



## Sample Information

**Patient Name:** 周海坤  
**Gender:** Male  
**ID No.:** D101455183  
**History No.:** 46318369  
**Age:** 63

**Ordering Doctor:** DOC3053B 林采榆  
**Ordering REQ.:** 0BKVJAW  
**Signing in Date:** 2021/09/09

**Path No.:** S110-99500  
**MP No.:** F21075  
**Assay:** Oncomine Focus Assay  
**Sample Type:** FFPE  
**Block No.:** S110-24996A+B  
**Percentage of tumor cells:** 40%

**Reporting Doctor:** DOC5466K 葉奕成 (Phone: 8#5466)

**Note:**

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

Table of Contents	Page
Variants (Exclude variant in Taiwan BioBank with >1% allele frequency)	2
Biomarker Descriptions	2
Relevant Therapy Summary	4
Relevant Therapy Details	5
Clinical Trials Summary	19
Alert Details	20

**Report Highlights**  
2 Relevant Biomarkers  
11 Therapies Available  
9 Clinical Trials

## Relevant Non-Small Cell Lung Cancer Variants

Gene	Finding	Gene	Finding
ALK	None detected	NTRK1	None detected
BRAF	None detected	NTRK2	None detected
EGFR	<b>EGFR p.(L861Q) c.2582T&gt;A</b>	NTRK3	None detected
ERBB2	None detected	RET	None detected
KRAS	<b>KRAS amplification</b>	ROS1	None detected
MET	None 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: 17.86%	<b>afatinib</b> <sup>1, 2</sup> <b>gefitinib</b> <sup>2</sup> afatinib + cetuximab bevacizumab + erlotinib bevacizumab + gefitinib dacomitinib erlotinib erlotinib + ramucirumab gefitinib + chemotherapy osimertinib osimertinib + chemotherapy	None	8
IIC	<b>KRAS amplification</b> KRAS proto-oncogene, GTPase	None	None	1

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.

## Variants (Exclude variant in Taiwan BioBank with >1% allele frequency)

### DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
EGFR	p.(L861Q)	c.2582T>A	COSM6213	chr7:55259524	17.86%	NM_005228.5	missense	1999

### Copy Number Variations

Gene	Locus	Copy Number
KRAS	chr12:25364761	7.38

## Biomarker Descriptions

### EGFR (epidermal growth factor receptor)

**Background:** The EGFR gene encodes the epidermal growth factor receptor (EGFR) tyrosine kinase, a member of the ERBB/human epidermal growth factor receptor (HER) family. In addition to EGFR/ERBB1/HER1, other members of the ERBB/HER family include ERBB2/HER2, ERBB3/HER3, and ERBB4/HER4<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 (TKD) of EGFR are observed in approximately 10-20% of lung adenocarcinoma, and at higher frequencies in never-smoker, female, and Asian populations<sup>4,5,6,7</sup>. The most common mutations occur near the ATP-binding pocket of the TKD 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 EGFR resulting in downstream signaling, and represent 80% of the EGFR mutations observed in lung cancer. A second group of less prevalent activating mutations include E709K, G719X, S768I, L861Q, and short in-frame insertion mutations 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>. In contrast, a different set of recurrent activating EGFR mutations in the extracellular domain include R108K, A289V and G598V and are primarily observed in glioblastoma<sup>8,14</sup>. Amplification of EGFR is observed in several cancer types including 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 and is observed in approximately 30% of glioblastoma<sup>16,17,18</sup>.

