

Comparative Efficacy of Osimertinib and Erlotinib Combination Therapy in EGFR-Mutated NSCLC with Malignant Pleural Effusion

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Background

Non-small cell lung cancer (NSCLC) with EGFR mutations often occurs with malignant pleural effusion (MPE), and previous studies have reported a positive correlation between MPE and EGFR mutations. Patients with EGFR mutations and MPE have poorer overall survival (OS) than those with EGFR mutations alone, underscoring the need for effective treatment strategies.

It remains unclear whether angiogenesis inhibitors are necessary for controlling pleural effusion in patients with EGFR-mutant NSCLC and pleural effusion. We conducted a multicenter retrospective study to verify whether the combination of erlotinib and anti-angiogenic agents contributes more effectively to survival prolongation compared to Osimertinib.

Methods

✓ **Design:** A multicenter retrospective study at 14 institutions in Japan.

✓ **Patients:**

- advanced EGFR-mutant NSCLC according to the TNM classification, 8th edition.
- who received either Osimertinib or erlotinib plus bevacizumab or erlotinib plus ramucirumab as first- or second-line treatment between November 2009 and October 2023.
- with pleural effusion at the start of treatment.
- who underwent drainage or pleurodesis for pleural effusion were included.

✓ The data cut-off date for follow-up was 2 July 2025.

