



Sample Information

Patient Name: 吳素珠  
Gender: Female  
ID No.: P221462667  
History No.: 14855222  
Age: 66  
  
Ordering Doctor: DOC1878G 沈佳儀  
Ordering REQ.: OCTARYK  
Signing in Date: 2023/11/09

Path No.: M112-00284  
MP No.: F23082  
Assay: Oncomine Focus Assay  
Sample Type: FFPE  
Block No.: S112-55570A+B  
Percentage of tumor cells: 30%

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

Note:

Sample Cancer Type: Non-Small Cell Lung Cancer

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Relevant Non-Small Cell Lung Cancer Variants

Gene	Finding	Gene	Finding
ALK	None detected	NTRK1	None detected
BRAF	None detected	NTRK2	None detected
EGFR	EGFR p.(L858R) c.2573T>G	NTRK3	None detected
ERBB2	None detected	RET	None detected
KRAS	None detected	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.(L858R) c.2573T&gt;G</b> epidermal growth factor receptor Allele Frequency: 34.37%	<b>afatinib</b> <sup>1,2</sup> <b>bevacizumab* + erlotinib</b> <sup>2</sup> <b>dacomitinib</b> <sup>1,2</sup> <b>erlotinib</b> <sup>1,2</sup> <b>erlotinib + ramucirumab</b> <sup>1,2</sup> <b>gefitinib</b> <sup>1,2</sup> <b>osimertinib</b> <sup>1,2</sup> atezolizumab + bevacizumab + chemotherapy gefitinib + chemotherapy	None	13

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.

\* Includes biosimilars/generics

## Variant Details

### DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
EGFR	p.(L858R)	c.2573T>G	COSM6224	chr7:55259515	34.37%	NM_005228.5	missense	1990
JAK1	p.(P733=)	c.2199A>G	.	chr1:65310489	50.55%	NM_002227.4	synonymous	2000
FGFR4	p.(P136L)	c.407C>T	.	chr5:176517797	99.45%	NM_213647.3	missense	2000

## 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>.

**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,

## Biomarker Descriptions (continued)

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>. However, in 2021, the irreversible tyrosine kinase inhibitor, mobocertinib<sup>27</sup> was FDA approved for the treatment of NSCLC with EGFR exon 20 insertion mutations. Additionally, in 2022, the FDA granted breakthrough therapy designation to the irreversible EGFR inhibitors, CLN-081 (TPC-064)<sup>28</sup> and sunvozertinib<sup>29</sup>, for locally advanced or metastatic non-small cell lung cancer harboring EGFR exon 20 insertion mutations. In lung cancer containing EGFR exon 19 or 21 activating mutations, treatment with TKIs is eventually associated with the emergence of drug resistance<sup>30</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>31</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>30</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>32</sup>. T790M and C797S can occur in either cis or trans allelic orientation<sup>32</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>32</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>32,33</sup>. However, C797S occurring in cis conformation with T790M, confers resistance to first- and third-generation TKIs<sup>32</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, amivantamab<sup>34</sup>, targeting EGFR and MET was approved (2021) for NSCLC tumors harboring EGFR exon 20 insertion mutations. CPO301<sup>35</sup> received a fast track designation (2023) from the FDA for EGFR mutations in patients with metastatic NSCLC who are relapsed/refractory or ineligible for EGFR targeting therapy such as 3rd-generation EGFR inhibitors including osimertinib. The Oncoprex immunogene therapy quaratusugene ozeplasmid<sup>36</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>37</sup> was granted a fast track designation (2020) for the treatment of solid tumors harboring an EGFR exon 20 insertion mutation.

## Relevant Therapy Summary

☒ In this cancer type
 ☐ In other cancer type
 ☒ In this cancer type and other cancer types
 ☒ No evidence

### EGFR p.(L858R) c.2573T>G

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
osimertinib	●	●	●	●	● (III)
afatinib	●	●	●	●	● (II)
dacomitinib	●	●	●	●	×
erlotinib	●	●	●	●	×
erlotinib + ramucirumab	●	●	●	●	×
gefitinib	●	●	●	●	×
bevacizumab + erlotinib	×	●	●	●	×
bevacizumab (Allergan) + erlotinib	×	×	●	×	×
bevacizumab (Celltrion) + erlotinib	×	×	●	×	×
bevacizumab (Mabxience) + erlotinib	×	×	●	×	×
bevacizumab (Pfizer) + erlotinib	×	×	●	×	×
bevacizumab (Samsung Bioepis) + erlotinib	×	×	●	×	×