## Biomarker Descriptions (continued)

**Potential relevance:** Approved first-generation EGFR tyrosine kinase inhibitors (TKIs) include erlotinib<sup>19</sup> (2004) and gefitinib<sup>20</sup> (2015), which block the activation of downstream signaling by reversible interaction with the ATP-binding site. Although initially approved for advanced lung cancer, the discovery that drug sensitivity was associated with exon 19 and exon 21 activating mutations allowed first-generation TKIs to become subsequently approved for front-line therapy in lung cancer tumors containing exon 19 or exon 21 activating mutations. Second-generation TKIs afatinib<sup>21</sup> (2013) and dacomitinib<sup>22</sup> (2018) bind EGFR and other ERBB/HER gene family members irreversibly and were subsequently approved. First- and second-generation TKIs afatinib, dacomitinib, erlotinib, and gefitinib are recommended for the treatment NSCLC harboring EGFR exon 19 insertions, exon 19 deletions, point mutations L861Q, L858R, S768I, and codon 719 mutations, whereas most EGFR exon 20 insertions, except p.A763\_Y764insFQEA, confer resistance to the same therapies<sup>23,24,25,26</sup>. In lung cancer containing EGFR exon 19 or 21 activating mutations, treatment with TKIs is eventually associated with the emergence of drug resistance<sup>27</sup>. The primary resistance mutation that emerges following treatment with first-generation TKI is T790M, accounting for 50-60% of resistant cases<sup>8</sup>. Third generation TKIs were developed to maintain sensitivity in the presence of T790M. Osimertinib<sup>28</sup> (2015) is an irreversible inhibitor indicated for metastatic EGFR T790M positive lung cancer and for the first-line treatment of metastatic NSCLC containing EGFR exon 19 deletions or exon 21 L858R mutations. Like first-generation TKIs, treatment with osimertinib is associated with acquired resistance. In this case, resistance is associated with the C797S mutation, and occurs in 22-44% of cases<sup>27</sup>. The T790M and C797S mutations may be each selected following sequential treatment with a first-generation TKI followed by a third-generation TKI or vice versa<sup>29</sup>. T790M and C797S can occur in either cis or trans allelic orientation<sup>29</sup>. If C797S is observed following progression after treatment with a third-generation TKI in the first-line setting, sensitivity may be retained to first-generation TKIs<sup>29</sup>. If C797S co-occurs in trans with T790M following sequential treatment with first- and third-generation TKIs, patients may exhibit sensitivity to combination first- and third-generation TKIs, but resistance to third-generation TKIs alone<sup>29,30</sup>. However, C797S occurring in cis conformation with T790M, confers resistance to first- and third-generation TKIs<sup>29</sup>. Fourth-generation TKIs are in development to overcome acquired C797S and T790M resistance mutations after osimertinib treatment. EGFR targeting antibodies including cetuximab (2004), panitumumab (2006), and necitumumab (2016) are under investigation in combination with EGFR-targeting TKIs for efficacy against EGFR mutations. The bispecific antibody, JNJ-61186372<sup>31</sup>, targeting EGFR and MET, and the TKI mobocertinib<sup>32</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>33</sup> in combination with osimertinib received a fast track designation from the FDA (2020) for NSCLC tumors harboring EGFR mutations that progressed on osimertinib alone. BDTX-189<sup>34</sup> was granted a fast track designation (2020) for the treatment of solid tumors harboring an EGFR exon 20 insertion mutation.

### KRAS (KRAS proto-oncogene, GTPase)

**Background:** The KRAS proto-oncogene encodes a GTPase that functions in signal transduction and is a member of the RAS superfamily which also includes NRAS and HRAS. RAS proteins mediate the transmission of growth signals from the cell surface to the nucleus via the PI3K/AKT/MTOR and RAS/RAF/MEK/ERK pathways, which regulate cell division, differentiation, and survival<sup>35,36,37</sup>.

**Alterations and prevalence:** Recurrent mutations in RAS oncogenes cause constitutive activation and are found in 20-30% of cancers. KRAS mutations are observed in up to 10-20% of uterine cancer, 30-35% of lung adenocarcinoma and colorectal cancer, and about 60% of pancreatic cancer<sup>6</sup>. The majority of KRAS mutations consist of point mutations occurring at G12, G13, and Q61<sup>6,38,39</sup>. Mutations at A59, K117, and A146 have also been observed but are less frequent<sup>7,40</sup>.

