Taipei Veterans General Hospital

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Sample Information

Patient Name: 王秉達
Gender: Male
ID No.: F129092597
History No.: 48946594
Age: 33

Ordering Doctor: DOC8202A 鍾沂廷
Ordering REQ.: 0CRXRFS
Signing in Date: 2023/10/13

Path No.: M112-00266
MP No.: F23075
Assay: Oncomine Focus Assay
Sample Type: FFPE
Block No.: S112-50488A
Percentage of tumor cells: 80%

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

Note:

Sample Cancer Type: Non-Small Cell Lung Cancer

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Relevant Non-Small Cell Lung Cancer Variants

Gene	Finding	Gene	Finding
ALK	None detected	NTRK1	None detected
BRAF	None detected	NTRK2	None detected
EGFR	***EGFR p.(L858R) c.2573T>G, EGFR p.(V834L) c.2500G>T***	NTRK3	None detected
ERBB2	None detected	RET	None detected
KRAS	None detected	ROS1	None detected
MET	***MET amplification***		

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	*EGFR p.(L858R) c.2573T>G* epidermal growth factor receptor Allele Frequency: 42.73%	**afatinib** [1, 2] **bevacizumab* + erlotinib** [2] **dacomitinib** [1, 2] **erlotinib** [1, 2] **erlotinib + ramucirumab** [1, 2] **gefitinib** [1, 2] **osimertinib** [1, 2] atezolizumab + bevacizumab + chemotherapy gefitinib + chemotherapy	None	13
IA	*MET amplification* MET proto-oncogene, receptor tyrosine kinase	capmatinib crizotinib tepotinib	None	3
IA	*EGFR p.(V834L) c.2500G>T* epidermal growth factor receptor Allele Frequency: 42.42%	None	None	3

Public data sources included in relevant therapies: FDA[1], NCCN, **EMA**[2], ESMO
Tier Reference: Li et al. *Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists.* J Mol Diagn. 2017 Jan;19(1):4-23.
*** Includes biosimilars/generics**

Prevalent cancer biomarkers without relevant evidence based on included data sources

FGFR4 amplification

Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
EGFR	p.(V834L)	c.2500G>T	.	chr7:55259442	42.42%	NM_005228.5	missense	1999
EGFR	p.(L858R)	c.2573T>G	COSM6224	chr7:55259515	42.73%	NM_005228.5	missense	1994
JAK1	p.(P733=)	c.2199A>G	.	chr1:65310489	63.75%	NM_002227.4	synonymous	1997
ALK	p.(D1529E)	c.4587C>G	.	chr2:29416366	9.61%	NM_004304.5	missense	1997
ALK	p.(G1125=)	c.3375C>A	.	chr2:29445458	8.10%	NM_004304.5	synonymous	1999
PDGFRA	p.(M648V)	c.1942A>G	.	chr4:55144113	23.25%	NM_006206.6	missense	2000
FGFR4	p.(P136L)	c.407C>T	.	chr5:176517797	99.35%	NM_213647.3	missense	2000
MAP2K2	p.(V64=)	c.192C>T	.	chr19:4117528	35.10%	NM_030662.4	synonymous	2000

Copy Number Variations

Gene	Locus	Copy Number
FGFR4	chr5:176517312	4.83
MET	chr7:116313480	38.56

Biomarker Descriptions

EGFR (epidermal growth factor receptor)

Background: The EGFR gene encodes the epidermal growth factor receptor (EGFR) tyrosine kinase, a member of the ERBB/human epidermal growth factor receptor (HER) family. In addition to EGFR/ERBB1/HER1, other members of the ERBB/HER family include ERBB2/HER2, ERBB3/HER3, and ERBB4/HER4[1]. 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[2,3].

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[4,5,6,7]. 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[8]. 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[9,10,11,12]. EGFR activating mutations in lung cancer tend to be mutually exclusive to KRAS activating mutations[13]. 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[8,14]. 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[5,6,7,14,15]. 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[16,17,18].

