Appendix 1

Inclusion criteria

1) Age of 19 years or more.
2) Previous response to first-line EGFR TKI treatment (CR, PR, or SD for at least 6 months).
3) Progressing after at least four cycles of cytotoxic chemotherapy.
4) Tested negative for T790M mutation but positive for other sensitizing EGFR mutations in tissues, cells, or blood-acquired post-disease progression.
5) At least one measurable lesion per RECIST version 1.1 criteria.
6) Estimated life expectancy of 12 weeks or more.
7) ECOG performance status ≤ 2.
8) Adequate hematologic, renal, and hepatic functions.
9) Brain metastasis patients who are asymptomatic, stable, and not receiving steroid treatment for at least two weeks prior to trial initiation.
10) Those who are willing and able to comply with the clinical trial protocol and have voluntary informed consent signed.

Exclusion criteria

1) Patients diagnosed with other types of cancer in the past 5 years or those who have a history of such cancers.
2) Patients suffering from clinically active interstitial lung disease (ILD), drug-induced ILD, or those with a history of radiation pneumonitis.
3) Individuals with clinically significant cardiac conditions or those who have experienced a myocardial infarction in the past 12 months.
4) Patients currently dealing with active infections or severe systemic illnesses.

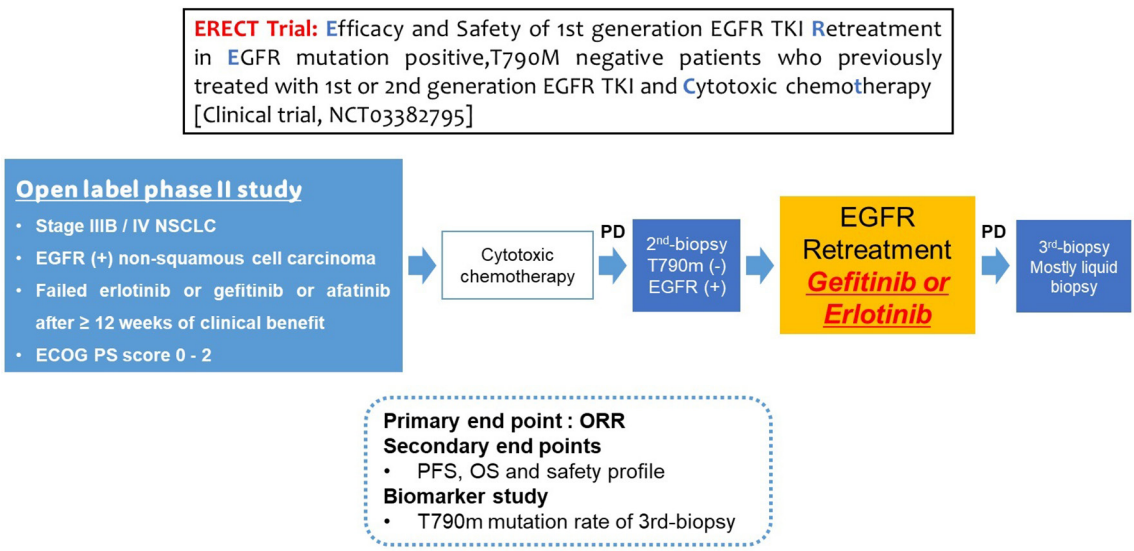

Figure S1 Study design and endpoints.

