



P1.192: Postoperative Outcomes by *EGFR* Mutation Subtype in Resected Pathological N1-2 Stage II-III NSCLC

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INTRODUCTION

BACKGROUND

Osimertinib and other EGFR-TKIs have broadened genotype-directed therapy after complete resection and after chemoradiotherapy for stage II-III *EGFR*-mutant NSCLC.

UNRESOLVED ISSUES

- Mutation subtype: Del19 and L858R are biologically distinct, but their prognostic impact after surgery remains uncertain.
- Nodal staging: Clinical staging may underestimate the extent of mediastinal disease in patients with clinically node-positive stage II-III disease.

OBJECTIVE

To compare postoperative outcomes between Del19 and L858R and to evaluate clinical-to-pathologic nodal upstaging, recurrence patterns, and postrecurrence outcomes.

STUDY OVERVIEW & METHODS

Multicenter Retrospective Study

2012-2020
Data from four Japanese institutions
(UOEH, Nagoya University, Nara Medical University, Kagoshima University)



66 patients
Analytic Cohort

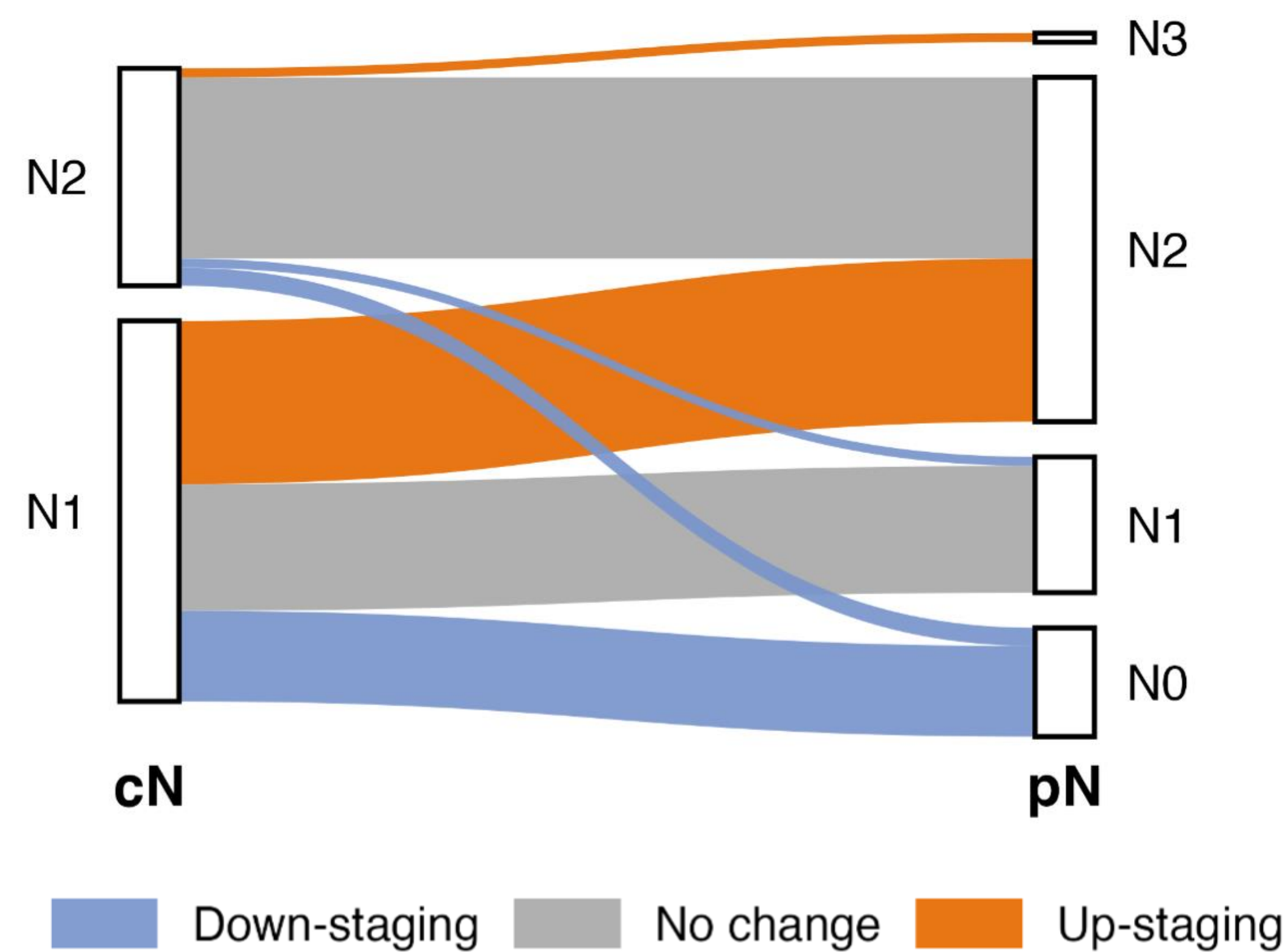
• Clinical N1-2 Stage II-III EGFR-Mutant