Potential relevance: Approved first-generation EGFR tyrosine kinase inhibitors (TKIs) include erlotinib[19] (2004) and gefitinib[20] (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[21] (2013) and dacomitinib[22] (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[23,24,25,26]. However, in 2021, the irreversible tyrosine kinase inhibitor, mobocertinib[27]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)[28] and sunvozertinib[29], 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[30]. The primary resistance mutation that emerges following treatment with first-generation TKI is T790M, accounting for 50-60% of resistant cases[8]. Third generation TKIs were developed to maintain sensitivity in the presence of T790M. Osimertinib[31] (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[30]. 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[32]. T790M and C797S can occur in either cis or trans allelic orientation[32]. 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[32]. 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[32,33]. However, C797S occurring in cis conformation with T790M, confers resistance to first- and third-generation TKIs[32]. Fourth-generation TKIs are in development to overcome acquired C797S and T790M resistance mutations after osimertinib treatment. EGFR targeting antibodies including cetuximab (2004), panitumumab (2006), and necitumumab (2016) are under investigation in combination with EGFR-targeting TKIs for efficacy against EGFR mutations. The bispecific antibody, amivantamab[34], targeting EGFR and MET was approved (2021) for NSCLC tumors harboring EGFR exon 20 insertion mutations. CPO301[35] received a fast track designation (2023) from the FDA for EGFR mutations in patients with metastatic NSCLC who are relapsed/refractory or ineligible for EGFR targeting therapy such as 3rd-generation EGFR inhibitors including osimertinib. The Oncoprex immunogene therapy quaratusugene ozeplasmid[36] 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[37] was granted a fast track designation (2020) for the treatment of solid tumors harboring an EGFR exon 20 insertion mutation.

FGFR4 (fibroblast growth factor receptor 4)

Background: The FGFR4 gene encodes fibroblast growth receptor 4, a member of the fibroblast growth-factor receptor (FGFR) family that also includes FGFR1, 2, and 3. These proteins are single-transmembrane receptors composed of three extracellular immunoglobulin (Ig)-type domains and an intracellular kinase domain. Upon FGF-mediated stimulation, FGFRs activate several oncogenic signaling pathways, including the RAS/RAF/MEK/ERK, PI3K/AKT/MTOR, PLC/PKC, and JAK/STAT pathways influencing cell

Biomarker Descriptions (continued)

proliferation, migration, and survival[38,39,40]. FGFR4 selectively binds the ligand FGF19, wherein FGF19-mediated aberrant signaling has been identified as an oncogenic driver in hepatocellular carcinoma[41,42].

Alterations and prevalence: Aberrations most common to the FGFR family are amplifications, followed by mutations and fusions. The majority of these aberrations result in gain of function[43]. FGFR4 exhibits amplification in up to 15% of clear-cell renal cell carcinomas, with somatic mutations observed in up to 6% of melanomas and uterine cancer[6,7].

Potential relevance: Currently, no targeted therapies are approved for FGFR4 aberrations. However, FDA-approved multi-kinase inhibitors known to inhibit FGFR family members, including regorafenib (2013), ponatinib (2012), lenvatinib (2015), nintedanib (2014), and pazopanib (2009), have demonstrated anti-tumor activity in select cancer types harboring FGFR alterations[44,45,46,47,48,49,50]. Selective, irreversible FGFR4 inhibitors, including BLU-554, have underwent clinical trial evaluation. In a phase-I clinical study of BLU-554 in patients with FGF19-positive advanced hepatocellular carcinoma, the overall response rate was 17%[51].

MET (MET proto-oncogene, receptor tyrosine kinase)

Background: The MET proto-oncogene encodes a receptor tyrosine kinase for the hepatocyte growth factor (HGF) protein, which is expressed by mesenchymal cells. MET is expressed as multiple isoforms with transcript variant 1 (NM_001127500.3) encoding a 1408 amino acid protein and transcript variant 2 (NM_000245.4) encoding a 1390 amino acid protein, both of which possess an intact protein kinase domain[52]. Ubiquitin-dependent proteolysis is responsible for regulating the steady state level of the MET protein via recognition of the tyrosine phosphorylation site Y1003(NM_000245.4), sometimes referred to as Y1021 (NM_001127500.3), in the MET Cbl-binding domain within the juxtamembrane region[53,54,55]. Growth factor signaling leads to MET dimerization and subsequent initiation of downstream effectors including those involved in the RAS/RAF/MEK/ERK and PI3K/AKT signaling pathways, which regulate cell migration, proliferation, and survival[56,57].

