



EP13.06: Benefit of Immune Checkpoint Inhibitor Therapy in Pulmonary Large Cell Neuroendocrine Carcinoma by Immunohistochemistry

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IASLC 2026 World
Conference on Lung Cancer

SEPTEMBER 12 - 15, 2026
SEOUL, REPUBLIC OF KOREA

BACKGROUND

- ✓ Large-cell neuroendocrine carcinoma (LCNEC) is a biologically heterogeneous disease with distinct transcription factor subtypes (ASCL1, NEUROD1, POU2F3, and YAP1)¹⁻³.
- ✓ However, biomarkers predicting the efficacy of immune checkpoint inhibitor (ICI)-containing therapy remain undefined¹.
- ✓ We investigated whether these transcription factor subtypes are associated with the efficacy of first-line ICI-containing therapy in advanced or recurrent pulmonary LCNEC.

METHODS

- ✓ We retrospectively analyzed patients with advanced or recurrent pulmonary LCNEC who initiated ICI-based therapy at our institution between July 2021 and April 2025. Clinical follow-up was updated through July 31, 2026.
- ✓ Tumor specimens were evaluated by immunohistochemistry (IHC) for RB1, p53, ASCL1, NEUROD1, POU2F3, and YAP1.
- ✓ IHC cut-offs were predefined (RB1 loss $\geq 90\%$; p53 abnormal expression $\geq 80\%$ overexpression or $\geq 90\%$ complete loss; others $\geq 10\%$ nuclear staining), and transcriptional subtypes were assigned according to the predominant expression of ASCL1, NEUROD1, POU2F3, or YAP1.

RESULTS

Patient Characteristics

	n = 9
Age, median (IQR)	72.0 (50-79)
Sex, n(%)	
Male	8 (88.9)
Smoking history, n(%)	
current	4 (44.4)
former	5 (55.6)
never	0 (0.0)
Stage, n(%)	
III	1 (11.1)
IV	4 (44.4)
Recurrence	4 (44.4)
ECOG PS, n(%)	
0-1	9 (100.0)
PD-L1, n(%)	
TPS < 1%	8 (88.9)
TPS 1-49%	0 (0.0)
TPS $\geq 50\%$	0 (0.0)
Not evaluable	1 (11.1)
Regimen, n (%)	
CBDCA + PTX + BEV + Atezolizumab	2 (22.2)
CBDCA + nab-PTX + Atezolizumab	3 (33.3)
CBDCA + PTX + Atezolizumab	1 (11.1)
CBDCA + ETP + Durvalumab	1 (11.1)
Ipi + Nivo	2 (22.2)

Abbreviations: CBDCA, carboplatin; PTX, paclitaxel; nab-PTX, nanoparticle albumin-bound paclitaxel; ETP, etoposide; BEV, bevacizumab; Ipi, ipilimumab; Nivo, nivolumab.

CONCLUSION

✓ **No clear association was observed between immunohistochemical transcription factor subtype and progression-free survival following first-line ICI-containing therapy in advanced or recurrent pulmonary LCNEC. A multicenter study is currently underway to further investigate this association.**