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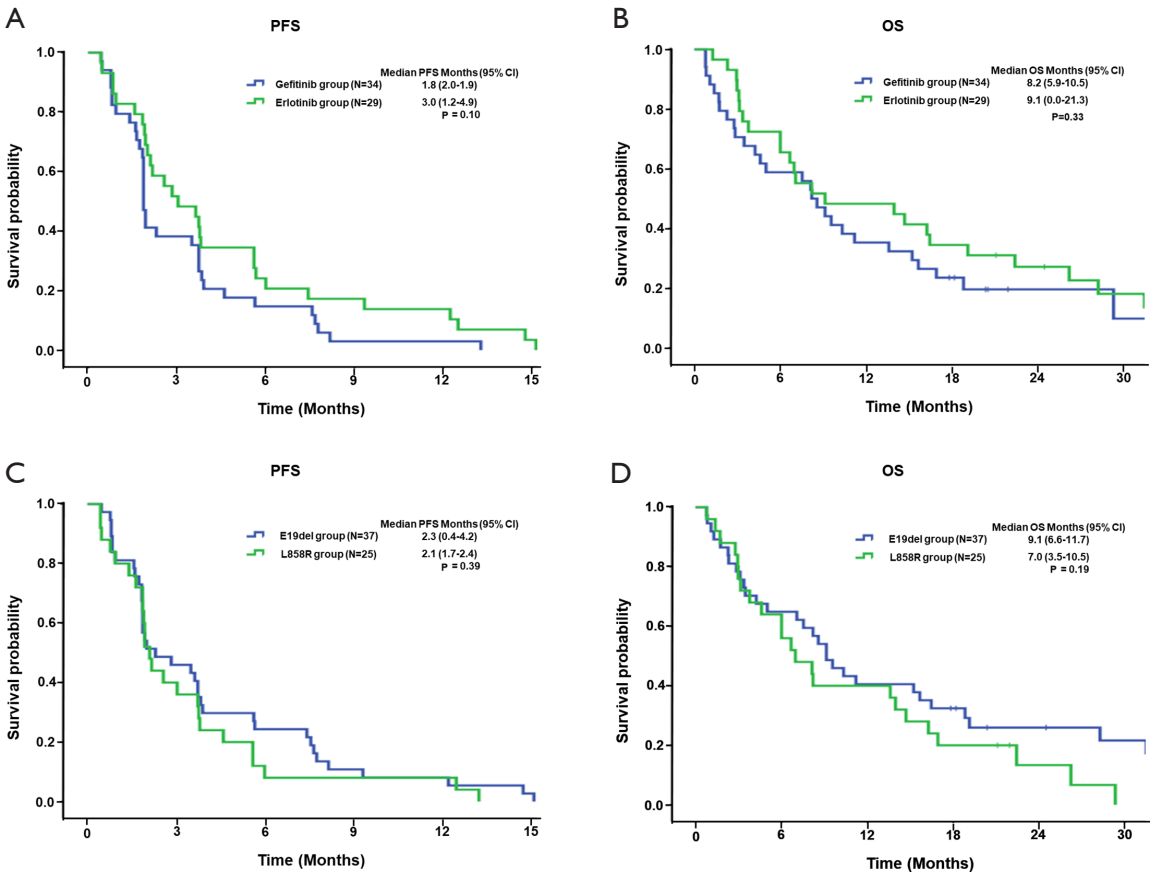

Figure S2 (A) Progression free survival analysis with EGFR drugs. (B) Overall survival analysis with EGFR drugs. (C) Progression free survival by EGFR mutation status. (D) Overall survival by EGFR mutation status.

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Table S1 Baseline characteristics stratified by the presence of T790M (+) conversion

Variables	Total patients (n=60)	T790m positive (n=20)	T790m negative (n=40)	P
Gender				0.85
Male	25 (41.7%)	8 (40.0%)	17 (42.5%)	
Female	35 (58.3%)	12 (60.0%)	23 (57.5%)	
Age, years	64.6±11.0	64.0±10.8	65.0±11.2	0.74
Smoking history				0.27
Never smoker	40 (66.7%)	16 (80.0%)	24 (60.0%)	
Ex-smoker	18 (30.0%)	4 (20.0%)	14 (35.0%)	
Current smoker	2 (3.3%)	0 (0.0%)	3 (5.0%)	
Baseline stage				>0.99
III	2 (3.3%)	19 (95.0%)	39 (97.5%)	
IV	58 (96.7%)	1 (5.0%)	1 (2.5%)	
Histologic type				0.33
Adenocarcinoma	59 (98.3%)	19 (95.0%)	40 (100.0%)	
Adenosquamous carcinoma	1 (1.7%)	1 (5.0%)	0 (0.0%)	
Baseline EGFR mutation type				0.15
E19del	36 (60.0%)	14 (70.0%)	22 (55.0%)	
L858R	23 (38.3%)	5 (25.0%)	18 (45.0%)	
G719X	1 (1.7%)	1 (5.0%)	0 (0.0%)	
Previous treatment line				0.28
2	24 (40.0%)	10 (50.0%)	14 (35.0%)	
3	26 (43.3%)	9 (45.0%)	17 (42.5%)	
4	6 (10.0%)	0 (0.0%)	6 (15.0%)	
5	4 (6.7%)	1 (5.0%)	3 (7.5%)	
Platinum doublet therapy or not	46 (76.7%)	16 (80.0%)	30 (75.0%)	0.76
Comorbidity				
Hypertension	23 (38.3%)	10 (50.0%)	13 (32.5%)	0.19
Diabetes mellitus	15 (25.0%)	4 (20.0%)	11 (27.5%)	0.53
COPD	4 (6.7%)	0 (0.0%)	4 (10.0%)	0.29

Continuous variables are presented as mean ± standard deviation. Categorical variables are expressed as numerical values and percentages. COPD, chronic obstructive pulmonary disease; EGFR, epidermal growth factor receptor.

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