



## Sample Information

**Patient Name:** 黃錦玫  
**Gender:** Female  
**ID No.:** P220080170  
**History No.:** 44356185  
**Age:** 51

**Ordering Doctor:** DOC3109L 邱昭華  
**Ordering REQ.:** D5CJNP8  
**Signing in Date:** 2020/09/09

**Path No.:** S109-99981  
**MP No.:** F20069  
**Assay:** Oncomine Focus Assay  
**Sample Type:** FFPE  
**Block No.:** S107-02072E  
**Percentage of tumor cells:** 60%  
**Note:**

## Sample Cancer Type: Non-Small Cell Lung Cancer

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## Relevant Non-Small Cell Lung Cancer Findings

Gene	Finding	Gene	Finding
ALK	Not detected	NTRK1	Not detected
BRAF	Not detected	NTRK2	Not detected
EGFR	<b>EGFR p.(L861Q) c.2582T&gt;A, EGFR p.(G719A) c.2156G&gt;C</b>	NTRK3	Not detected
ERBB2	Not detected	RET	Not detected
KRAS	Not detected	ROS1	Not detected
MET	Not detected		



## Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	<b>EGFR p.(L861Q) c.2582T&gt;A</b> epidermal growth factor receptor Allele Frequency: 50.93%	<b>afatinib</b> <sup>1,2</sup> dacomitinib erlotinib <b>gefitinib</b> <sup>2</sup> osimertinib afatinib + cetuximab bevacizumab + erlotinib erlotinib + ramucirumab gefitinib + chemotherapy bevacizumab + gefitinib	None	136
IA	<b>EGFR p.(G719A) c.2156G&gt;C</b> epidermal growth factor receptor Allele Frequency: 49.22%	<b>afatinib</b> <sup>1,2</sup> dacomitinib erlotinib <b>gefitinib</b> <sup>2</sup> osimertinib afatinib + cetuximab bevacizumab + erlotinib erlotinib + ramucirumab gefitinib + chemotherapy bevacizumab + gefitinib	None	124

Public data sources included in relevant therapies: FDA<sup>1</sup>, NCCN, EMA<sup>2</sup>, ESMO

**Tier Reference:** Li et al. *Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists.* J Mol Diagn. 2017 Jan;19(1):4-23.

## Variant Details

DNA Sequence Variants								
Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
EGFR	p.(G719A)	c.2156G>C	COSM6239	chr7:55241708	49.22%	NM_005228.4	missense	1999
EGFR	p.(L861Q)	c.2582T>A	COSM6213	chr7:55259524	50.93%	NM_005228.4	missense	1999
JAK1	p.(=)	c.2199A>G	.	chr1:65310489	54.14%	NM_002227.3	synonymous	1993
ALK	p.(D1529E)	c.4587C>G	.	chr2:29416366	99.95%	NM_004304.4	missense	1991
ALK	p.(I1461V)	c.4381A>G	.	chr2:29416572	99.55%	NM_004304.4	missense	1997
ALK	p.(=)	c.3375C>A	.	chr2:29445458	99.95%	NM_004304.4	synonymous	1993
FGFR3	p.(=)	c.1953G>A	.	chr4:1807894	99.75%	NM_000142.4	synonymous	1994
PDGFRA	p.(=)	c.939T>G	.	chr4:55133726	52.48%	NM_006206.5	synonymous	1993
PDGFRA	p.(=)	c.1701A>G	.	chr4:55141055	99.45%	NM_006206.5	synonymous	1997
PDGFRA	p.(=)	c.2472C>T	.	chr4:55152040	50.35%	NM_006206.5	synonymous	2000
FGFR4	p.(P136L)	c.407C>T	.	chr5:176517797	99.45%	NM_213647.2	missense	2000
RET	p.(=)	c.2307G>T	.	chr10:43613843	63.45%	NM_020975.4	synonymous	1992



## Biomarker Descriptions

### EGFR (epidermal growth factor receptor)

**Background:** The EGFR gene encodes the epidermal growth factor receptor (EGFR) tyrosine kinase, a member of the human epidermal growth factor receptor (HER) family. Along with EGFR/ERBB1/HER1, ERBB2/HER2, ERBB3/HER3, and ERBB4/HER4 make up the HER protein family<sup>1</sup>. EGFR ligand induced dimerization results in kinase activation and leads to stimulation of oncogenic signaling pathways including the PI3K/AKT/MTOR and RAS/RAF/MEK/ERK pathways. Activation of these pathways promote cell proliferation, differentiation, and survival<sup>2,3</sup>.

**Alterations and prevalence:** Recurrent somatic mutations in the tyrosine kinase domain of EGFR are observed in approximately 10-20% of lung adenocarcinoma and at higher frequencies in never-smoker, female, and in Asian populations with lung cancer<sup>4,5,6,7</sup>. The most common mutations occur near the ATP-binding pocket of the kinase domain and include short in-frame deletions in exon 19 (EGFR exon 19 deletion) and the L858R amino acid substitution in exon 21<sup>8</sup>. These mutations constitutively activate the EGFR kinase resulting in downstream signaling and represent 80% of the EGFR mutations observed in lung cancer. A second group of recurrent activating mutations that are less common include E709K, G719X, S768I, L861Q, and short in-frame insertions in exon 20<sup>9,10,11,12</sup>. EGFR activating mutations in lung cancer tend to be mutually exclusive to KRAS activating mutations<sup>13</sup>. Although these variants are common in lung cancer, they are rare in other cancer types. In glioblastoma, recurrent activating EGFR mutations in the extracellular domain include R108K, A289V and G598V<sup>8,14</sup>. The recurrent focal amplification of the EGFR gene leads to an increase in expression in several cancer types. EGFR is amplified in up to 30% of glioblastoma, 12% of esophageal cancer, 10% of head and neck cancer, 5% of bladder cancer, and 5% of lung squamous cell carcinoma<sup>5,6,7,14,15</sup>. Deletion of exons 2-7 encoding the extracellular domain of EGFR (EGFRvIII) results in overexpression of a ligand-independent constitutively active protein which is frequently observed in glioblastoma and has been shown to lead to lung cancer development as well as sensitivity to TKIs<sup>16,17,18</sup>.

