progression-free survival of first-line immune checkpoint inhibitor-containing therapy in advanced-stage lung cancer. 1- and 2-year PFS rates were 53.6% and 49.1% in NY-ESO-negative patients and 37.5% and 0% in NY-ESO-positive patients, respectively. NY-ESO-positive patients showed shorter PFS than NY-ESO-negative patients (median PFS, 7.0 vs 17.9 months; unadjusted HR = 2.41, 95% CI 0.78–7.47; p = 0.041).

DISCUSSION AND CONCLUSION

- NY-ESO expression is consistent regardless of organ site and was not affected by ICIs treatment.
- NY-ESO expression may have a predictive value for poor response to ICIs therapy in LUSC and could be a potential target in those who have limited benefit from ICIs.

Future Direction for Research

- Elucidation of the molecular mechanisms by which NY-ESO contributes to ICI resistance.
- Development of NY-ESO-targeted therapeutic strategies to overcome ICI resistance and improve clinical outcomes in patients with LUSC.