

Supplementary

Table S1 Treatment received following PD

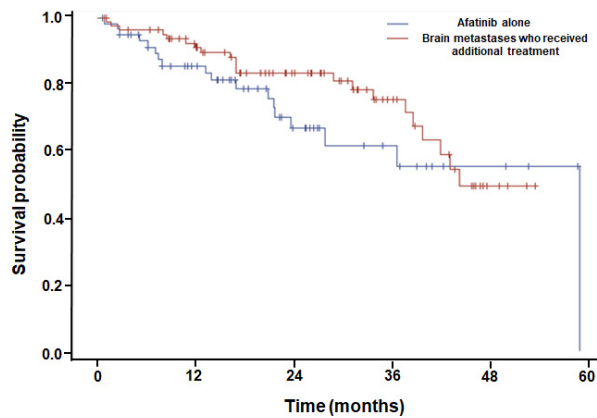
Treatment following PD	N	%
Cytotoxic chemotherapy	90	71.4
Gefitinib, erlotinib	9	7.1
3rd generation EGFR TKI	21	16.7
ALK TKI	1	0.8
IND	5	4.0

PD, progressive disease; EGFR, epidermal growth factor receptor; TKI, tyrosine kinase inhibitor; ALK, anaplastic lymphoma kinase; IND, investigational new drug.

Table S2 Treatment of patients with brain metastasis at time of initial lung cancer diagnosis and their afatinib treatment duration

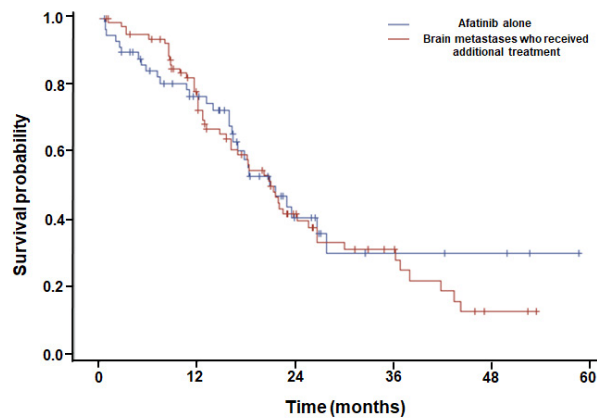
Brain metastasis treatment	N (%)	Afatinib treatment duration (start to end of administration)	
		Mean (SD)	Median [Q1, Q3]
No treatment	60 (41.4)	324.6 (247.4)	308 [125, 464]
Surgery	7 (4.8)	452.1 (300.4)	430 [261, 752]
GKRS	21 (14.5)	457.9 (292.2)	435 [231, 614]
CyberKife	4 (2.8)	259.8 (136.1)	209.5 [168, 351.5]
WBRT	51 (35.1)	290.1 (188.1)	258 [167, 376]
SRS	2 (1.4)	178.0 (8.5)	178 [172, 184]

GKRS, gamma knife radiosurgery; WBRT, whole brain radiation therapy; SRS, stereotactic surgery; SD, standard deviation; Q1, 25th percentile; Q3, 75th percentile.



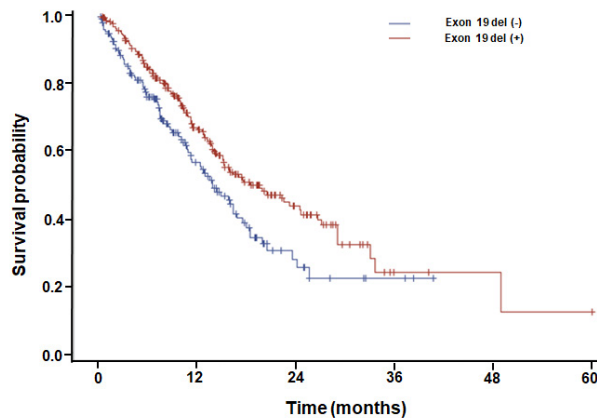
Subgroup	No. of patients	Median OS (95% CI) (months)	36-mo OS rate (%)	60-mo OS rate (%)	P value
Treated	85	30.6 (27.5–NR)	49.6	49.6	0.220
Not treated	60	40.9 (19.2–40.9)	55.6	0	

Figure S1 Kaplan-Meier OS curves in patients with baseline brain metastases who received additional treatment *vs.* afatinib alone. CI, confidence interval; OS, overall survival; mo, months; NR, not reached.