**Potential relevance:** Erlotinib<sup>19</sup> (2004), afatinib<sup>20</sup> (2013), gefitinib<sup>21</sup> (2015), osimertinib<sup>22</sup> (2015), and dacomitinib<sup>23</sup> (2018) are small molecule TKIs that are FDA approved for non-small cell lung cancer (NSCLC) patients with sensitizing exon 19 deletions and exon 21 L858R mutations. Acquired secondary mutations often confer resistance to first line TKI therapy with the T790M amino acid substitution accounting for 50-60% of cases<sup>8</sup>. Osimertinib is also indicated for NSCLC patients harboring EGFR T790M mutations whose disease has progressed on or after treatment with a first line TKI. EGFR targeting antibodies including cetuximab<sup>24</sup> (2004), panitumumab<sup>25</sup> (2006), and necitumumab<sup>26</sup> (2016) are also under investigation in combination with EGFR-targeting TKIs for efficacy against EGFR mutations. The bispecific antibody, JNJ-61186372<sup>27</sup>, targeting EGFR and MET, and the tyrosine kinase inhibitor<sup>28</sup> each received a breakthrough designation from the FDA (2020) for NSCLC tumors harboring EGFR exon 20 insertion mutations. The Oncoprex immunogene therapy CNVN-202<sup>29</sup> in combination with the EGFR inhibitor, osimertinib, received a fast track designation from the FDA (2020) for NSCLC tumors harboring EGFR mutations. The use of cetuximab in combination with afatinib is currently recommended by the NCCN for patients who have progressed after receiving erlotinib, afatinib, dacomitinib, or gefitinib and chemotherapy<sup>30</sup>.

## Relevant Therapy Summary

● In this cancer type    ○ In other cancer type    ● In this cancer type and other cancer types    ❌ Contraindicated    ⚠ Both for use and contraindicated    ✕ No evidence

### EGFR p.(L861Q) c.2582T>A

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
afatinib	●	●	●	●	● (IV)
gefitinib	✕	●	●	●	● (III)
bevacizumab + erlotinib	✕	●	✕	●	● (II)

\* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.



## Relevant Therapy Summary (continued)

● In this cancer type    ○ In other cancer type    ● In this cancer type and other cancer types    ⚡ Contraindicated    ⚠ Both for use and contraindicated    ✕ No evidence

### EGFR p.(L861Q) c.2582T>A (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
erlotinib	✕	●	✕	●	● (II)
osimertinib	✕	●	✕	●	● (II)
dacomitinib	✕	●	✕	●	● (I)
erlotinib + ramucirumab	✕	●	✕	●	✕
afatinib + cetuximab	✕	●	✕	✕	✕
bevacizumab + gefitinib	✕	✕	✕	●	✕
gefitinib + carboplatin + pemetrexed	✕	✕	✕	●	✕
anlotinib hydrochloride, toripalimab	✕	✕	✕	✕	● (IV)
apatinib + EGFR tyrosine kinase inhibitor	✕	✕	✕	✕	● (IV)
apatinib, gefitinib	✕	✕	✕	✕	● (IV)
bevacizumab + osimertinib, osimertinib	✕	✕	✕	✕	● (IV)
EGFR tyrosine kinase inhibitor	✕	✕	✕	✕	● (IV)
erlotinib, gefitinib, icotinib hydrochloride, chemotherapy	✕	✕	✕	✕	● (IV)
gefitinib, radiation therapy	✕	✕	✕	✕	● (IV)
icotinib hydrochloride	✕	✕	✕	✕	● (IV)
icotinib hydrochloride, radiation therapy	✕	✕	✕	✕	● (IV)
bevacizumab, atezolizumab, chemotherapy	✕	✕	✕	✕	● (III)
bevacizumab, erlotinib	✕	✕	✕	✕	● (III)
BPI-7711, gefitinib	✕	✕	✕	✕	● (III)
durvalumab, chemotherapy	✕	✕	✕	✕	● (III)
erlotinib, erlotinib + chemotherapy	✕	✕	✕	✕	● (III)
gefitinib, apatinib	✕	✕	✕	✕	● (III)
gefitinib, erlotinib	✕	✕	✕	✕	● (III)
gefitinib, icotinib hydrochloride, erlotinib	✕	✕	✕	✕	● (III)
HS-10296, gefitinib	✕	✕	✕	✕	● (III)

\* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.



## Relevant Therapy Summary (continued)

In this cancer type
  In other cancer type
  In this cancer type and other cancer types
  Contraindicated
  Both for use and contraindicated
  No evidence

### EGFR p.(L861Q) c.2582T>A (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
icotinib hydrochloride, chemotherapy	×	×	×	×	● (III)
nivolumab, chemotherapy	×	×	×	×	● (III)
AZD-3759, erlotinib, gefitinib	×	×	×	×	● (II/III)
afatinib, bevacizumab	×	×	×	×	● (II)
afatinib, chemotherapy, radiation therapy	×	×	×	×	● (II)
anlotinib hydrochloride	×	×	×	×	● (II)
anlotinib hydrochloride, gefitinib	×	×	×	×	● (II)
avitinib, AZD-3759	×	×	×	×	● (II)
bevacizumab + gefitinib + chemotherapy	×	×	×	×	● (II)
bevacizumab, erlotinib, chemotherapy	×	×	×	×	● (II)
bevacizumab, osimertinib	×	×	×	×	● (II)
bintrafusp alfa, chemoradiation therapy, durvalumab	×	×	×	×	● (II)
chemotherapy, atezolizumab, bevacizumab	×	×	×	×	● (II)
chemotherapy, durvalumab	×	×	×	×	● (II)
EGFR tyrosine kinase inhibitor + chemotherapy	×	×	×	×	● (II)
EGFR tyrosine kinase inhibitor + chemotherapy, EGFR tyrosine kinase inhibitor	×	×	×	×	● (II)
EGFR tyrosine kinase inhibitor, apatinib	×	×	×	×	● (II)
EGFR tyrosine kinase inhibitor, radiation therapy	×	×	×	×	● (II)
erlotinib + chemotherapy	×	×	×	×	● (II)
erlotinib, chemotherapy	×	×	×	×	● (II)
erlotinib, chemotherapy, sintilimab, anlotinib hydrochloride	×	×	×	×	● (II)
erlotinib, gefitinib	×	×	×	×	● (II)
erlotinib, gefitinib, icotinib hydrochloride, erlotinib + chemotherapy, gefitinib + chemotherapy, icotinib hydrochloride + chemotherapy	×	×	×	×	● (II)

\* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.