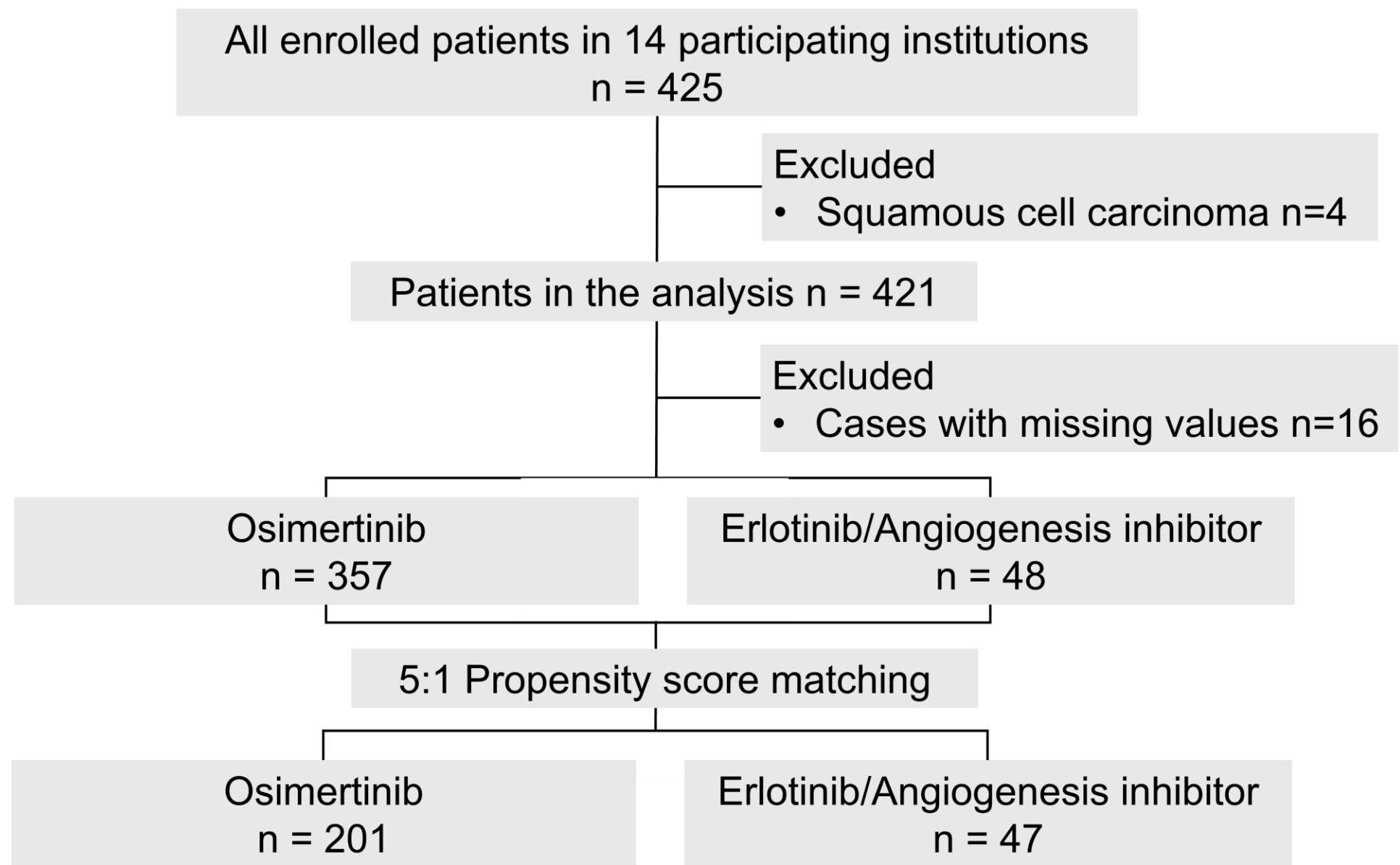


Table 1. Patient Characteristics

After propensity score matching	Osimertinib n=201 (%)	Erlotinib/angiogenesis inhibitor n=47 (%)	p value
Age, years [median, IQR]	74 [67-79]	72 [64.5-75.5]	0.11
Men	74 (37)	19 (40)	0.74
ECOG PS 0-1	176 (88)	40 (85)	0.63
Current/former smoker	70 (35)	18 (38)	0.74
Histology			
Adenocarcinoma	200 (99.5)	47 (100)	> 0.99
EGFR mutation			
exon19 deletion	83 (41)	16 (34)	0.41
exon21 L858R	118 (59)	31 (66)	
Stage			
IV / Recurrence	183 (91)/18 (9)	44 (94)/3 (6)	0.77
T790M mutation	19 (9)	1 (2)	0.15
Brain metastasis	51 (25)	11 (23)	0.85
Pleural effusion			
small amount	89 (44)	22 (47)	0.87
large amount	112 (56)	25 (53)	
Pleurodesis before treatment	40 (20)	8 (19)	0.84

Table 2. Adverse events of grade 3 or higher in the overall cohort

	Osimertinib N=373 (%)	Erlotinib/BEV N=19 (%)	Erlotinib/RAM N=29 (%)	P
ALL	77 (21)	6 (33)	12 (41)	0.02
Hematologic AEs				
Neutropenia	3 (0.8)	0 (0)	0 (0)	
Anemia	0 (0)	0 (0)	1 (3)	
Thrombocytopenia	1 (0.3)	0 (0)	0 (0)	
Non-hematologic AEs†				
Pneumonitis	29 (8)	1 (5)	1 (3)	
Liver dysfunction	8 (2)	1 (5)	4 (14)	
Diarrhea	8 (2)	0 (0)	3 (10)	
Rash	5 (1)	1 (5)	2 (7)	
Renal dysfunction	5 (1)	0 (0)	0 (0)	
Pneumonia	4 (1)	0 (0)	0 (0)	
Anorexia	3 (0.8)	0 (0)	0 (0)	
Heart failure	3 (0.8)	0 (0)	0 (0)	
Fatigue	2 (0.5)	0 (0)	0 (0)	
Elevated CPK	2 (0.5)	0 (0)	0 (0)	
Hyponatremia	2 (0.5)	0 (0)	0 (0)	

†: Adverse events that occurred in two or more cases.

Results

Figure 1. PFS (A) and OS (B) of propensity score matched cohort

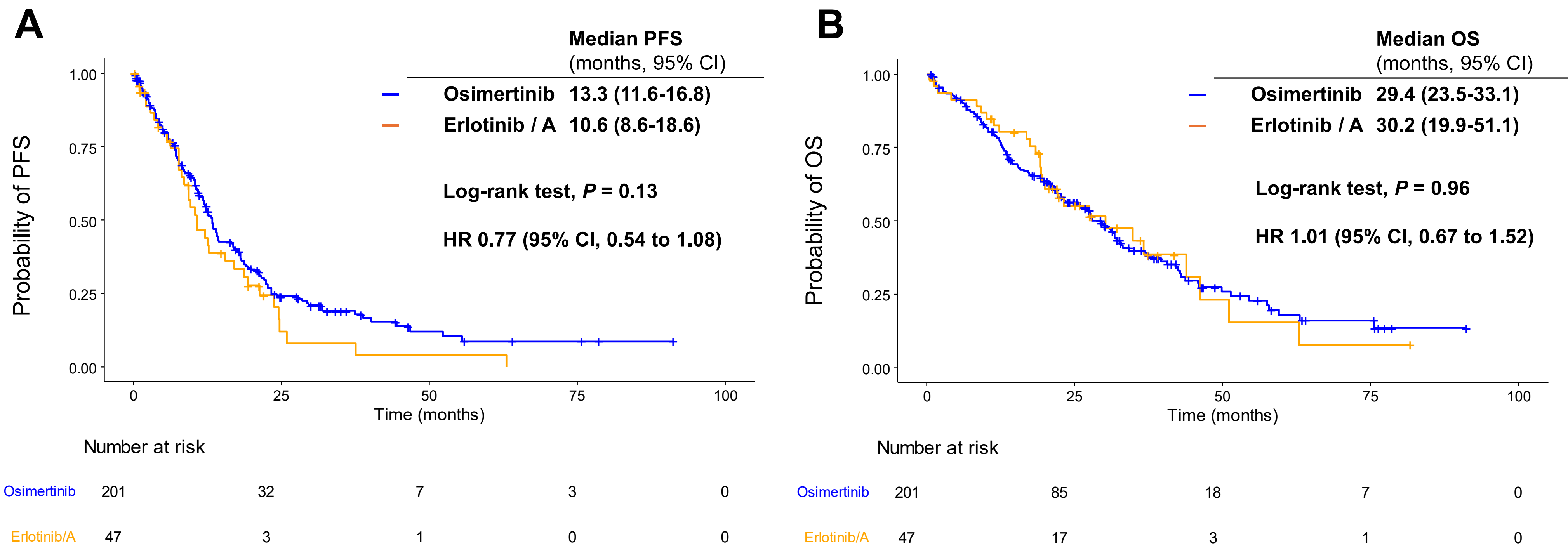


Figure 2. PFS and OS based on EGFR mutation subtype (A, B: exon19, C, D: L858R)