Fig.1 PFS and Immunohistochemical Profiles of All Patients

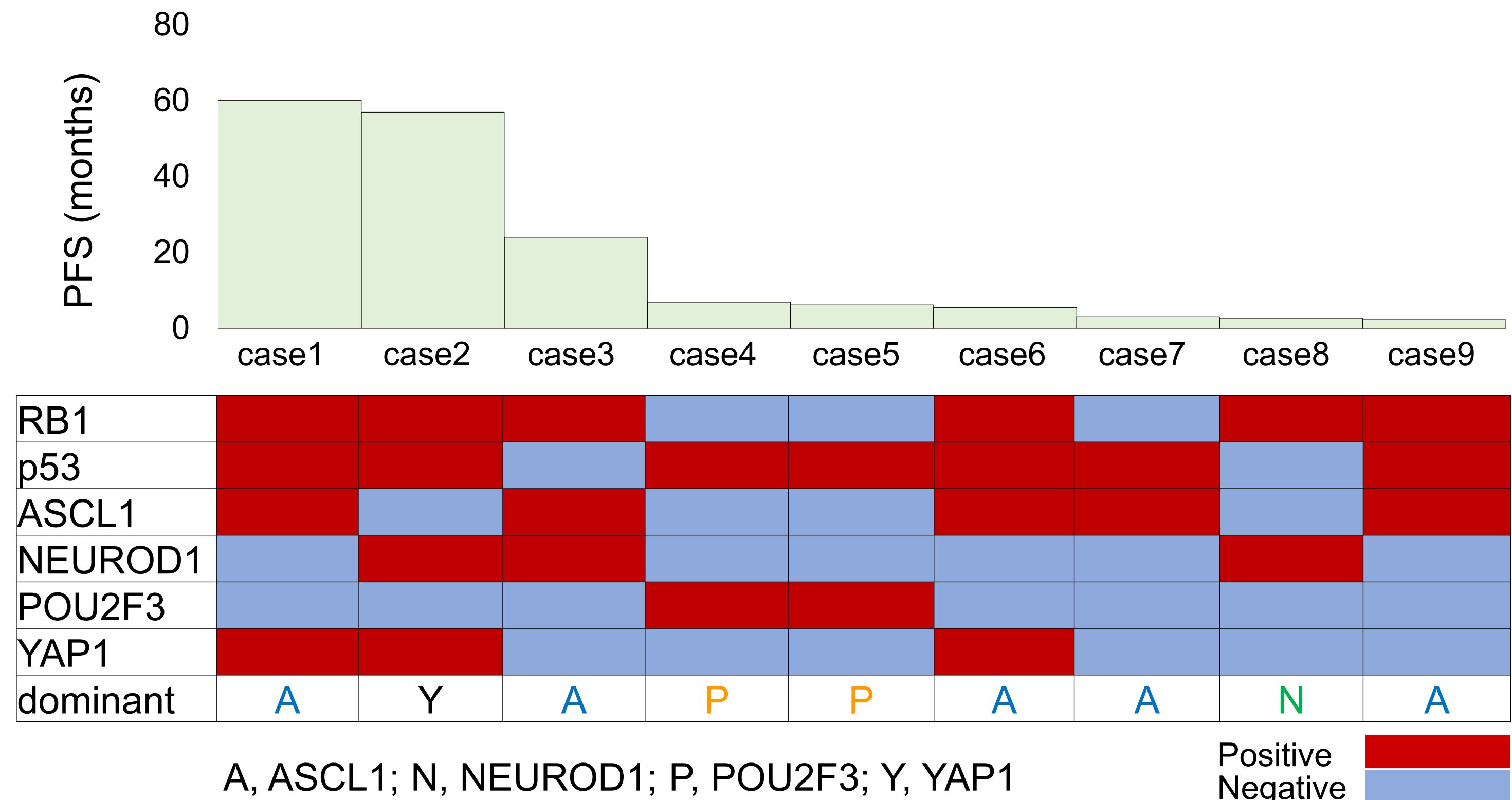
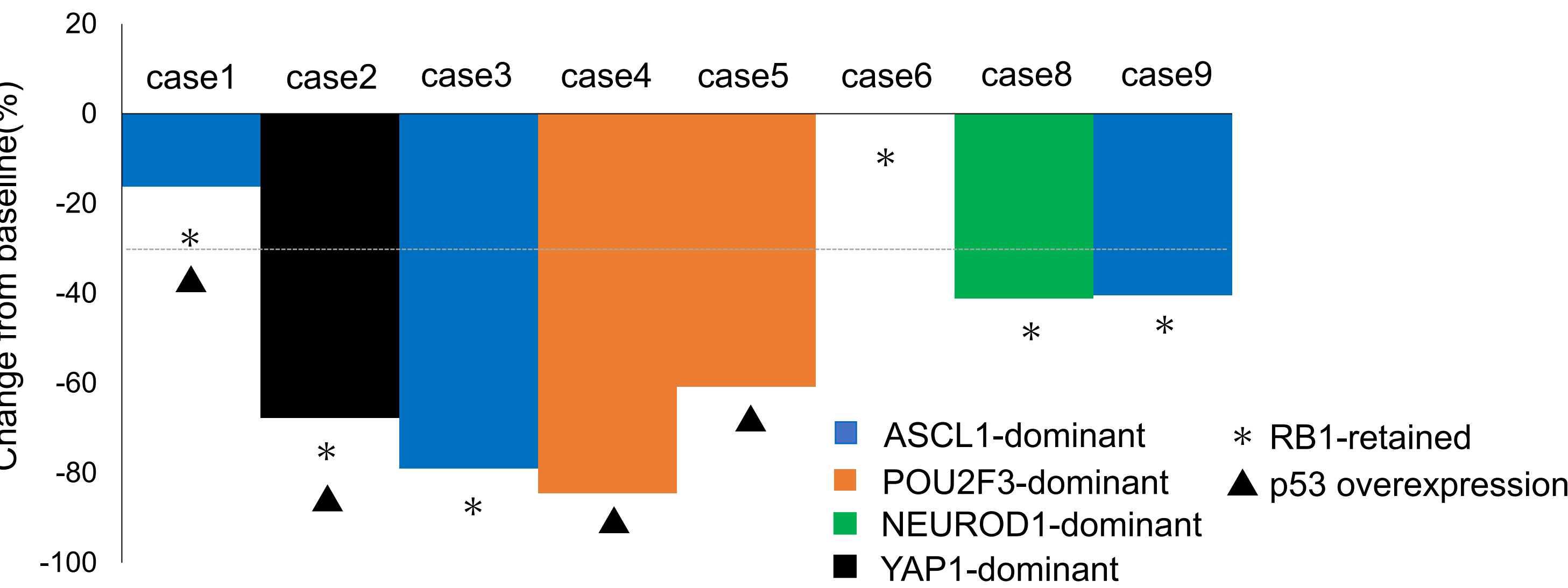


