



## Sample Information

**Patient Name:** 劉美滿  
**Gender:** Female  
**ID No.:** F221621203  
**History No.:** 47011121  
**Age:** 50

**Ordering Doctor:** DOC3182F 陳均嘉  
**Ordering REQ.:** 0BWMRMN  
**Signing in Date:** 2022/06/23

**Path No.:** S111-99610  
**MP No.:** F22062  
**Assay:** Oncomine Focus Assay  
**Sample Type:** FFPE  
**Block No.:** C111-16879  
**Percentage of tumor cells:** 20%

**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  
17 Therapies Available  
15 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 exon 19 deletion, EGFR amplification</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 exon 19 deletion</b> epidermal growth factor receptor Allele Frequency: 85.46%	<b>afatinib</b> <sup>1, 2</sup> <b>bevacizumab* + erlotinib</b> <sup>2</sup> <b>dacomitinib</b> <sup>1, 2</sup> <b>erlotinib</b> <sup>1, 2</sup> <b>erlotinib + ramucirumab</b> <sup>1, 2</sup> <b>gefitinib*</b> <sup>1, 2</sup> <b>osimertinib</b> <sup>1, 2</sup> atezolizumab + bevacizumab + chemotherapy bevacizumab + gefitinib gefitinib + chemotherapy osimertinib + chemotherapy	None	15
IIC	<b>AR amplification</b> androgen receptor	None	hormone therapy	0

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

### Prevalent cancer biomarkers without relevant evidence based on included data sources

PIK3CA amplification, EGFR amplification, MYCN amplification

## 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. (L747_A750delinsP)	c.2239_2248delTTAA GAGAAGinsC	COSM12382	chr7:55242469	85.46%	NM_005228.5	nonframeshift Block Substitution	1967

### Copy Number Variations

Gene	Locus	Copy Number
MYCN	chr2:16080663	30.4
PIK3CA	chr3:178916683	9.75
EGFR	chr7:55198956	42.8
AR	chrX:66776186	12.2

## Biomarker Descriptions

### AR (androgen receptor)

**Background:** The AR gene encodes the androgen receptor protein (AR), a ligand-activated transcription factor regulated by the binding of the hormones testosterone and dihydrotestosterone<sup>1,2</sup>. Hormone binding to AR results in receptor dimerization, nuclear translocation, and target gene transcription, thus activating the RAS/RAF/MEK/ERK and PI3K/AKT/MTOR signaling pathways, which promote cell proliferation and survival<sup>2,3,4</sup>.

## Biomarker Descriptions (continued)

**Alterations and prevalence:** Alterations in AR function can result from overexpression, gene amplification, or mutations. AR mutations, including L702H, W742C/L, H875Y, and T878A, are commonly observed in 10-30% of castration-resistant prostate cancer and result in decreased ligand specificity, allowing other nuclear hormones to activate AR<sup>5</sup>. Androgen receptor splice variants have been reported in castration resistant prostate cancer<sup>6,7</sup>. The androgen receptor splice variant 7 (AR-V7) is a result of aberrant mRNA splicing of AR exons 1-3 and a cryptic exon 3, resulting in the expression of a constitutively active protein<sup>7</sup>.

**Potential relevance:** The FDA has granted fast track designation (2022) to the selective androgen receptor targeting agonist, enobosarm, for the treatment of patients with androgen AR-positive, estrogen receptor (ER)-positive, HER2-negative metastatic breast cancer<sup>8</sup>. The FDA also granted fast track designation (2016) to the small-molecule CYP17 lyase-selective inhibitor, seviteronel, for AR-positive triple-negative breast cancer (TNBC) patients<sup>9</sup>. Androgen deprivation therapy (ADT) such as abiraterone<sup>10</sup> (2011) and enzalutamide<sup>11</sup> (2011) are FDA approved for use in locally advanced and metastatic prostate cancers. Although many men initially respond to ADT, most will develop hormone resistance. Resistance to ADT is also associated with other aberrations of the AR gene including mutations within the ligand binding domain and gene amplification<sup>5,12,13</sup>. The androgen receptor splice variant, AR-V7, lacks the ligand binding domain, resulting in constitutive activation and is associated with resistance to androgen deprivation therapy (ADT) in advanced prostate cancer<sup>6</sup>.

### 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>17,18,19,20</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>21</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>22,23,24,25</sup>. EGFR activating mutations in lung cancer tend to be mutually exclusive to KRAS activating mutations<sup>26</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>21,27</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>18,19,20,27,28</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>29,30,31</sup>.