Characteristic	n (%)
Del19	33 (50.0)
L858R	28 (42.4)
Uncommon variants	5 (7.6)
Clinical N1 / N2	42 / 24
Pathologic N2	38 (57.6)
Adenocarcinoma	56 (84.8)
R0 resection	48 (72.7)
Lobectomy	54 (81.8)

• Endpoints and analysis

OS and PFS were measured from the date of surgery.
Primary comparison: Del19 versus L858R in clinical and pathologic cohorts.
Exploratory outcomes: nodal migration, recurrence sites, first treatment after recurrence, and postrecurrence survival.
Kaplan-Meier, log-rank tests, and multivariable Cox models

Frequent Nodal Upstaging (Clinical to Pathological N)



42.9%

cN1 → pN2 upstaging

- 42.9% of cN1 Patients Upstaged to pN2
- Substantial nodal migration suggests clinical staging frequently underestimates disease extent in *EGFR*-mutant NSCLC.
- Pathologic assessment revealed a high burden occult Mediastinal disease.

Nodal stage cross-tabulation

Clinical N	pN0	pN1	pN2	pN3	Total
cN1	10	14	18	0	42
cN2	2	1	20	1	24
Overall	12	15	38	1	66

Percentages within cN category: cN1→pN2 42.9%; cN2→pN2 83.3%.