Alterations and prevalence: Somatic mutations in MET are observed in 10% of uterine corpus endometrial carcinoma, 9% of skin cutaneous melanoma, 8% of papillary renal cell carcinoma (PRCC), and 4% of lung adenocarcinoma, colorectal adenocarcinoma, bladder urothelial carcinoma, and uterine carcinosarcoma[6,7]. Recurrent somatic MET alterations include activating mutations, gene amplification, and translocations generating MET gene fusions. Recurrent somatic mutations fall into two classes, mutations in the MET kinase domain, which are uncommon, and splice-site mutations affecting exon 14. Recurrent kinase domain mutations are observed in PRCC and include M1250T, H1094Y, and V1070E (NM_000245.4)[6,7]. Mutation of the Y1003 phosphorylation site is reported in approximately 2% of MET altered lung cancer[58]. In contrast, splice-site mutations flanking exon 14 are observed in 3-4% of all non-small cell lung cancer (NSCLC)[59]. These mutations include canonical splice site mutations affecting exon 14 and deletions that extend into the splicing motifs within intron 13[58,60]. Such mutations disrupt splicing leading to the formation of an alternative transcript that joins exon 13 directly to exon 15 and skips exon 14 entirely. The MET exon 14 skipping transcript lacks the juxtamembrane domain that contains the recognition motif for ubiquitin-dependent proteolysis and thus leads to a marked increase in the steady-state level of the MET protein[61]. MET exon 14 skipping mutations act as oncogenic drivers in lung cancer mutually exclusive to activating mutations in EGFR and KRAS and other oncogenic fusions such as ALK and ROS1[60,62,63]. MET is amplified in 2-5% of ovarian cancer, esophageal adenocarcinoma, stomach adenocarcinoma, glioblastoma, and lung adenocarcinoma[7,14,64]. Recurrent MET fusions, although infrequent, are observed in adult and pediatric glioblastoma, papillary renal cell carcinoma, lung cancer, liver cancer, thyroid cancer, and melanoma[65,66,67]. MET alterations are believed to be enriched in late-stage cancers where they drive tumor progression and metastasis[68,69,70].

Potential relevance: In 2020, the FDA granted accelerated approval to capmatinib[71] for NSCLC harboring MET exon 14 skipping positive as detected by an FDA-approved test. The kinase inhibitor, tepotinib[72], is also approved (2021) for MET exon 14 skipping mutations in NSCLC. MET exon 14 skipping mutations confer sensitivity to approved kinase inhibitors including crizotinib (2011), which is recommended for MET amplifications and exon 14 skipping mutations[23,60,62,63]. The FDA also granted breakthrough therapy designation (2018) to crizotinib for metastatic non-small cell lung cancer (NSCLC) with MET exon 14 alterations with disease progression on or after platinum-based chemotherapy[73]. Conversely, amplification of MET has been observed to mediate resistance to EGFR tyrosine kinase inhibitors (TKIs)[74,75,76,77,78]. However, the FDA has granted Fast Track designation (2021) to the MET/CSF1R/SRC small molecule inhibitor, TPX-0022[79], for MET amplified advanced or metastatic gastric cancer, including gastroesophageal junction adenocarcinoma (GEJ) after prior chemotherapy. Tepotinib has also been recommended for treatment of NSCLC with high-level MET amplification[23]. In a phase II trial testing the MET inhibitor savolitinib, patients with advanced PRCC exhibited median progression free survival (PFS) of 6.2 and 1.4 months for MET-driven and MET-independent PRCC, respectively[80].

Relevant Therapy Summary

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ✖ No evidence

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

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
osimertinib	●	●	●	●	● (III)
afatinib	●	●	●	●	● (II)
dacomitinib	●	●	●	●	✖
erlotinib	●	●	●	●	✖
erlotinib + ramucirumab	●	●	●	●	✖
gefitinib	●	●	●	●	✖
bevacizumab + erlotinib	✖	●	●	●	✖
bevacizumab (Allergan) + erlotinib	✖	✖	●	✖	✖
bevacizumab (Celltrion) + erlotinib	✖	✖	●	✖	✖
bevacizumab (Mabxience) + erlotinib	✖	✖	●	✖	✖
bevacizumab (Pfizer) + erlotinib	✖	✖	●	✖	✖
bevacizumab (Samsung Bioepis) + erlotinib	✖	✖	●	✖	✖
bevacizumab (Stada) + erlotinib	✖	✖	●	✖	✖
atezolizumab + bevacizumab + carboplatin + paclitaxel	✖	✖	✖	●	✖
gefitinib + carboplatin + pemetrexed	✖	✖	✖	●	✖
amivantamab, lazertinib, chemotherapy	✖	✖	✖	✖	● (III)
osimertinib, chemotherapy	✖	✖	✖	✖	● (III)
patritumab deruxtecan	✖	✖	✖	✖	● (III)
savolitinib, osimertinib	✖	✖	✖	✖	● (III)
erlotinib, OBI-833	✖	✖	✖	✖	● (II)
osimertinib, savolitinib	✖	✖	✖	✖	● (II)
BLU-451, chemotherapy	✖	✖	✖	✖	● (I/II)
sunvozertinib	✖	✖	✖	✖	● (I/II)
ABBV 400	✖	✖	✖	✖	● (I)
BAY-2927088	✖	✖	✖	✖	● (I)
TNO-155, nazartinib	✖	✖	✖	✖	● (I)