**Potential relevance:** Approved first-generation EGFR tyrosine kinase inhibitors (TKIs) include erlotinib<sup>32</sup> (2004) and gefitinib<sup>33</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>34</sup> (2013) and dacomitinib<sup>35</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>36,37,38,39</sup>. However, in 2021, the irreversible tyrosine kinase inhibitor, mobocertinib<sup>40</sup> was FDA approved for the treatment of NSCLC with EGFR exon 20 insertion mutations. Additionally, in 2022, the FDA granted breakthrough therapy designation to the irreversible EGFR inhibitors, CLN-081 (TPC-064)<sup>41</sup> and DZD-9008<sup>42</sup>, for locally advanced or metastatic non-small cell lung cancer harboring EGFR exon 20 insertion mutations. In lung cancer containing EGFR exon 19 or 21 activating mutations, treatment with TKIs is eventually associated with the emergence of drug resistance<sup>43</sup>. The primary resistance mutation that emerges following treatment with first-generation TKI is T790M, accounting for 50-60% of resistant cases<sup>21</sup>. Third generation TKIs were developed to maintain sensitivity in the presence of T790M. Osimertinib<sup>44</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>43</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>45</sup>. T790M and C797S can occur in either cis or trans allelic orientation<sup>45</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>45</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>45,46</sup>. However, C797S occurring in cis conformation with T790M, confers resistance to first- and third-generation TKIs<sup>45</sup>. Fourth-generation TKIs are in development to overcome acquired C797S and T790M resistance

## Biomarker Descriptions (continued)

mutations after osimertinib treatment. EGFR targeting antibodies including cetuximab (2004), panitumumab (2006), and necitumumab (2016) are under investigation in combination with EGFR-targeting TKIs for efficacy against EGFR mutations. The bispecific antibody, amivantamab<sup>47</sup>, targeting EGFR and MET was approved (2021) NSCLC tumors harboring EGFR exon 20 insertion mutations. The Oncoprex immunogene therapy quaratusugene ozeplasmid<sup>48</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>49</sup> was granted a fast track designation (2020) for the treatment of solid tumors harboring an EGFR exon 20 insertion mutation.

### MYCN (MYCN proto-oncogene, bHLH transcription factor)

**Background:** The MYCN gene encodes the MYCN proto-oncogene (n-MYC), a basic helix-loop-helix transcription factor. MYCN is a member of the MYC oncogene family that regulates the expression of numerous genes that control cell cycle progression, apoptosis, metabolic pathways, and cellular transformation<sup>50,51,52,53,54</sup>. MYCN amplification is correlated with failure of cells to arrest in G1 phase of the cell cycle, leading to uncontrolled proliferation<sup>55</sup>. Like MYC, MYCN functions as a heterodimer in complex with the transcription factor MAX<sup>52,56</sup>.

**Alterations and prevalence:** Recurrent somatic mutations in MYCN, including codon P44, are observed in approximately 2% of neuroblastoma with the same variants observed in Wilms' tumor<sup>57,58</sup>. MYCN amplification is found in 20 to 30% of neuroblastoma<sup>59</sup>. Amplification and overexpression of MYCN is also common in other central nervous system cancers as well as prostate cancer, hematologic malignancies, and pancreatic cancer<sup>60</sup>.

**Potential relevance:** Currently, no therapies are approved for MYCN aberrations. Dysregulation of MYCN is associated with poor prognosis of several pediatric tumor types including neuroblastoma, Wilms' tumor, retinoblastoma, medulloblastoma, and rhabdomyosarcoma<sup>55</sup>. In neuroblastoma, increased MYCN signaling is directly related to tumor aggressiveness and increased metastatic potential<sup>55,61</sup>. Strategies targeting MYCN driven cancers currently focus on targeting MYCN expression, transcription, and synthetic lethality associated with MYCN overexpression<sup>60</sup>.