**Potential relevance:** The KRAS inhibitor, sotorasib<sup>41</sup>, is approved (2021) for the treatment of adult patients with KRAS G12C-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC). The small molecular inhibitor, RO-5126766, was granted breakthrough designation (2021) alone for KRAS G12V mutant non-small cell lung cancer or in combination with defactinib, for KRAS mutant endometrial carcinoma and KRAS G12V mutant non-small cell lung cancer<sup>42</sup>. Additionally, onvansertib<sup>43</sup> was granted fast track designation (2020) for second-line treatment of patients with KRAS-mutated metastatic colorectal cancer (mCRC). The EGFR antagonists, cetuximab<sup>44</sup> and panitumumab<sup>45</sup>, are contraindicated for treatment of colorectal cancer patients with KRAS mutations in exon 2 (codons 12 and 13), exon 3 (codons 59 and 61), and exon 4 (codons 117 and 146)<sup>40</sup>. Additionally, KRAS mutations are associated with poor prognosis in NSCLC<sup>46</sup>.

## Relevant Therapy Summary

● In this cancer type    
 ○ In other cancer type    
 ● In this cancer type and other cancer types    
 ✕ No evidence

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

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
afatinib	●	●	●	●	✕
gefitinib	✕	●	●	●	✕
bevacizumab + erlotinib	✕	●	✕	●	✕
dacomitinib	✕	●	✕	●	✕
erlotinib	✕	●	✕	●	✕
erlotinib + ramucirumab	✕	●	✕	●	✕
osimertinib	✕	●	✕	●	✕
afatinib + cetuximab	✕	●	✕	✕	✕
osimertinib + chemotherapy	✕	●	✕	✕	✕
osimertinib + chemotherapy + surgical intervention	✕	●	✕	✕	✕
bevacizumab + gefitinib	✕	✕	✕	●	✕
gefitinib + carboplatin + pemetrexed	✕	✕	✕	●	✕
atezolizumab, bevacizumab, chemotherapy	✕	✕	✕	✕	● (II)
bintrafusp alfa, chemoradiation therapy, durvalumab	✕	✕	✕	✕	● (II)
datopotamab deruxtecan	✕	✕	✕	✕	● (II)
osimertinib, savolitinib	✕	✕	✕	✕	● (II)
DZD-9008	✕	✕	✕	✕	● (I/II)
amivantamab	✕	✕	✕	✕	● (I)
lazertinib, amivantamab, chemotherapy	✕	✕	✕	✕	● (I)
TNO-155, nazartinib	✕	✕	✕	✕	● (I)

### KRAS amplification

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
RMC-4630, pembrolizumab	✕	✕	✕	✕	● (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

FDA information is current as of 2021-07-14. 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)

## Current NCCN Information

- ☒ In this cancer type
 ☐ In other cancer type
 ☒ In this cancer type and other cancer types

NCCN information is current as of 2021-07-01. 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, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

#### 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, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

#### 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, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

#### 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, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

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

### ● 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, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (First-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

### ● 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, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

### ● afatinib + cetuximab

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L861Q mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Progression, Symptomatic, Metastatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

### ● 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, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (First-line therapy); Other recommended intervention
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

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

### ● 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, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (Subsequent therapy)

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

### ● 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, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (Subsequent therapy)

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

### ● 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, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (First-line therapy); Other recommended intervention
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (Subsequent therapy)

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

### ● 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, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (Subsequent therapy)

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]



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

### ● 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, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (Subsequent therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

### ● osimertinib + chemotherapy

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L861Q mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Stage IIB, Stage IIIA, Stage IIIB (Adjuvant therapy)
- Stage IIIA; Resectable (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