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

Relevant Therapy Summary (continued)

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ✖ No evidence

MET amplification

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
capmatinib	✖	●	✖	✖	✖
crizotinib	✖	●	✖	✖	✖
tepotinib	✖	●	✖	✖	✖
savolitinib, osimertinib	✖	✖	✖	✖	● (III)
osimertinib, savolitinib	✖	✖	✖	✖	● (II)
HLX55	✖	✖	✖	✖	● (I)

EGFR p.(V834L) c.2500G>T

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
BLU-451, chemotherapy	✖	✖	✖	✖	● (I/II)
sunvozertinib	✖	✖	✖	✖	● (I/II)
ABBV 400	✖	✖	✖	✖	● (I)

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

Relevant Therapy Details

Current FDA Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types

FDA information is current as of 2023-08-16. For the most up-to-date information, search www.fda.gov.

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

● afatinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2022-04-07 **Variant class:** EGFR L858R mutation

Indications and usage:

GILOTRIF® is a kinase inhibitor indicated for:

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

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

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

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/201292s017lbl.pdf

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

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

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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

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erlotinib + ramucirumab

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2022-03-22 **Variant class:** EGFR L858R mutation

Indications and usage:

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

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

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/125477s042lbl.pdf

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

gefitinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2021-05-05 **Variant class:** EGFR L858R mutation

Indications and usage:

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

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

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/206995s004lbl.pdf

osimertinib

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

Indications and usage:

TAGRISSO® is a kinase inhibitor indicated for:

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

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/208065Orig1s028lbl.pdf

Current NCCN Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types

NCCN information is current as of 2023-08-01. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/what-we-do/international-adaptations.

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

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

● afatinib

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

NCCN Recommendation category: 1

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

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

● dacomitinib

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

NCCN Recommendation category: 1

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

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

● erlotinib

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

NCCN Recommendation category: 1

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

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

● gefitinib

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

NCCN Recommendation category: 1

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

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

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

osimertinib

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

NCCN Recommendation category: 1

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

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

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afatinib

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

NCCN Recommendation category: 2A

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

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

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afatinib

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

Other criteria: EGFR T790M mutation negative

NCCN Recommendation category: 2A

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

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

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bevacizumab + erlotinib

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

NCCN Recommendation category: 2A

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

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

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

bevacizumab + erlotinib

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

Other criteria: EGFR T790M mutation negative

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Non-squamous Cell; Advanced, Metastatic, Progression, Symptomatic, Asymptomatic (Subsequent therapy)

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

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dacomitinib

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

NCCN Recommendation category: 2A

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

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

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dacomitinib

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

Other criteria: EGFR T790M mutation negative

NCCN Recommendation category: 2A

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

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

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erlotinib

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

NCCN Recommendation category: 2A

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

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

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

erlotinib

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

Other criteria: EGFR T790M mutation negative

NCCN Recommendation category: 2A

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

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

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erlotinib + ramucirumab

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

NCCN Recommendation category: 2A

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

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

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erlotinib + ramucirumab

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

Other criteria: EGFR T790M mutation negative

NCCN Recommendation category: 2A

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

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

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gefitinib

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

NCCN Recommendation category: 2A

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

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

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

gefitinib

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

Other criteria: EGFR T790M mutation negative

NCCN Recommendation category: 2A

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

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

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osimertinib

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

NCCN Recommendation category: 2A

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

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

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osimertinib

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

NCCN Recommendation category: 2A

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

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

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erlotinib

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

NCCN Recommendation category: 2B

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

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

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

afatinib

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

NCCN Recommendation category: 2B

Population segment (Line of therapy):
- Brain Metastases (Line of therapy not specified); Other recommended intervention