### PIK3CA (phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha)

**Background:** The PIK3CA gene encodes the phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha of the class I phosphatidylinositol 3-kinase (PI3K) enzyme<sup>62</sup>. PI3K is a heterodimer that contains a p85 regulatory subunit, which couples one of four p110 catalytic subunits to activated tyrosine protein kinases<sup>63,64</sup>. The p110 catalytic subunits include p110α, β, δ, γ and are encoded by genes PIK3CA, PIK3CB, PIK3CD, and PIK3CG, respectively<sup>63</sup>. PI3K catalyzes the conversion of phosphatidylinositol (4,5)-bisphosphate (PI(4,5)P2) into phosphatidylinositol (3,4,5)-trisphosphate (PI(3,4,5)P3) while the phosphatase and tensin homolog (PTEN) catalyzes the reverse reaction<sup>65,66</sup>. The reversible phosphorylation of inositol lipids regulates diverse aspects of cell growth and metabolism<sup>65,66,67,68</sup>. Recurrent somatic alterations in PIK3CA are frequent in cancer and result in the activation of PI3K/AKT/MTOR pathway, which can influence several hallmarks of cancer including cell proliferation, apoptosis, cancer cell metabolism and invasion, and genetic instability<sup>69,70,71</sup>.

**Alterations and prevalence:** Recurrent somatic activating mutations in PIK3CA are common in diverse cancers and are observed in 20-30% of breast, cervical, and uterine cancers and 10-20% of bladder, gastric, head and neck, and colorectal cancers<sup>19,20</sup>. Activating mutations in PIK3CA commonly cluster in two regions corresponding to the exon 9 helical (codons E542/E545) and exon 20 kinase (codon H1047) domains, each having distinct mechanisms of activation<sup>72,73,74</sup>. PIK3CA resides in the 3q26 cytoband, a region frequently amplified (10-30%) in diverse cancers including squamous carcinomas of the lung, cervix, head and neck, and esophagus, and in serous ovarian and uterine cancers<sup>19,20</sup>.

**Potential relevance:** The PI3K inhibitor, alpelisib<sup>75</sup>, is FDA approved (2019) in combination with fulvestrant for the treatment of patients with PIK3CA-mutated, hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, advanced or metastatic breast cancer. Additionally, a phase Ib study of alpelisib with letrozole in patients with metastatic estrogen receptor (ER)-positive breast cancer, the clinical benefit rate, defined as lack of disease progression ≥ 6 months, was 44% (7/16) in PIK3CA-mutated tumors and 20% (2/20) in PIK3CA wild-type tumors<sup>76</sup>. Specifically, exon 20 H1047R mutations were associated with more durable clinical responses in comparison to exon 9 E545K mutations<sup>76</sup>. However, alpelisib did not improve response when administered with letrozole in patients with ER+ early breast cancer with PIK3CA mutations<sup>77</sup>. Case studies with MTOR inhibitors sirolimus and temsirolimus report isolated cases of clinical response in PIK3CA mutated refractory cancers<sup>78,79</sup>.

## Relevant Therapy Summary

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

### EGFR exon 19 deletion

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
osimertinib	●	●	●	●	● (III)
afatinib	●	●	●	●	● (II)
dacomitinib	●	●	●	●	✕
erlotinib	●	●	●	●	✕
erlotinib + ramucirumab	●	●	●	●	✕
gefitinib	●	●	●	●	✕
bevacizumab + erlotinib	✕	●	●	●	✕
osimertinib + chemotherapy	✕	●	✕	✕	✕
bevacizumab (Allergan) + erlotinib	✕	✕	●	✕	✕
bevacizumab (Fujifilm Kyowa Kirin Biologics) + erlotinib	✕	✕	●	✕	✕
bevacizumab (Mabxience) + erlotinib	✕	✕	●	✕	✕
bevacizumab (Pfizer) + erlotinib	✕	✕	●	✕	✕
bevacizumab (Samsung Bioepis) + erlotinib	✕	✕	●	✕	✕
bevacizumab (Stada) + erlotinib	✕	✕	●	✕	✕
gefitinib (Mylan)	✕	✕	●	✕	✕
atezolizumab + bevacizumab + carboplatin + paclitaxel	✕	✕	✕	●	✕
bevacizumab + gefitinib	✕	✕	✕	●	✕
gefitinib + carboplatin + pemetrexed	✕	✕	✕	●	✕
amivantamab, lazertinib, chemotherapy	✕	✕	✕	✕	● (III)
amivantamab, lazertinib, osimertinib	✕	✕	✕	✕	● (III)
durvalumab, chemotherapy	✕	✕	✕	✕	● (III)
osimertinib, chemotherapy	✕	✕	✕	✕	● (III)
atezolizumab, bevacizumab, chemotherapy	✕	✕	✕	✕	● (II)
durvalumab, tremelimumab, chemotherapy	✕	✕	✕	✕	● (II)
osimertinib, savolitinib	✕	✕	✕	✕	● (II)
BLU-945	✕	✕	✕	✕	● (I/II)
sunvozertinib	✕	✕	✕	✕	● (I/II)
amivantamab, lazertinib	✕	✕	✕	✕	● (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 exon 19 deletion (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
lazertinib, amivantamab	×	×	×	×	● (I)
telisotuzumab vedotin, osimertinib	×	×	×	×	● (I)
TNO-155, nazartinib	×	×	×	×	● (I)

