



P2-278: Clinical Predictors of Second-Line Platinum-Pemetrexed Efficacy After EGFR-TKI Progression in EGFR-Mutant NSCLC

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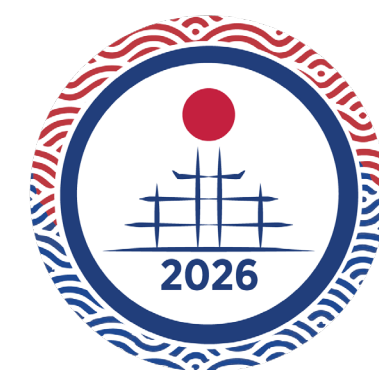
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INTRODUCTION

Background

- Although first-line EGFR tyrosine kinase inhibitor (TKI) therapy is the standard of care for advanced EGFR-mutant non-small cell lung cancer (NSCLC), disease progression invariably occurs.
- Platinum-based chemotherapy combined with pemetrexed remains a key second-line treatment option; however, significant heterogeneity exists in treatment response.

Aim of the Study

- To identify clinical predictors of second-line platinum-pemetrexed efficacy in patients with EGFR-mutant NSCLC following progression on first-line EGFR-TKI therapy.

METHODS

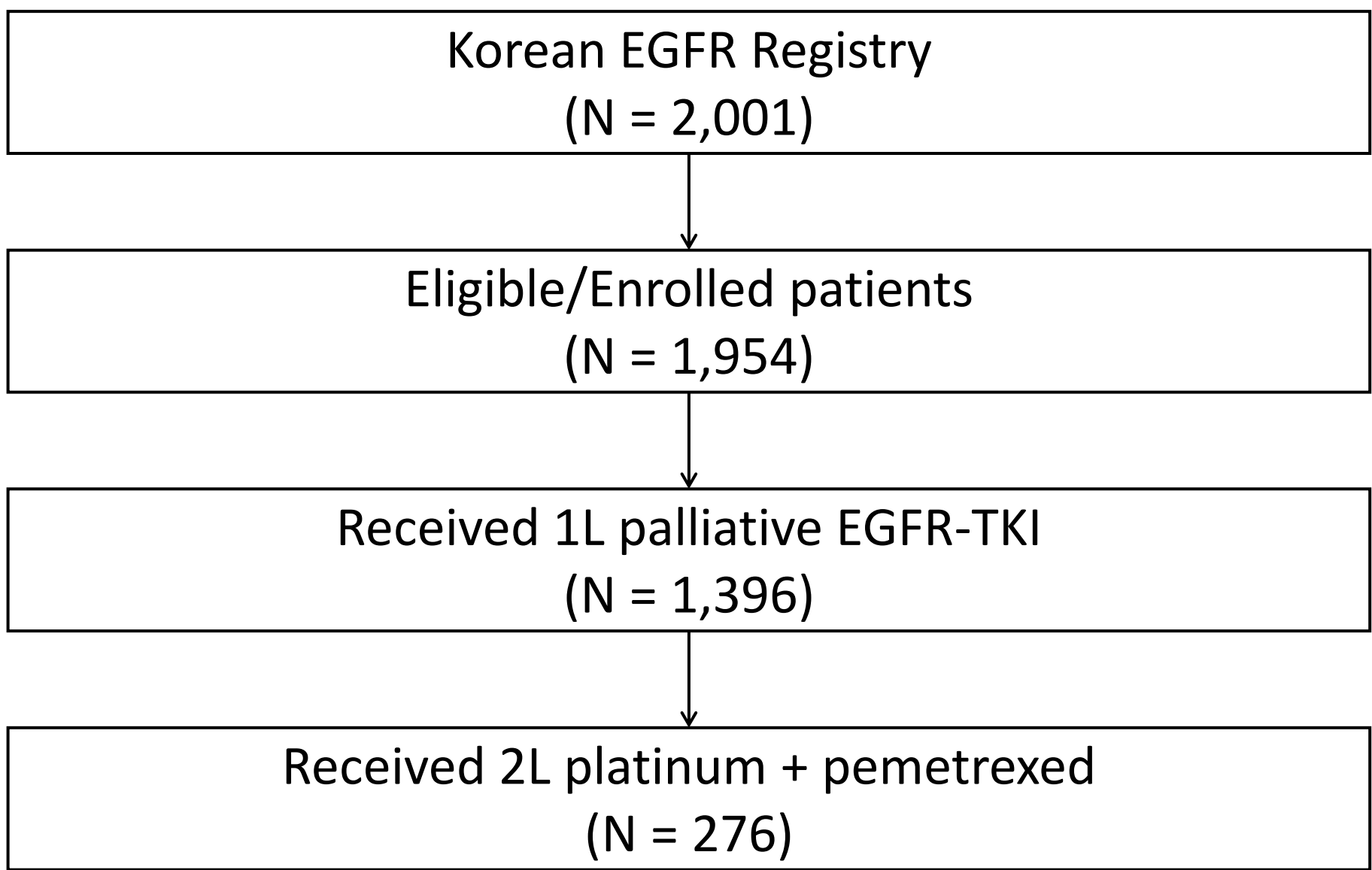
Study Design

- Multicenter, real-world cohort study using the Korean EGFR Registry
- Prospective and retrospective registry from 40 institutions across Korea

Study Population

- Advanced EGFR-mutant NSCLC
- First-line palliative EGFR-TKI therapy
- Subsequent second-line platinum + pemetrexed

Figure. Flowchart of study patients



Outcome & Statistical Analysis

- Primary outcome: PFS from initiation of second-line platinum-pemetrexed
- Survival analysis: Kaplan-Meier method and log-rank test
- Predictor analysis: Univariable and multivariable Cox proportional hazards regression