## Relevant Therapy Summary (continued)

● In this cancer type    ○ In other cancer type    ⓘ In this cancer type and other cancer types    ⛔ Contraindicated    ⚠ Both for use and contraindicated    ✕ No evidence

### EGFR p.(L861Q) c.2582T>A (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
erlotinib, radiation therapy	✕	✕	✕	✕	● (II)
famitinib, HS-10296	✕	✕	✕	✕	● (II)
gefitinib + chemotherapy	✕	✕	✕	✕	● (II)
gefitinib, chemotherapy	✕	✕	✕	✕	● (II)
gefitinib, hormone therapy	✕	✕	✕	✕	● (II)
gefitinib, surgical intervention	✕	✕	✕	✕	● (II)
maiHuatinib	✕	✕	✕	✕	● (II)
nazartinib, gefitinib	✕	✕	✕	✕	● (II)
nivolumab, ipilimumab	✕	✕	✕	✕	● (II)
osimertinib, bevacizumab	✕	✕	✕	✕	● (II)
osimertinib, radiation therapy	✕	✕	✕	✕	● (II)
osimertinib, savolitinib	✕	✕	✕	✕	● (II)
pembrolizumab, chemotherapy	✕	✕	✕	✕	● (II)
poziotinib	✕	✕	✕	✕	● (II)
ramucirumab, chemotherapy, cytokine	✕	✕	✕	✕	● (II)
SH-1028	✕	✕	✕	✕	● (II)
sutetinib	✕	✕	✕	✕	● (II)
targeted therapy, chemotherapy	✕	✕	✕	✕	● (II)
tyrosine kinase inhibitors, radiation therapy	✕	✕	✕	✕	● (II)
zoledronic acid, gefitinib	✕	✕	✕	✕	● (II)
anlotinib hydrochloride, chemotherapy	✕	✕	✕	✕	● (I/II)
bevacizumab + erlotinib + chemotherapy	✕	✕	✕	✕	● (I/II)
CBT-502, anlotinib hydrochloride	✕	✕	✕	✕	● (I/II)
DZD-9008	✕	✕	✕	✕	● (I/II)
EMB01	✕	✕	✕	✕	● (I/II)

\* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.



## Relevant Therapy Summary (continued)

● In this cancer type    ○ In other cancer type    ● In this cancer type and other cancer types    ⛔ Contraindicated    ⚠ Both for use and contraindicated    ✕ No evidence

### EGFR p.(L861Q) c.2582T>A (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
icotinib hydrochloride + chemotherapy	✕	✕	✕	✕	● (I/II)
KP-673	✕	✕	✕	✕	● (I/II)
ningetinib, gefitinib	✕	✕	✕	✕	● (I/II)
U3-1402	✕	✕	✕	✕	● (I/II)
AB-928, zimberelimab, chemotherapy	✕	✕	✕	✕	● (I)
afatinib, chemotherapy	✕	✕	✕	✕	● (I)
afatinib, immunostimulant	✕	✕	✕	✕	● (I)
afatinib, osimertinib	✕	✕	✕	✕	● (I)
alisertib, osimertinib	✕	✕	✕	✕	● (I)
dacomitinib, osimertinib	✕	✕	✕	✕	● (I)
DS-1205c, osimertinib	✕	✕	✕	✕	● (I)
genolimzumab, fruquintinib	✕	✕	✕	✕	● (I)
JNJ-61186372	✕	✕	✕	✕	● (I)
lazertinib, JNJ-61186372	✕	✕	✕	✕	● (I)
nazartinib + trametinib, nazartinib + ribociclib, LXH254 + nazartinib, capmatinib + nazartinib, gefitinib + nazartinib	✕	✕	✕	✕	● (I)
neratinib, palbociclib, everolimus, trametinib	✕	✕	✕	✕	● (I)
niraparib, osimertinib	✕	✕	✕	✕	● (I)
osimertinib, necitumumab	✕	✕	✕	✕	● (I)
pirotinib	✕	✕	✕	✕	● (I)
telisotuzumab vedotin, osimertinib	✕	✕	✕	✕	● (I)
TNO-155	✕	✕	✕	✕	● (I)
TP-0903	✕	✕	✕	✕	● (I)
TQB 3804	✕	✕	✕	✕	● (I)

\* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.



## Relevant Therapy Summary (continued)

● In this cancer type    ○ In other cancer type    ● In this cancer type and other cancer types    ⚡ Contraindicated    ⚠ Both for use and contraindicated    ✕ No evidence

### EGFR p.(L861Q) c.2582T>A (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
tyrosine kinase inhibitors, tyrosine kinase inhibitors + chemotherapy	✕	✕	✕	✕	● (I)
WSD-0922	✕	✕	✕	✕	● (I)

### EGFR p.(G719A) c.2156G>C

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
afatinib	●	●	●	●	● (IV)
gefitinib	✕	●	●	●	● (III)
erlotinib	✕	●	✕	●	● (III)
osimertinib	✕	●	✕	●	● (II)
dacomitinib	✕	●	✕	●	● (I)
bevacizumab + erlotinib	✕	●	✕	●	✕
erlotinib + ramucirumab	✕	●	✕	●	✕
afatinib + cetuximab	✕	●	✕	✕	✕
bevacizumab + gefitinib	✕	✕	✕	●	✕
gefitinib + carboplatin + pemetrexed	✕	✕	✕	●	✕
anlotinib hydrochloride, toripalimab	✕	✕	✕	✕	● (IV)
apatinib + EGFR tyrosine kinase inhibitor	✕	✕	✕	✕	● (IV)
apatinib, gefitinib	✕	✕	✕	✕	● (IV)
bevacizumab + osimertinib, osimertinib	✕	✕	✕	✕	● (IV)
EGFR tyrosine kinase inhibitor	✕	✕	✕	✕	● (IV)
erlotinib, gefitinib, icotinib hydrochloride, chemotherapy	✕	✕	✕	✕	● (IV)
gefitinib, radiation therapy	✕	✕	✕	✕	● (IV)
icotinib hydrochloride, radiation therapy	✕	✕	✕	✕	● (IV)
bevacizumab, atezolizumab, chemotherapy	✕	✕	✕	✕	● (III)

\* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.