### AR amplification

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
bicalutamide	×	○	×	×	×
leuprorelin	×	○	×	×	×

\* 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 2022-04-13. For the most up-to-date information, search [www.fda.gov](https://www.fda.gov).

### EGFR exon 19 deletion

#### ● afatinib

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

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

**Variant class:** EGFR exon 19 deletion

#### Indications and usage:

GILOTRIF® is a kinase inhibitor indicated for:

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

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

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

#### Reference:

[https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2022/201292s017lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/201292s017lbl.pdf)

## EGFR exon 19 deletion (continued)

### ● dacomitinib

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

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

**Variant class:** EGFR exon 19 deletion

**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)

### ● erlotinib

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

**Label as of:** 2016-10-18

**Variant class:** EGFR exon 19 deletion

**Indications and usage:**

TARCEVA® is a kinase inhibitor indicated for:

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

**Limitations of Use:**

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

**Reference:**

[https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2016/021743s025lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/021743s025lbl.pdf)

### ● erlotinib + ramucirumab

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

**Label as of:** 2022-03-22

**Variant class:** EGFR exon 19 deletion

**Indications and usage:**

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

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

**Reference:**

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

## EGFR exon 19 deletion (continued)

### ● gefitinib

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

**Label as of:** 2021-05-05

**Variant class:** EGFR exon 19 deletion

**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:** 2022-01-19

**Variant class:** EGFR exon 19 deletion

**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/2022/208065s025lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/208065s025lbl.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 2022-03-31. 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 exon 19 deletion

#### ● afatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

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 3.2022]

#### ● dacomitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

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 3.2022]

#### ● erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

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 3.2022]

#### ● gefitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

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 3.2022]

## EGFR exon 19 deletion (continued)

### ● osimertinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

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 3.2022]

### ● afatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

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 3.2022]

### ● bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Non-squamous Cell; Advanced, Metastatic (First-line therapy); Other recommended intervention
- Non-squamous Cell; Advanced, Metastatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2022]

### ● dacomitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

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 3.2022]

## EGFR exon 19 deletion (continued)

### ● erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

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 2.2021]

### ● erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

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 3.2022]

### ● erlotinib + ramucirumab

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

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 3.2022]

### ● gefitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR exon 19 deletion

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 3.2022]

## EGFR exon 19 deletion (continued)

### ● osimertinib

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

**Variant class:** EGFR exon 19 deletion

**NCCN Recommendation category:** 2A

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

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

**Reference:** NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 2.2021]

### ● osimertinib

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

**Variant class:** EGFR exon 19 deletion

**NCCN Recommendation category:** 2A

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

- Stage IB , Stage IIA, Stage IIB, Stage IIIA, Stage IIIB; Resected (Adjuvant therapy)
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (Subsequent therapy); Preferred intervention
- Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Leptomeningeal Metastases, Progression (Subsequent therapy); Consider

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2022]

### ● osimertinib + chemotherapy

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

**Variant class:** EGFR exon 19 deletion

**NCCN Recommendation category:** 2A

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

- Stage IB , Stage IIA, Stage IIB, Stage IIIA; Resected (Adjuvant therapy)

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2022]

### ● erlotinib

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

**Variant class:** EGFR exon 19 deletion

**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 2.2021]

## EGFR exon 19 deletion (continued)

### ● afatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFRi sensitizing mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Brain Metastases (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 2.2021]

### ● gefitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFRi sensitizing mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Brain Metastases (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 2.2021]

## AR amplification

### ○ bicalutamide

Cancer type: Head and Neck Cancer

Variant class: AR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Salivary Gland Neoplasm; Recurrent, Unresectable, Distant Metastases (Line of therapy not specified); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Head and Neck Cancers [Version 1.2022]

### ○ leuprorelin

Cancer type: Head and Neck Cancer

Variant class: AR positive

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Salivary Gland Neoplasm; Recurrent, Unresectable, Distant Metastases (Line of therapy not specified); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Head and Neck Cancers [Version 1.2022]

## 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 2022-04-13. For the most up-to-date information, search [www.ema.europa.eu/ema](https://www.ema.europa.eu/ema).