DISCUSSION AND CONCLUSION

Actionable Take Away Message

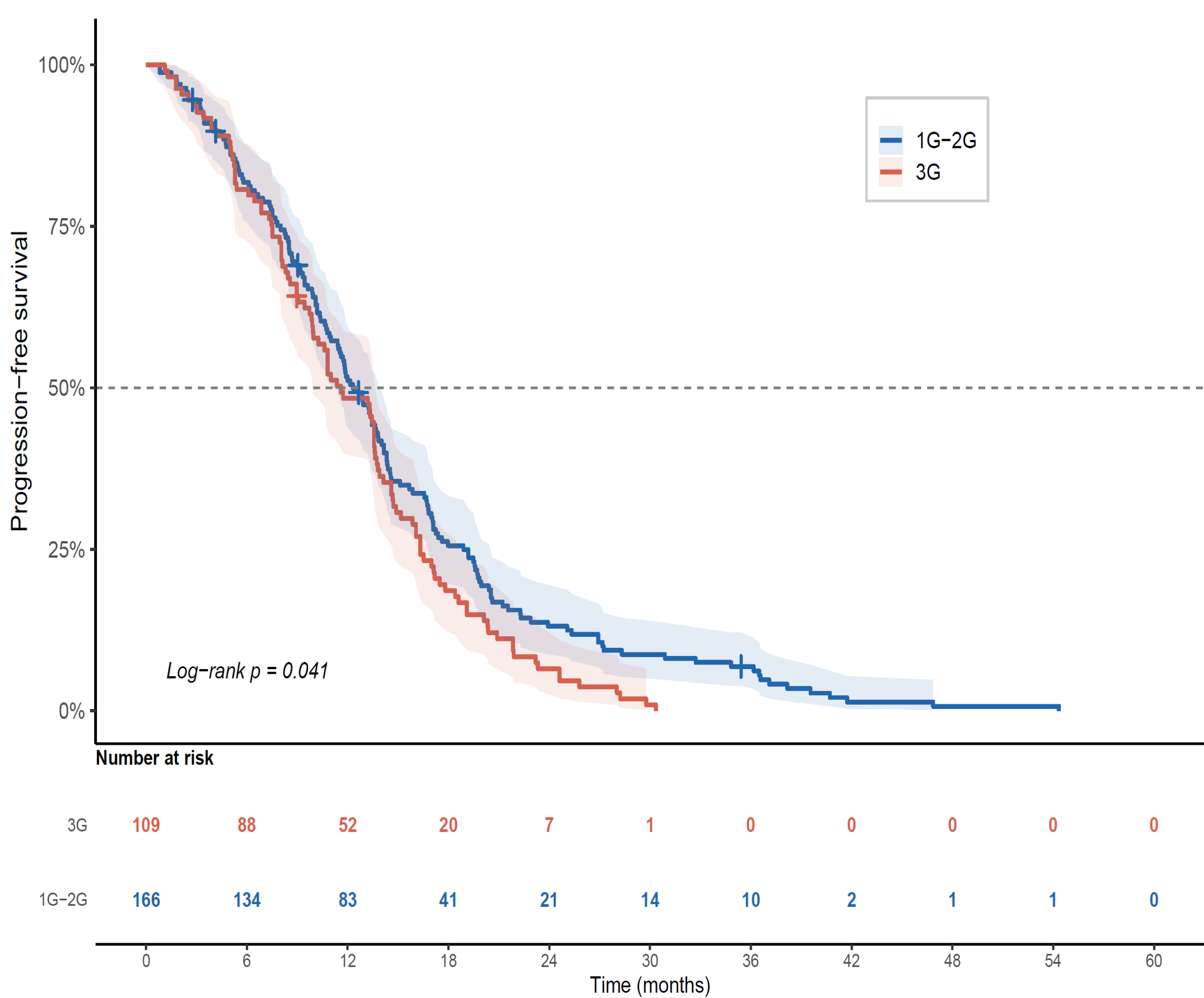
- In this real-world multicenter analysis, second-line platinum-pemetrexed chemotherapy showed heterogeneous outcomes in EGFR-mutant NSCLC following TKI failure.
- Longer first-line EGFR-TKI duration (≥ 12 months) was associated with longer PFS with subsequent platinum-pemetrexed and remained significant in multivariable analysis.
- Patients previously treated with third-generation EGFR-TKIs showed shorter PFS in unadjusted analysis, but TKI generation was not significant in multivariable analysis.
- This finding should be interpreted with caution, as the third-generation TKI group may include a higher proportion of early progressors, while patients with longer TKI benefit may not yet have reached second-line chemotherapy.

Future Direction for Research

- Further analyses with extended follow-up, along with investigation of potential molecular biomarkers, will be needed to better characterize which patients are most likely to benefit from this treatment strategy.

RESULTS

Figure. PFS by 1st Line TKI (1G/2G vs. 3G)



RESULTS