Interpretation and clinical implication

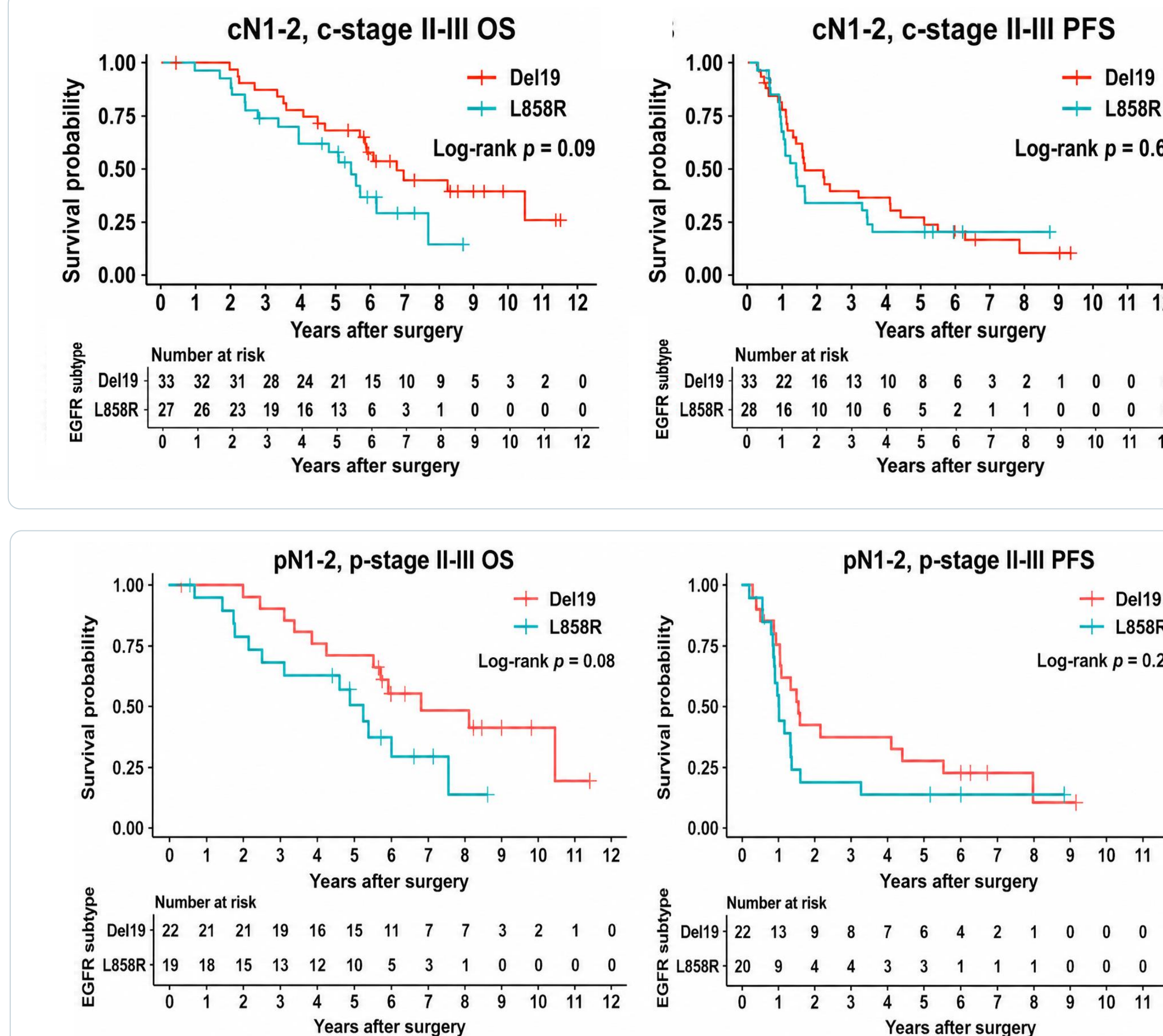
Clinical-stage-only analyses may underestimate nodal burden and dilute mutation-specific prognostic signals.

Upstaging was observed across participating institutions rather than being driven by a single center.

Pathologic reclassification provides a more precise framework for postoperative risk assessment.

In clinically node-positive *EGFR*-mutant NSCLC, rigorous mediastinal staging and systematic nodal assessment should remain central.