### EGFR exon 19 deletion

#### ● afatinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2021-04-21

Variant class: EGFR exon 19 deletion

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: 2021-09-06

Variant class: EGFR exon 19 deletion

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: 2021-06-23

Variant class: EGFR exon 19 deletion

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: 2021-12-21

Variant class: EGFR exon 19 deletion

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: 2022-03-29

Variant class: EGFR exon 19 deletion

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 exon 19 deletion

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 exon 19 deletion (continued)

### ● bevacizumab (Samsung Bioepis) + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2021-06-21

Variant class: EGFR exon 19 deletion

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 (Stada) + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2022-03-17

Variant class: EGFR exon 19 deletion

Reference:

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

### ● bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2022-04-11

Variant class: EGFR exon 19 deletion

Reference:

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

### ● bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2022-03-16

Variant class: EGFR exon 19 deletion

Reference:

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

### ● dacomitinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2021-07-21

Variant class: EGFR exon 19 deletion

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: 2021-08-18

Variant class: EGFR exon 19 deletion

Reference:

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

## EGFR exon 19 deletion (continued)

### ● erlotinib + ramucirumab

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2022-01-28

Variant class: EGFR exon 19 deletion

Other criteria: EGFR T790M mutation negative

Reference:

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

### ● gefitinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2021-03-05

Variant class: EGFR exon 19 deletion

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)

### ● gefitinib (Mylan)

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2021-12-15

Variant class: EGFR exon 19 deletion

Reference:

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

### ● osimertinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2022-04-07

Variant class: EGFR exon 19 deletion

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 2022-03-31. For the most up-to-date information, search [www.esmo.org](http://www.esmo.org).

### EGFR exon 19 deletion

#### ● osimertinib

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR exon 19 deletion

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

Population segment (Line of therapy):

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

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

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

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR exon 19 deletion

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.]

## EGFR exon 19 deletion (continued)

### ● erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFRi sensitizing mutation

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

Population segment (Line of therapy):

- Advanced (First-line therapy)

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

### ● gefitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFRi sensitizing mutation

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

Population segment (Line of therapy):

- Advanced (First-line therapy)

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

### ● osimertinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFRi sensitizing mutation

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

Population segment (Line of therapy):

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

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

### ● 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.]

## EGFR exon 19 deletion (continued)

### ● erlotinib

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

**Variant class:** EGFRi sensitizing mutation

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

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

- Non-squamous Cell (Maintenance therapy)

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

### ● afatinib

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

**Variant class:** EGFR activating mutation

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

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

- Stage IV (First-line therapy)

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

### ● bevacizumab + erlotinib

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

**Variant class:** EGFR activating mutation

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

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

- Stage IV (First-line therapy)

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

### ● 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.]

## EGFR exon 19 deletion (continued)

### ● dacomitinib

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

**Variant class:** EGFR activating mutation

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

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

- Stage IV (First-line therapy)

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

### ● erlotinib

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

**Variant class:** EGFR activating mutation

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

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

- Stage IV (First-line therapy)

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

### ● erlotinib + ramucirumab

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

**Variant class:** EGFR activating mutation

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

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

- Stage IV (First-line therapy)

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

### ● 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.]

## EGFR exon 19 deletion (continued)

### ● gefitinib + carboplatin + pemetrexed

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

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

Population segment (Line of therapy):

- Stage IV (First-line therapy)

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

### ● bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

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

Population segment (Line of therapy):

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

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

### ● bevacizumab + gefitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

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

Population segment (Line of therapy):

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

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

### ● 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.]

## EGFR exon 19 deletion (continued)

### ● gefitinib + carboplatin + pemetrexed

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

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

Population segment (Line of therapy):

- Advanced (First-line therapy)

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

### ● afatinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

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

Population segment (Line of therapy):

- Stage IV (First-line therapy)

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

### ● bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

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

Population segment (Line of therapy):

- Stage IV (First-line therapy)

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

### ● 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.]

## EGFR exon 19 deletion (continued)

### ● dacomitinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

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

Population segment (Line of therapy):

- Stage IV (First-line therapy)

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

### ● erlotinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

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

Population segment (Line of therapy):

- Stage IV (First-line therapy)