## Relevant Therapy Summary (continued)

● In this cancer type    ○ In other cancer type    ● In this cancer type and other cancer types    ⛔ Contraindicated    ⚠ Both for use and contraindicated    ✕ No evidence

### EGFR p.(G719A) c.2156G>C (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
bevacizumab, erlotinib	✕	✕	✕	✕	● (III)
BPI-7711, gefitinib	✕	✕	✕	✕	● (III)
durvalumab, chemotherapy	✕	✕	✕	✕	● (III)
erlotinib, erlotinib + chemotherapy	✕	✕	✕	✕	● (III)
gefitinib, apatinib	✕	✕	✕	✕	● (III)
gefitinib, erlotinib	✕	✕	✕	✕	● (III)
HS-10296, gefitinib	✕	✕	✕	✕	● (III)
icotinib hydrochloride, chemotherapy	✕	✕	✕	✕	● (III)
nivolumab, chemotherapy	✕	✕	✕	✕	● (III)
AZD-3759, erlotinib, gefitinib	✕	✕	✕	✕	● (II/III)
afatinib, bevacizumab	✕	✕	✕	✕	● (II)
afatinib, chemotherapy, radiation therapy	✕	✕	✕	✕	● (II)
anlotinib hydrochloride	✕	✕	✕	✕	● (II)
anlotinib hydrochloride, gefitinib	✕	✕	✕	✕	● (II)
avitinib, AZD-3759	✕	✕	✕	✕	● (II)
bevacizumab + gefitinib + chemotherapy	✕	✕	✕	✕	● (II)
bevacizumab, erlotinib, chemotherapy	✕	✕	✕	✕	● (II)
bevacizumab, osimertinib	✕	✕	✕	✕	● (II)
bintrafusp alfa, chemoradiation therapy, durvalumab	✕	✕	✕	✕	● (II)
chemotherapy, durvalumab	✕	✕	✕	✕	● (II)
EGFR tyrosine kinase inhibitor + chemotherapy	✕	✕	✕	✕	● (II)
EGFR tyrosine kinase inhibitor + chemotherapy, EGFR tyrosine kinase inhibitor	✕	✕	✕	✕	● (II)
EGFR tyrosine kinase inhibitor, apatinib	✕	✕	✕	✕	● (II)
EGFR tyrosine kinase inhibitor, radiation therapy	✕	✕	✕	✕	● (II)
erlotinib + chemotherapy	✕	✕	✕	✕	● (II)

\* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.



## Relevant Therapy Summary (continued)

● In this cancer type    ○ In other cancer type    ● In this cancer type and other cancer types    
 ⚡ Contraindicated    ⚠ Both for use and contraindicated    ✕ No evidence

### EGFR p.(G719A) c.2156G>C (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
erlotinib, chemotherapy	✕	✕	✕	✕	● (II)
erlotinib, chemotherapy, sintilimab, anlotinib hydrochloride	✕	✕	✕	✕	● (II)
erlotinib, gefitinib	✕	✕	✕	✕	● (II)
erlotinib, gefitinib, icotinib hydrochloride, erlotinib + chemotherapy, gefitinib + chemotherapy, icotinib hydrochloride + chemotherapy	✕	✕	✕	✕	● (II)
erlotinib, radiation therapy	✕	✕	✕	✕	● (II)
famitinib, HS-10296	✕	✕	✕	✕	● (II)
gefitinib + chemotherapy	✕	✕	✕	✕	● (II)
gefitinib, chemotherapy	✕	✕	✕	✕	● (II)
gefitinib, hormone therapy	✕	✕	✕	✕	● (II)
icotinib hydrochloride	✕	✕	✕	✕	● (II)
maiHuatinib	✕	✕	✕	✕	● (II)
nazartinib, gefitinib	✕	✕	✕	✕	● (II)
neratinib	✕	✕	✕	✕	● (II)
nivolumab, ipilimumab	✕	✕	✕	✕	● (II)
osimertinib, bevacizumab	✕	✕	✕	✕	● (II)
osimertinib, radiation therapy	✕	✕	✕	✕	● (II)
osimertinib, savolitinib	✕	✕	✕	✕	● (II)
pembrolizumab, chemotherapy	✕	✕	✕	✕	● (II)
poziotinib	✕	✕	✕	✕	● (II)
ramucirumab, chemotherapy, cytokine	✕	✕	✕	✕	● (II)
SH-1028	✕	✕	✕	✕	● (II)
sutetinib	✕	✕	✕	✕	● (II)
targeted therapy, chemotherapy	✕	✕	✕	✕	● (II)

\* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.



## Relevant Therapy Summary (continued)

In this cancer type
  In other cancer type
  In this cancer type and other cancer types
  Contraindicated
  Both for use and contraindicated
  No evidence

### EGFR p.(G719A) c.2156G>C (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
tyrosine kinase inhibitors, radiation therapy	×	×	×	×	● (II)
zoledronic acid, gefitinib	×	×	×	×	● (II)
anlotinib hydrochloride, chemotherapy	×	×	×	×	● (I/II)
bevacizumab + erlotinib + chemotherapy	×	×	×	×	● (I/II)
CBT-502, anlotinib hydrochloride	×	×	×	×	● (I/II)
DZD-9008	×	×	×	×	● (I/II)
EMB01	×	×	×	×	● (I/II)
icotinib hydrochloride + chemotherapy	×	×	×	×	● (I/II)
KP-673	×	×	×	×	● (I/II)
ningetinib, gefitinib	×	×	×	×	● (I/II)
U3-1402	×	×	×	×	● (I/II)
AB-928, zimberelimab, chemotherapy	×	×	×	×	● (I)
afatinib, chemotherapy	×	×	×	×	● (I)
afatinib, immunostimulant	×	×	×	×	● (I)
afatinib, osimertinib	×	×	×	×	● (I)
alisertib, osimertinib	×	×	×	×	● (I)
dacomitinib, osimertinib	×	×	×	×	● (I)
DS-1205c, osimertinib	×	×	×	×	● (I)
genolimzumab, fruquintinib	×	×	×	×	● (I)
JNJ-61186372	×	×	×	×	● (I)
lazertinib, JNJ-61186372	×	×	×	×	● (I)
nazartinib + trametinib, nazartinib + ribociclib, LXH254 + nazartinib, capmatinib + nazartinib, gefitinib + nazartinib	×	×	×	×	● (I)
neratinib, palbociclib, everolimus, trametinib	×	×	×	×	● (I)
niraparib, osimertinib	×	×	×	×	● (I)

\* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.