Worse Prognosis In L858R Patients



Cox model summary: L858R versus Del19

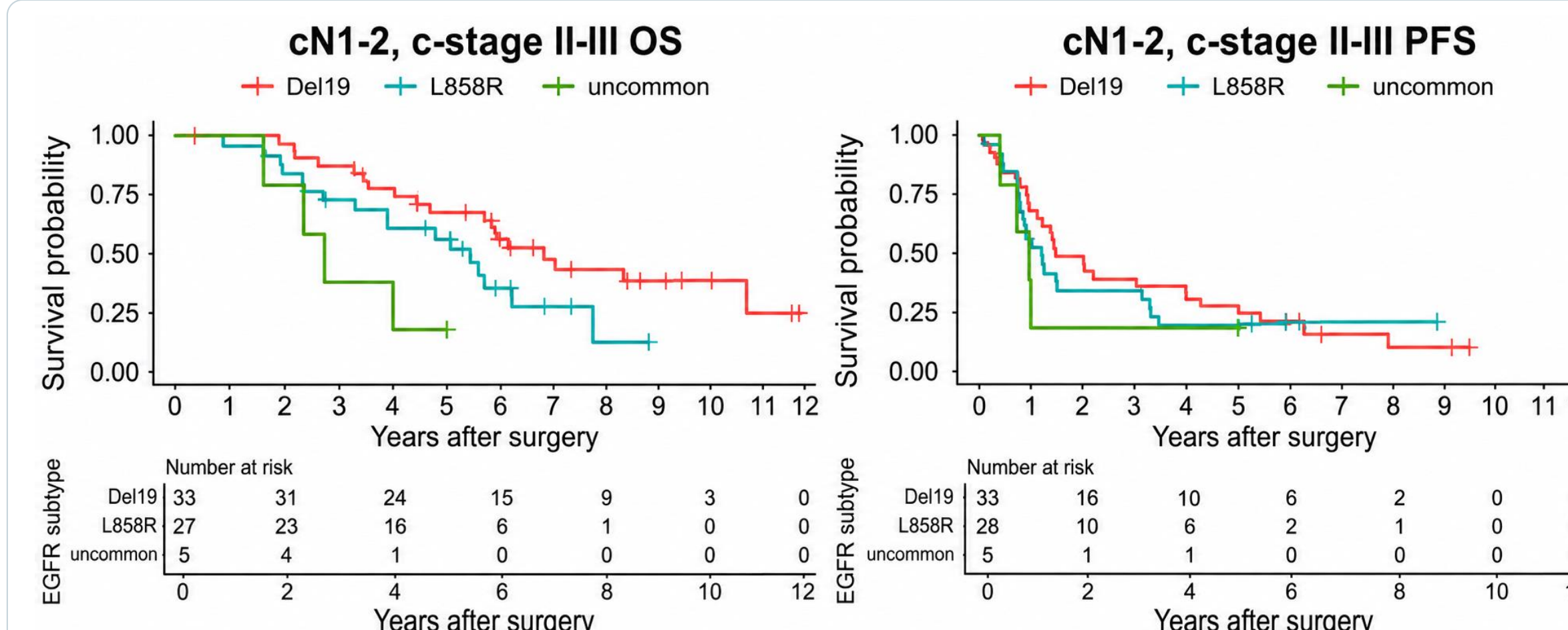
Analysis	Adjusted OS HR (95% CI)	P	Adjusted PFS HR (95% CI)	P
Clinical cohort	1.99 (0.97–4.09)	0.062	0.99 (0.54–1.81)	0.965
Pathologic cohort	1.95 (0.85–4.48)	0.117	1.34 (0.66–2.72)	0.420

Pattern: an unfavorable direction for OS with L858R; surgery-to-PFS was not clearly different.