### ● osimertinib + chemotherapy + surgical intervention

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L861Q mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Stage IIB (Adjuvant therapy)
- Stage IIIA; Resectable (Adjuvant therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2021]

### ● erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFRi sensitizing mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Brain Metastases (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2021]

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

### ● afatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFRi sensitizing mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Brain Metastases (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2021]

### ● gefitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFRi sensitizing mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Brain Metastases (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2021]

### ● osimertinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Leptomeningeal Metastases, Spine Metastases (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2021]

## Current EMA Information

☒ In this cancer type    ☐ In other cancer type    ☒ In this cancer type and other cancer types

EMA information is current as of 2021-07-14. For the most up-to-date information, search [www.ema.europa.eu/ema](https://www.ema.europa.eu/ema).

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

#### ☒ afatinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2021-04-21

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: 2021-03-05

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)

## Current ESMO Information

- ☒ In this cancer type
 ☐ In other cancer type
 ☒ In this cancer type and other cancer types

ESMO information is current as of 2021-07-01. 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 (First-line therapy)

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - <https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer>); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

#### 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 (First-line therapy)

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - <https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer>); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

#### 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 (First-line therapy)

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - <https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer>); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

#### 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 (First-line therapy); ESMO-MCBS v1.1 score: 4

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - <https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer>); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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

### ● 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):**

- Advanced (First-line therapy); ESMO-MCBS v1.1 score: 3

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - <https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer>); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

### ● 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 Cell (Maintenance therapy)

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - <https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer>); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

### ● 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 (First-line therapy)

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - <https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer>); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

### ● bevacizumab + 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 (First-line therapy)

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - <https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer>); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

## 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: I / A

Population segment (Line of therapy):

- Stage IV (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - <https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer>); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

### ● dacomitinib

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 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - <https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer>); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

### ● 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 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - <https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer>); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

### ● erlotinib + ramucirumab

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 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - <https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer>); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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

### ● 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 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - <https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer>); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

### ● gefitinib + carboplatin + pemetrexed

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 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - <https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer>); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

### ● bevacizumab + erlotinib

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):

- Stage IV (First-line therapy); ESMO-MCBS v1.1 score: 3

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - <https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer>); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

### ● bevacizumab + gefitinib

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):

- Stage IV (First-line therapy); ESMO-MCBS v1.1 score: 3

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - <https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer>); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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

### ● erlotinib + ramucirumab

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):

- Stage IV (First-line therapy); ESMO-MCBS v1.1 score: 3

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - <https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer>); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

### ● 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 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - <https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer>); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

### ● 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 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - <https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer>); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

### ● bevacizumab + 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 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - <https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer>); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]



## 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: III / A

Population segment (Line of therapy):

- Stage IV (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - <https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer>); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

### ● 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 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - <https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer>); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

### ● 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 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - <https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer>); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

### ● erlotinib + ramucirumab

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 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - <https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer>); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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

### ● 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 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - <https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer>); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

### ● gefitinib + carboplatin + pemetrexed

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 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Online Guideline (15SEP2020 - <https://www.esmo.org/guidelines/lung-and-chest-tumours/clinical-practice-living-guidelines-metastatic-non-small-cell-lung-cancer>); Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