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

### ● erlotinib + ramucirumab

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

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

Population segment (Line of therapy):

- Stage IV (First-line therapy)

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

### ● 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.]

## EGFR exon 19 deletion (continued)

### ● gefitinib + carboplatin + pemetrexed

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR activating mutation

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

Population segment (Line of therapy):

- Stage IV (First-line therapy)

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



## Clinical Trials in Taiwan region:

### Clinical Trials Summary

#### EGFR exon 19 deletion

NCT ID	Title	Phase
NCT04988295	A Phase III, Open-Label, Randomized Study of Amivantamab and Lazertinib in Combination With Platinum-Based Chemotherapy Compared With Platinum-Based Chemotherapy in Patients With EGFR-Mutated Locally Advanced or Metastatic Non-Small Cell Lung Cancer After Osimertinib Failure	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
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
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
NCT05215548	A Phase II Study of Primary Tumor Resection for Stage IV Non-small-cell Lung Cancer Without Progression After First-line Epidermal Growth Factor Receptor-tyrosine Kinase Inhibitor	II
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
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
NCT03778229	A Phase II, Single Arm Study Assessing Efficacy of Osimertinib With Savolitinib in Patients With EGFRm + MET+, Locally Advanced or Metastatic Non Small Cell Lung Cancer Who Have Progressed Following Osimertinib Treatment (SAVANNAH Study)	II
NCT02609776	A Phase I, First-in-Human, Open-Label, Dose Escalation Study of JNJ-61186372, a Human Bispecific EGFR and cMet Antibody, in Subjects With Advanced Non-Small Cell Lung Cancer	I
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
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
NCT04862780	A Phase I/II Study Targeting Acquired Resistance Mechanisms in Patients With EGFR Mutant Non-Small Cell Lung Cancer	I/II
NCT03114319	An Open-label, Multi-center, Phase I, Dose Finding Study of Oral TNO155 in Adult Patients With Advanced Solid Tumors.	I
NCT03974022	A Phase I/II, Open-Label, Multicenter Study to Assess the Safety, Tolerability, Pharmacokinetics and Anti-tumor Efficacy of DZD9008 in Patients With Advanced Non-Small Cell Lung Cancer (NSCLC) with EGFR or HER2 Mutation	I/II
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

## Alerts Informed By Public Data Sources

### Current FDA Information

 Contraindicated
  Not recommended
  Resistance
  Breakthrough
  Fast Track

FDA information is current as of 2022-04-13. For the most up-to-date information, search [www.fda.gov](https://www.fda.gov).

### EGFR exon 19 deletion

#### patritumab deruxtecan

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

**Variant class:** EGFR exon 19 deletion

**Supporting Statement:**

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

**Reference:**

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

#### osimertinib + quaratusugene ozeplasmid

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

**Variant class:** EGFR mutation

**Supporting Statement:**

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

**Reference:**

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

### AR amplification

#### enobosarm

**Cancer type:** Breast Cancer

**Variant class:** AR positive

**Other criteria:** ERBB2 negative, ER positive

**Supporting Statement:**

The FDA has granted Fast Track Designation to enobosarm for AR+/ER+/HER2- in metastatic breast cancer.

**Reference:**

<https://www.cancernetwork.com/view/fda-grants-fast-track-designation-to-enobosarm-in-ar-er-her2--metastatic-breast-cancer>

## AR amplification (continued)

### **seviteronel**

**Cancer type:** Triple Negative Breast Cancer

**Variant class:** AR positive

#### Supporting Statement:

The FDA has granted Fast Track Designation to the small-molecule CYP17 lyase-selective inhibitor, seviteronel, for:

- Androgen receptor (AR) positive advanced triple negative breast cancer (TNBC).
- Estrogen receptor (ER) positive advanced breast cancer.

#### Reference:

<https://www.businesswire.com/news/home/20160106006206/en/Innocrin-Pharmaceuticals-Granted-Fast-Track-Designation-FDA>

## Current NCCN Information

 Contraindicated

 Not recommended

 Resistance

 Breakthrough

 Fast Track

NCCN information is current as of 2022-03-31. 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 exon 19 deletion

### **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 rearrangements."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2022]

### **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 rearrangements."

**Reference:** NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2022]

## EGFR exon 19 deletion (continued)

### pembrolizumab

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR mutation

#### Summary:

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

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

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2022]

## Signatures

Testing Personnel:

Laboratory Supervisor:

Pathologist:

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