## Relevant Therapy Summary (continued)

● In this cancer type    ○ In other cancer type    ⓘ In this cancer type and other cancer types    ⛔ Contraindicated    ⚠ Both for use and contraindicated    ✕ No evidence

### EGFR p.(G719A) c.2156G>C (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
osimertinib, necitumumab	✕	✕	✕	✕	● (I)
pirotinib	✕	✕	✕	✕	● (I)
telisotuzumab vedotin, osimertinib	✕	✕	✕	✕	● (I)
TNO-155	✕	✕	✕	✕	● (I)
TP-0903	✕	✕	✕	✕	● (I)
TQB 3804	✕	✕	✕	✕	● (I)
tyrosine kinase inhibitors, tyrosine kinase inhibitors + chemotherapy	✕	✕	✕	✕	● (I)
WSD-0922	✕	✕	✕	✕	● (I)

\* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

## Relevant Therapy Details

### Current FDA Information

● In this cancer type    ○ In other cancer type    ⓘ In this cancer type and other cancer types    ⛔ Contraindicated    ⚠ Not recommended    🛑 Resistance

FDA information is current as of 2020-05-26. For the most up-to-date information, search [www.fda.gov](http://www.fda.gov).

### EGFR p.(L861Q) c.2582T>A

#### ● afatinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2019-10-11

Variant class: EGFR L861Q mutation

#### Indications and usage:

GILOTRIF® is a kinase inhibitor indicated for:

- First-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have non-resistant epidermal growth factor receptor (EGFR) mutations as detected by an FDA-approved test.

Limitation of Use: Safety and efficacy of GILOTRIF® were not established in patients whose tumors have resistant EGFR mutations

- Treatment of patients with metastatic, squamous NSCLC progressing after platinum-based chemotherapy

#### Reference:

[https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2019/201292s015lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/201292s015lbl.pdf)



## EGFR p.(G719A) c.2156G>C

### ● afatinib

**Cancer type:** Non-Small Cell Lung Cancer

**Label as of:** 2019-10-11

**Variant class:** EGFR G719 mutation

#### Indications and usage:

GILOTRIF® is a kinase inhibitor indicated for:

- First-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have non-resistant epidermal growth factor receptor (EGFR) mutations as detected by an FDA-approved test.

Limitation of Use: Safety and efficacy of GILOTRIF® were not established in patients whose tumors have resistant EGFR mutations

- Treatment of patients with metastatic, squamous NSCLC progressing after platinum-based chemotherapy

#### Reference:

[https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2019/201292s015lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/201292s015lbl.pdf)



## Current NCCN Information

☒ In this cancer type  
 ☐ In other cancer type  
 ☒ In this cancer type and other cancer types  
 ☒ Contraindicated  
 ☒ Not recommended  
 ☒ Resistance

NCCN information is current as of 2020-05-01. For the most up-to-date information, search [www.nccn.org](http://www.nccn.org).  
 For NCCN International Adaptations & Translations, search [www.nccn.org/global/international\\_adaptations.aspx](http://www.nccn.org/global/international_adaptations.aspx).

### EGFR p.(L861Q) c.2582T>A

#### ● afatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L861Q mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Sensitizing EGFR mutation discovered prior to first-line systemic therapy (First-line therapy) (Other Recommended)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

#### ● dacomitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L861Q mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Sensitizing EGFR mutation discovered prior to first-line systemic therapy (First-line therapy) (Other Recommended)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

#### ● erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L861Q mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Sensitizing EGFR mutation discovered prior to first-line systemic therapy (First-line therapy) (Other Recommended)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]



## EGFR p.(L861Q) c.2582T>A (continued)

### ● gefitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L861Q mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Sensitizing EGFR mutation discovered prior to first-line systemic therapy (First-line therapy) (Other Recommended)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

### ● osimertinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L861Q mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; EGFR sensitizing mutation discovered prior to first-line systemic therapy (First-line therapy) (Preferred)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

### ● afatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L861Q mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Sensitizing EGFR mutation discovered during first-line systemic therapy; Interrupt or complete planned systemic therapy, including maintenance therapy (First-line therapy)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Progression on erlotinib +/- (ramucirumab or bevacizumab), afatinib, gefitinib, or dacomitinib; Asymptomatic or symptomatic with brain metastases or isolated lesions (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

### ● afatinib + cetuximab

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L861Q mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Non-Small Cell Lung Cancer; Progression on erlotinib, afatinib, dacomitinib, gefitinib, chemotherapy, or osimertinib; Systemic multiple lesions (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]



## EGFR p.(L861Q) c.2582T>A (continued)

### ● bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L861Q mutation

NCCN Recommendation category: 2A

#### Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Progression on erlotinib +/- (ramucirumab or bevacizumab), afatinib, gefitinib, or dacomitinib; Asymptomatic or symptomatic with brain metastases or isolated lesions (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

### ● dacomitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L861Q mutation

NCCN Recommendation category: 2A

#### Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Sensitizing EGFR mutation discovered during first-line systemic therapy; Interrupt or complete planned systemic therapy, including maintenance therapy (First-line therapy)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Progression on erlotinib +/- (ramucirumab or bevacizumab), afatinib, gefitinib, or dacomitinib; Asymptomatic or symptomatic with brain metastases or isolated lesions (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

### ● erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L861Q mutation

NCCN Recommendation category: 2A

#### Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Sensitizing EGFR mutation discovered during first-line systemic therapy; Interrupt or complete planned systemic therapy, including maintenance therapy (First-line therapy)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Progression on erlotinib +/- (ramucirumab or bevacizumab), afatinib, gefitinib, or dacomitinib; Asymptomatic or symptomatic with brain metastases or isolated lesions (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]