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

gefitinib

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

NCCN Recommendation category: 2B

Population segment (Line of therapy):
- Brain Metastases (Line of therapy not specified); Other recommended intervention

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

MET amplification

capmatinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** MET amplification

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Metastatic (Line of therapy not specified)

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

crizotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** MET amplification

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Metastatic (Line of therapy not specified)

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

MET amplification (continued)

tepotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** MET amplification

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Metastatic (Line of therapy not specified)

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

Current EMA Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types

EMA information is current as of 2023-08-16. For the most up-to-date information, search www.ema.europa.eu/ema.

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

● afatinib

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

Reference:

https://www.ema.europa.eu/en/documents/product-information/giotrif-epar-product-information_en.pdf

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● bevacizumab (Allergan) + erlotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2023-01-05 **Variant class:** EGFR L858R mutation

Reference:

https://www.ema.europa.eu/en/documents/product-information/mvasi-epar-product-information_en.pdf

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● bevacizumab (Celltrion) + erlotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2023-05-10 **Variant class:** EGFR L858R mutation

Reference:

https://www.ema.europa.eu/en/documents/product-information/vegzelma-epar-product-information_en.pdf

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● bevacizumab (Mabxience) + erlotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2023-07-26 **Variant class:** EGFR L858R mutation

Reference:

https://www.ema.europa.eu/en/documents/product-information/alymsys-epar-product-information_en.pdf

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● bevacizumab (Pfizer) + erlotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2023-01-05 **Variant class:** EGFR L858R mutation

Reference:

https://www.ema.europa.eu/en/documents/product-information/zirabev-epar-product-information_en.pdf

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● bevacizumab (Samsung Bioepis) + erlotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2023-04-11 **Variant class:** EGFR L858R mutation

Reference:

https://www.ema.europa.eu/en/documents/product-information/aybintio-epar-product-information_en.pdf

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

bevacizumab (Samsung Bioepis) + erlotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2023-04-11 **Variant class:** EGFR L858R mutation

Reference:
https://www.ema.europa.eu/en/documents/product-information/onbevzi-epar-product-information_en.pdf

bevacizumab (Stada) + erlotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2023-07-14 **Variant class:** EGFR L858R mutation

Reference:
https://www.ema.europa.eu/en/documents/product-information/oyavas-epar-product-information_en.pdf

bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2022-12-15 **Variant class:** EGFR L858R mutation

Reference:
https://www.ema.europa.eu/en/documents/product-information/abevmy-epar-product-information_en.pdf

bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2023-03-17 **Variant class:** EGFR L858R mutation

Reference:
https://www.ema.europa.eu/en/documents/product-information/avastin-epar-product-information_en.pdf

dacomitinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2021-07-21 **Variant class:** EGFR L858R mutation

Reference:
https://www.ema.europa.eu/en/documents/product-information/vizimpro-epar-product-information_en.pdf

erlotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2023-05-16 **Variant class:** EGFR L858R mutation

Reference:
https://www.ema.europa.eu/en/documents/product-information/tarceva-epar-product-information_en.pdf

erlotinib + ramucirumab

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2022-12-13 **Variant class:** EGFR L858R mutation

Other criteria: EGFR T790M mutation negative

Reference:
https://www.ema.europa.eu/en/documents/product-information/cyramza-epar-product-information_en.pdf

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

gefitinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2023-07-27 **Variant class:** EGFR L858R mutation

Reference:

https://www.ema.europa.eu/en/documents/product-information/gefitinib-mylan-epar-product-information_en.pdf

gefitinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2023-07-17 **Variant class:** EGFR L858R mutation

Reference:

https://www.ema.europa.eu/en/documents/product-information/iressa-epar-product-information_en.pdf

osimertinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2023-08-11 **Variant class:** EGFR L858R mutation

Reference:

https://www.ema.europa.eu/en/documents/product-information/tagrisso-epar-product-information_en.pdf

Current ESMO Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types

ESMO information is current as of 2023-08-01. For the most up-to-date information, search www.esmo.org.

