



## Sample Information

**Patient Name:** 李彭桂花**Gender:** Female**ID No.:** F200108296**History No.:** 37383907**Age:** 81**Ordering Doctor:** DOC8725A 林怡均**Ordering REQ.:** 0BHWKEG**Signing in Date:** 2021/07/14**Path No.:** S110-99091**MP No.:** F21057**Assay:** Oncomine Focus Assay**Sample Type:** FFPE**Block No.:** C110-13903**Percentage of tumor cells:** 70%**Reporting Doctor:** DOC5466K 葉奕成 (Phone: 8#5466)**Note:**

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

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### Report Highlights

2 Relevant Biomarkers  
15 Therapies Available  
196 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.(L858R) c.2573_2574delTGinsGT</b>	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)</b> <b>c.2573_2574delTGinsGT</b> epidermal growth factor receptor Allele Frequency: 45.00%	<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> afatinib + cetuximab atezolizumab + bevacizumab + chemotherapy bevacizumab + gefitinib gefitinib + chemotherapy osimertinib + chemotherapy	None	192
IIC	<b>CDK4 p.(R24H) c.71G&gt;A</b> cyclin dependent kinase 4 Allele Frequency: 33.35%	None	None	7

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

## 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.(L858R)	c.2573_2574delTGinsGT	COSM12429	chr7:55259515	45.00%	NM_005228.5	missense	1991
CDK4	p.(R24H)	c.71G>A	COSM1989836	chr12:58145430	33.35%	NM_000075.4	missense	2000
FGFR4	p.(A657S)	c.1969G>T	.	chr5:176523312	18.58%	NM_213647.3	missense	1997

## Biomarker Descriptions

### CDK4 (cyclin dependent kinase 4)

**Background:** The CDK4 gene encodes the cyclin-dependent kinase 4 protein, a homologue of CDK6. Both proteins are serine/threonine protein kinases that are involved in the regulation of the G1/S phase transition of the mitotic cell cycle<sup>1,2</sup>. CDK4 kinase is activated by complex formation with D-type cyclins (e.g., CCND1, CCND2, or CCND3), which leads to the phosphorylation of retinoblastoma protein (RB), followed by E2F activation, DNA replication, and cell-cycle progression<sup>3</sup>. Germline mutations in CDK4 are associated with familial melanoma<sup>4,5,6</sup>.

**Alterations and prevalence:** Recurrent somatic mutations of CDK4 codon K22 and R24 are observed in melanoma (1-2%) and lung cancer (approximately 0.1%). Codons K22 and R24 are necessary for binding and inhibition by p16/CDKN2A<sup>7,8,9</sup>. CDK4 is recurrently amplified in several cancer types, most notably in sarcomas (15-20%), glioma (10-15%), adrenocortical carcinoma (5%), lung adenocarcinoma (5%), and melanoma (3%)<sup>10,11,12,13</sup>.

**Potential relevance:** Currently, no therapies are approved for CDK4 aberrations. Small molecule inhibitors targeting CDK4/6 including palbociclib (2015), abemaciclib (2017), and ribociclib (2017), are FDA approved in combination with an aromatase inhibitor or fulvestrant for the treatment of hormone receptor-positive, HER2-negative advanced or metastatic breast cancer.

## Biomarker Descriptions (continued)

### 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>14</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>15,16</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>10,11,12,17</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>18</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>19,20,21,22</sup>. EGFR activating mutations in lung cancer tend to be mutually exclusive to KRAS activating mutations<sup>23</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>13,18</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>10,11,12,13,24</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>25,26,27</sup>.

**Potential relevance:** Approved first-generation EGFR tyrosine kinase inhibitors (TKIs) include erlotinib<sup>28</sup> (2004) and gefitinib<sup>29</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>30</sup> (2013) and dacomitinib<sup>31</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>32,33,34,35</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>36</sup>. The primary resistance mutation that emerges following treatment with first-generation TKI is T790M, accounting for 50-60% of resistant cases<sup>18</sup>. Third generation TKIs were developed to maintain sensitivity in the presence of T790M. Osimertinib<sup>37</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>36</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>38</sup>. T790M and C797S can occur in either cis or trans allelic orientation<sup>38</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>38</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>38,39</sup>. However, C797S occurring in cis conformation with T790M, confers resistance to first- and third-generation TKIs<sup>38</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>40</sup>, targeting EGFR and MET, and the TKI mobocertinib<sup>41</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>42</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>43</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.2573\_2574delTGinsGT

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
afatinib	●	●	●	●	● (IV)
dacomitinib	●	●	●	●	● (IV)
gefitinib	●	●	●	●	● (IV)
osimertinib	●	●	●	●	● (III)
erlotinib	●	●	●	●	● (II)
erlotinib + ramucirumab	●	●	●	●	×
bevacizumab + erlotinib	×	●	●	●	×
afatinib + cetuximab	×	●	×	×	×
osimertinib + chemotherapy	×	●	×	×	×
osimertinib + chemotherapy + surgical intervention	×	●	×	×	×
bevacizumab (Allergan) + erlotinib	×	×	●	×	×
bevacizumab (Fujifilm Kyowa Kirin Biologics) + erlotinib	×	×	●	×	×
bevacizumab (Mabxience) + erlotinib	×	×	●	×	×
bevacizumab (Pfizer) + erlotinib	×	×	●	×	×
bevacizumab (Samsung Bioepis) + erlotinib	×	×	●	×	×
atezolizumab + bevacizumab + carboplatin + paclitaxel	×	×	×	●	×
bevacizumab + gefitinib	×	×	×	●	×
gefitinib + carboplatin + pemetrexed	×	×	×	●	×
afatinib, osimertinib	×	×	×	×	● (IV)
anlotinib hydrochloride, toripalimab	×	×	×	×	● (IV)
apatinib + EGFR tyrosine kinase inhibitor	×	×	×	×	● (IV)
apatinib, gefitinib	×	×	×	×	● (IV)
bevacizumab + osimertinib, osimertinib	×	×	×	×	● (IV)
EGFR tyrosine kinase inhibitor	×	×	×	×	● (IV)
gefitinib, chemotherapy	×	×	×	×	● (IV)
gefitinib, endostatin	×	×	×	×	● (IV)
gefitinib, radiation therapy	×	×	×	×	● (IV)
icotinib hydrochloride	×	×	×	×	● (IV)

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

**Disclaimer:** The data presented here is from a curated knowledgebase of publicly available information, but may not be exhaustive. The data version is 2021.06(007).

## 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.2573\_2574delT GINS GT (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
icotinib hydrochloride, chemotherapy	×	×	×	×	● (IV)
icotinib hydrochloride, radiation therapy	×	×	×	×	● (IV)
natural product, gefitinib, erlotinib, icotinib hydrochloride	×	×	×	×	● (IV)
almonertinib	×	×	×	×	● (III)
amivantamab, lazertinib, osimertinib	×	×	×	×	● (III)
ASK120067, gefitinib	×	×	×	×	● (III)
atezolizumab, bevacizumab, chemotherapy	×	×	×	×	● (III)
atezolizumab, PF-06744547	×	×	×	×	● (III)
BPI-7711, gefitinib	×	×	×	×	● (III)
CK-101, gefitinib	×	×	×	×	● (III)
durvalumab, chemotherapy	×	×	×	×	● (III)
erlotinib, chemotherapy	×	×	×	×	● (III)
gefitinib + chemotherapy	×	×	×	×	● (III)
gefitinib, anlotinib hydrochloride	×	×	×	×	● (III)
gefitinib, icotinib hydrochloride, erlotinib, radiation therapy	×	×	×	×	● (III)
icotinib hydrochloride, anlotinib hydrochloride	×	×	×	×	● (III)
lazertinib, gefitinib	×	×	×	×	● (III)
maiHuatinib, gefitinib	×	×	×	×	● (III)
osimertinib, bevacizumab	×	×	×	×	● (III)
osimertinib, chemotherapy	×	×	×	×	● (III)
SH-1028, gefitinib	×	×	×	×	● (III)
zorifertinib, erlotinib, gefitinib	×	×	×	×	● (II/III)
afatinib, chemotherapy	×	×	×	×	● (II)
almonertinib, radiation therapy	×	×	×	×	● (II)
anlotinib hydrochloride	×	×	×	×	● (II)
anlotinib hydrochloride, chemotherapy	×	×	×	×	● (II)
anlotinib hydrochloride, erlotinib, icotinib hydrochloride, gefitinib	×	×	×	×	● (II)