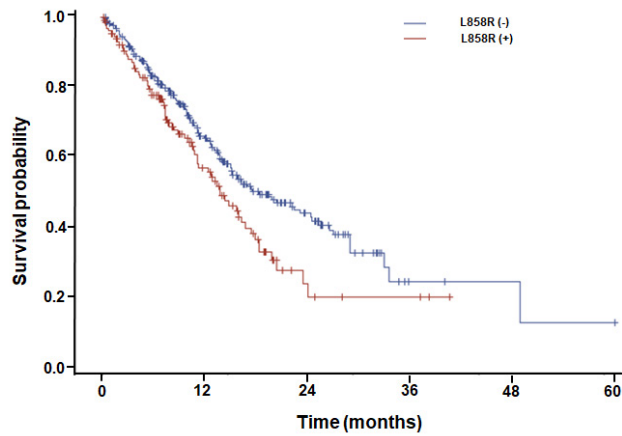
Subgroup	No of patients	Median PFS (95% CI) (months)	36-mo PFS rate (%)	60-mo PFS rate (%)	P value
Treated	85	14.5 (11.2–17.8)	12.4	12.4	0.683
Not treated	60	14.4 (11.4–19.2)	29.9	29.9	

Figure S2 Kaplan-Meier PFS curves in patients with baseline brain metastases who received additional treatment *vs.* afatinib alone. PFS, progression-free survival; CI, confidence interval; mo, months.



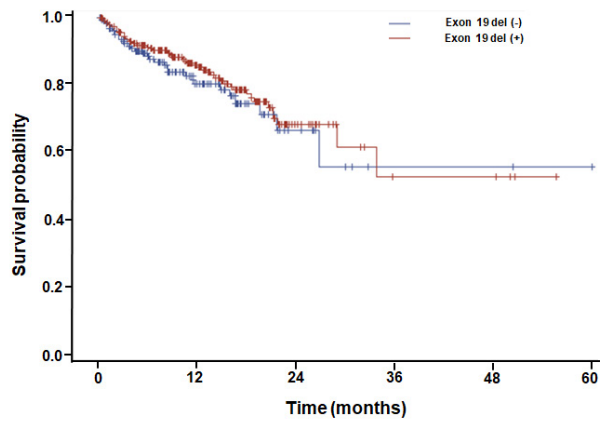
Mutations	No. of patients	Median PFS (95% CI) (months)	36-mo PFS rate (%)	60-mo PFS rate (%)	P value
Del19	252	20.8 (17.1–27.8)	32.1	12.0	0.009
Others	163	15.6 (12.6–19.0)	22.2	22.2	

Figure S3 Kaplan-Meier PFS curves in patients with Del19 mutation *vs.* without. PFS, progression-free survival; CI, confidence interval; mo, months.



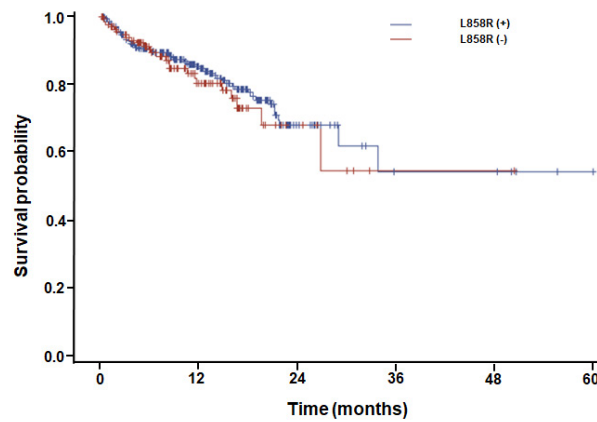
Mutations	No. of patients	Median PFS (95% CI) (months)	36-mo PFS rate (%)	60-mo PFS rate (%)	P value
L858R	129	15.6 (12.6–19.0)	19.4	19.4	0.017
Others	286	19.9 (17.1–27.7)	32.0	12.0	

Figure S4 Kaplan-Meier PFS curves in patients with *vs.* without L858R mutation. PFS, progression-free survival; CI, confidence interval; mo, months.



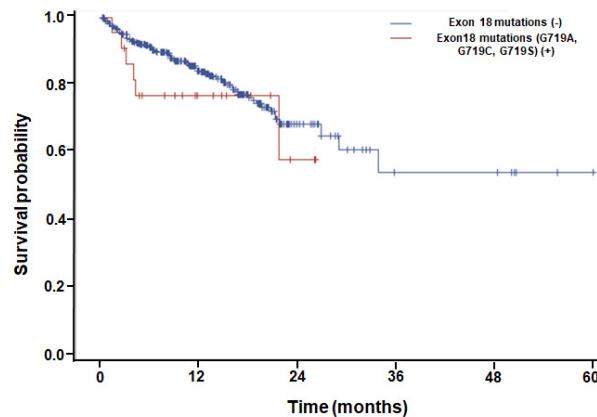
Mutations	No. of patients	Median OS (95% CI) (months)	36-mo OS rate (%)	60-mo OS rate (%)	P value
Del19	256	NR (40.9–NR)	68.1	52.5	0.432
Others	161	NR (37.7–NR)	66.4	55.4	

Figure S5 Kaplan-Meier OS curves in patients with Del19 mutation *vs.* without. OS, overall survival; CI, confidence interval; mo, months; NR, not reached.



