

PD-L1 Expression Is Associated With Inferior Outcomes Independent of EGFR Subtype in Advanced NSCLC With Uncommon EGFR Mutations

POSTER #

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Background

- Uncommon EGFR mutations represent ~10% of EGFR alterations and show marked biological heterogeneity.
- Outcome prediction for second-generation EGFR-TKIs still mainly relies on mutation subtype.

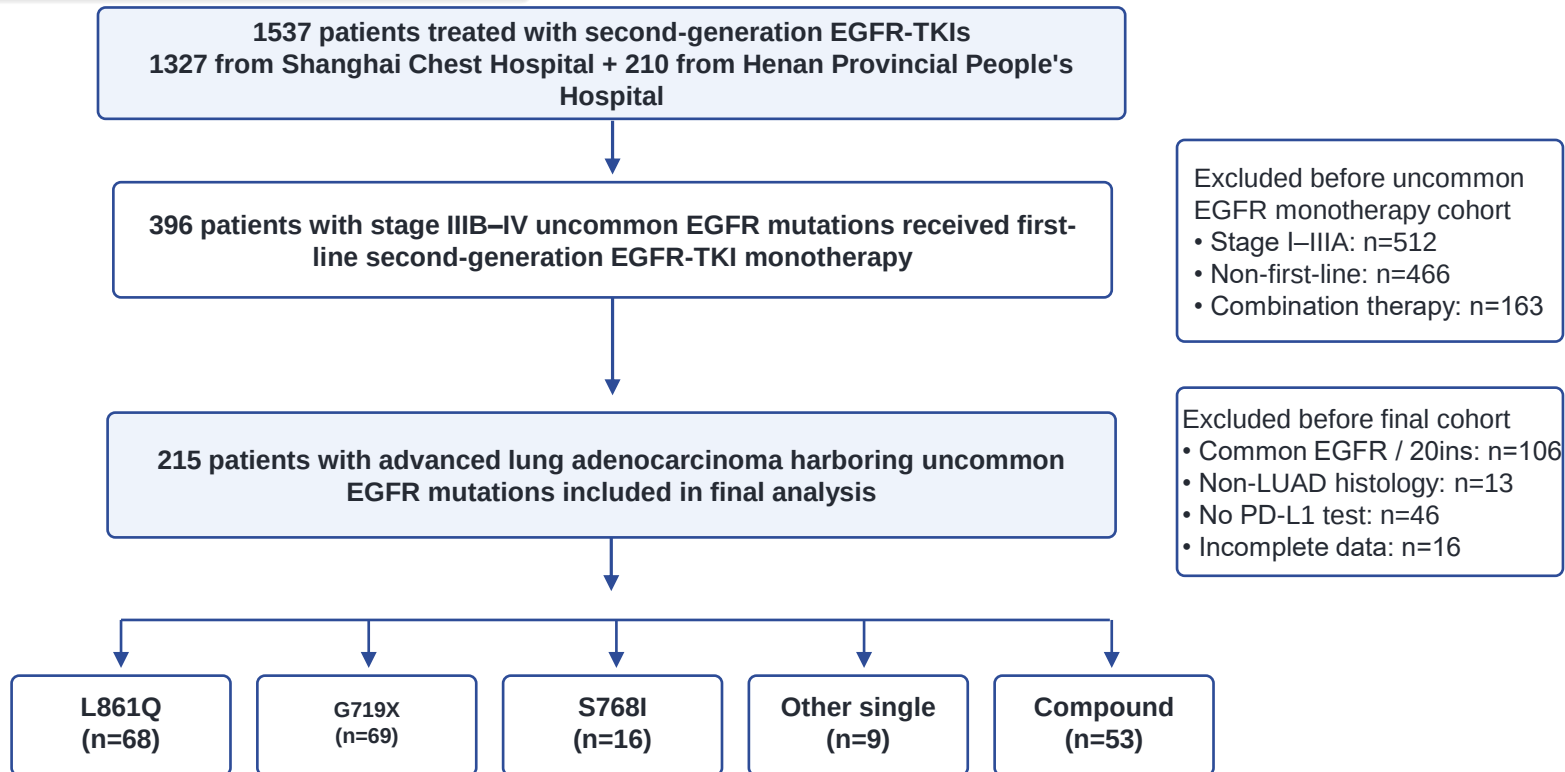
Objective & Methods

- Dual-center retrospective real-world cohort (January 2018–December 2024).
- Included stage IIIB–IV lung adenocarcinoma with uncommon EGFR mutations treated with first-line afatinib or dacomitinib monotherapy.
- PD-L1 assessed using DAKO 22C3 TPS (<1%, 1%–49%, ≥50%); endpoints: PFS, ORR, DCR.

