Online Supplementary Tables

Online Supplementary Table S1. EGFR-TKI Treatment

Dose reduction of EGFR-TKI N, %		
Dose reduction performed	192	33.3
No dose modification	384	66.5
Unknown	1	0.2

EGFR, epidermal growth factor receptor; TKI, tyrosine kinase inhibitor.

Online Supplementary Table S2. Patient Characteristics of Each Study Group

Characteristics	Group (number, %)				
	A	B	C	D	E
	(N = 168)	(N = 186)	(N = 97)	(N = 96)	(N = 30)
TKI agent					
Gefitinib	160 (95.2)	167 (89.8)	91 (93.8)	82 (85.4)	29 (96.7)
Erlotinib	8 (4.8)	19 (10.2)	6 (6.2)	14 (14.6)	1 (3.3)
Gender					
Men/women	52/116	62/124	21/76	29/67	13/17
	31.0/69.0	33.3/66.7	21.7/78.4	30.2/69.8	43.3/56.7
Age (years)					
Median	67	68.5	69	75	71
Range	38-93	31-88	27-93	45-89	57-88
PS					
0	45 (26.8)	68 (36.6)	32 (33.0)	27(28.1)	16 (53.3)
1	75 (44.6)	80 (43.0)	42 (43.3)	40 (41.7)	9 (30.0)
2	27 (16.1)	23 (12.4)	16 (16.5)	15 (15.6)	3 (10.0)
3	16 (9.5)	11 (5.9)	6 (6.2)	11 (11.5)	1 (3.3)
4	5 (3.0)	4 (2.2)	1 (1.0)	1 (1.0)	0 (0)
Unknown	0 (0)	0 (0)	0 (0)	2 (2.1)	1 (3.3)
Cancer staging					
IIIA	145 (97.3)	156 (94.5)	78 (97.5)	73 (91.3)	14 (77.8)
IIIB	3 (2.0)	8 (4.8)	2 (2.5)	3 (3.7)	2 (11.1)
IV	1 (0.7)	1 (0.7)	0 (0)	4 (5.0)	2 (11.1)
Site of metastasis					
Bone	92 (37.3)	65 (32.0)	43 (31.8)	44 (37.9)	9 (39.1)
Lung	65 (26.3)	74 (36.4)	51 (37.8)	39 (33.6)	11 (47.8)
Brain	69 (27.9)	46 (22.7)	32 (23.7)	22 (19.0)	2 (8.7)
Liver	21 (8.5)	18 (8.9)	9 (6.7)	11 (9.5)	1 (4.4)

Online Supplementary Table S2. Patient Characteristics of Each Study Group (Continued)

Characteristics	Group (number, %)				
	A	B	C	D	E
	(N = 168)	(N = 186)	(N = 97)	(N = 96)	(N = 30)
Histology					
Adenocarcinoma	165 (98.2)	181 (97.3)	96 (99.0)	95 (99.0)	30 (100)
NSCLC (not otherwise specified)	1 (0.6)	4 (2.2)	1 (1.0)	1 (1.0)	0 (0.0)
Other	2 (1.2)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
EGFR mutation subtype					
Exon 19 deletion	86 (51.2)	93 (50.0)	37 (38.2)	45 (46.9)	18 (60.0)
Exon 21 L858R	77 (45.8)	84 (45.2)	56 (57.7)	45 (46.9)	12 (40.0)
Other	5 (3.0)	9 (4.8)	4 (4.1)	6 (6.2)	0 (0.0)
Smoking status					
Never smoked	102 (60.7)	119 (64.0)	75 (77.3)	67 (69.8)	18 (60.0)
Current smoker	20 (11.9)	11 (5.9)	6 (6.2)	5 (5.2)	12 (40.0)
Previous smoker	44 (26.2)	56 (30.1)	16 (16.5)	24 (25.0)	0 (0.0)
Unknown	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Comorbidity					
COPD	4 (2.4)	6 (3.2)	2 (2.1)	9 (9.4)	1 (3.3)
Hepatic disease	1 (0.6)	3 (1.6)	0 (0.0)	2 (2.1)	1 (3.3)
Interstitial lung disease	1 (0.6)	1 (0.6)	0 (0.0)	1 (1.0)	0 (0.0)
None of the above	162 (96.4)	176 (94.6)	95 (97.9)	84 (87.5)	28 (93.4)
Previous treatment					
None	108 (64.3)	138(74.2)	64 (66.0)	69 (71.9)	17 (56.7)
Surgery	10 (5.9)	16 (8.6)	12 (12.4)	13 (13.5)	9 (30.0)
Radiation	45 (26.8)	25 (13.4)	18 (18.5)	12 (12.5)	1 (3.3)
Surgery + radiation	5 (3.0)	7 (3.8)	3 (3.1)	2 (2.1)	3 (10.0)

COPD, chronic obstructive pulmonary disease; EGFR, epidermal growth factor receptor; NSCLC, non-small-cell lung carcinoma; PS, performance status; TKI, tyrosine kinase inhibitor.