\* 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    
 ✕ No evidence

### EGFR p.(L858R) c.2573T>G (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
bevacizumab (Stada) + erlotinib	✕	✕	●	✕	✕
atezolizumab + bevacizumab + carboplatin + paclitaxel	✕	✕	✕	●	✕
gefitinib + carboplatin + pemetrexed	✕	✕	✕	●	✕
osimertinib, chemotherapy	✕	✕	✕	✕	● (III)
patritumab deruxtecan	✕	✕	✕	✕	● (III)
savolitinib, osimertinib	✕	✕	✕	✕	● (III)
erlotinib, OBI-833	✕	✕	✕	✕	● (II)
osimertinib, savolitinib	✕	✕	✕	✕	● (II)
BLU-451, chemotherapy	✕	✕	✕	✕	● (I/II)
BLU-945, osimertinib	✕	✕	✕	✕	● (I/II)
sunvozertinib	✕	✕	✕	✕	● (I/II)
ABBV 400	✕	✕	✕	✕	● (I)
BAY-2927088	✕	✕	✕	✕	● (I)
TNO-155, nazartinib	✕	✕	✕	✕	● (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 2023-09-13. For the most up-to-date information, search [www.fda.gov](https://www.fda.gov).

#### EGFR p.(L858R) c.2573T>G

##### ● afatinib

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

**Label as of:** 2022-04-07

**Variant class:** EGFR L858R 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.

Limitations 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/2022/201292s017lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/201292s017lbl.pdf)

##### ● dacomitinib

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

**Label as of:** 2020-12-18

**Variant class:** EGFR L858R mutation

##### Indications and usage:

VIZIMPRO® is a kinase inhibitor indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletion or exon 21 L858R substitution mutations as detected by an FDA-approved test.

##### Reference:

[https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2020/211288s003lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/211288s003lbl.pdf)

**EGFR p.(L858R) c.2573T>G (continued)****● erlotinib****Cancer type:** Non-Small Cell Lung Cancer**Label as of:** 2016-10-18**Variant class:** EGFR L858R mutation**Indications and usage:**

TARCEVA® is a kinase inhibitor indicated for:

- The treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test receiving first-line, maintenance, or second or greater line treatment after progression following at least one prior chemotherapy regimen.
- First-line treatment of patients with locally advanced, unresectable or metastatic pancreatic cancer, in combination with gemcitabine.

**Limitations of Use:**

- Safety and efficacy of TARCEVA® have not been established in patients with NSCLC whose tumors have other EGFR mutations.
- TARCEVA® is not recommended for use in combination with platinum-based chemotherapy.

**Reference:**[https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2016/021743s025lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/021743s025lbl.pdf)**● erlotinib + ramucirumab****Cancer type:** Non-Small Cell Lung Cancer**Label as of:** 2022-03-22**Variant class:** EGFR L858R mutation**Indications and usage:**

CYRAMZA® is a human vascular endothelial growth factor receptor 2 (VEGFR2) antagonist indicated:

- as a single agent or in combination with paclitaxel, for treatment of advanced or metastatic gastric or gastro-esophageal junction adenocarcinoma with disease progression on or after prior fluoropyrimidine- or platinum-containing chemotherapy.
- in combination with erlotinib, for first-line treatment of metastatic non-small cell lung cancer with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) mutations.
- in combination with docetaxel, for treatment of metastatic non-small cell lung cancer with disease progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving CYRAMZA®.
- in combination with FOLFIRI, for the treatment of metastatic colorectal cancer with disease progression on or after prior therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine.
- as a single agent, for the treatment of hepatocellular carcinoma in patients who have an alpha fetoprotein of  $\geq 400$  ng/mL and have been treated with sorafenib.

**Reference:**[https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2022/125477s042lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/125477s042lbl.pdf)

**EGFR p.(L858R) c.2573T>G (continued)****● gefitinib****Cancer type:** Non-Small Cell Lung Cancer**Label as of:** 2021-05-05**Variant class:** EGFR L858R mutation**Indications and usage:**

IRESSA® is a tyrosine kinase inhibitor indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test.

Limitation of Use: Safety and efficacy of IRESSA® have not been established in patients whose tumors have EGFR mutations other than exon 19 deletions or exon 21 (L858R) substitution mutations.