Cohort Features

- N=215; median age 64.5 years; females 50.2%; never-smokers 76.3%.
- Stage IV disease: 89.3%.
- Afatinib 78.6%; dacomitinib 21.4%.
- PD-L1 TPS <1%: 51.2%; 1%–49%: 29.3%; ≥50%: 19.5%.

Patient Enrollment



Final cohort: 215 patients. Major subtypes were balanced between L861Q and G719X, with additional S768I, other single-site, and compound mutations.

Overall efficacy and mutation subtype analysis

14.07

months median PFS

95% CI, 12.54-15.60

49.3%

objective response

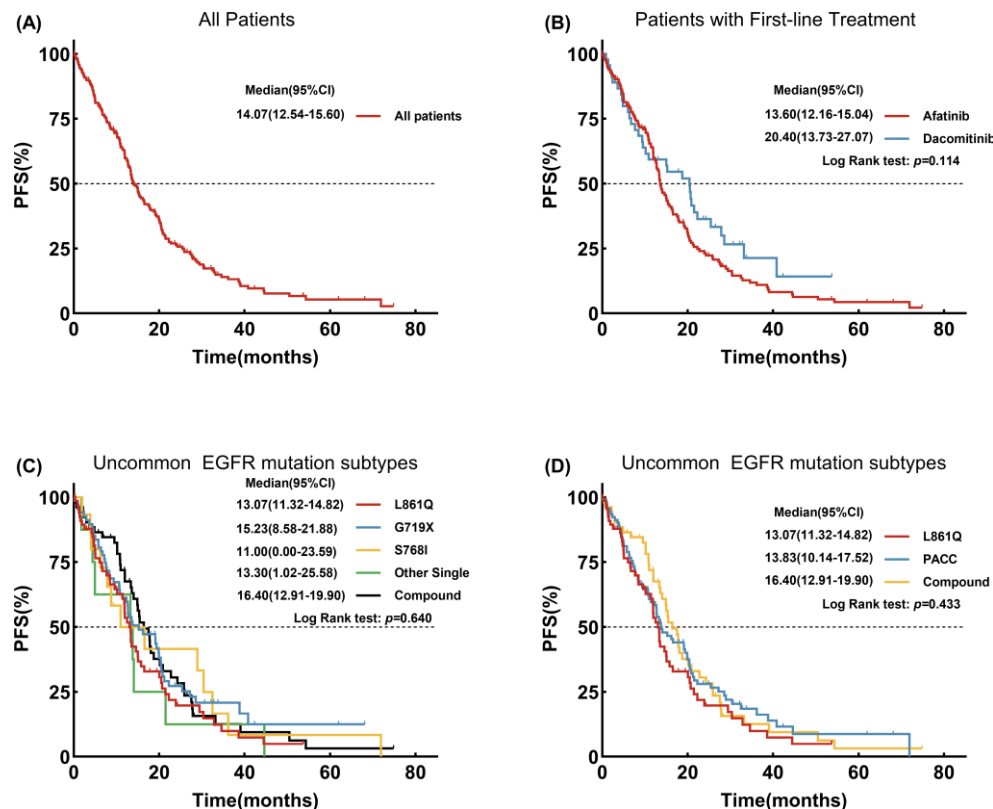
ORR; 106 partial responses

89.8%

disease control rate

PR + SD in 193/215

Kaplan–Meier PFS Curves



Key Findings

- No statistically significant efficacy differences were observed across uncommon EGFR mutation subtypes.
- Structural regrouping (L861Q, PACC, compound) also showed comparable PFS ($p=0.433$).