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## 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.2573\_2574delT GainsGT (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
anlotinib hydrochloride, gefitinib	×	×	×	×	● (II)
atezolizumab, bevacizumab	×	×	×	×	● (II)
atezolizumab, chemotherapy	×	×	×	×	● (II)
avitinib, zorifertinib	×	×	×	×	● (II)
bevacizumab, atezolizumab	×	×	×	×	● (II)
bevacizumab, atezolizumab, chemotherapy	×	×	×	×	● (II)
bevacizumab, erlotinib	×	×	×	×	● (II)
bevacizumab, gefitinib	×	×	×	×	● (II)
bevacizumab, osimertinib	×	×	×	×	● (II)
bintrafusp alfa, chemoradiation therapy, durvalumab	×	×	×	×	● (II)
camrelizumab, apatinib	×	×	×	×	● (II)
chemotherapy, atezolizumab, bevacizumab	×	×	×	×	● (II)
chemotherapy, durvalumab	×	×	×	×	● (II)
crizotinib	×	×	×	×	● (II)
dacomitinib, osimertinib	×	×	×	×	● (II)
datopotamab deruxtecan	×	×	×	×	● (II)
durvalumab, tremelimumab, chemotherapy	×	×	×	×	● (II)
EGFR tyrosine kinase inhibitor + chemotherapy, EGFR tyrosine kinase inhibitor	×	×	×	×	● (II)
EGFR tyrosine kinase inhibitor, radiation therapy	×	×	×	×	● (II)
erlotinib, bevacizumab	×	×	×	×	● (II)
erlotinib, gefitinib, icotinib hydrochloride, chemotherapy	×	×	×	×	● (II)
famitinib, almonertinib	×	×	×	×	● (II)
gefitinib, bevacizumab, chemotherapy	×	×	×	×	● (II)
gefitinib, erlotinib	×	×	×	×	● (II)
gefitinib, erlotinib, afatinib	×	×	×	×	● (II)
gefitinib, thalidomide	×	×	×	×	● (II)
nazartinib, gefitinib	×	×	×	×	● (II)
nivolumab	×	×	×	×	● (II)

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

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## 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.2573\_2574delTGinsGT (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
olaparib, durvalumab	×	×	×	×	● (II)
osimertinib, abemaciclib	×	×	×	×	● (II)
osimertinib, radiation therapy	×	×	×	×	● (II)
osimertinib, ramucirumab	×	×	×	×	● (II)
osimertinib, savolitinib	×	×	×	×	● (II)
osimertinib, selumetinib	×	×	×	×	● (II)
patritumab deruxtecan	×	×	×	×	● (II)
PD-1 Inhibitor, chemotherapy	×	×	×	×	● (II)
poziotinib	×	×	×	×	● (II)
ramucirumab, chemotherapy, cytokine	×	×	×	×	● (II)
ramucirumab, pembrolizumab	×	×	×	×	● (II)
SH-1028	×	×	×	×	● (II)
tyrosine kinase inhibitors, radiation therapy	×	×	×	×	● (II)
BBT-176, cetuximab	×	×	×	×	● (I/II)
BDTX-189	×	×	×	×	● (I/II)
BLU-945	×	×	×	×	● (I/II)
CBT-502, anlotinib hydrochloride	×	×	×	×	● (I/II)
DZD-9008	×	×	×	×	● (I/II)
EMB01	×	×	×	×	● (I/II)
erlotinib, chemotherapy, bevacizumab	×	×	×	×	● (I/II)
JFAN-1001	×	×	×	×	● (I/II)
KP-673	×	×	×	×	● (I/II)
mobocertinib	×	×	×	×	● (I/II)
necitumumab, trastuzumab, osimertinib	×	×	×	×	● (I/II)
ningetinib, gefitinib	×	×	×	×	● (I/II)
osimertinib, anlotinib hydrochloride	×	×	×	×	● (I/II)
telaglenastat, osimertinib	×	×	×	×	● (I/II)
alisertib, osimertinib	×	×	×	×	● (I)
alisertib, sapanisertib, 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    
 ✕ No evidence

### EGFR p.(L858R) c.2573\_2574delTGinsGT (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
amivantamab, lazertinib	✕	✕	✕	✕	● (I)
BBP-398	✕	✕	✕	✕	● (I)
BCA101	✕	✕	✕	✕	● (I)
bevacizumab + erlotinib + chemotherapy	✕	✕	✕	✕	● (I)
C-005	✕	✕	✕	✕	● (I)
chemotherapy, osimertinib	✕	✕	✕	✕	● (I)
CK-101	✕	✕	✕	✕	● (I)
EGFR tyrosine kinase inhibitor, anlotinib hydrochloride	✕	✕	✕	✕	● (I)
etrumadenant, zimberelimab, chemotherapy	✕	✕	✕	✕	● (I)
FT500, nivolumab, pembrolizumab, atezolizumab	✕	✕	✕	✕	● (I)
genolimzumab, fruquintinib	✕	✕	✕	✕	● (I)
lazertinib, amivantamab, chemotherapy	✕	✕	✕	✕	● (I)
MRX-2843, osimertinib	✕	✕	✕	✕	● (I)
nazartinib, trametinib, ribociclib, LXH254 , capmatinib, gefitinib	✕	✕	✕	✕	● (I)
neratinib, palbociclib, everolimus, trametinib	✕	✕	✕	✕	● (I)
niraparib, osimertinib	✕	✕	✕	✕	● (I)
nivolumab, ipilimumab, radiation therapy	✕	✕	✕	✕	● (I)
osimertinib, ipilimumab	✕	✕	✕	✕	● (I)
pirotinib	✕	✕	✕	✕	● (I)
PLB-1004	✕	✕	✕	✕	● (I)
ramucirumab, erlotinib, osimertinib	✕	✕	✕	✕	● (I)
telaglenastat, sapanisertib	✕	✕	✕	✕	● (I)
telisotuzumab vedotin, osimertinib	✕	✕	✕	✕	● (I)
TNO-155, nazartinib	✕	✕	✕	✕	● (I)
TQB 3804	✕	✕	✕	✕	● (I)
WSD-0922	✕	✕	✕	✕	● (I)
ZZ06	✕	✕	✕	✕	● (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
 ☒ No evidence

### CDK4 p.(R24H) c.71G>A

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
abemaciclib	×	×	×	×	● (II)
palbociclib	×	×	×	×	● (II)
SY-5609	×	×	×	×	● (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 2021-05-12. For the most up-to-date information, search [www.fda.gov](http://www.fda.gov).

### EGFR p.(L858R) c.2573\_2574delTGinsGT

#### ● afatinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2019-10-11

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.

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)

#### ● 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.2573\_2574delTGinsGT (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:** 2020-07-06

**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/2020/125477s037lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/125477s037lbl.pdf)

## EGFR p.(L858R) c.2573\_2574delTGinsGT (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:** 2020-12-18

**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/2020/208065s021lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/208065s021lbl.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 2021-05-03. 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.(L858R) c.2573\_2574delTGinsGT

#### ● 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 (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

#### ● 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 (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

#### ● 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 (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

#### ● 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 (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

**EGFR p.(L858R) c.2573\_2574delTGinsGT (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 (First-line therapy); Preferred intervention

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]**● 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 (Subsequent therapy)

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]**● afatinib + cetuximab****Cancer type:** Non-Small Cell Lung Cancer**Variant class:** EGFR L858R mutation**NCCN Recommendation category:** 2A**Population segment (Line of therapy):**

- Progression (Subsequent therapy)

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]**● bevacizumab + 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 (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 4.2021]

## EGFR p.(L858R) c.2573\_2574delTGinsGT (continued)

### ● 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 (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

### ● 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 (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

### ● 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 (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 4.2021]

### ● 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 (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

## EGFR p.(L858R) c.2573\_2574delTGinsGT (continued)

### ● osimertinib

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 (Subsequent therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 4.2021]

### ● osimertinib + chemotherapy

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R 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 4.2021]

### ● osimertinib + chemotherapy + surgical intervention

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R 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 4.2021]

### ● erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):

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

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 5.2020]

## EGFR p.(L858R) c.2573\_2574delTGinsGT (continued)

### ● 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 5.2020]

### ● 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 5.2020]

### ● 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 5.2020]



## 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 2021-05-12. For the most up-to-date information, search [www.ema.europa.eu/ema](http://www.ema.europa.eu/ema).