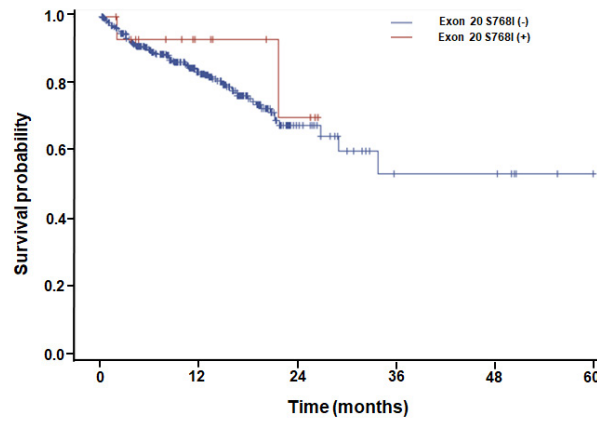
Mutations	No. of patients	Median OS (95% CI) (months)	36-mo OS rate (%)	60-mo OS rate (%)	P value
L858R	137	NR (37.7–NR)	68.0	54.4	0.553
Others	280	NR (40.9–NR)	67.7	53.9	

Figure S6 Kaplan-Meier OS curves in patients with *vs.* without L858R mutation. OS, overall survival; CI, confidence interval; mo, months; NR, not reached.



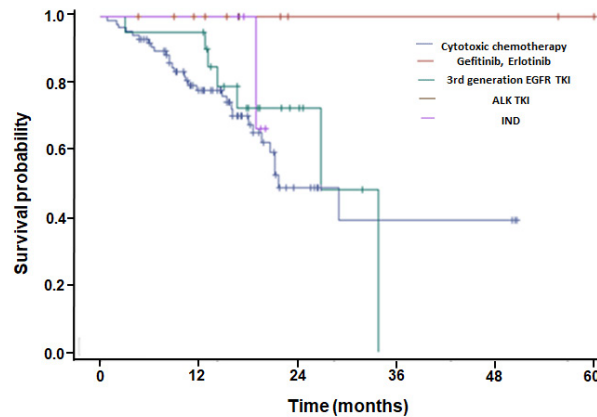
Mutations	No. of patients	Median OS (95% CI) (months)	36-mo OS rate (%)	60-mo OS rate (%)	P value
Exon 18 mutations (G719A, G719C, G719S)	22	NR (30.5–NR)	57.4	57.4	0.315
Others	395	NR (40.9–NR)	68.1	53.7	

Figure S7 Kaplan-Meier OS curves in patients according to the presence or absence of Exon18 mutations (G719A, G719C, G719S). OS, overall survival; CI, confidence interval; mo, months; NR, not reached.



Mutations	No. of patients	Median OS (95% CI) (months)	36-mo OS rate (%)	60-mo OS rate (%)	P value
Exon 20 (S768I)	16	NR (30.5–NR)	70.0	70.0	0.503
Others	401	NR (40.9–NR)	67.6	53.3	

Figure S8 Kaplan-Meier OS curves in patients according to the presence or absence of exon 20 S768I. OS, overall survival; CI, confidence interval; mo, months; NR, not reached.



Treatments	No. of patients	Median OS (95% CI) (months)	36-mo OS rate (%)	60-mo OS rate (%)	P value
Cytotoxic chemotherapy	90	20.5 (27.5–NR)	49.1	39.3	0.239
Gefitinib, Erlotinib	9	NR (NR–NR)	100	100	
3 rd generation EGFR TKI	21	37.7 (23.4–47.6)	72.7		
ALK TKI	1	NR (NR–NR)	100	100	
IND	5	NR (NR–NR)	66.7	66.7	

Figure S9 Kaplan-Meier curves OS in patients according to treatment received after PD. EGFR, epidermal growth factor receptor; TKI, tyrosine kinase inhibitors; ALK, anaplastic lymphoma kinase; IND, investigational new drug; OS, overall survival; CI, confidence interval; mo, months; NR, not reached; PD, progressive disease.