Online Supplementary Table S3. EGFR-TKI Therapy of Each Study Group

Characteristics	Group (number, %)				
	A	B	C	D	E
	(N = 168)	(N = 186)	(N = 97)	(N = 96)	(N = 30)
Best response					
CR	2(1.2)	5(2.7)	0(0.0)	3(3.1)	1(3.3)
PR	109(64.9)	136(73.1)	78(80.4)	45(46.9)	19(63.3)
SD	38(22.6)	24(12.9)	17(17.5)	28(29.2)	7(23.3)
PD	11(6.5)	18(9.7)	2(2.1)	2(2.1)	0(0.0)
NE	8(4.8)	3(1.6)	0(0.0)	17(17.7)	2(6.7)
Unknown	0(0.0)	0(0.0)	0(0.0)	1(1.0)	1(3.4)
Dose reduction and change in EGFR-TKI					
Dose reduction and/or change in schedule	53(31.6)	54(29.0)	44(45.3)	32(30.3)	9(30.0)
None	115(68.4)	132(71.0)	53(54.7)	64(66.7)	20(66.7)
Unknown	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(3.3)
Combined treatment modality during EGFR-TKI					
Surgery	2(1.2)	8(4.3)	1(1.0)	1(1.0)	0(0.0)
Radiotherapy	32(19.0)	22(11.8)	43(44.3)	7(7.3)	4(13.3)
Chemotherapy	2(1.2)	5(2.7)	7(7.2)	0(0.0)	0(0.0)
None	132(78.6)	151(81.2)	46(47.4)	88(91.7)	26(86.7)
Combined treatment location during EGFR-TKI					
Brain	20(48.8)	13(38.2)	22(50.0)	4(44.4)	0(0.0)
Vertebra	7(17.1)	6(17.7)	12(27.3)	4(44.4)	4(100)
Bone (other than vertebra)	11(26.8)	12(35.3)	7(15.9)	0(0.0)	0(0.0)
Primary tumor	2(4.9)	0(0.0)	2(4.5)	1(11.2)	0(0.0)
Mediastinum	0(0.0)	1(2.9)	1(2.3)	0(0.0)	0(0.0)
Liver	0(0.0)	2(5.9)	0(0.0)	0(0.0)	0(0.0)
Pericardium	1(2.4)	0(0.0)	0(0.0)	0(0.0)	0(0.0)

Online Supplementary Table S3. EGFR-TKI Therapy of Each Study Group (Continued)

Characteristics	Group (number, %)				
	A	B	C	D	E
	(N = 168)	(N = 186)	(N = 97)	(N = 96)	(N = 30)
Adverse events (≥ Grade 3)					
Skin					
Grade 3	7(20.6)	10(25.6)	4(14.8)	6(10.7)	1(20.0)
Diarrhea					
Grade 3	0(0.0)	2(5.1)	3(11.1)	3(5.3)	0(0.0)
Liver dysfunction					
Grade 3	24(70.6)	17(43.6)	16(59.3)	24(42.8)	4(80.0)
Grade 4	0(0.0)	0(0.0)	0(0.0)	2(3.6)	0(0.0)
Interstitial lung disease					
Grade 3	1(2.9)	1(2.6)	0(0.0)	7(12.5)	0(0.0)
Grade 4	0(0.0)	0(0.0)	0(0.0)	1(1.8)	0(0.0)
Grade 5	0(0.0)	0(0.0)	0(0.0)	2(5.4)	0(0.0)
Other					
Grade 3	1(2.9)	8(20.5)	4(14.8)	7(12.5)	0(0.0)
Grade 4	1(2.9)	1(2.6)	0(0.0)	2(3.6)	0(0.0)
Grade 5	0(0.0)	0(0.0)	0(0.0)	1(1.8)	0(0.0)

Online Supplementary Table S4. Reasons for Physicians Choosing to Discontinue EGFR-TKI Therapy

Characteristics	Total		Group C	
	N = 536	(%)	n = 87	(%)
RECIST PD	251	46.8	8*	9.2
Clinical PD	242	45.2	86	98.9
Adverse Event	77	14.4	1	1.2
Patient's preference	9	1.7	0	0
Physician's decision	7	1.3	0	0
Other	16	3.0	3	3.5

*EGFR-TKI therapy was discontinued, at the discretion of the attending physicians, in eight patients due to secondary radiological progression after continuation of first radiological progression.

EGFR, epidermal growth factor receptor; PD, progressive disease; RECIST, Response Evaluation Criteria in Solid Tumors; TKI, tyrosine kinase inhibitor.

Online Supplementary Table S5. Details of Clinical Progression

Characteristics	Group A	Group C	Total
	(n = 168)	(n = 97)	
Emergence of symptoms	92 (54.8%)	43 (44.3%)	135 (50.9%)
Deterioration of PS	59 (35.1%)	33 (34.0%)	92 (34.7%)
Threat to major organs	50 (29.8%)	14 (14.4%)	64 (24.2%)
Unequivocal multiorgan progression	46 (27.4%)	43 (44.3%)	89 (33.6%)

PS, performance status