Fig.2 IHC Profiles in Patients with PFS ≥ 12 Months

	RB1	p53	ASCL1	NEUROD1	POU2F3	YAP1
case 1	Retained	overexpression	+	-	-	+ (partial)
case 2	Retained	overexpression	-	+ (partial)	-	+
case 3	Retained	-	+	+	-	-

Fig.3 Best Percentage Change in Tumor Size from Baseline



One patient was not evaluable for tumor response due to clinical deterioration after one cycle.

REFERENCES

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- Hung YP, et al. Histopathology. 2026;88(4):810-830.

Fig.4 Treatment Duration and Clinical Course in All Patients

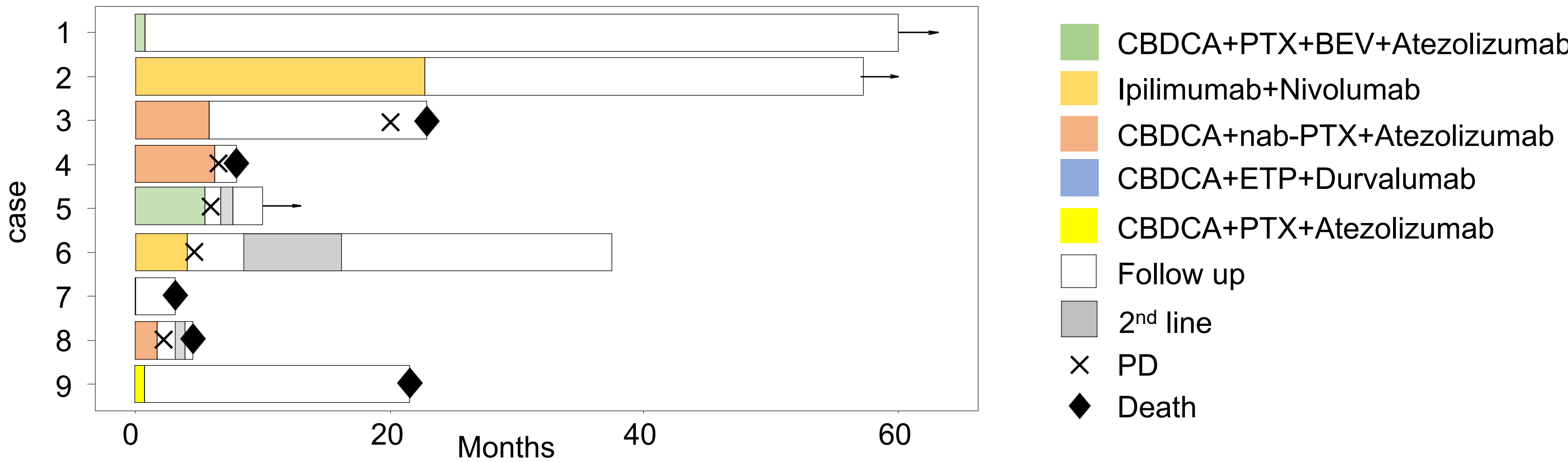