### EGFR p.(L858R) c.2573\_2574delTGinsGT

#### ● afatinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2021-04-21

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: 2020-11-03

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 (Fujifilm Kyowa Kirin Biologics) + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2021-04-19

Variant class: EGFR L858R mutation

Reference:

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

#### ● bevacizumab (Mabxience) + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2021-04-26

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: 2021-01-07

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: 2021-05-18

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)

**EGFR p.(L858R) c.2573\_2574delTGinsGT (continued)****● bevacizumab (Samsung Bioepis) + erlotinib**

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2021-05-05

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)**● bevacizumab + erlotinib**

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2021-01-28

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: 2021-02-22

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: 2019-04-24

Variant class: EGFR L858R mutation

Reference:

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

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2020-07-02

Variant class: EGFR L858R mutation

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)**● gefitinib**

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2021-03-05

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: 2020-10-16

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 2021-05-03. For the most up-to-date information, search [www.esmo.org](http://www.esmo.org).

### EGFR p.(L858R) c.2573\_2574delTGinsGT

#### ● atezolizumab + bevacizumab + carboplatin + paclitaxel

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R mutation

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

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

- Non-squamous Cell; Metastatic (First-line therapy); ESMO-MCBS v1.1 score: 3
- Metastatic (Second-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: 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.]

## EGFR p.(L858R) c.2573\_2574delTGinsGT (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 (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.]

### ● 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.]

**EGFR p.(L858R) c.2573\_2574delTGinsGT (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 (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.]

**● 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.]

## EGFR p.(L858R) c.2573\_2574delTGinsGT (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 (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.]

### ● 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.]

## EGFR p.(L858R) c.2573\_2574delTGinsGT (continued)

### ● 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.]

### ● 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.]

## EGFR p.(L858R) c.2573\_2574delTGinsGT (continued)

### ● 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.]

### ● 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.]



## EGFR p.(L858R) c.2573\_2574delTGinsGT (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 (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.]

### ● 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 Summary

### EGFR p.(L858R) c.2573\_2574delTGinsGT

NCT ID	Title	Phase
No NCT ID	The Efficacy and Safety of Osimertinib Combined with Bevacizumab in the Treatment of SD Patients with Non-Squamous Cell Lung Cancer	IV
NCT03264794	Evaluation of the Efficacy of Domestic Gefitinib Tablets in the Treatment of Locally Advanced or Metastatic Non-small Cell Lung Cancer Patients Using a Multicenter, Randomized, Positive Drug Gefitinib Pharmacodynamics and Pharmacodynamics	IV
NCT02103257	Sequential Icotinib Plus Chemotherapy Versus Icotinib Alone as First-line Treatment in Stage IIIB/IV Lung Adenocarcinoma: a Randomized, Open-label, Multicenter Study	IV
NCT04401059	Synergistic Real-World Study and Evidence-based Medicine Evaluation of Eleme Combined With Tyrosine Kinase Inhibitors(TKIs)in the Treatment of Advanced Non-small Cell Lung Cancer (NSCLC): Prospective Study	IV
No NCT ID	A Randomized, Placebo-Controlled, Double-Blind, Phase III Study To Evaluate the Safety and Efficacy HS-10296 in Patients With Unresectable Locally Advanced Epidermal Growth Factor Receptors That Have Not Progressed After Platinum-Containing Radical Radiotherapy And Chemotherapy (CCRT/ SCRT)	III
NCT04687241	Efficacy and Safety of Almonertinib Versus Placebo as Adjuvant Therapy for Subjects With Resected Stage II-IIIb NSCLC Harboring EGFR-sensitive Mutations: A Randomized, Controlled, Double-blind, Phase III and Multicenter Clinical Study	III
NCT04487080	A Phase III, Randomized Study of Amivantamab and Lazertinib Combination Therapy Versus Osimertinib Versus Lazertinib as First-Line Treatment in Patients With EGFR-Mutated Locally Advanced or Metastatic Non-Small Cell Lung Cancer.	III
NCT04143607	A Phase III,Double-Blind, Randomised Study to Assess the Efficacy and Safety of ASK120067 Versus Gefitinib as First-Line Treatment in Patients With Epidermal Growth Factor Receptor Mutation Positive, Locally Advanced or Metastatic Non-Small Cell Lung Cancer	III
NCT02886195	EGFR-TKIs Combine Chemotherapy as First-line Therapy for Patients With Advanced EGFR Mutation-positive NSCLC	III
NCT02518802	Pemetrexed Disodium and Cisplatin Chemotherapy Combined With Synchronous Gefitinib vs Chemotherapy Alone as Adjuvant Therapy in Patient With Stage II-IIIa, Epidermal Growth Factor Receptor Mutant Expressing Lung Adenocarcinoma	III
NCT04028778	A Multicenter, Randomized, Double-Blind Study of Gefitinib in Combination With Anlotinib or Placebo in Previously Untreated Patients With EGFR Mutation-Positive Advanced Non-Small-Cell Lung Cancer	III
NCT03381066	A Phase III, Randomized, Multi-center Study to Determine the Efficacy of the Intercalating Combination Treatment of Chemotherapy and Gefitinib or Chemotherapy as Adjuvant Treatment in NSCLC With Common EGFR Mutations.	III
NCT04797806	Phase III Study Comparing Anlotinib Plus Icotinib to Icotinib in Patients With Untreated Non-squamous NSCLC Harboring EGFR Concomitant Mutations	III
NCT04058704	A Multi-center, Prospective Study to Determine the Efficiency of Icotinib Combined With Radiation Therapy Early Intervention or Late Intervention For NSCLC Patients With Brain Metastases and EGFR(Epidermal Growth Factor Receptor) Mutation	III
NCT04248829	A Phase III, Randomized, Double-blind Study to Assess the Efficacy and Safety of Lazertinib Versus Gefitinib as the First-line Treatment in Patients With Epidermal Growth Factor Receptor Sensitizing Mutation Positive, Locally Advanced or Metastatic Non-Small Cell Lung Cancer	III
No NCT ID	A Phase III Trial for Mefatinib (MET-306) Versus Gefitinib in the Treatment of 1st Line EGFR Mutation of Patients with Advanced Non-Small Cell Lung Cancer	III