Table. Baseline Characteristics of Study Population

Variable	Total (N=276)
Age	65 (34-86)
Sex	
Male	131 (47.5%)
Female	145 (52.5%)
Smoking status	
Never-smoker	159 (57.6%)
Ever-smoker	116 (42.0%)
ECOG Performance Status	
0-1	246 (89.1%)
2-3	11 (4.0%)
EGFR mutation subtype	
Exon 19 deletion	118 (42.8%)
L858R	124 (44.9%)
Others	34 (12.3%)
1st line TKI generation	
1st Generation (Gefitinib or erlotinib)	33 (12.0%)
2nd Generation (Afatinib or dacomitinib)	132 (47.8%)
3rd Generation (Osimertinib or Lazertinib)	109 (39.5%)
Duration of 1st line TKI	
<12 months	139 (50.4%)
≥12 months	136 (49.3%)
CNS metastasis at baseline	112 (40.6%)
Liver metastasis at baseline	29 (10.5%)
Bone metastasis at baseline	124 (44.9%)
Number of metastatic sites	
≤3	228 (82.6%)
≥4	48 (17.4%)
Progression pattern on TKI	
Extracranial	216 (78.3%)
Intracranial	15 (5.4%)
Extra and intracranial	38 (13.8%)
Unknown	7 (2.5%)
Platinum regimen	
Cisplatin	121 (43.8%)
Carboplatin	154 (55.8%)

Data are presented as n (%) or median (interquartile range). Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; TKI, tyrosine kinase inhibitor; CNS, central nervous system.