## Clinical Trials in Taiwan region:

### Clinical Trials Summary

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

NCT ID	Title	Phase
NCT04147351	A Phase II Study of Atezolizumab in Combination With Bevacizumab, Carboplatin or Cisplatin, and Pemetrexed for EGFR-mutant Metastatic Non-small Cell Lung Cancer Patients After Failure of EGFR Tyrosine Kinase Inhibitors.	II
NCT03840902	A Multicenter, Double Blind, Randomized, Controlled Study of M7824 With Concurrent Chemoradiation Followed by M7824 Versus Concurrent Chemoradiation Plus Placebo Followed by Durvalumab in Participants With Unresectable Stage III Non-small Cell Lung Cancer	II
NCT03778229	A Phase II, Single Arm Study Assessing Efficacy of Osimertinib With Savolitinib in Patients With EGFRm + MET+, Locally Advanced or Metastatic Non Small Cell Lung Cancer Who Have Progressed Following Osimertinib Treatment (SAVANNAH Study)	II
NCT02609776	A Phase I, First-in-Human, Open-Label, Dose Escalation Study of JNJ-61186372, a Human Bispecific EGFR and cMet Antibody, in Subjects With Advanced Non-Small Cell Lung Cancer.	I
NCT04484142	Phase II, Single-arm, Open-label Study of DS-1062a in Advanced or Metastatic Non-small Cell Lung Cancer With Actionable Genomic Alterations and Progressed on or After Kinase Inhibitor Therapy and Platinum Based Chemotherapy (TROPION-Lung05)	II
NCT03114319	An Open-label, Multi-center, Phase I, Dose Finding Study of Oral TNO155 in Adult Patients With Advanced Solid Tumors.	I
NCT03974022	A Phase I/II, Open-Label, Multicenter Study to Assess the Safety, Tolerability, Pharmacokinetics and Anti-tumor Efficacy of DZD9008 in Patients With Advanced Non-Small Cell Lung Cancer (NSCLC) With EGFR or HER2 Mutation	I/II
NCT04077463	An Open-label Phase I/Ib Study to Evaluate the Safety and Pharmacokinetics of JNJ-73841937 (Lazertinib), a Third Generation EGFR-TKI, as Monotherapy or in Combinations With JNJ-61186372, a Human Bispecific EGFR and cMet Antibody in Participants With Advanced Non-Small Cell Lung Cancer	I

#### KRAS amplification

NCT ID	Title	Phase
NCT04418661	A Phase I, Open-label, Multicenter, Safety Study of SAR442720 in Combination With Pembrolizumab in Patients With Advanced Malignancies	I

## Alerts Informed By Public Data Sources

### Current FDA Information

 Contraindicated
  Not recommended
  Resistance
  Breakthrough
  Fast Track

FDA information is current as of 2021-07-14. For the most up-to-date information, search [www.fda.gov](http://www.fda.gov).

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

#### osimertinib + quaratusugene ozeplasmid

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

**Variant class:** EGFR mutation

##### Supporting Statement:

The FDA has granted Fast Track Designation to the immunogene therapy, quaratusugene ozeplasmid, in combination with EGFR inhibitor osimertinib for the treatment of non-small cell lung cancer (NSCLC) with EGFR mutations that progressed after treatment with osimertinib alone.

##### Reference:

<https://www.genprex.com/news/genprex-receives-u-s-fda-fast-track-designation-for-gene-therapy-that-targets-lung-cancer/>

### Current NCCN Information

 Contraindicated
  Not recommended
  Resistance
  Breakthrough
  Fast Track

NCCN information is current as of 2021-07-01. 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

#### alectinib

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

**Variant class:** EGFRi sensitizing mutation

##### Summary:

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

- "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 5.2021]

#### brigatinib

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

**Variant class:** EGFRi sensitizing mutation

##### Summary:

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

- "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 5.2021]

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

### – ceritinib

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

**Variant class:** EGFRi sensitizing mutation

**Summary:**

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

- "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 5.2021]

### – crizotinib

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

**Variant class:** EGFRi sensitizing mutation

**Summary:**

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

- "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 5.2021]

### – lorlatinib

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

**Variant class:** EGFRi sensitizing mutation

**Summary:**

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

- "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 5.2021]

### – atezolizumab

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

**Variant class:** EGFR mutation

**Summary:**

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

- "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 5.2021]

### – nivolumab

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

**Variant class:** EGFR mutation

**Summary:**

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

- "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 5.2021]

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

### pembrolizumab

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR mutation

#### Summary:

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

- "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 5.2021]

## Signatures

Testing Personnel:

Laboratory Supervisor:

Pathologist:

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