## Clinical Trials Summary (continued)

### EGFR p.(L858R) c.2573\_2574delTGinsGT (continued)

NCT ID	Title	Phase
NCT03521154	A Phase III, Randomized, Double-blind, Placebo-controlled, Multicenter, International Study of Osimertinib as Maintenance Therapy in Patients With Locally Advanced, Unresectable EGFR Mutation-positive Non-Small Cell Lung Cancer (Stage III) Whose Disease Has Not Progressed Following Definitive Platinum-based Chemoradiation Therapy (LAURA)	III
NCT04181060	Randomized Phase III Study of Combination AZD9291 (Osimertinib) and Bevacizumab Versus AZD9291 (Osimertinib) Alone as First-Line Treatment for Patients With Metastatic EGFR-Mutant Non-Small Cell Lung Cancer (NSCLC)	III
NCT04035486	A Phase III, Open-label, Randomized Study of Osimertinib With or Without Platinum Plus Pemetrexed Chemo, as First-line Treatment in Patients With Epidermal Growth Factor Receptor (EGFR) Mutation Positive, Locally Advanced or Metastatic Non-small Cell Lung Cancer (FLAURA2)	III
NCT04351555	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
NCT04239833	A Phase III, Double-blind, Randomised Study of SH-1028 Tablets Versus Gefitinib as First Line Treatment in Patients With Epidermal Growth Factor Receptor Mutation Positive, Locally Advanced or Metastatic Non Small Cell Lung Cancer	III
NCT02338011	Gefitinib Alone or With Concomitant Whole Brain Radiotherapy for Patients Harboring an EGFR Mutation With Multiple Brain Metastases From Non-Small-cell Lung Cancer: a Phase II/III Randomized Controlled Trial	II/III
NCT03653546	A Randomized, Open-label, Controlled, Multi-Center Phase II/III Study to Assess the Efficacy and Safety of AZD3759 vs. a Standard of Care EGFR TKI, as First Line Treatment to EGFR Mutation Positive Advanced NSCLC With CNS Metastases	II/III
No NCT ID	Multicenter, Prospective Interventional Study To Evaluate Therapeutic Effect of Afatinib in Patients With Advanced Non-Small Cell Lung Cancer, EGFR Mutation Positive And Brain Metastasis.	II
No NCT ID	The feasibility study and biomarker research of afatinib in patients with previously treated advanced NSCLC harboring EGFR mutation.	II
No NCT ID	A phase II study of afatinib in combination with pemetrexed and carboplatin in Japanese patients with EGFR mutation positive (mEGFR +) non-squamous (SQ), advanced non-small cell lung cancer (NSCLC) refractory to first-line osimertinib treatment (NEJ025B)	II
NCT04636593	Almonertinib With Concurrent Radiotherapy in The Treatment of Unresectable, Stage III Non-small-cell Lung Cancer Harboring EGFR Mutations: A Phase II Cohort Study	II
NCT03720873	An Multicenter,Phase II Trial of EGFR-TKIs Combine With Anlotinib as First-line Treatment for Patients With Advanced EGFR Mutation-positive NSCLC	II
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
NCT04245085	A Randomised Non-comparative Open Label Phase II Trial of Atezolizumab Plus Bevacizumab, With Carboplatin-paclitaxel or Pemetrexed, in EGFR-mutant Non-small Cell Lung Carcinoma With Acquired Resistance	II
No NCT ID	Phase II Study of Platinum-Based Doublet Chemotherapy Plus Atezolizumab, In Completely Resected, P-Stage II-IIIA NSCLC Patients Harboring EGFR Mutation. (WJOG11719L Investigator-Initiated Clinical Trial)	II

## Clinical Trials Summary (continued)

### EGFR p.(L858R) c.2573\_2574delTGinsGT (continued)

NCT ID	Title	Phase
NCT04099836	Single Arm Phase II Trial of Atezolizumab and Bevacizumab in Epidermal Growth Factor Receptor (EGFR) Mutant Non-Small Cell Lung Cancer in Patients With Progressive Disease After Receiving Osimertinib (TOP 1901).	II
NCT02655536	A Phase II, Open Label, Multicenter Study of Bevacizumab in Combination With Erlotinib Versus Erlotinib Alone in Patients With EGFR Mutant Non-small Cell Lung Cancer Who Have Brain Metastases	II
NCT04425187	Bevacizumab Combined With Gefitinib in the Treatment of Advanced NSCLC Clinical Study of L858R Positive Mutation Patients	II
No NCT ID	Clinical Study of Camrelizumab Combined With Apatinib in the Treatment of EGFR-TKI Resistance in NSCLC	II
No NCT ID	A Phase IIa Clinical Study of crizotinib in the Treatment of Advanced Non-small Cell Lung Cancer	II
NCT04027647	A Single-arm, Open-label, Phase II Study of Dacomitinib With or Without Dose Titration for the First-line Treatment of Locally Advanced or Metastatic Non-small Cell Lung Cancer in Subjects With Epidermal Growth Factor Receptor (EGFR) Activation Mutation	II
NCT04675008	A Phase II Study of Dacomitinib in Advanced Epidermal Growth Factor Receptor (EGFR)-Mutant Non-small Cell Lung Cancer (NSCLC) Patients Who Have Non-irradiated Brain Metastasis	II
NCT04811001	A Randomised Non-comparative, Phase II Study Investigating the Best Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor (EGFR-TKI) Sequence in Advanced or Metastatic Non Small-Cell Lung Cancer (NSCLC) Harboring EGFR Mutations	II
NCT03994393	A Phase II Trial of Durvalumab (MEDI4736) and Tremelimumab With Chemotherapy in Metastatic EGFR Mutant Non-squamous Non-small Cell Lung Cancer (NSCLC) Following Progression on EGFR Tyrosine Kinase Inhibitors (TKIs)	II
No NCT ID	A Phase II Trial of Induction Erlotinib Followed by Surgical Resection in Patients with Pathologically Confirmed Stage IIIA-N2 EGFR Mutated Non-small cell lung cancer	II
NCT03126799	A Randomized Phase II Study of Erlotinib Alone Versus Erlotinib Plus Bevacizumab for Advanced Non-small Cell Lung Cancer With Epidermal Growth Factor Receptor Activating Mutations	II
NCT02098954	Second Line Erlitinib Combination With Gemcitabine Cisplatin in Non-small Cell Lung Cancer Patients Who Harbored EGFR Sensitive Mutation Developed Resistance After First Line TKI Treatment	II
NCT03267654	Gefitinib Versus Combination of Gefitinib With Chemotherapy or Anti-angiogenesis as 1st Line Treatment in Advanced NSCLC Patients Detected With Bim Deletion or Low EGFR Activating Mutation Abundance:A Randomized, Multicentre, Phase II Study	II
No NCT ID	A randomized phase II trial of docetaxel or pemetrexed with or without gefitinib in elderly advanced non-small cell lung cancer patients harboring activating EGFR mutation after failure of the therapy as first-line treatment.	II
No NCT ID	Gefitinib Plus Pemetrexed Combined With Bevacizumab Or Carboplatin In First-LineTreatment Of Stage IV EGFR Mutant Non-Squamous Non-Small Cell Lung Cancer	II
NCT03457337	A Randomized, Controlled, Open-label, Prospective Trial of S-1 Plus Gefitinib Versus Gefitinib Monotherapy for First-line Treatment of Advanced Non-squamous Non-small Cell Lung Cancer With EGFR-sensitive Mutation	II
NCT03382795	Retreatment With 1st Generation EGFR TKIs in Sensitizing EGFR Mutation Positive Non-Squamous Cell Carcinoma Patients Who Previously Treated With EGFR TKI and Cytotoxic Chemotherapy	II
NCT03341494	A Randomized Phase II Study of Gefitinib Alone Versus Gefitinib Plus Thalidomide for Advanced Non-small Cell Lung Cancer With Epidermal Growth Factor Receptor Activating Mutations	II

