

Figure S1. Kaplan-Meier survival curves for the PFS of patients with EGFR mutation vs. patients without EGFR mutation (median PFS time, 12.2 vs. 11.6 months; 95% CI, 9.7-14.7 vs. 7.7-15.5, respectively; $P=0.369$). HR, hazard ratio; PFS, progression-free survival; EGFR, epidermal growth factor receptor; CI, confidence interval.

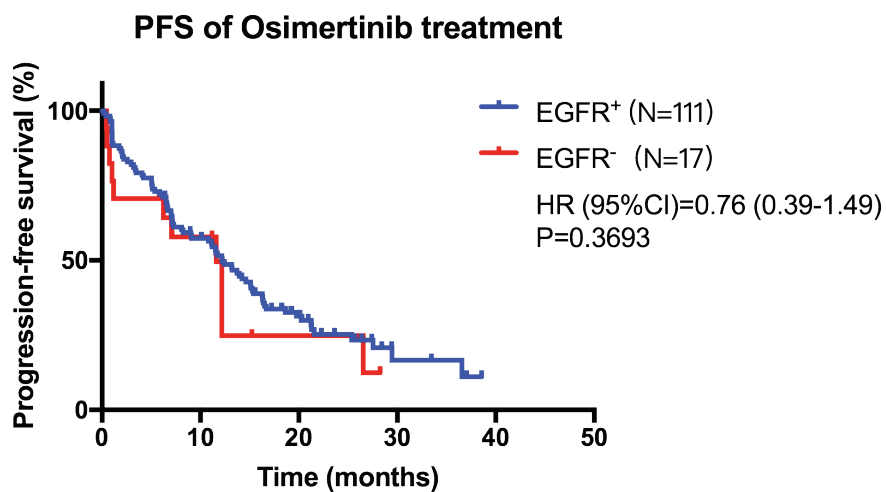


Figure S2. Kaplan-Meier survival curves for the median PFS of all the patients was 12.17 months (95% CI, 10.6-13.8) and the median OS was 29.33 months (95% CI, 27.1-31.6). PFS, progression-free survival; OS, overall survival; confidence interval.

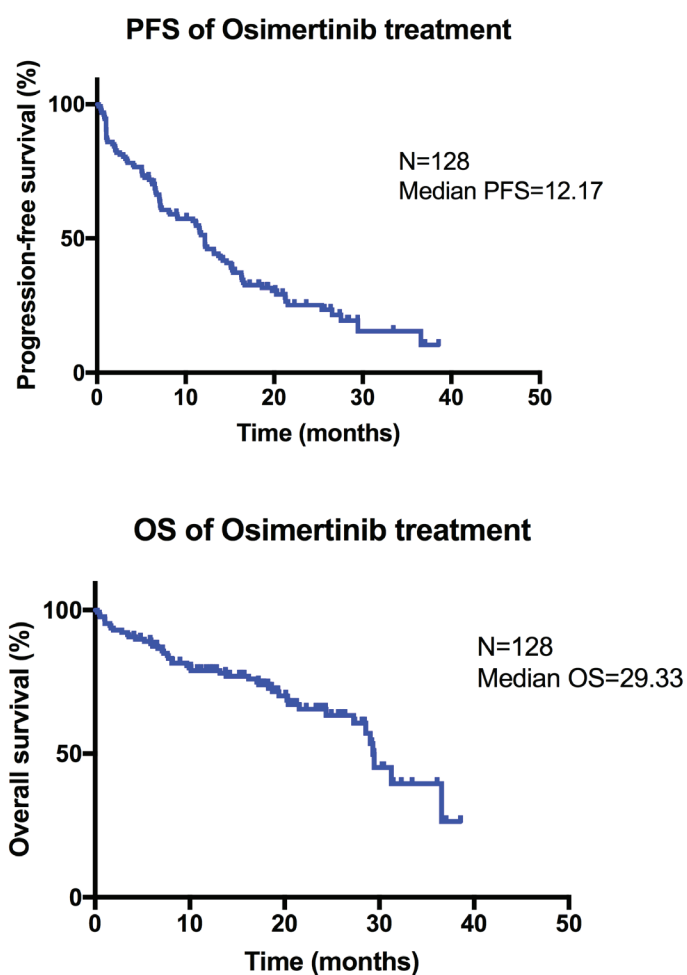


Figure S3. Kaplan-Meier survival curves for the PFS of 14 patients with acquired complex mutations vs. 87 patients with single EGFR mutations (median PFS time, 11.2 vs. 14.6 months; 95% CI, 8.5-13.9 vs. 10.6-18.6, respectively; $P=0.0206$). HR, hazard ratio; PFS, progression-free survival; EGFR, epidermal growth factor receptor; CI, confidence interval.