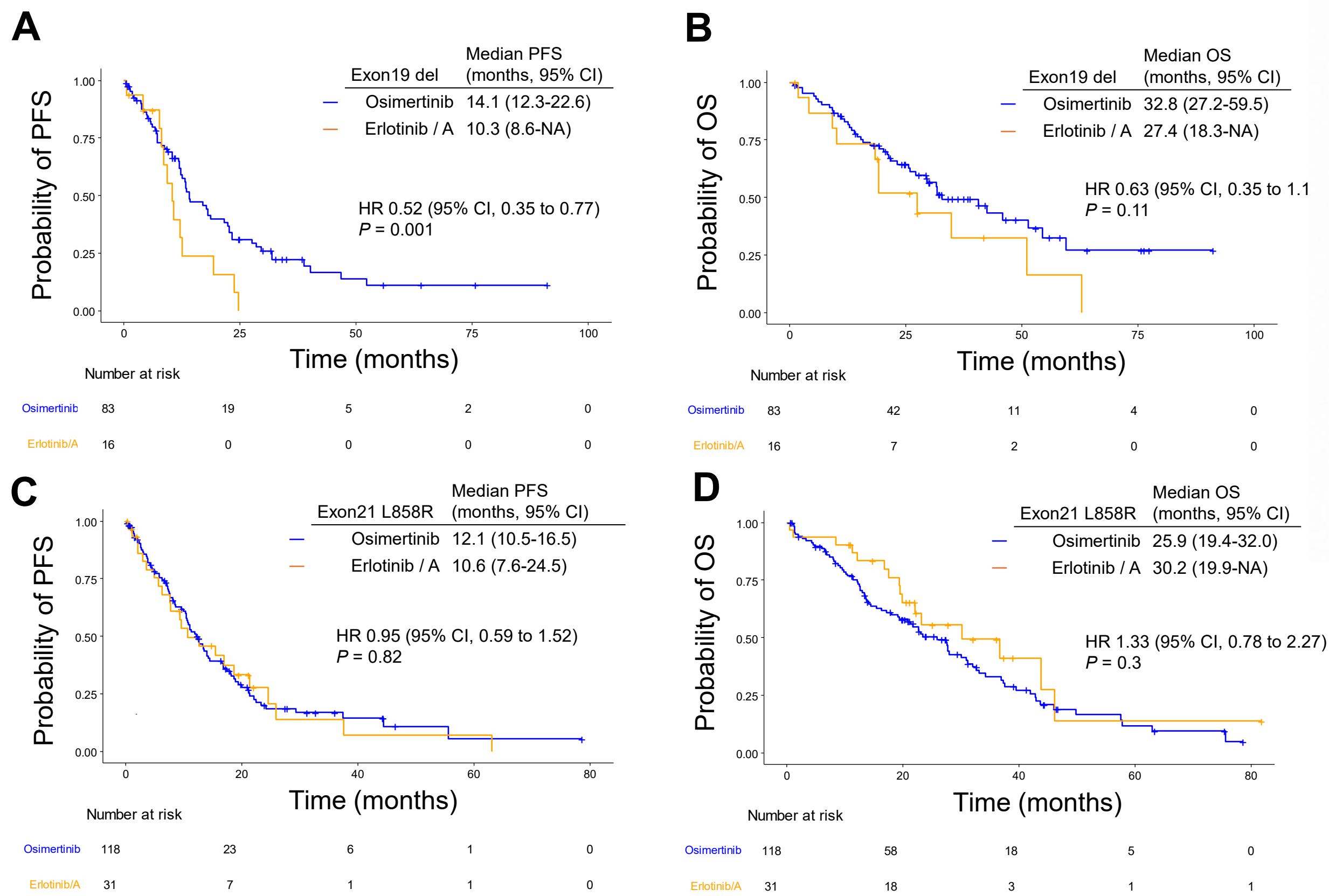


Figure 3. Multivariable Cox Regression

	HR (95% CI)	P	Interaction P
Overall			
PFS	0.87 (0.60–1.25)	0.448	
OS	0.95 (0.63–1.44)	0.825	
Exon 19 deletion			
PFS	0.47 (0.26–0.84)	0.011	0.024
OS	0.58 (0.31–1.09)	0.092	0.079
L858R			
PFS	1.04 (0.64–1.68)	0.870	
OS	1.20 (0.70–2.05)	0.503	

Conclusions

For patients with EGFR-mutated NSCLC and malignant PE, osimertinib showed survival outcomes comparable to those of erlotinib combined with an anti-angiogenic agent. Notably, osimertinib significantly prolonged PFS in patients with exon 19 deletion, suggesting that it may be a preferred therapeutic option for this subgroup.

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