**Reference:**

[https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2021/206995s004lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/206995s004lbl.pdf)

**● osimertinib****Cancer type:** Non-Small Cell Lung Cancer**Label as of:** 2023-06-21**Variant class:** EGFR L858R mutation**Indications and usage:**

TAGRISSO® is a kinase inhibitor indicated for:

- as adjuvant therapy after tumor resection in adult patients with non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test
- the first-line treatment of adult patients with metastatic NSCLC whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test.
- the treatment of adult patients with metastatic EGFR T790M mutation-positive NSCLC, as detected by an FDA-approved test, whose disease has progressed on or after EGFR TKI therapy.

**Reference:**

[https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2023/208065Orig1s028lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/208065Orig1s028lbl.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 2023-09-01. 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/what-we-do/international-adaptations](http://www.nccn.org/global/what-we-do/international-adaptations).

Some variant specific evidence in this report may be associated with a broader set of alterations from the NCCN Guidelines. Specific variants listed in this report were sourced from approved therapies or scientific literature. These therapeutic options are appropriate for certain population segments with cancer. Refer to the NCCN Guidelines® for full recommendation.

### EGFR p.(L858R) c.2573T>G

#### ● afatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Biomarker discovered prior to first line therapy (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

#### ● dacomitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Biomarker discovered prior to first line therapy (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

#### ● erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Biomarker discovered prior to first line therapy (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

#### ● gefitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Biomarker discovered prior to first line therapy (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]



## EGFR p.(L858R) c.2573T>G (continued)

### ● osimertinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Biomarker discovered prior to first line therapy (First-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

### ● afatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Biomarker discovered during first line therapy (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

### ● afatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R mutation

Other criteria: EGFR T790M mutation negative

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Progression, Symptomatic, Asymptomatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

### ● bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Non-squamous Cell; Advanced, Metastatic, Biomarker discovered prior to first line therapy (First-line therapy); Other recommended intervention
- Non-squamous Cell; Advanced, Metastatic, Biomarker discovered during first line therapy (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

## EGFR p.(L858R) c.2573T>G (continued)

### ● bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R mutation

Other criteria: EGFR T790M mutation negative

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Non-squamous Cell; Advanced, Metastatic, Progression, Symptomatic, Asymptomatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

### ● dacomitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Biomarker discovered during first line therapy (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

### ● dacomitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R mutation

Other criteria: EGFR T790M mutation negative

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Progression, Symptomatic, Asymptomatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

### ● erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Biomarker discovered during first line therapy (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

**EGFR p.(L858R) c.2573T>G (continued)****● erlotinib**

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R mutation

Other criteria: EGFR T790M mutation negative

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Progression, Symptomatic, Asymptomatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

**● erlotinib + ramucirumab**

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Biomarker discovered prior to first line therapy (First-line therapy); Other recommended intervention
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Biomarker discovered during first line therapy (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

**● erlotinib + ramucirumab**

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R mutation

Other criteria: EGFR T790M mutation negative

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Progression, Symptomatic, Asymptomatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

**● gefitinib**

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Biomarker discovered during first line therapy (First-line therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]

**EGFR p.(L858R) c.2573T>G (continued)****● gefitinib****Cancer type:** Non-Small Cell Lung Cancer**Variant class:** EGFR L858R mutation**Other criteria:** EGFR T790M mutation negative**NCCN Recommendation category:** 2A**Population segment (Line of therapy):**

- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Progression, Symptomatic, Asymptomatic (Subsequent therapy)

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]**● osimertinib****Cancer type:** Non-Small Cell Lung Cancer**Variant class:** EGFR L858R mutation**NCCN Recommendation category:** 2A**Population segment (Line of therapy):**

- Brain Metastases, Leptomeningeal Metastases (Line of therapy not specified); Preferred intervention

**Reference:** NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2023]**● osimertinib****Cancer type:** Non-Small Cell Lung Cancer**Variant class:** EGFR L858R mutation**NCCN Recommendation category:** 2A**Population segment (Line of therapy):**

- Stage IB , Stage IIA, Stage IIB, Stage IIIA, Stage IIIB; Resected (Adjuvant therapy)
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Biomarker discovered during first line therapy (First-line therapy); Preferred intervention
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic, Progression, Asymptomatic, Symptomatic (Subsequent therapy)
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Leptomeningeal Metastases, Progression (Subsequent therapy); Consider

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2023]**● erlotinib****Cancer type:** Non-Small Cell Lung Cancer**Variant class:** EGFR L858R mutation**NCCN Recommendation category:** 2B**Population segment (Line of therapy):**

- Leptomeningeal Metastases (Line of therapy not specified); Other recommended intervention

**Reference:** NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2023]

## EGFR p.(L858R) c.2573T>G (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); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2023]

### ● 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); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 1.2023]

## 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 2023-09-13. For the most up-to-date information, search [www.ema.europa.eu/ema](https://www.ema.europa.eu/ema).