## EGFR p.(L861Q) c.2582T>A (continued)

### ● erlotinib + ramucirumab

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFR L861Q mutation

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Sensitizing EGFR mutation discovered prior to or during first-line systemic therapy (First-line therapy) (Other Recommended)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Progression on erlotinib +/- (ramucirumab or bevacizumab), afatinib, gefitinib, or dacomitinib; Asymptomatic or symptomatic with brain metastases or isolated lesions (Subsequent therapy)

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

### ● gefitinib

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFR L861Q mutation

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Sensitizing EGFR mutation discovered during first-line systemic therapy; Interrupt or complete planned systemic therapy, including maintenance therapy (First-line therapy)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Progression on erlotinib +/- (ramucirumab or bevacizumab), afatinib, gefitinib, or dacomitinib; Asymptomatic or symptomatic with brain metastases or isolated lesions (Subsequent therapy)

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

### ● osimertinib

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFR L861Q mutation

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Sensitizing EGFR mutation discovered during first-line systemic therapy; Interrupt or complete planned systemic therapy, including maintenance therapy (First-line therapy) (Preferred)
- Progression on osimertinib; Advanced or metastatic disease; Asymptomatic or symptomatic with brain or isolated lesions (Subsequent therapy)

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]



## EGFR p.(L861Q) c.2582T>A (continued)

### ● bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L861Q mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Sensitizing EGFR mutation discovered prior to or during first-line systemic therapy (First-line therapy) (Useful in Certain Circumstances)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

### ● erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFRi sensitizing mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Non-Small Cell Lung Cancer; Brain metastases; Use agents active against primary tumor; Pulsatile erlotinib (Not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 2.2020]

### ● afatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFRi sensitizing mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Non-Small Cell Lung Cancer; Brain metastases; Use agents active against primary tumor (Not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 2.2020]

### ● gefitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFRi sensitizing mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Non-Small Cell Lung Cancer; Brain metastases; Use agents active against primary tumor (Not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 2.2020]



## EGFR p.(L861Q) c.2582T>A (continued)

### – alectinib

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFRi sensitizing mutation

**Summary:**

NCCN Guidelines® include the following supporting statement(s):

- "Thus, crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended as subsequent therapy for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

### – brigatinib

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFRi sensitizing mutation

**Summary:**

NCCN Guidelines® include the following supporting statement(s):

- "Thus, crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended as subsequent therapy for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

### – ceritinib

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFRi sensitizing mutation

**Summary:**

NCCN Guidelines® include the following supporting statement(s):

- "Thus, crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended as subsequent therapy for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

### – crizotinib

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFRi sensitizing mutation

**Summary:**

NCCN Guidelines® include the following supporting statement(s):

- "Thus, crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended as subsequent therapy for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]



## EGFR p.(L861Q) c.2582T>A (continued)

### – lorlatinib

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFRi sensitizing mutation

**Summary:**

NCCN Guidelines® include the following supporting statement(s):

- "Thus, crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended as subsequent therapy for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

### – atezolizumab

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFR mutation

**Summary:**

NCCN Guidelines® include the following supporting statement(s):

- "Therefore, subsequent therapy with pembrolizumab, nivolumab, or atezolizumab is not recommended in patients with EGFR mutations or ALK fusions."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

### – nivolumab

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFR mutation

**Summary:**

NCCN Guidelines® include the following supporting statement(s):

- "Therefore, subsequent therapy with pembrolizumab, nivolumab, or atezolizumab is not recommended in patients with EGFR mutations or ALK fusions."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

### – pembrolizumab

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFR mutation

**Summary:**

NCCN Guidelines® include the following supporting statement(s):

- "Therefore, subsequent therapy with pembrolizumab, nivolumab, or atezolizumab is not recommended in patients with EGFR mutations or ALK fusions."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]



## EGFR p.(L861Q) c.2582T>A (continued)

### — pembrolizumab

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR mutation

Other criteria: CD274 overexpression

#### Summary:

NCCN Guidelines® include the following supporting statement(s):

- "A small study suggests that single-agent pembrolizumab is not effective as first-line therapy in patients with metastatic NSCLC and EGFR mutations, even those with PD-L1 levels more than 50%."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

## EGFR p.(G719A) c.2156G>C

### ● afatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR G719 mutation

NCCN Recommendation category: 1

#### Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Sensitizing EGFR mutation discovered prior to first-line systemic therapy (First-line therapy) (Other Recommended)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

### ● dacomitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR G719 mutation

NCCN Recommendation category: 1

#### Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Sensitizing EGFR mutation discovered prior to first-line systemic therapy (First-line therapy) (Other Recommended)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

### ● erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR G719 mutation

NCCN Recommendation category: 1

#### Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Sensitizing EGFR mutation discovered prior to first-line systemic therapy (First-line therapy) (Other Recommended)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]



## EGFR p.(G719A) c.2156G>C (continued)

### ● gefitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR G719 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Sensitizing EGFR mutation discovered prior to first-line systemic therapy (First-line therapy) (Other Recommended)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

### ● osimertinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR G719 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; EGFR sensitizing mutation discovered prior to first-line systemic therapy (First-line therapy) (Preferred)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

### ● afatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR G719 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Sensitizing EGFR mutation discovered during first-line systemic therapy; Interrupt or complete planned systemic therapy, including maintenance therapy (First-line therapy)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Progression on erlotinib +/- (ramucirumab or bevacizumab), afatinib, gefitinib, or dacomitinib; Asymptomatic or symptomatic with brain metastases or isolated lesions (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

### ● afatinib + cetuximab

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR G719 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Non-Small Cell Lung Cancer; Progression on erlotinib, afatinib, dacomitinib, gefitinib, chemotherapy, or osimertinib; Systemic multiple lesions (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]



## EGFR p.(G719A) c.2156G>C (continued)

### ● bevacizumab + erlotinib

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFR G719 mutation

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Progression on erlotinib +/- (ramucirumab or bevacizumab), afatinib, gefitinib, or dacomitinib; Asymptomatic or symptomatic with brain metastases or isolated lesions (Subsequent therapy)

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

### ● dacomitinib

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFR G719 mutation

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Sensitizing EGFR mutation discovered during first-line systemic therapy; Interrupt or complete planned systemic therapy, including maintenance therapy (First-line therapy)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Progression on erlotinib +/- (ramucirumab or bevacizumab), afatinib, gefitinib, or dacomitinib; Asymptomatic or symptomatic with brain metastases or isolated lesions (Subsequent therapy)