## Clinical Trials Summary (continued)

### EGFR p.(L858R) c.2573\_2574delTGinsGT (continued)

NCT ID	Title	Phase
NCT03349203	Icotinib as Neoadjuvant and Adjuvant Therapy in EGFR-mutant Stage IIIB or Oligometastasis Non-small Cell Lung Cancer: a Single Arm, Phase II Clinical Study	II
NCT03396185	Icotinib as Consolidation Therapy After Synchronous or Sequential Chemoradiotherapy in Stage IIIA-IIIB Non-small Cell Lung Cancer With EGFR Sensitive Mutation: A Single Center, Single Arm, Open Label and Prospective Clinical Study	II
NCT03749213	Icotinib as Neoadjuvant Therapy in EGFR-mutant Stage IIIA-N2 Non-small Cell Lung Cancer: a Single Arm, Phase II Clinical Study	II
NCT03151161	A Prospective, Multi-center, Open-labeled Phase II Randomized and Comparative Clinical Study of First Line Intermittent and Maintenance of Icotinib in Combination With Pemetrexed/Carboplatin Compared With Icotinib Single Drug in IIIB/IV Non Small Cell Lung Cancer With Epidermal Growth Factor Receptor (EGFR) Mutation	II
NCT02726568	A Phase II Study to Determine the Efficacy and Safety of High Dose Icotinib Combined With Stereotactic Radiosurgery for NSCLC Patients Harboring EGFR Mutation With Brain Metastases	II
NCT03292133	A Phase II Study of EGF816 and Gefitinib in TKI-naïve EGFR-mutant Non-Small Cell Lung Cancer	II
No NCT ID	A Phase II, Noncomparative, Open Label, Multicentre, Study Of AZD9291 In Patients With Locally Advanced Or Metastatic EGFR Mutated "T790M Undetectable Or Unknown" Non-Small Cell Lung Cancer (Stage IIIB-IV) After No Immediate Prior EGFR TKI (OSIRIS Study)	II
NCT02736513	Pilot, Phase II Study Assessing Intracranial Activity of AZD9291 (TAGRISSO) in Advanced EGFRm(EGFR Mutation) NSCLC Patients With Asymptomatic Brain Metastases	II
NCT03433469	A Phase II Study to Evaluate Neoadjuvant Osimertinib Therapy in Patients with Surgically Resectable, EGFR-Mutant Non-Small Cell Lung Cancer	II
NCT03586453	A Phase II Study of Osimertinib With On-study and Post-progression Biopsy in the First Line Treatment of EGFR Inhibitor naïve Advanced EGFR Mutant Lung Cancer	II
NCT04233021	A Phase II, Multi-centre Study, to Evaluate the Efficacy and Safety of Osimertinib Treatment for Patients With EGFR-mutated Non-small Cell Lung Cancer (NSCLC) With Brain or Leptomeningeal Metastases	II
NCT04545710	A Phase II Trial of Osimertinib and Abemaciclib With a Focus on Non-Small Cell Lung Cancer Patients With EGFR Activating Mutations With Osimertinib Resistance	II
NCT03497767	A Randomised Phase II Trial of Osimertinib With or Without Stereotactic Radiosurgery for EGFR Mutated Non-Small Cell Lung Cancer (NSCLC) With Brain Metastases	II
NCT03769103	Open Label, Multicenter, Phase II Study of Patients With Treatment Naïve Metastatic Epidermal Growth Factor Receptor (EGFR) Mutation-Positive Non-Small Cell Lung Cancer (NSCLC) With Brain Metastases Randomized to Stereotactic Radiosurgery (SRS) and Osimertinib or Osimertinib Alone	II
NCT03909334	An Open-Label Randomized Phase II Study of Combining Osimertinib With and Without Ramucirumab in Tyrosine Kinase Inhibitor (TKI)-naïve Epidermal Growth Factor Receptor (EGFR)-Mutant Locally Advanced or Metastatic NSCLC	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
NCT03392246	A Phase II Study of Osimertinib in Combination With Selumetinib in EGFR Inhibitor naïve Advanced EGFR Mutant Lung Cancer	II
NCT04619004	HERTHENA-Lung01: A Phase II Randomized Open-Label Study of Patritumab Deruxtecan (U3-1402) in Subjects With Previously Treated Metastatic or Locally Advanced EGFR-mutated Non-Small Cell Lung Cancer (NSCLC)	II

## Clinical Trials Summary (continued)

### EGFR p.(L858R) c.2573\_2574delTGinsGT (continued)

NCT ID	Title	Phase
NCT03823807	A Multicenter, Open-label, Phase II Study to Evaluate the Safety and Efficacy of SH-1028 in Locally Advanced or Metastatic NSCLC	II
No NCT ID	Afatinib Translational Study in Patients with EGFR Mutation-Positive Non-Squamous Non-small Cell Lung Cancer Acquired Resistance to Osimertinib (ASPEC)	I/II
NCT03706287	Efficacy and Safety of Anlotinib Combined With Platinum Plus Pemetrexed in T790M Mutation Negative Metastatic Non-squamous Non-small-cell Lung Cancer After Progression on First-line EGFR TKI: a Phase II, Multi-center, Single Arm Study	I/II
NCT04820023	A Phase I/II, Open-Label Study to Assess the Safety, Tolerability, Pharmacokinetics, and Anti-tumor Activity of BBT-176 in Patients With Advanced Non-Small Cell Lung Cancer (NSCLC) Who Progressed Following Prior Therapy With an Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor (EGFR TKI) Agent	I/II
No NCT ID	A single/multicenter, open phase I/II clinical trial to evaluate the safety, tolerability, pharmacokinetics and antitumor activity of JFAN-1001 capsules in the treatment of patients with locally advanced or metastatic non-squamous non-small cell lung cancer	I/II
NCT03446417	A Phase 1/2 Open Label, Multicenter Study to Assess the Safety, Tolerability, Pharmacokinetics, and Anti-tumor Activity of ZN-e4 (KP-673) in Patients With Advanced Non-Small Cell Lung Cancer with Activating Epidermal Growth Factor Receptor (EGFR) Mutations	I/II
NCT02716116	A Phase I/II Study of the Safety, Pharmacokinetics, and Anti-Tumor Activity of the Oral EGFR/HER2 Inhibitor TAK-788 (AP32788) in Non-Small Cell Lung Cancer	I/II
NCT04285671	UCLA L-08: A Phase Ib/II Study of Combined HER Inhibition Adding Necitumumab and Trastuzumab to Osimertinib in Patients With Refractory EGFR-Mutated Lung Cancer	I/II
NCT04770688	Safety and Efficacy of Osimertinib Combined With Anlotinib in EGFRm+, Treatment-naïve IIIb/IV NSCLC Patients: a Prospective, Single Arm, Phase Ib/IIa Study	I/II
NCT03831932	A Phase I/II Study of AZD9291 (Osimertinib) and CB-839 HCl in Patients With EGFR Mutant Non-Small Cell Lung Cancer	I/II
No NCT ID	A Non-interventional, Single-arm, Prospective Clinical Study for the Efficacy and Safety of Low-dose Alfaatinib Combined with Pemetrexed and Carboplatin in First-line Treatment of Advanced EGFR Mutant Non-squamous Non-small Cell Lung Cancer	I
NCT04085315	A Phase I/Ib Study of Alisertib in Combination With Osimertinib in Metastatic EGFR-mutant Lung Cancer	I
NCT04479306	A Ph Ib Study of Osimertinib + Alisertib or Sapanisertib for Osimertinib-Resistant EGFR Mutant Non-Small Cell Lung Cancer (NSCLC) (Crossover Study)	I
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
No NCT ID	Phase I Clinical Study of C-005 Tablet In The Treatment Of Advanced Non-Small Cell Lung Cancer	I
NCT04541407	A Phase I Study of Temozolomide in Combination with Targeted Therapy for NSCLC Patients With CNS Progression on Either Osimertinib or Lorlatinib	I
No NCT ID	Phase I Clinical Study of Safety, Tolerability, Pharmacokinetics and Initial Efficacy of RX518 in Patients with Advanced Non-small Cell Lung Cancer	I
No NCT ID	Study for Efficacy and Safety of Continuing to Treat with TKI Combined with Anlotinib Monotherapy in Advanced NSCLC Patients with T790M Mutation-negative after Tki Treatment Failure	I