### EGFR p.(L858R) c.2573T>G

#### ● afatinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2023-06-21

Variant class: EGFR L858R 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)

#### ● bevacizumab (Allergan) + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2023-01-05

Variant class: EGFR L858R mutation

Reference:

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

#### ● bevacizumab (Celltrion) + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2023-09-12

Variant class: EGFR L858R mutation

Reference:

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

#### ● bevacizumab (Mabxience) + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2023-07-26

Variant class: EGFR L858R mutation

Reference:

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

#### ● bevacizumab (Pfizer) + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2023-01-05

Variant class: EGFR L858R mutation

Reference:

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

#### ● bevacizumab (Samsung Bioepis) + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2023-04-11

Variant class: EGFR L858R mutation

Reference:

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

**EGFR p.(L858R) c.2573T>G (continued)****● bevacizumab (Samsung Bioepis) + erlotinib**

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2023-04-11

Variant class: EGFR L858R mutation

Reference:

[https://www.ema.europa.eu/en/documents/product-information/onbevzi-epar-product-information\\_en.pdf](https://www.ema.europa.eu/en/documents/product-information/onbevzi-epar-product-information_en.pdf)**● bevacizumab (Stada) + erlotinib**

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2023-07-14

Variant class: EGFR L858R mutation

Reference:

[https://www.ema.europa.eu/en/documents/product-information/oyavas-epar-product-information\\_en.pdf](https://www.ema.europa.eu/en/documents/product-information/oyavas-epar-product-information_en.pdf)**● bevacizumab + erlotinib**

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2022-12-15

Variant class: EGFR L858R mutation

Reference:

[https://www.ema.europa.eu/en/documents/product-information/abevmy-epar-product-information\\_en.pdf](https://www.ema.europa.eu/en/documents/product-information/abevmy-epar-product-information_en.pdf)**● bevacizumab + erlotinib**

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2023-03-17

Variant class: EGFR L858R mutation

Reference:

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

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2021-07-21

Variant class: EGFR L858R mutation

Reference:

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

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2023-05-16

Variant class: EGFR L858R mutation

Reference:

[https://www.ema.europa.eu/en/documents/product-information/tarceva-epar-product-information\\_en.pdf](https://www.ema.europa.eu/en/documents/product-information/tarceva-epar-product-information_en.pdf)**● erlotinib + ramucirumab**

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2022-12-13

Variant class: EGFR L858R mutation

Other criteria: EGFR T790M mutation negative

Reference:

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

## EGFR p.(L858R) c.2573T>G (continued)

### ● gefitinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2023-07-27

Variant class: EGFR L858R mutation

Reference:

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

### ● gefitinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2023-07-17

Variant class: EGFR L858R 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)

### ● osimertinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2023-08-11

Variant class: EGFR L858R mutation

Reference:

[https://www.ema.europa.eu/en/documents/product-information/tagrisso-epar-product-information\\_en.pdf](https://www.ema.europa.eu/en/documents/product-information/tagrisso-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 2023-09-01. For the most up-to-date information, search [www.esmo.org](http://www.esmo.org).

### EGFR p.(L858R) c.2573T>G

#### ● osimertinib

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L858R mutation

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

Population segment (Line of therapy):

- Stage IB , Stage IIA, Stage IIB, Stage IIIA; Resected (Adjuvant therapy); ESMO-MCBS v1.1 score: A

Reference: ESMO Clinical Practice Guidelines - ESMO-Early-Stage and Locally Advanced (non-metastatic) Non-Small-Cell Lung Cancer [Ann Oncol (2017) 28 (suppl 4): iv1–iv21. (eUpdate: 01 September 2021, 04 May 2020)]

#### ● osimertinib

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L858R mutation

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

Population segment (Line of therapy):

- Stage IV; Advanced, Metastatic (First-line therapy); ESMO-MCBS v1.1 score: 4

Reference: ESMO Clinical Practice Guidelines - ESMO-Oncogene-addicted Metastatic Non-Small-Cell Lung Cancer [Annals of Oncology (2023), doi: <https://doi.org/10.1016/j.annonc.2022.12.009> (Published)]