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

### ● erlotinib

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFR G719 mutation

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Sensitizing EGFR mutation discovered during first-line systemic therapy; Interrupt or complete planned systemic therapy, including maintenance therapy (First-line therapy)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Progression on erlotinib +/- (ramucirumab or bevacizumab), afatinib, gefitinib, or dacomitinib; Asymptomatic or symptomatic with brain metastases or isolated lesions (Subsequent therapy)

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]



## EGFR p.(G719A) c.2156G>C (continued)

### ● erlotinib + ramucirumab

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFR G719 mutation

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Sensitizing EGFR mutation discovered prior to or during first-line systemic therapy (First-line therapy) (Other Recommended)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Progression on erlotinib +/- (ramucirumab or bevacizumab), afatinib, gefitinib, or dacomitinib; Asymptomatic or symptomatic with brain metastases or isolated lesions (Subsequent therapy)

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

### ● gefitinib

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFR G719 mutation

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Sensitizing EGFR mutation discovered during first-line systemic therapy; Interrupt or complete planned systemic therapy, including maintenance therapy (First-line therapy)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Progression on erlotinib +/- (ramucirumab or bevacizumab), afatinib, gefitinib, or dacomitinib; Asymptomatic or symptomatic with brain metastases or isolated lesions (Subsequent therapy)

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

### ● osimertinib

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFR G719 mutation

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Sensitizing EGFR mutation discovered during first-line systemic therapy; Interrupt or complete planned systemic therapy, including maintenance therapy (First-line therapy) (Preferred)
- Progression on osimertinib; Advanced or metastatic disease; Asymptomatic or symptomatic with brain or isolated lesions (Subsequent therapy)

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]





## EGFR p.(G719A) c.2156G>C (continued)

### ● bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR G719 mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Sensitizing EGFR mutation discovered prior to or during first-line systemic therapy (First-line therapy) (Useful in Certain Circumstances)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

### ● erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFRi sensitizing mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Non-Small Cell Lung Cancer; Brain metastases; Use agents active against primary tumor; Pulsatile erlotinib (Not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 2.2020]

### ● afatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFRi sensitizing mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Non-Small Cell Lung Cancer; Brain metastases; Use agents active against primary tumor (Not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 2.2020]

### ● gefitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFRi sensitizing mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Non-Small Cell Lung Cancer; Brain metastases; Use agents active against primary tumor (Not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 2.2020]



## EGFR p.(G719A) c.2156G>C (continued)

### – alectinib

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFRi sensitizing mutation

**Summary:**

NCCN Guidelines® include the following supporting statement(s):

- "Thus, crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended as subsequent therapy for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

### – brigatinib

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFRi sensitizing mutation

**Summary:**

NCCN Guidelines® include the following supporting statement(s):

- "Thus, crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended as subsequent therapy for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

### – ceritinib

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFRi sensitizing mutation

**Summary:**

NCCN Guidelines® include the following supporting statement(s):

- "Thus, crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended as subsequent therapy for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

### – crizotinib

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFRi sensitizing mutation

**Summary:**

NCCN Guidelines® include the following supporting statement(s):

- "Thus, crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended as subsequent therapy for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]



## EGFR p.(G719A) c.2156G>C (continued)

### – lorlatinib

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFRi sensitizing mutation

**Summary:**

NCCN Guidelines® include the following supporting statement(s):

- "Thus, crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended as subsequent therapy for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

### – atezolizumab

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFR mutation

**Summary:**

NCCN Guidelines® include the following supporting statement(s):

- "Therefore, subsequent therapy with pembrolizumab, nivolumab, or atezolizumab is not recommended in patients with EGFR mutations or ALK fusions."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

### – nivolumab

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFR mutation

**Summary:**

NCCN Guidelines® include the following supporting statement(s):

- "Therefore, subsequent therapy with pembrolizumab, nivolumab, or atezolizumab is not recommended in patients with EGFR mutations or ALK fusions."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]

### – pembrolizumab

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFR mutation

**Summary:**

NCCN Guidelines® include the following supporting statement(s):

- "Therefore, subsequent therapy with pembrolizumab, nivolumab, or atezolizumab is not recommended in patients with EGFR mutations or ALK fusions."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]



## EGFR p.(G719A) c.2156G>C (continued)

### — pembrolizumab

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFR mutation

**Other criteria:** CD274 overexpression

#### Summary:

NCCN Guidelines® include the following supporting statement(s):

- "A small study suggests that single-agent pembrolizumab is not effective as first-line therapy in patients with metastatic NSCLC and EGFR mutations, even those with PD-L1 levels more than 50%."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2020]



## Current EMA Information

☒ In this cancer type  
 ☐ In other cancer type  
 ☒ In this cancer type and other cancer types  
 ☒ Contraindicated  
 ☒ Not recommended  
 ☒ Resistance

EMA information is current as of 2020-05-26. For the most up-to-date information, search [www.ema.europa.eu/ema](http://www.ema.europa.eu/ema).

### EGFR p.(L861Q) c.2582T>A

#### ● afatinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2020-02-13

Variant class: EGFR L861Q mutation

Reference:

[https://www.ema.europa.eu/en/documents/product-information/giotrif-epar-product-information\\_en.pdf](https://www.ema.europa.eu/en/documents/product-information/giotrif-epar-product-information_en.pdf)

#### ● gefitinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2019-05-28

Variant class: EGFR L861Q mutation

Reference:

[https://www.ema.europa.eu/en/documents/product-information/iressa-epar-product-information\\_en.pdf](https://www.ema.europa.eu/en/documents/product-information/iressa-epar-product-information_en.pdf)

### EGFR p.(G719A) c.2156G>C

#### ● afatinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2020-02-13

Variant class: EGFR G719 mutation

Reference:

[https://www.ema.europa.eu/en/documents/product-information/giotrif-epar-product-information\\_en.pdf](https://www.ema.europa.eu/en/documents/product-information/giotrif-epar-product-information_en.pdf)

#### ● gefitinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2019-05-28

Variant class: EGFR G719 mutation

Reference:

[https://www.ema.europa.eu/en/documents/product-information/iressa-epar-product-information\\_en.pdf](https://www.ema.europa.eu/en/documents/product-information/iressa-epar-product-information_en.pdf)



## Current ESMO Information

☒ In this cancer type  
 ☐ In other cancer type  
 ☒ In this cancer type and other cancer types  
 ☒ Contraindicated  
 ☒ Not recommended  
 ☒ Resistance

ESMO information is current as of 2020-05-01. For the most up-to-date information, search [www.esmo.org](http://www.esmo.org).