Subtype Outcomes

Subtype	n	ORR	DCR	mPFS
L861Q	68	51.5%	85.3%	13.07 mo
G719X	69	56.5%	94.2%	15.23 mo
S768I	16	25.0%	93.8%	11.00 mo
Other single	9	66.7%	88.9%	13.30 mo
Compound	53	41.5%	88.7%	16.40 mo

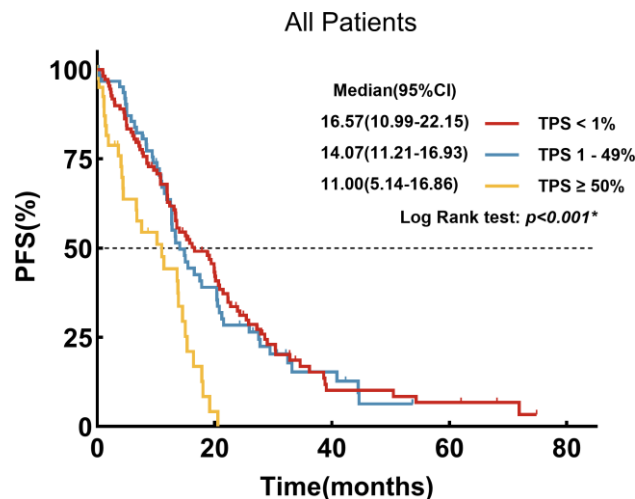
No statistically significant differences were observed across subtype groups (ORR $p=0.102$; DCR $p=0.463$; PFS $p=0.640$).

Interpretation

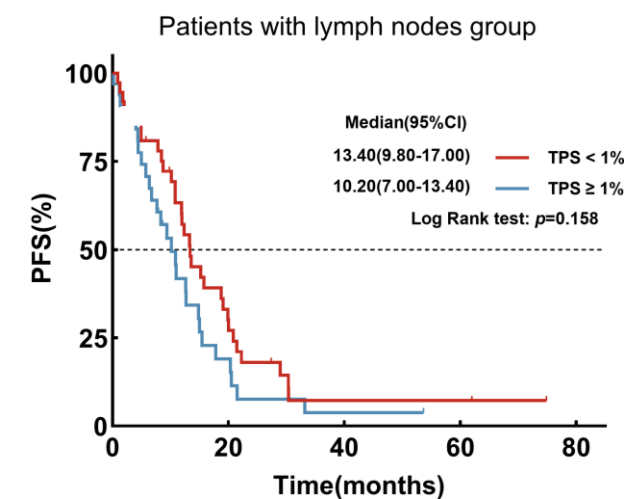
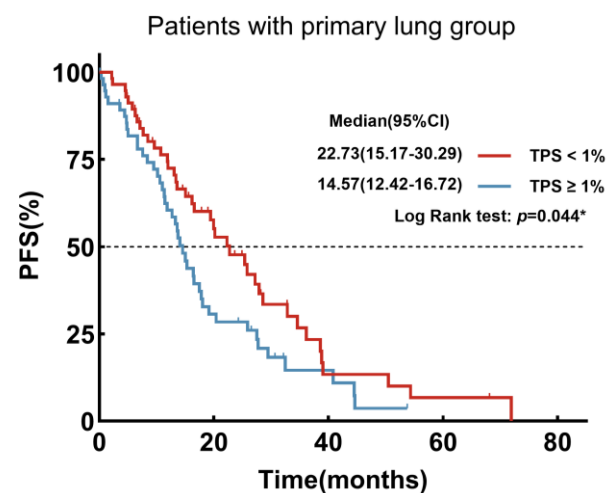
- Numerical differences were seen, but subtype alone did not reliably stratify benefit from second-generation EGFR-TKIs.
- Additional biomarkers beyond EGFR subtype are needed for risk stratification.

PD-L1 expression, tissue sampling site, and take-home messages

PFS by PD-L1 Expression



Exploratory Analysis by Sampling Site



PFS Predictors

- TPS ≥ 50% was independently associated with shorter PFS (HR 2.359 vs TPS < 1%).
- Bone metastasis remained an adverse factor (HR 1.417).
- Age ≥ 65 years was associated with longer PFS (HR 0.699).

Results Summary

- Median PFS decreased with increasing PD-L1 expression: 16.57 → 14.07 → 11.00 months ($p < 0.001$).
- ORR and DCR were not significantly different across PD-L1 groups.
- Primary-tumor PD-L1, but not lymph-node PD-L1, was associated with shorter PFS.

Conclusions

- EGFR mutation subtype alone did not clearly discriminate outcomes.
- PD-L1 provided prognostic information beyond EGFR subtype.
- Tissue sampling site should be considered when interpreting PD-L1 for risk stratification.

LIMITATIONS

Retrospective dual-center design; small mutation and site subgroups; OS immature; no paired primary-node PD-L1 testing; co-occurring alterations not systematically analyzed.

ARTICLE, CORRESPONDENCE & DISCLOSURES

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