Exploratory clinical-stage subgroups

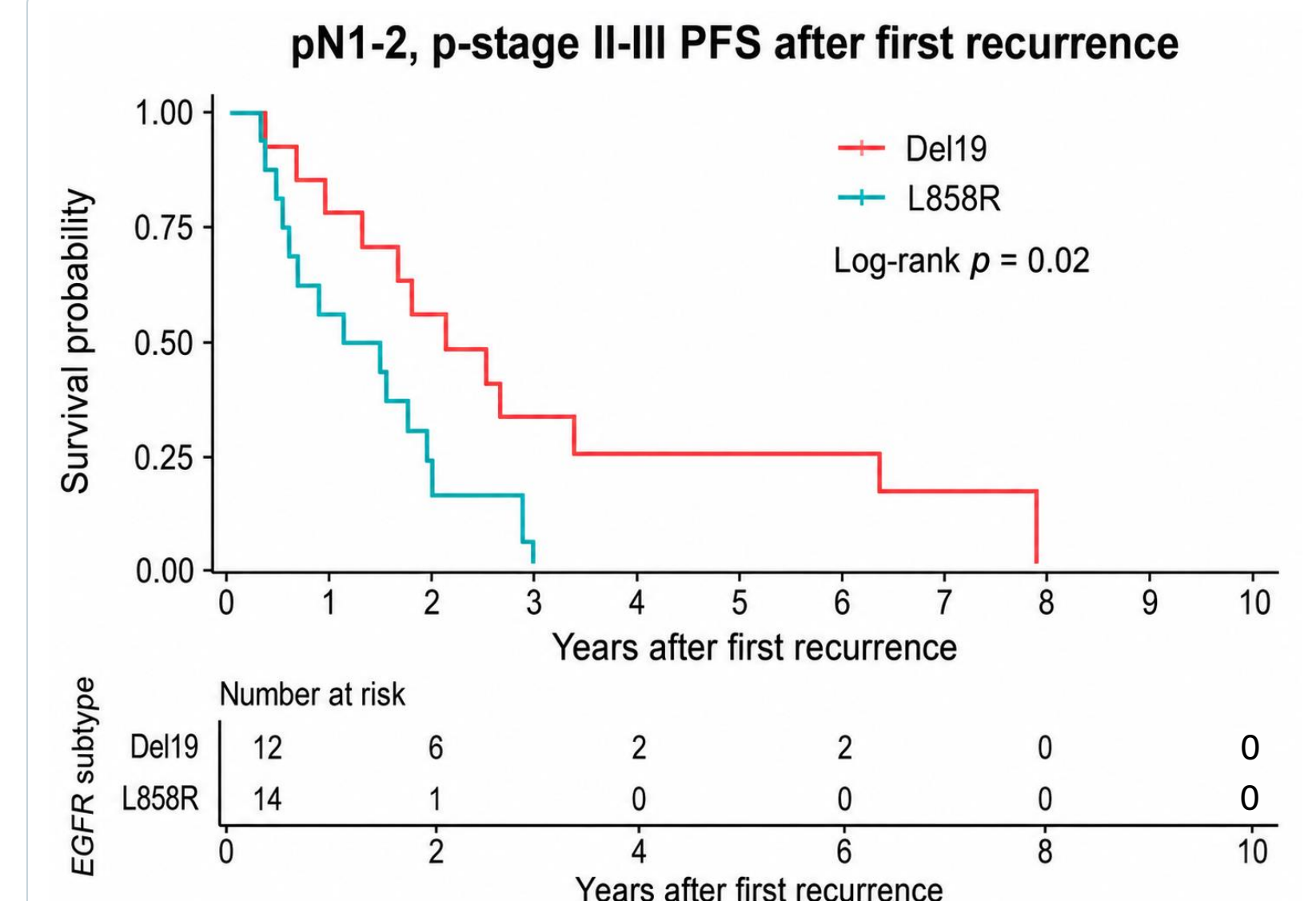
Subgroup	OS p	PFS p
cN2, stage III	0.081	0.215
cN1, stage II	0.513	0.893

Primary message: mutation subtype and pathologic nodal burden provide complementary—not interchangeable—risk information.



Compared to Del19, the OS hazard ratio was 1.99 for L858R (95% confidence interval, 0.97–4.09; $P = 0.06$) and 5.93 for uncommon variants (1.77–19.83; $P = 0.004$). *EGFR* subtype was not associated with PFS.

Post-Recurrence Outcome



Recurrence profile (n = 56)

28.6%

lung

26.8%

lymph nodes

25.0%

brain/meninges

Brain/meningeal recurrence

L858R 37.5% (9/24)

Del19 17.9% (5/28)

First treatments after recurrence: gefitinib and osimertinib, 13 patients each (23.2%).

Postrecurrence interpretation

- Postrecurrence PFS was significantly shorter with L858R.
- Postrecurrence OS was similar ($p = 0.514$).
- Findings are exploratory because recurrence treatment was heterogeneous and molecular data at recurrence were unavailable.

Key messages

- 1 Frequent cN1→pN2 upstaging highlights the limits of clinical staging alone.
- 2 L858R showed a consistently less favorable OS trajectory than Del19.
- 3 Mutation subtype plus pathologic nodal burden may refine postoperative risk assessment.

Limitations

- Retrospective design and modest sample size.
- Heterogeneous perioperative and recurrence treatments.
- Noncentralized testing and incomplete data for some analyses.
- Only five patients had uncommon variants.

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