### EGFR p.(L861Q) c.2582T>A

#### ● afatinib

Cancer type: Non-Small Cell Lung Cancer      Variant class: EGFRi sensitizing mutation

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):

- Advanced stage (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]

#### ● erlotinib

Cancer type: Non-Small Cell Lung Cancer      Variant class: EGFRi sensitizing mutation

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):

- Advanced stage (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]

#### ● gefitinib

Cancer type: Non-Small Cell Lung Cancer      Variant class: EGFRi sensitizing mutation

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):

- Advanced stage (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]



## EGFR p.(L861Q) c.2582T>A (continued)

### ● osimertinib

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFRi sensitizing mutation

**ESMO Level of Evidence/Grade of Recommendation:** I / A

**Population segment (Line of therapy):**

- Advanced stage; ESMO-Magnitude of Clinical Benefit Scale Version 1.1 Score: 4 (First-line therapy)

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]

### ● dacomitinib

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFRi sensitizing mutation

**ESMO Level of Evidence/Grade of Recommendation:** I / B

**Population segment (Line of therapy):**

- Stage IV; Magnitude of Clinical Benefit Scale Version v1.1 Score: 3 (First-line therapy)

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]

### ● erlotinib

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFRi sensitizing mutation

**ESMO Level of Evidence/Grade of Recommendation:** III / B

**Population segment (Line of therapy):**

- Non-Squamous (Maintenance therapy)

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]

### ● afatinib

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFR activating mutation

**ESMO Level of Evidence/Grade of Recommendation:** I / A

**Population segment (Line of therapy):**

- Stage IV; PS 0-2 (First-line therapy)

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]



## EGFR p.(L861Q) c.2582T>A (continued)

### ● erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):

- Stage IV; PS 0-2 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]

### ● gefitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):

- Stage IV; PS 0-2 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]

### ● gefitinib + carboplatin + pemetrexed

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: I / B

Population segment (Line of therapy):

- Advanced stage (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]

### ● bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: II / B

Population segment (Line of therapy):

- Stage IV; ESMO-Magnitude of Clinical Benefit Scale Version 1.1 Score: 3 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]





## EGFR p.(L861Q) c.2582T>A (continued)

### ● bevacizumab + gefitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: II / B

Population segment (Line of therapy):

- Stage IV; ESMO-Magnitude of Clinical Benefit Scale Version 1.1 Score: 3 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]

### ● erlotinib + ramucirumab

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: II / B

Population segment (Line of therapy):

- Stage IV (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]

### ● afatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: III / A

Population segment (Line of therapy):

- Stage IV; PS 3-4 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]

### ● dacomitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: III / A

Population segment (Line of therapy):

- Stage IV; PS 3-4 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]



## EGFR p.(L861Q) c.2582T>A (continued)

### ● erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: III / A

Population segment (Line of therapy):

- Stage IV; PS 3-4 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]

### ● gefitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: III / A

Population segment (Line of therapy):

- Stage IV; PS 3-4 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]

## EGFR p.(G719A) c.2156G>C

### ● afatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFRi sensitizing mutation

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):

- Advanced stage (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]

### ● erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFRi sensitizing mutation

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):

- Advanced stage (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]



## EGFR p.(G719A) c.2156G>C (continued)

### ● gefitinib

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFRi sensitizing mutation

**ESMO Level of Evidence/Grade of Recommendation:** I / A

**Population segment (Line of therapy):**

- Advanced stage (First-line therapy)

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]

### ● osimertinib

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFRi sensitizing mutation

**ESMO Level of Evidence/Grade of Recommendation:** I / A

**Population segment (Line of therapy):**

- Advanced stage; ESMO-Magnitude of Clinical Benefit Scale Version 1.1 Score: 4 (First-line therapy)

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]

### ● dacomitinib

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFRi sensitizing mutation

**ESMO Level of Evidence/Grade of Recommendation:** I / B

**Population segment (Line of therapy):**

- Stage IV; Magnitude of Clinical Benefit Scale Version v1.1 Score: 3 (First-line therapy)

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]

### ● erlotinib

**Cancer type:** Non-Small Cell Lung Cancer

**Variant class:** EGFRi sensitizing mutation

**ESMO Level of Evidence/Grade of Recommendation:** III / B

**Population segment (Line of therapy):**

- Non-Squamous (Maintenance therapy)

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]



## EGFR p.(G719A) c.2156G>C (continued)

### ● afatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):

- Stage IV; PS 0-2 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]

### ● erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):

- Stage IV; PS 0-2 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]

### ● gefitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):

- Stage IV; PS 0-2 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]

### ● gefitinib + carboplatin + pemetrexed

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: I / B

Population segment (Line of therapy):

- Advanced stage (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]



## EGFR p.(G719A) c.2156G>C (continued)

### ● bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: II / B

Population segment (Line of therapy):

- Stage IV; ESMO-Magnitude of Clinical Benefit Scale Version 1.1 Score: 3 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]

### ● bevacizumab + gefitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: II / B

Population segment (Line of therapy):

- Stage IV; ESMO-Magnitude of Clinical Benefit Scale Version 1.1 Score: 3 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]

### ● erlotinib + ramucirumab

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: II / B

Population segment (Line of therapy):

- Stage IV (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]

### ● afatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: III / A

Population segment (Line of therapy):

- Stage IV; PS 3-4 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]



## EGFR p.(G719A) c.2156G>C (continued)

### ● dacomitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: III / A

Population segment (Line of therapy):

- Stage IV; PS 3-4 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]

### ● erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: III / A

Population segment (Line of therapy):

- Stage IV; PS 3-4 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]

### ● gefitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

ESMO Level of Evidence/Grade of Recommendation: III / A

Population segment (Line of therapy):

- Stage IV; PS 3-4 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237; <https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer>]



## Signatures

Testing Personnel:

Laboratory Supervisor:

Pathologist:



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