Figure. 2nd Line PFS by 1L TKI Duration (<12mon vs ≥12 months)

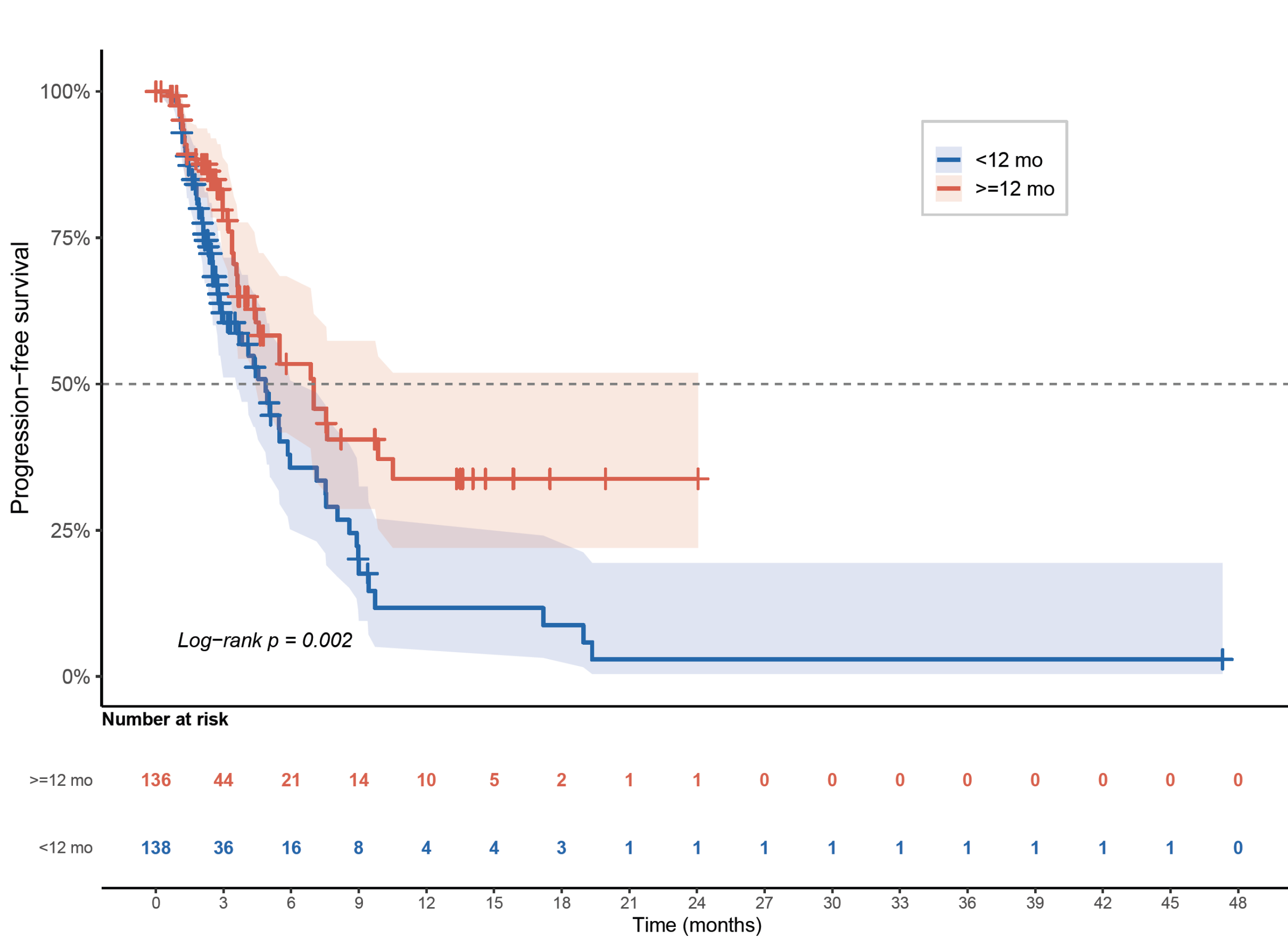
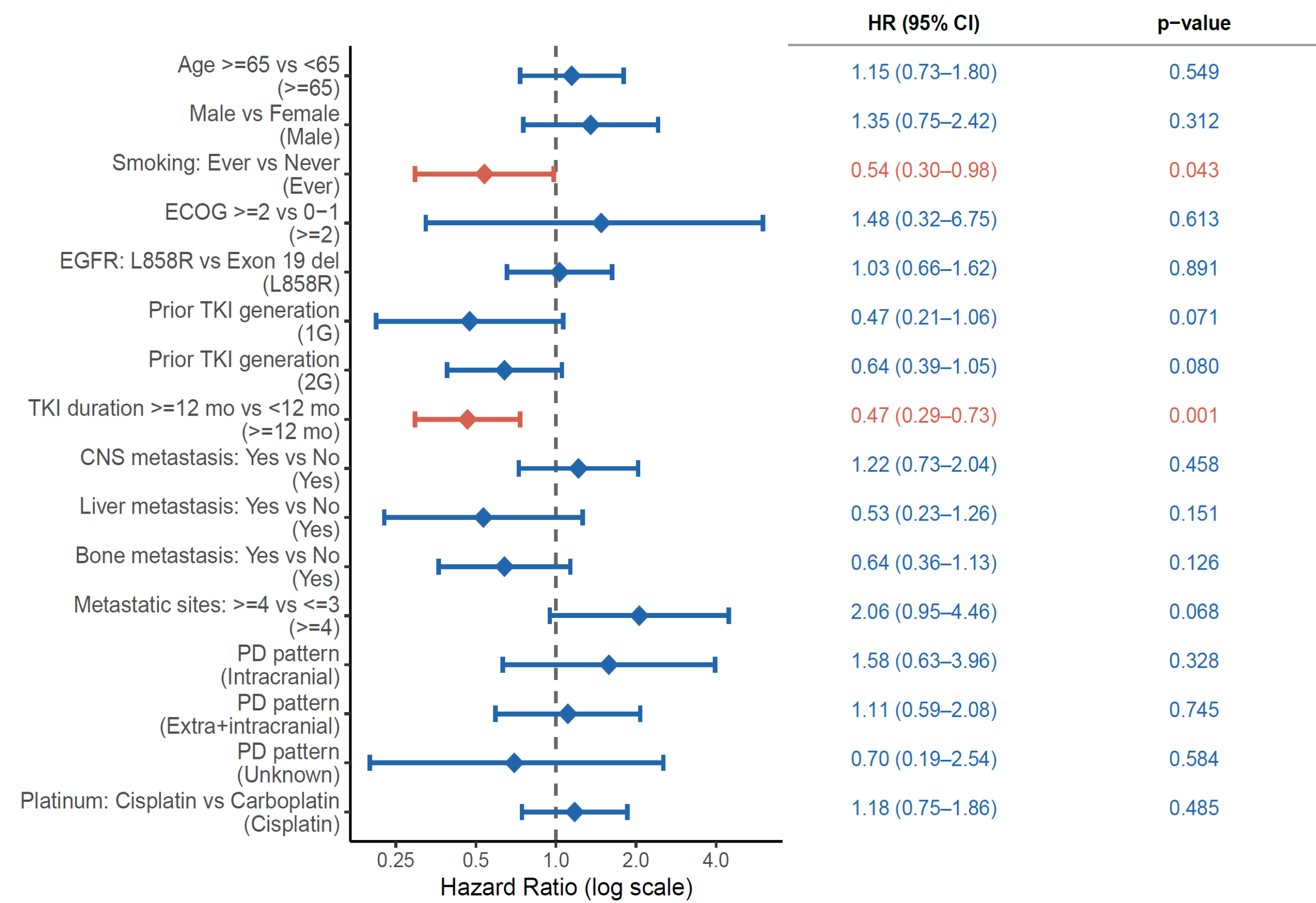


Figure. Subgroup Forest Plot for Predictors of PFS (multivariable)



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