#### ● afatinib

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L858R mutation

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

Population segment (Line of therapy):

- Stage IV; Advanced, Metastatic (First-line therapy); ESMO-MCBS v1.1 score: 5

Reference: ESMO Clinical Practice Guidelines - ESMO-Oncogene-addicted Metastatic Non-Small-Cell Lung Cancer [Annals of Oncology (2023), doi: <https://doi.org/10.1016/j.annonc.2022.12.009> (Published)]

#### ● bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L858R mutation

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

Population segment (Line of therapy):

- Stage IV; Advanced, Metastatic (First-line therapy); ESMO-MCBS v1.1 score: 2

Reference: ESMO Clinical Practice Guidelines - ESMO-Oncogene-addicted Metastatic Non-Small-Cell Lung Cancer [Annals of Oncology (2023), doi: <https://doi.org/10.1016/j.annonc.2022.12.009> (Published)]

**EGFR p.(L858R) c.2573T>G (continued)****● dacomitinib****Cancer type:** Non-Small Cell Lung Cancer**Variant class:** EGFR L858R mutation**ESMO Level of Evidence/Grade of Recommendation:** I / B**Population segment (Line of therapy):**

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

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Oncogene-addicted Metastatic Non-Small-Cell Lung Cancer [Annals of Oncology (2023), doi: <https://doi.org/10.1016/j.annonc.2022.12.009> (Published)]

**● erlotinib****Cancer type:** Non-Small Cell Lung Cancer**Variant class:** EGFR L858R mutation**ESMO Level of Evidence/Grade of Recommendation:** I / B**Population segment (Line of therapy):**

- Stage IV; Advanced, Metastatic (First-line therapy); ESMO-MCBS v1.1 score: 4

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Oncogene-addicted Metastatic Non-Small-Cell Lung Cancer [Annals of Oncology (2023), doi: <https://doi.org/10.1016/j.annonc.2022.12.009> (Published)]

**● erlotinib + ramucirumab****Cancer type:** Non-Small Cell Lung Cancer**Variant class:** EGFR L858R mutation**ESMO Level of Evidence/Grade of Recommendation:** I / B**Population segment (Line of therapy):**

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

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Oncogene-addicted Metastatic Non-Small-Cell Lung Cancer [Annals of Oncology (2023), doi: <https://doi.org/10.1016/j.annonc.2022.12.009> (Published)]

**● gefitinib****Cancer type:** Non-Small Cell Lung Cancer**Variant class:** EGFR L858R mutation**ESMO Level of Evidence/Grade of Recommendation:** I / B**Population segment (Line of therapy):**

- Stage IV; Advanced, Metastatic (First-line therapy); ESMO-MCBS v1.1 score: 4

**Reference:** ESMO Clinical Practice Guidelines - ESMO-Oncogene-addicted Metastatic Non-Small-Cell Lung Cancer [Annals of Oncology (2023), doi: <https://doi.org/10.1016/j.annonc.2022.12.009> (Published)]

**EGFR p.(L858R) c.2573T>G (continued)****● gefitinib + carboplatin + pemetrexed**

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R mutation

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

Population segment (Line of therapy):

- Stage IV; Advanced, Metastatic (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Oncogene-addicted Metastatic Non-Small-Cell Lung Cancer [Annals of Oncology (2023), doi: <https://doi.org/10.1016/j.annonc.2022.12.009> (Published)]

**● atezolizumab + bevacizumab + carboplatin + paclitaxel**

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R mutation

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

Population segment (Line of therapy):

- Stage IV; Advanced, Metastatic, Progression (Subsequent therapy); ESMO-MCBS v1.1 score: 3

Reference: ESMO Clinical Practice Guidelines - ESMO-Oncogene-addicted Metastatic Non-Small-Cell Lung Cancer [Annals of Oncology (2023), doi: <https://doi.org/10.1016/j.annonc.2022.12.009> (Published)]