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

● osimertinib

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

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

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

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

● osimertinib

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

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

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

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

● afatinib

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

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

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

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

● bevacizumab + erlotinib

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

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

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

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

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

dacomitinib

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

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

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

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

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erlotinib

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

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

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

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

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erlotinib + ramucirumab

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

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

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

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

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gefitinib

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

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

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

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

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

gefitinib + carboplatin + pemetrexed

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

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

Population segment (Line of therapy):
- Stage IV; Advanced, Metastatic (First-line therapy)

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

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atezolizumab + bevacizumab + carboplatin + paclitaxel

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

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

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

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

Clinical Trials in Taiwan region:

Clinical Trials Summary

EGFR p.(L858R) c.2573T>G + MET amplification

NCT ID	Title	Phase
NCT05261399	A Phase III, Randomised, Open-Label Study of Savolitinib in Combination With Osimertinib Versus Platinum-Based Doublet Chemotherapy in Participants With EGFR Mutated, MET-Overexpressed and/or Amplified, Locally Advanced or Metastatic Non-Small Cell Lung Cancer Who Have Progressed on Treatment With Osimertinib (SAFFRON).	III
NCT03778229	A Phase II Study Assessing the Efficacy of Osimertinib in Combination With Savolitinib in Patients With EGFRm+ and MET+, Locally Advanced or Metastatic Non Small Cell Lung Cancer Who Have Progressed Following Treatment With Osimertinib.	II

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

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
NCT05120349	A Phase III, Double-blind, Randomised, Placebo-Controlled, International Study to Assess the Efficacy and Safety of Adjuvant Osimertinib Versus Placebo in Participants With EGFR Mutation-positive Stage IA2-IA3 Non-small Cell Lung Cancer, Following Complete Tumour Resection	III
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
NCT05338970	HERTHENA–Lung02: Phase III, Randomized, Open-label Study of Patritumab Deruxtecan Versus Platinum-Based Chemotherapy in Metastatic or Locally Advanced Non-Small Cell Lung Cancer (NSCLC) With Epidermal Growth Factor Receptor (EGFRm) Mutation After Failure treatment with epidermal growth factor (EGFR) tyrosine kinase inhibitors (TKIs)	III
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
NCT05442060	A Randomized, Open-Label, Phase 2 Study to Evaluate OBI-833/OBI-821 in Combination With First-Line Erlotinib in Patients With EGFR-Mutated, Globo H-Positive, Locally Advanced or Metastatic Non-Small Cell Lung Cancer	II
NCT05099172	An Open Label, First-in-human Study of BAY 2927088 in Participants With Advanced Non-small Cell Lung Cancer (NSCLC) Harboring an EGFR and/or HER2 Mutation	I
NCT03114319	An Open-label, Multi-center, Phase I, Dose Finding Study of Oral TNO155 in Adult Patients With Advanced Solid Tumors.	I
NCT05241873	Phase I/II Study of BLU-451 in Advanced Cancers With EGFR Exon 20 Insertion Mutations	I/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
NCT05029882	A Phase I First in Human Study Evaluating Safety, Pharmacokinetics and Efficacy of ABBV-400 in Adult Subjects With Advanced Solid Tumors	I

Clinical Trials Summary (continued)

MET amplification

NCT ID	Title	Phase
NCT04169178	A Phase I Dose Finding/Expansion Study of HLX55, A Monoclonal Antibody Targeting Tyrosine-Protein Kinase MET (C-MET) in Patients With Advanced Solide Tumors Refactory to Standard Therapy	I

EGFR p.(V834L) c.2500G>T

NCT ID	Title	Phase
NCT05241873	Phase I/II Study of BLU-451 in Advanced Cancers With EGFR Exon 20 Insertion Mutations	I/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
NCT05029882	A Phase I First in Human Study Evaluating Safety, Pharmacokinetics and Efficacy of ABBV-400 in Adult Subjects With Advanced Solid Tumors	I

Alerts Informed By Public Data Sources

Current FDA Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

FDA information is current as of 2023-08-16. For the most up-to-date information, search www.fda.gov.

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

patritumab deruxtecan

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR L858R mutation or EGFRi sensitizing mutation

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

Reference:

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

CPO-301

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR mutation

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

Reference:

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

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

osimertinib + quaratusugene ozeplasmid

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

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

Reference:

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

EGFR p.(V834L) c.2500G>T

CPO-301

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

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

Reference:

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

osimertinib + quaratusugene ozeplasmid

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

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

Reference:

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

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