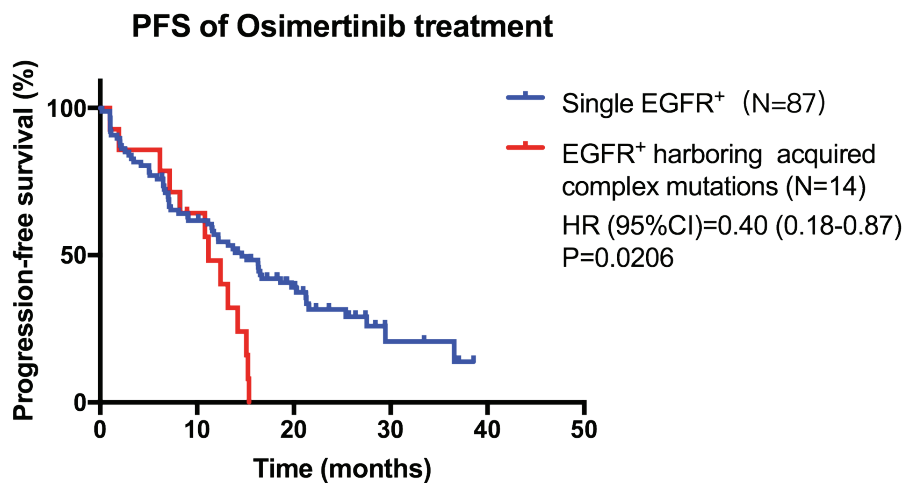


Table SI. Characteristics of T790M⁺ patients with or without complex mutations.

Characteristic	T790M ⁺ (n=41)	T790M ⁺ and complex mutations (n=13)	P-value
Age (range), years	61.5 (34-83)	52 (30-72)	0.779
Sex, n (%)			0.322
Female	27 (50.0)	7 (13.0)	
Male	14 (25.9)	6 (11.1)	
Smoking history, n (%)			0.126
Yes	10 (18.5)	6 (11.1)	
No	31 (57.4)	7 (13.0)	
ECOG performance status at osimertinib treatment, n (%)			0.417
0-1	36 (87.8)	13 (100.0)	
2	3 (7.3)	0 (0)	
3	2 (4.9)	0 (0)	
Objective response rate, n (%)	32 (78.0)	7 (53.8)	0.180
Disease control rate, n (%)	38 (92.7)	10 (76.9)	0.143

Differences between groups were analyzed with a Student's t-test for age and with a χ^2 test/Fisher's exact test for all other variables. ECOG, Eastern Cooperative Oncology Group.

Table SII. Characteristics of patients with or without additional complex- mutations.

Characteristic	EGFR ⁺ (n=87)	EGFR ⁺ and complex-mutations (n=24)	P-value
Median age (range), years	57 (34-83)	51.5 (28-72)	0.094
Sex, n (%)			0.949
Female	55 (63.2)	15 (62.5)	
Male	32 (36.8)	9 (37.5)	
Smoking history, n (%)			0.154
Yes	20 (23.0)	9 (37.5)	
No	67 (77.0)	15 (62.5)	
ECOG performance status at osimertinib treatment, n (%)			0.128
0-1	67 (77.0)	20 (83.3)	
2	15 (17.3)	1 (4.2)	
3	5 (5.7)	3 (12.5)	
Treatment line, n (%)			0.074
First line	4 (4.6)	0 (0)	
Second line	52 (59.8)	21 (87.5)	
Third line and after	31 (35.6)	3 (12.5)	
Objective response rate, n (%)	61 (71.1)	9 (37.5)	0.014
Disease control rate, n (%)	75 (86.2)	17 (70.8)	0.076

Differences between groups were analyzed with a Student's t-test for age and with a χ^2 test/Fisher's exact test for all other variables. EGFR, epidermal growth factor receptor; ECOG, Eastern Cooperative Oncology Group.