## Clinical Trials Summary (continued)

### EGFR p.(L858R) c.2573\_2574delTGinsGT (continued)

NCT ID	Title	Phase
NCT03976856	A Phase Ib Clinical Study With Extension Phase to Evaluate Safety and Efficacy of Genolimzumab (GB226) in Combination With Fruquintinib in the Treatment of Relapsed or Metastatic NSCLC Patients	I
NCT03333343	A Phase Ib, Open Label, Multi-center Study to Characterize the Safety, Tolerability and Preliminary Efficacy of EGF816 in Combination With Selected Targeted Agents in EGFR Mutant NSCLC	I
No NCT ID	Study Of Immunologic Factor In Re-Biopsy Specimen, Peritumoral BALF, And The Peripheral Blood For Predicting Response To Osimertinib In NSCLC Patients	I
No NCT ID	To Evaluate the Safety and Effectiveness of PLB1004 in the Treatment of Advanced Non-Small Cell Lung Cancer	I
No NCT ID	Single-arm Phase I Study of Erlotinib or Osmeltinib plus Ramcilmab in Patients with Untreated EGFR Gene Mutation-Positive Non-Small Cell Lung Cancer with Brain Metastases	I
NCT02099058	A Multicenter, Phase I/Ib, Open-Label, Dose-Escalation Study of ABBV-399, an Antibody Drug Conjugate, in Subjects With Advanced Solid Tumors	I
NCT04197934	Phase I Study to Evaluate Safety, Tolerability, Pharmacokinetics and Anti-Tumor Activity of WSD0922-FUFU	I
NCT04132102	An Open-label, Single-arm Clinical Study to Evaluate the Efficacy of Afatinib in Advanced Lung Squamous Cell Carcinoma With EGFR Sensitive Mutation	IV
NCT04116918	Efficacy and Safety of the Combination of Anlotinib and JS001 in EGFR-TKI Resistant T790M-Negative NSCLC	IV
No NCT ID	Gefitinib Combined with Vinorelbine Soft Capsules vs Gefitinib Monotherapy in the Treatment of Stage IIIB-IV NSCLC Patients with EGFR-sensitive Mutation	IV
No NCT ID	Phase III Study of Afatinib or Chemotherapy in Patients with Non-small Cell Lung Cancer Harboring Sensitizing Uncommon Epidermal Growth Factor Receptor Mutations (ACHILLES study/TORG1834)	III
NCT03735121	A Randomized, Multicenter, Phase Ib/III Study to Investigate the Pharmacokinetics, Efficacy, and Safety of Atezolizumab Subcutaneous Compared With Atezolizumab Intravenous in Patients With Previously Treated Locally Advanced or Metastatic Non-Small Cell Lung Cancer	III
NCT03866499	A Randomized, Double-blind, Positive Controlled Phase III Study to Evaluate the Efficacy and Safety of BPI-7711 Capsule in Locally Advanced or Recurrent/Metastatic Treatment-naïve Non-small Cell Lung Cancer Patients With EGFR Mutation	III
No NCT ID	Phase III Clinical Study Of The Effectiveness And Safety Of RX518 As The First-line Treatment For Patients With Locally Advanced Or Metastatic Non-small Cell Lung Cancer With EGFR Mutations	III
No NCT ID	A Randomized Phase III Study Of Erlotinib Compared To Intercalated Erlotinib With Cisplatin Pemetrexed As First-Line Therapy For Advanced EGFR Mutated Non-Small-Cell Lung Cancer. The NVALT-17 Study	III
NCT01996098	A Multicenter, Randomized, Phase III Trial of Chemotherapy Followed by 6-month or 12-month Icotinib Versus Chemotherapy as Adjuvant Therapy in Stage IIA-IIIA Non-small Cell Lung Cancer Harboring Epidermal Growth Factor Receptor Mutation	III
NCT02183883	Deciphering Afatinib Response and Resistance With INtratumour Heterogeneity	II
NCT04201756	Neoadjuvant Afatinib Therapy for Resectable Stage III EGFR Mutation-Positive Lung Adenocarcinoma: A Single-Arm, Open-Label, Phase II Clinical Trial	II
No NCT ID	Hypothesis generative H2H study comparing the efficacy between afatinib and osimertinib based on the immunological biomarker in the NSCLC patients with EGFR mutations (HeaT ON BeaT)	II

## Clinical Trials Summary (continued)

### EGFR p.(L858R) c.2573\_2574delTGinsGT (continued)

NCT ID	Title	Phase
NCT04426825	A Single Arm, Phase II Study of Atezolizumab (MPDL3280A, Anti-PD-L1 Antibody) in Combination With Bevacizumab in Patients With EGFR Mutation Positive Stage IIIB/IV Non-Squamous Non-Small Cell Lung Cancer Pretreated With Epidermal Growth Factor Receptor Tyrosine-Kinase Inhibitors	II
NCT03574402	An Open-label, Multi-center, Phase II Umbrella Study to Assess Efficacy of Targeted Therapy or Immunotherapy Directed by Next Generation Sequencing (NGS) in Chinese Patients With Advanced NSCLC (TRUMP)	II
NCT04042558	A Multicentre Phase II, Open-label, Non-randomized Study Evaluating Platinum-Pemetrexed-Atezolizumab (+/- Bevacizumab) for Patients With Stage IIIB/IV Non-squamous Non-small Cell Lung Cancer With EGFR Mutations, ALK Rearrangement or ROS1 Fusion Progressing After Targeted Therapies	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
NCT03944772	A Biomarker-directed Phase II Platform Study in Patients With Advanced Non-Small Lung Cancer Whose Disease Has Progressed on First-Line Osimertinib Therapy	II
No NCT ID	The Clinical Effect of EGFR-TKI Combined with Chemotherapy on Patients with EGFR Multiple Gene Mutations	II
NCT02264210	A Randomized, Phase II Trial of Icotinib Versus Observation as Adjuvant Treatment in Stage IB Non-Small Cell Lung Cancer Harboring Activating Epidermal Growth Factor Receptor Mutation	II
NCT02820116	An Open-label, Multicenter, Single-arm, Phase II Clinical Study of Icotinib for IIIA - IIIB NSCLC Patients with Epidermal Growth Factor Receptor Mutation	II
NCT02824952	Neo-adjuvant Trial With AZD9291 in EGFRm+ Stage IIIA/B NSCLC - a Phase II Open-label Study	II
NCT04120454	An Investigator-Sponsored Phase II Single Arm Trial of Ramucirumab and Pembrolizumab in Patients With EGFR Mutant Non-Small Cell Lung Cancer	II
NCT03983928	A Phase Ib, Open-label, Single Center, Non-randomized Study for Safety and Efficacy of TQB2450 Combined With Anlotinib in Subjects With Advanced Mutation Positive Non-Small Cell Lung Cancer	I/II
NCT03846310	A Phase I/Ib Study to Evaluate the Safety and Tolerability of Immunotherapy Combinations in Participants With Lung Cancer	I
NCT04141644	A Phase Ib Study to Evaluate the Safety and Efficacy of Osimertinib in Combination With Ipilimumab in Patients With EGFR Mutated Non-Small-Cell Lung Cancer Tumors	I
NCT04511533	Single Arm Study to Evaluate the Safety of Dacomitinib for the First-Line Treatment of Participants in India With Metastatic Non-Small Cell Lung Cancer With Epidermal Growth Factor Receptor (EGFR)-Activating Mutations	IV
No NCT ID	The Continuous Evaluation of EGFR Mutation in EGFR-mutation Positive Lung Cancer Patients During EGFR TKI Treatment.	IV
No NCT ID	Clinical Study of Gefitinib Combined with Recombinant Human Endostatin or Single-agent Gefitinib in The Treatment of EGFR Mutation-Positive Advanced NSCLC	IV
NCT02404675	High Dose Icotinib in Advanced Non-small Cell Lung Cancer With EGFR 21 Exon Mutation (INCREASE): a Randomized, Open-label Study	IV
NCT03991403	Study of Atezolizumab in Combination With Carboplatin + Paclitaxel + Bevacizumab vs With Pemetrexed + Cisplatin or Carboplatin With Stage IV Non-Squamous Non-Small Cell Lung Cancer with EGFR (+) or ALK (+)	III



