

Supplemental Table for:
Clinical benefit of tyrosine kinase inhibitors in advanced lung cancer with EGFR-G719A and other uncommon EGFR mutations
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Supplemental Table 1. Additional Studies of EGFR Inhibitors in Patients with Advanced Non-Small Cell Lung Cancer with Uncommon (or Rare) *EGFR*

Mutations

Study	Study Type	Study Location	Type of <i>EGFR</i> mutations	Drug(s)	N	Objective response rate (%)	Median PFS, months (95% CI)	Median OS, months (95% CI)
<i>First generation EGFR inhibitors only</i>								
Wu <i>et al</i> , 2011 ¹¹	Retrospective	Taiwan	Uncommon mutations	Gefitinib/ erlotinib	62	48.4	5.0 (0.2 – 37.5)	15.0 (1.1 – 59.3)
De Pas <i>et al</i> , 2011 ¹²	Retrospective	Italy	Rare mutations	Gefitinib/ erlotinib	10	30	Not reported	Not reported
Beau-Faller <i>et al</i> , 2014 ¹³	Observational	France	Rare exon 18 & exon 20 mutations ^a	Gefitinib/ erlotinib	50	15	4.0 (2 – NE)	14.0 (6 – 21)
Keam <i>et al</i> , 2014 ¹⁴	Retrospective	Korea	Rare mutations	Gefitinib/ erlotinib	16	25	1.4 (0.3 – 2.5)	Not reported
Chiu <i>et al</i> , 2015 ¹⁵	Retrospective	Taiwan	G719X/ L861Q/ S768I/ mutations	Gefitinib/ erlotinib	161	41.6	7.7	17.2
Lohinai <i>et al</i> , 2015 ¹⁶	Retrospective	Hungary	Rare mutations	Gefitinib/ erlotinib	20	37	6.2	7.4
Baek <i>et al</i> , 2015 ¹⁷	Retrospective	Korea	Any mutation other than exon 19 del or L858R ^a	Gefitinib/ erlotinib	54	20.4	2.6 (0.0 – 5.4)	12.7 (7.2 – 18.2)

Oyeart <i>et al</i> , 2015 ¹⁸	Retrospective	Belgium	Rare mutations ^a	Gefitinib/ erlotinib	6	33.3	3.0	Not reported
Chen <i>et al</i> , 2016 ¹⁹	Retrospective	China	Exon 20 mutations ^a	Gefitinib/ erlotinib/ icotinib	62	8.1	2.1	13.3
Xu <i>et al</i> , 2016 ²⁰	Retrospective	China	Uncommon mutations ^a	Gefitinib/ erlotinib/ icotinib	95	Not reported	Not reported	18.96 (16.65 – 21.26)
Shi <i>et al</i> , 2017 ²¹	Retrospective	China	Uncommon EGFR mutations ^a	Gefitinib/ erlotinib/ icotinib	30	23.3	7.1	Not reported
Pilotto <i>et al</i> , 2018 ²²	Retrospective	Italy	Any mutation other than exon 19 del or L858R ^a	Gefitinib/ erlotinib	35	25.7	5.2 (2.7 – 10.3)	14.5 (8.1 – 22.5)
Li <i>et al</i> , 2019 ²³	Observational prospective	China	G719X/ L861Q/ S768I/ mutations	Gefitinib/ erlotinib/ icotinib	51	33	7.2	14.3
Kate <i>et al</i> , 2019 ²⁴	Retrospective	India	TKI sensitive single mutation (G719X/ S768I/ L861Q)	Gefitinib/ erlotinib	9	37.5	12.8 (4.7 – 20.9)	Not reported

First AND second generation EGFR inhibitors only

Arrieta <i>et al</i> , 2015 ²⁵	Observational prospective	Mexico, Colombia, Costa Rica	Rare mutations ^a	Gefitinib/ erlotinib/ afatinib	38	32.4	3.9 (1.9 – 5.9)	17.4 (12.9 – 21.8)
Krawczyk <i>et al</i> , 2017 ²⁶	Retrospective	Poland	Rare mutations ^a	Gefitinib/ erlotinib/ afatinib	13	53.8	5.0	22.0

Hunter <i>et al</i> , 2017 ²⁷	Retrospective	UK	Uncommon mutations ^a	Gefitinib/ erlotinib/ afatinib	29	38	8.1	Not reported
Passaro <i>et al</i> , 2019 ²⁸	Retrospective	Italy	<i>EGFR</i> exon 18 mutations	Gefitinib/ erlotinib/ afatinib	42	31	8.3 (4.8 – 11.7)	17.0 (8.2 – 25.7)
<i>First VS. second generation EGFR inhibitors only</i>								
Shen <i>et al</i> , 2017 ³²	Retrospective	Taiwan	Non-classical mutations (alone or in combination)	Gefitinib/ erlotinib VS. Afatinib	21 VS. 13	52.4 VS. 69.2	2.8 (2.1 – 3.4) VS. 18.3 (3.2 – 33.4)	Not reported
Kim <i>et al</i> , 2019 ³³	Retrospective	Korea	Uncommon mutations [excluding / including <i>de novo</i> T790M mutations]	Gefitinib VS. Erlotinib VS. Afatinib	9 / 12 VS. 5 / 5 VS. 10 / 14	44.4 / 33.3 VS. 20 / 20 VS. 80 / 57.1	Not reported / 5.0 VS. Not reported / 6.1 VS. Not reported / NR	Not reported
Lau <i>et al</i> , 2019 ³⁴	Retrospective	Canada	Uncommon mutation subgroup	Gefitinib/ erlotinib VS. Afatinib	7 VS. 9	Not reported	Not reported	32.7 (1.1 – NR) VS. 48.5 (6.4 – NR)
Chang <i>et al</i> , 2019 ³⁵	Retrospective	Taiwan	Non-resistant uncommon mutations	Gefitinib/ erlotinib VS. Afatinib	39 VS. 33	35.8 VS. 60.6	8.8 (4.8 – 12.8) VS. 12.0 (9.5 – 14.5)	29.0 (22.8 – 35.2) VS. 27.6 (2.1 – 53.1)
<i>Second generation EGFR inhibitors only</i>								
Heigener <i>et al</i> ,	Observational	Germany	Uncommon	Afatinib	58	22	Not reported	Not reported

2015 ⁴²	prospective		mutations ^a					
Moran <i>et al</i> , 2020 ⁴³	Retrospective	Spain	Uncommon mutations ^a including	Afatinib	67	44.8	Not reported	19.9 (9.7 – 30.1)
			Single mutations		24	54.1		19.9 (10.8 – 29.0)
			and		and	and		and
			Complex mutations		20	70		28.8 (20.8 – 36.8)

^a Included T790M mutations, exon 20 insertions, and/or complex mutations involving exon 19 deletion and L858R

Abbreviations: CI = Confidence intervals, del = deletion, N = number of patients, NE = Not estimable, NR = not reached, OS = Overall survival, PFS = Progression-free survival,

TKI = Tyrosine kinase inhibitor.