Supplemental Table 1 Patient Disposition and Study Drug Exposure

	Linsitinib + Erlotinib (N = 43) N (%)		Placebo + Erlotinib (N = 44) N (%)	
	Linsitinib	Erlotinib	Placebo	Erlotinib
Drug exposure (d)				
Mean (SD)	199.3 (147.6)	225.2 (156.8)	287.5 (121.5)	311.9 (127.8)
Median (range)	197.0 (15-548)	228.0 (14-576)	279.0 (43-548)	305.0 (43-551)
Dose intensity (mg/dosing days)				
Mean (SD)	273.4 (36.2)	135.5 (21.4)	287.7 (35.2)	140.0 (21.2)
Median (range)	298.0 (203-300)	150.0 (86-150)	299.6 (154-304)	150.0 (67-150)
Dose intensity (mg/days on study)				
Mean (SD)	243.7 (69.7)	129.6 (24.4)	282.3 (39.0)	137.6 (21.8)
Median (range)	266.2 (8-300)	145.3 (73-150)	299.2 (146-300)	149.3 (64-150)
Duration of exposure, d				
≤7 to <21	2 (4.7)	2 (4.7)	0 (0)	0 (0)
≥21 to <42	4 (9.3)	3 (7.0)	0 (0)	0 (0)
≥42 to <63	6 (14.0)	6 (14.0)	1 (2.3)	1 (2.3)
≥63 to <84	2 (4.7)	1 (2.3)	1 (2.3)	1 (2.3)
≥84 to <105	1 (2.3)	1 (2.3)	0 (0)	0 (0)
≥105 to <126	0 (0)	0 (0)	2 (4.5)	2 (4.5)
≥126 to <147	0 (0)	0 (0)	1 (2.3)	1 (2.3)
≥147 to <168	3 (7.0)	2 (4.7)	0 (0)	0 (0)
≥168	25 (58.1)	28 (65.1)	39 (88.6)	39 (88.6)
Dose modification				
Interruptions	26 (60.5)	26 (60.5)	20 (45.5)	21 (47.7)
Reductions	30 (69.8)	15 (34.9)	26 (59.1)	10 (22.7)
Reasons for reduction				
Treatment-related AE	11 (25.6)	9 (20.9)	4 (9.1)	8 (18.2)
Nontreatment-related AE	0 (0)	0 (0)	4 (9.1)	0 (0)
Patient noncompliance	13 (30.2)	0 (0)	12 (27.3)	0 (0)
Toxicity improved	11 (25.6)	8 (18.6)	4 (9.1)	5 (11.4)
Other	17 (39.5)	4 (9.3)	14 (31.8)	4 (9.1)
Discontinued treatment	32 (74.4)		24 (54.5)	
Primary reason for discontinued treatment, n (% of discontinued)				
Disease progression	24 (75.0)		22 (91.7)	
AE	5 (15.6)		0 (0)	
Withdrew consent	2 (6.3)		2 (8.3)	
Medical or ethical	1 (3.1)		0 (0)	

Abbreviations: AE = Adverse event; SD = standard deviation.

Supplemental Table 2 Subgroup Analysis of Progression-Free Survival

Subgroup	Linsitinib + Erlotinib (N = 44)			Placebo + Erlotinib (N = 44)			HR (95% CI)
	N	Events N (%)	Median, mos	N	Events N (%)	Median, mos	
EGFR mutation status							
Exon 19 deletion	26	15 (57.7)	8.4	25	11 (44.0)	12.9	2.09 (0.94-4.64)
Exon 21 single-point mutation	18	8 (44.4)	9.4	19	13 (68.4)	11.7	0.83 (0.34-2.01)
ECOG performance status							
0	21	11 (52.4)	10.4	21	11 (52.4)	13.2	1.03 (0.43-2.44)
1	23	12 (52.2)	7.1	23	13 (56.5)	11.7	1.91 (0.86-4.24)
Age group, years							
≤65	29	15 (51.7)	8.2	32	14 (43.8)	16.1	1.51 (0.72-3.19)
>65	15	8 (53.3)	8.4	12	10 (83.3)	10.4	1.35 (0.49-3.73)
Gender							
Male	14	7 (50.0)	10.4	12	8 (66.7)	16.1	1.59 (0.50-5.04)
Female	30	16 (53.3)	8.2	32	16 (50.0)	12.5	1.63 (0.80-3.34)
Race							
Asian	20	12 (60.0)	8.2	16	8 (50.0)	11.0	1.48 (0.59-3.69)
Other	24	11 (45.8)	8.5	28	16 (57.1)	12.9	1.42 (0.66-3.09)
Cigarette smoking history							
Current or former smoker	11	4 (36.4)	13.8	12	10 (83.3)	9.7	0.58 (0.18-1.86)
Never smoked	33	19 (57.6)	8.4	32	14 (43.8)	12.9	1.96 (0.97-3.96)
Histology							
Adenocarcinoma	41	20 (48.8)	8.5	42	22 (52.4)	12.9	1.28 (0.69-2.37)
Other	3	3 (100)	1.5	2	2 (100)	5.7	3.35 (0.34-33.4)

Abbreviations: CI = Confidence interval; ECOG = Eastern Cooperative Oncology Group; EGFR = epidermal growth factor receptor; HR = hazard ratio.