## Clinical Trials in Taiwan region:

### Clinical Trials Summary

#### EGFR p.(L858R) c.2573T>G

NCT ID	Title	Phase
<a href="#">NCT05120349</a>	A Phase III, Double-blind, Randomised, Placebo-Controlled, International Study to Assess the Efficacy and Safety of Adjuvant Osimertinib Versus Placebo in Participants With EGFR Mutation-positive Stage IA2-IA3 Non-small Cell Lung Cancer, Following Complete Tumour Resection	III
<a href="#">NCT04351555</a>	A Phase III, Randomised, Controlled, Multi-center, 3-Arm Study of Neoadjuvant Osimertinib as Monotherapy or in Combination With Chemotherapy Versus Standard of Care Chemotherapy Alone for the Treatment of Patients With Epidermal Growth Factor Receptor Mutation Positive, Resectable Non-small Cell Lung Cancer	III
<a href="#">NCT05338970</a>	HERTHENA–Lung02: Phase III, Randomized, Open-label Study of Patritumab Deruxtecan Versus Platinum-Based Chemotherapy in Metastatic or Locally Advanced Non-Small Cell Lung Cancer (NSCLC) With Epidermal Growth Factor Receptor (EGFRm) Mutation After Failure treatment with epidermal growth factor (EGFR) tyrosine kinase inhibitors (TKIs)	III
<a href="#">NCT05261399</a>	A Phase III, Randomised, Open-Label Study of Savolitinib in Combination With Osimertinib Versus Platinum-Based Doublet Chemotherapy in Participants With EGFR Mutated, MET-Overexpressed and/or Amplified, Locally Advanced or Metastatic Non-Small Cell Lung Cancer Who Have Progressed on Treatment With Osimertinib (SAFFRON).	III
<a href="#">NCT05215548</a>	A Phase II Study of Primary Tumor Resection for Stage IV Non-small-cell Lung Cancer Without Progression After First-line Epidermal Growth Factor Receptor-tyrosine Kinase Inhibitor	II
<a href="#">NCT05442060</a>	A Randomized, Open-Label, Phase 2 Study to Evaluate OBI-833/OBI-821 in Combination With First-Line Erlotinib in Patients With EGFR-Mutated, Globo H-Positive, Locally Advanced or Metastatic Non-Small Cell Lung Cancer	II
<a href="#">NCT03778229</a>	A Phase II Study Assessing the Efficacy of Osimertinib in Combination With Savolitinib in Patients With EGFRm+ and MET+, Locally Advanced or Metastatic Non Small Cell Lung Cancer Who Have Progressed Following Treatment With Osimertinib.	II
<a href="#">NCT04862780</a>	A Phase I/II Study Targeting Acquired Resistance Mechanisms in Patients With EGFR Mutant Non-Small Cell Lung Cancer.	I/II
<a href="#">NCT05099172</a>	An Open Label, First-in-human Study of BAY 2927088 in Participants With Advanced Non-small Cell Lung Cancer (NSCLC) Harboring an EGFR and/or HER2 Mutation	I
<a href="#">NCT03114319</a>	An Open-label, Multi-center, Phase I, Dose Finding Study of Oral TNO155 in Adult Patients With Advanced Solid Tumors.	I
<a href="#">NCT05241873</a>	Phase I/II Study of BLU-451 in Advanced Cancers With EGFR Exon 20 Insertion Mutations	I/II
<a href="#">NCT03974022</a>	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
<a href="#">NCT05029882</a>	A Phase I First in Human Study Evaluating Safety, Pharmacokinetics and Efficacy of ABBV-400 in Adult Subjects With Advanced Solid Tumors	I

## Alerts Informed By Public Data Sources

### Current FDA Information

 Contraindicated  Not recommended  Resistance  Breakthrough  Fast Track

FDA information is current as of 2023-09-13. For the most up-to-date information, search [www.fda.gov](https://www.fda.gov).

### EGFR p.(L858R) c.2573T>G

#### patritumab deruxtecan

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

**Variant class:** EGFR L858R mutation or EGFRi sensitizing mutation

**Supporting Statement:**

The FDA has granted Breakthrough Therapy Designation to a potential first-in-class HER3 directed antibody-drug conjugate, patritumab deruxtecan, for metastatic or locally advanced, EGFR-mutant non-small cell lung cancer.

**Reference:**

<https://www.cancernetwork.com/view/fda-grants-breakthrough-therapy-status-to-patritumab-deruxtecan-for-egfr-metastatic-nscl>

#### CPO-301

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

**Variant class:** EGFR mutation

**Supporting Statement:**

The FDA has granted Fast Track Designation to a first-in-class antibody drug conjugate, CPO301, for EGFR mutations in patients with metastatic non-small cell lung cancer (NSCLC) who are relapsed/refractory to or ineligible for EGFR targeting therapy such as 3rd-generation EGFR inhibitors including Osimertinib.

**Reference:**

<http://iis.aastocks.com/20230612/10770455-0.PDF>

#### 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 EGFR mutations in non-small cell lung cancer (NSCLC) patients 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/>

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