Fig.5 Overall Survival and Progression-Free Survival in All Patients

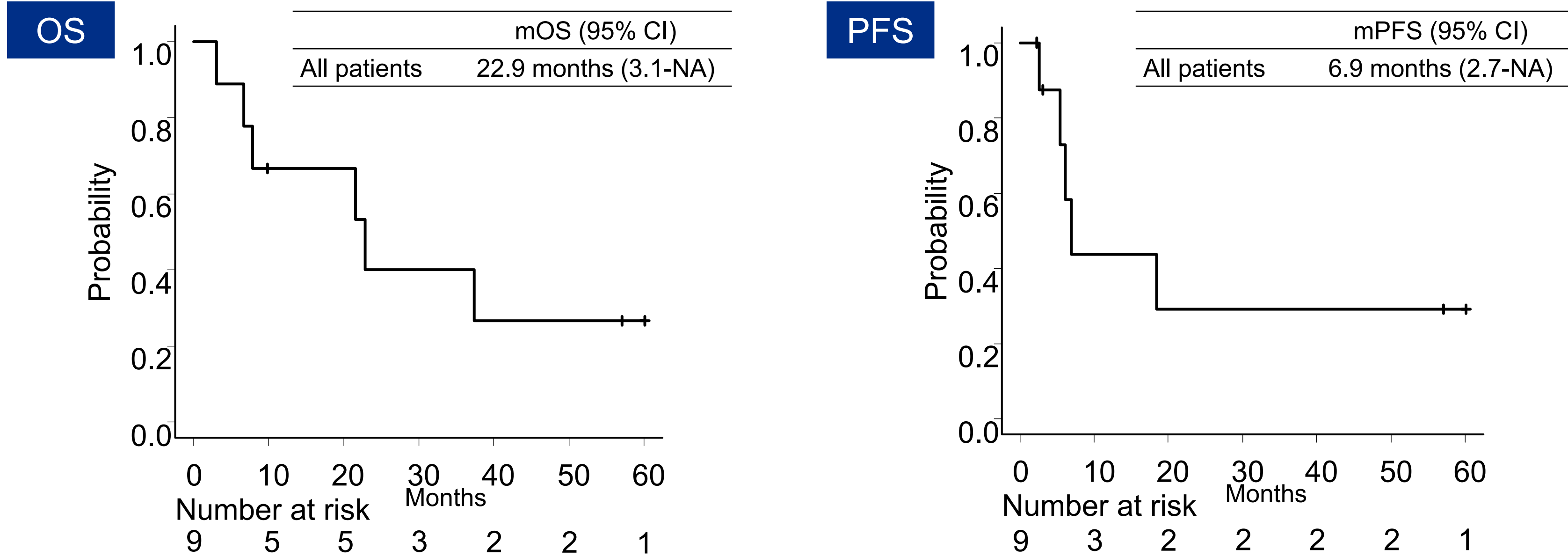
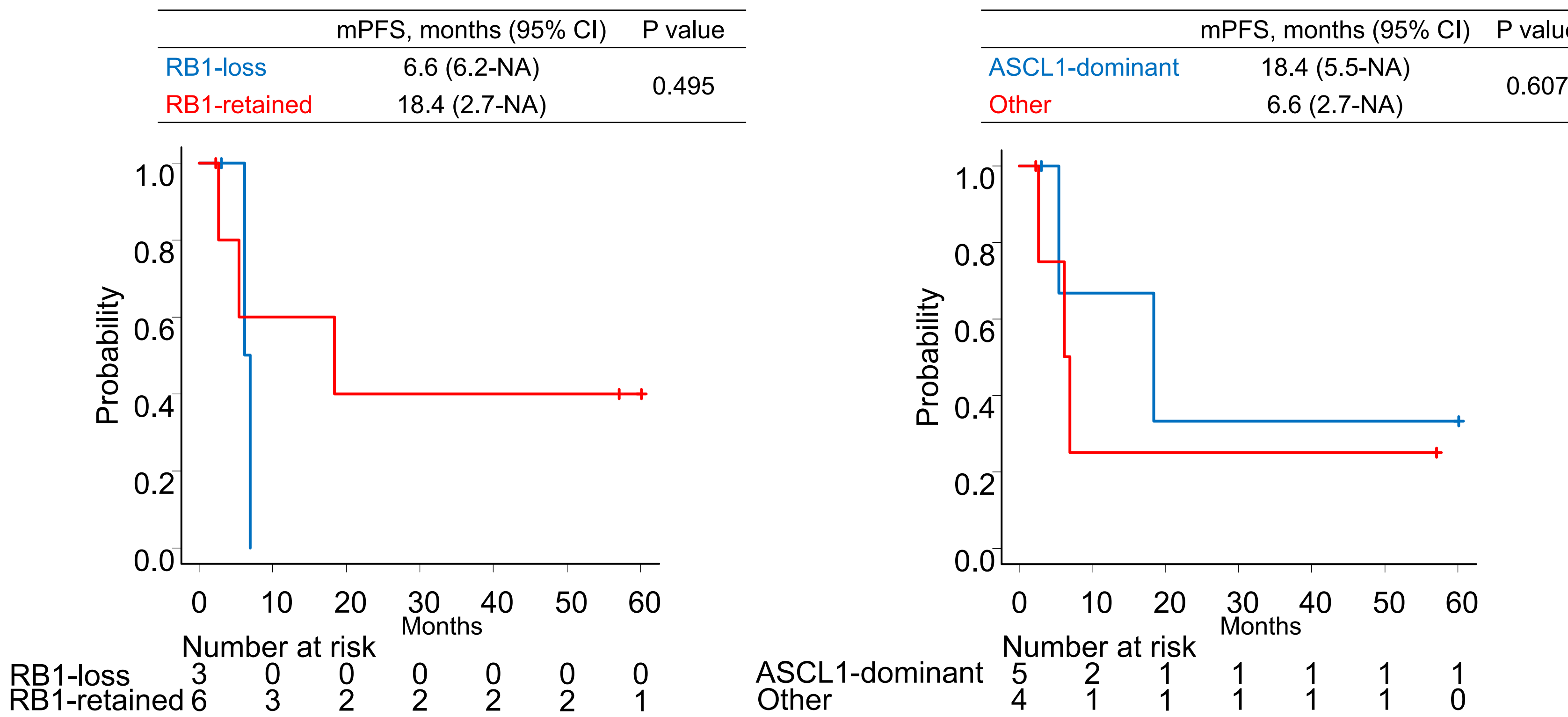


Fig.6 Exploratory PFS by RB1 Status and ASCL1 Subtype



DISCUSSION

- ✓ No significant association was observed between transcription factor subtype and PFS following first-line ICI-containing therapy.
- ✓ In an exploratory subgroup analysis, RB1-retained and ASCL1-dominant tumors showed a numerically longer PFS, without reaching statistical significance.
- ✓ Given the small sample size and exploratory nature of this study, these findings should be interpreted with caution.