## Clinical Trials Summary (continued)

### EGFR p.(L858R) c.2573\_2574delTGinsGT (continued)

NCT ID	Title	Phase
NCT02714010	Whole Brain Radiotherapy Concurrent With EGFR-TKI Versus EGFR-TKI Alone in the Treatment of Non-small Cell Lung Cancer Patients With Brain Metastasis	III
NCT03786692	TH-138: Phase II Randomized Trial of Carboplatin + Pemetrexed + Bevacizumab, With or Without Atezolizumab in Stage IV Non-squamous NSCLC Patients Who Harbor a Sensitizing EGFR Mutation or Have Never Smoked	II
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
NCT01470716	A Phase II Study of Neo-adjuvant Erlotinib for Operable Stage IIB or IIIA Non-small Cell Lung Cancer With Epidermal Growth Factor Receptor Activation Mutations	II
No NCT ID	ITAC 2 TRIAL: Intermittent TKI and Chemotherapy for Patients with Advanced Non-Small Cell Lung Cancer	II
NCT01951469	Multicenter Phase II Study of Gefitinib Mono-therapy or Gefitinib Combined With Pemetrexed/Cisplatin in Patients With Brain Metastases From Non-small Cell Lung Cancer Harboring EGFR Mutation	II
NCT02044328	Icotinib as an Adjuvant Therapy for Patients With Stage IIA-IIIA Adenocarcinoma With EGFR Mutation: a Prospective, Exploratory Study	II
NCT03804580	First-Line Treatment With Osimertinib In EGFR-Mutated Non-Small Cell Lung Cancer, Coupled To Extensive Translational Studies	II
NCT04335292	Osimertinib Then Chemotherapy in EGFR-mutated Lung Cancer With Osimertinib Third-line Rechallenge	II
NCT04410796	A Phase II Randomized Study of Osimertinib Versus Osimertinib Plus Chemotherapy for Patients With Metastatic EGFR-Mutant Lung Cancers That Have Detectable EGFR-Mutant cfDNA in Plasma After Initiation of Osimertinib	II
NCT03667820	Phase II Trial of Osimertinib in Combination With Stereotactic Ablative Radiation (SABR) in EGFR Mutant Advanced Non-Small Cell Lung Cancer (NSCLC)	II
NCT03318939	A Phase II Study of Pozitotinib in Patients With Non-Small Cell Lung Cancer (NSCLC), Locally Advanced or Metastatic, With EGFR or HER2 Exon 20 Insertion Mutation (ZENITH20).	II
NCT04862780	A Phase I/II Study Targeting Acquired Resistance Mechanisms in Patients With EGFR Mutant Non-Small Cell Lung Cancer	I/II
No NCT ID	A Phase I Study Afatinib In Combination Of Osimertinib In Patients With Relapsed Non-Small Cell Lung Cancer After Failure of Prior Osimertinib	I
NCT03755102	A Pilot Study of Dacomitinib With or Without Osimertinib for Patients With Metastatic EGFR Mutant Lung Cancers With Disease Progression on Osimertinib	I
NCT04762199	A Phase Ib Safety and Pharmacodynamic Study of MER Tyrosine Kinase Inhibitor, MRX-2843, in Combination With Osimertinib in Advanced EGFR Mutant Non-Small Cell Lung Cancer	I
NCT03891615	Phase I Study of Niraparib in Combination With Osimertinib in EGFR-Mutated Advanced Lung Cancer	I
NCT04250545	A Phase I Trial of MLN0128 (Sapanisertib) and CB-839 HCl (Telaglenastat) in Advanced NSCLC Patients	I
NCT03114319	An Open-label, Multi-center, Phase I, Dose Finding Study of Oral TNO155 in Adult Patients With Advanced Solid Tumors	I

## Clinical Trials Summary (continued)

### EGFR p.(L858R) c.2573\_2574delTGinsGT (continued)

NCT ID	Title	Phase
NCT04413201	AFAMOSI: Prospective, Randomized, Multicenter Phase IV Study to Evaluate the Efficacy and Safety of Afatinib Followed by Osimertinib Compared to Osimertinib in Patients With EGFRmutated/T790M Mutation Negative Non-squamous NSCLC in the First-line Setting	IV
No NCT ID	Apatinib Combined With EGFR-TKI For Patients With EGFR Mutation Who Failed EGFR-TKI: A Prospective Study	IV
No NCT ID	A Real World Study Of Apatinib Combined With Gefitinib In The Treatment Of EGFRm+ Advanced Non-Squamous Non-Small Cell Lung Cancer	IV
No NCT ID	Clinical Study Of Combined Action Of Gefitinib And Brain Radiotherapy On EGFR-Mutated Non-Small-Cell Lung Cancer Patients With Brain Metastasis	IV
No NCT ID	Clinical Study Of Combined Action Of Icotinib And Brain Radiotherapy On EGFR-Mutated Non-Small-Cell Lung Cancer Patients With Brain Metastasis	IV
NCT03800134	A Phase III, Double-blind, Placebo-controlled, Multi-center International Study of Neoadjuvant/Adjuvant Durvalumab for the Treatment of Patients With Resectable Stages II and III Non-small Cell Lung Cancer (AEGEAN)	III
NCT03656393	Observational Clinical Trial of Adjuvant Chemotherapy for Non-squamous Cell Carcinoma of Non-small Cell Lung Cancer	III
NCT03992885	Combination Therapy With Icotinib, Pemetrexed and Platinum in Patients With Metastatic Non-squamous Non-small Cell Lung Cancer With EGFR Mutations Who Did Not Progress After Pemetrexed in Combination With Platinum-based Chemotherapy:a Single-arm, Open, Multicenter Clinical Study.	III
No NCT ID	A Phase II Study Of Afatinib For Advanced Non-Small Cell Lung Cancer With Uncommon Epidermal Growth Factor Receptor (EGFR) Mutation Including Compound Mutation Detected By Next Generation Sequencing	II
No NCT ID	A Single-center, Open Label, Phase II Study of Anlotinib as Second/Third-line Treatment for Advanced Non-small Cell Lung Cancer	II
NCT04619563	A Single-arm Exploratory Clinical Study of Anlotinib Hydrochloride Combined With Docetaxel in EGFR Mutations Advanced Non Small Cell Lung Cancer Patients Who Have Progressed After Targeted Therapy and Chemotherapy	II
No NCT ID	Clinical Study And Safety Analysis On The Treatment Of Advanced Non-Small Cell Lung Cancer With Anlotinib And Gefitinib	II
No NCT ID	Osimertinib Combined Bevacizumab in Untreated Epidermal Growth Factor Receptor Mutated Non-small-cell Lung Cancer Patients with Malignant Pleural And/Or Pericardial Effusion -phase II Trial	II
No NCT ID	Randomized Controlled Trial for EGFR-TKIs Plus S-1 or EGFR-TKIs as the First-Line Therapy for Patients with Advanced Non-small Cell Lung Cancer Harboring EGFR Mutations	II
No NCT ID	EGFR-TKI Combined With Stereotactic Body Radiation Therapy Versus TKI alone for Stage IV Oncogene-Driven Non-Small Cell Lung Cancer.	II
No NCT ID	Efficacy and Safety of Erlotinib in Elderly Patients With Non-small-cell Lung Cancer Harboring Epidermal Growth Factor Receptor Mutations	II
NCT04591431	The Rome Trial From Histology to Target: the Road to Personalize Target Therapy and Immunotherapy	II
NCT03904823	An Open, Single-arm, Multi-center, Phase II Clinical Trial of Famitinib Combined With Epidermal Growth Factor Receptor (EGFR) Inhibitor HS-10296 in Patients With Advanced EGFR-mutant Non-Small Cell Lung Cancer (NSCLC)	II

## Clinical Trials Summary (continued)

### EGFR p.(L858R) c.2573\_2574delTGinsGT (continued)

NCT ID	Title	Phase
NCT01784549	A Multi-center Phase II Randomized Study of Customized Neoadjuvant Therapy Versus Standard Chemotherapy in Non-small Cell Lung Cancer (NSLC) Patients With Resectable Stage IIIA (N2) Disease	II
NCT02960607	A Phase II Study of High-dose Icotinib in Previously Treated Non-small Cell Lung Cancer Patients With Epidermal Growth Factor Receptor Mutation	II
No NCT ID	Open-Label, Single arm, Phase II trial to Evaluate Efficacy and Safety of Nivolumab as Maintenance Therapy Following Platinum-based Chemotherapy in Non-Small Cell Lung Cancer Patients after Tyrosine Kinase Inhibitor Therapy	II
NCT04538378	Phase II Trial of Olaparib (LYNPARZA) Plus Durvalumab (IMFINZI) in EGFR-Mutated Adenocarcinomas That Transform to Small Cell Lung Cancer (SCLC) and Other Neuroendocrine Tumors.	II
NCT03460275	Osimertinib as First-line Therapy for Patients With EGFR Mutation-positive Locally Advanced or Metastatic Non-squamous Non-Small Cell Lung Cancer(NSCLC), a Single-Arm, Open-Label, Prospective, Multicenter, Phase II Clinical Trial	II
No NCT ID	Efficacy Of Osimertinib With Platinum And Pemetrexed In EGFR Mutant Non-Small Cell Lung Cancer Patients Bearing CNS Metastasis, And Have Systemic Progression But Stable Intracranial Disease On Osimertinib Resistance. (EPONA)	II
No NCT ID	An Exploratory Clinical Study Of PD-1 Inhibitor Combined With Chemotherapy In The Treatment Of Advanced Non-small Cell Lung Cancer With EGFR Mutation Positive And T790M Negative After Failure Of TKI Combined With Antiangiogenic Drugs	II
No NCT ID	Phase II Trial Of Docetaxel Plus Ramucirumab Combination Therapy In Patients With Advanced EGFR Gene Mutation Positive Advanced Stage Non-Squamous Cell Non small Cell Lung Cancer	II
No NCT ID	Clinical Study of Combined Action of the First Generation of TKIs and Brain Radiotherapy on EGFR-Mutated Non-Small-Cell Lung Cancer Patients with Brain Metastasis	II
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
NCT03797391	First-in-human, Phase I/II, Multicenter, Open-Label Study of EMB-01 in Patients With Advanced/ Metastatic Solid Tumors	I/II
No NCT ID	A phase I/II study of erlotinib/carboplatin/pemetrexed/bevacizumab in chemotherapy-naïve patients with EGFR mutation positive advanced non-squamous non-small-cell lung cancer	I/II
NCT03758287	A Phase Ib, Multi-center, Open Label Study of Ningetinib (CT053PTSA) in Combination With Gefitinib in Stage IIIB or IV NSCLC Patients With EGFR Mutation and T790M Negative Who Have Progressed After EGFR TKI Therapy	I/II
NCT03711422	A Dose Finding Study of Continuous and Intermittent High-dose (HDI) Afatinib (EGFR TKI) on CNS Metastases and Leptomeningeal Disease (LMD) in Patients With Advanced Refractory EGFR Mutation Positive Non-small Cell Lung Cancer	I
NCT04528836	A Phase I/IB First-in-Human Study of the SHP2 Inhibitor BBP-398 (Formerly Known as IACS-15509) in Patients With Advanced Solid Tumors	I
No NCT ID	Feasibility Study of Pemetrexed / Bevacizumab / Erlotinib in Chemotherapy Naïve Patients With Non-Small Cell Lung Cancer Harboring EGFR Mutation	I
No NCT ID	Phase I Study of DZD9008 in EGFR or HER2 Mutant NSCLC Chinese Patients	I
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

## Clinical Trials Summary (continued)

### EGFR p.(L858R) c.2573\_2574delTGinsGT (continued)

NCT ID	Title	Phase
NCT04013542	A Pilot Trial of Ipilimumab-Nivolumab in Local-Regionally Advanced Non Small Cell Lung Cancer (NSCLC)	I
No NCT ID	Pharmacokinetic and dose finding study of osimertinib in patients with impaired renal function and low body weight	I
No NCT ID	A Pilot Study for Apatinib Mesylate Combined with Gefitinib in First-line Treatment of Lung Adenocarcinoma with Malignant Pleural Effusion or Pericardial Effusion	IV
NCT04209465	MasterKey-01: A Phase I/II, Open-label, Two-part, Multicenter Study to Assess the Safety, Tolerability, Pharmacokinetics & Antitumor Activity of BDTX-189, an Inhibitor of Allosteric ErbB Mutations, in Patients w/ Advanced Solid Malignancies	I/II
NCT03618043	A Phase I, Open-label Study to Assess the Safety and Tolerability of Ascending Doses of SH-1028 Tablets in Patients With Advanced Solid Cancer.	I
NCT03810872	An Open Explorative Phase II, Open Label Study of Afatinib in the Treatment of Advanced Cancer Carrying an EGFR, a HER2 or a HER3 Mutation	II
NCT02465060	Molecular Analysis for Therapy Choice (MATCH).	II
NCT03239015	Efficacy and Safety of Targeted Precision Therapy in Refractory Tumor With Druggable Molecular Event	II
NCT03065387	Phase I Study of the Pan-ERBB Inhibitor Neratinib Given in Combination With Everolimus, Palbociclib, or Trametinib in Advanced Cancer Subjects With EGFR Mutation/Amplification, HER2 Mutation/Amplification, or HER3/4 Mutation or KRAS Mutation	I
No NCT ID	Phase I Clinical Study With Advanced Solid Tumors KBP-5209 Treatment	I
NCT04128085	A Phase I, Open-label, Multicenter, Dose Escalation and Expansion Study to Evaluate the Tolerance and Pharmacokinetics of TQB3804 in Subjects With Advanced Malignant Tumors	I
NCT03841110	FT500 as Monotherapy and in Combination With Immune Checkpoint Inhibitors in Subjects With Advanced Solid Tumors (Phase I)	I
NCT04412616	A Phase I, Multicenter, Open-label Study to Evaluate the Safety, Tolerability, Pharmacokinetics, Immunogenicity, and Preliminary Evidence of Antitumor Activity of ZZ06 in Adult Patients With Advanced EGFR Positive Solid Tumor Malignancies	I
NCT03297606	Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR): A Phase II Basket Trial	II
NCT04429542	First-in-Human, Phase I/Ib, Open-label, Multicenter Study of Bifunctional EGFR/TGFβ Fusion Protein BCA101 Alone and in Combination With Pembrolizumab in Patients With EGFR-Driven Advanced Solid Tumors	I

### CDK4 p.(R24H) c.71G>A

NCT ID	Title	Phase
NCT04591431	The Rome Trial From Histology to Target: the Road to Personalize Target Therapy and Immunotherapy	II
NCT03239015	Efficacy and Safety of Targeted Precision Therapy in Refractory Tumor With Druggable Molecular Event	II
NCT03994796	Genomically-Guided Treatment Trial in Brain Metastases	II
NCT03297606	Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR): A Phase II Basket Trial	II
NCT03155620	NCI-COG Pediatric MATCH (Molecular Analysis for Therapy Choice) Screening Protocol	II



## Clinical Trials Summary (continued)

### CDK4 p.(R24H) c.71G>A (continued)

NCT ID	Title	Phase
NCT03526250	NCI-COG Pediatric MATCH (Molecular Analysis for Therapy Choice) - Phase 2 Subprotocol of Palbociclib in Patients With Tumors Harboring Activating Alterations in Cell Cycle Genes	II
NCT04247126	A Phase I Study of SY 5609, an Oral, Selective CDK7 Inhibitor, in Adult Patients With Select 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 2021-05-12. For the most up-to-date information, search [www.fda.gov](http://www.fda.gov).

### EGFR p.(L858R) c.2573\_2574delTGinsGT

#### 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 EFGR 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 2021-05-03. 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.(L858R) c.2573\_2574delTGinsGT

#### 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 4.2021]

## EGFR p.(L858R) c.2573\_2574delTGinsGT (continued)

### – 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 4.2021]

### – 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 4.2021]

### – 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 4.2021]

### – 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 4.2021]

### – 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 4.2021]

## EGFR p.(L858R) c.2573\_2574delTGinsGT (continued)

### — 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 4.2021]

### — 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 4.2021]

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## Signatures

Testing Personnel:

Laboratory Supervisor:

Pathologist:



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