Taipei Veterans General Hospital

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Sample Information

Patient Name: 林慶銘
Gender: Male
ID No.: F120179486
History No.: 45859630
Age: 30

Ordering Doctor: DOC3109L 邱昭華
Ordering REQ.: 0BKSAVN
Signing in Date: 2021/09/03

Path No.: S110-99444
MP No.: F21072
Assay: Oncomine Focus Assay
Sample Type: FFPE
Block No.: S109-64795A+B
Percentage of tumor cells: 30%

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

Note:

Sample Cancer Type: Non-Small Cell Lung Cancer

Report Highlights

2 Relevant Biomarkers
11 Therapies Available
14 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	***EGFR p.(L858R) c.2573T>G, EGFR p.(T790M) c.2369C>T***	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	*EGFR p.(L858R) c.2573T>G* epidermal growth factor receptor Allele Frequency: 11.25%	**bevacizumab* + erlotinib** [2] **erlotinib + ramucirumab** [1, 2] **osimertinib** [1, 2] afatinib + cetuximab atezolizumab + bevacizumab + chemotherapy bevacizumab + gefitinib gefitinib + chemotherapy osimertinib + chemotherapy	None	14
IA	*EGFR p.(T790M) c.2369C>T* epidermal growth factor receptor Allele Frequency: 5.30%	**osimertinib** [1, 2] osimertinib + chemotherapy	None	7

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**

Alerts informed by public data sources: ⊘ Contraindicated, Resistance

EGFR p.(T790M) c.2369C>T	⊘ **gefitinib** [2] afatinib, dacomitinib, erlotinib, gefitinib

Public data sources included in alerts: FDA[1], NCCN, **EMA**[2], ESMO

Prevalent cancer biomarkers without relevant evidence based on included data sources

MAP2K1 p.(C121Y) c.362G>A, JAK3 p.(S493C) c.1477A>T

Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
EGFR	p.(T790M)	c.2369C>T	COSM6240	chr7:55249071	5.30%	NM_005228.5	missense	1999
EGFR	p.(L858R)	c.2573T>G	COSM6224	chr7:55259515	11.25%	NM_005228.5	missense	1991
MAP2K1	p.(C121Y)	c.362G>A	.	chr15:66729154	17.20%	NM_002755.4	missense	2000
JAK3	p.(S493C)	c.1477A>T	COSM48455	chr19:17949164	4.31%	NM_000215.4	missense	1994
JAK1	p.(P743L)	c.2228C>T	.	chr1:65310460	8.60%	NM_002227.4	missense	2000
DDR2	p.(R133=)	c.399G>A	.	chr1:162724627	6.06%	NM_006182.4	synonymous	742
ALK	p.(*1621R)	c.4861T>C	.	chr2:29416092	8.71%	NM_004304.5	stoploss	402
ALK	p.(G1137E)	c.3410G>A	.	chr2:29445423	4.60%	NM_004304.5	missense	2000
IDH1	p.(T106=)	c.318G>A	.	chr2:209113189	8.10%	NM_005896.3	synonymous	2000
CTNNB1	p.(A13V)	c.38C>T	.	chr3:41266041	6.09%	NM_001904.4	missense	476
CTNNB1	p.(Q28*)	c.82C>T	.	chr3:41266085	6.33%	NM_001904.4	nonsense	474
PIK3CA	p.(K111=)	c.333G>A	.	chr3:178916946	63.17%	NM_006218.4	synonymous	714
PIK3CA	p.(W552*)	c.1656G>A	.	chr3:178936114	5.73%	NM_006218.4	nonsense	262

Variant Details (continued)

DNA Sequence Variants (continued)

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
FGFR3	p.(V82M)	c.244G>A	.	chr4:1801115	15.56%	NM_000142.4	missense	257
FGFR3	p.(N262D)	c.784A>G	.	chr4:1803606	8.30%	NM_000142.4	missense	1988
PDGFRA	p.(G829E)	c.2486G>A	.	chr4:55152054	10.56%	NM_006206.6	missense	1999
FGFR4	p.(P136L)	c.407C>T	.	chr5:176517797	99.82%	NM_213647.3	missense	1107
FGFR4	p.(P178S)	c.532C>T	.	chr5:176518034	10.64%	NM_213647.3	missense	799
FGFR4	p.(S422L)	c.1265C>T	.	chr5:176520420	13.40%	NM_213647.3	missense	2000
ESR1	p.(H567R)	c.1700A>G	.	chr6:152420013	5.60%	NM_001122740.1	missense	2000
EGFR	p.(E736=)	c.2208G>A	.	chr7:55242438	10.17%	NM_005228.5	synonymous	1997
MET	p.(H1097Y)	c.3289C>T	.	chr7:116415141	5.29%	NM_001127500.3	missense	1492
SMO	p.(V411L)	c.1231G>C	.	chr7:128846395	7.41%	NM_005631.5	missense	1998
BRAF	p.(G474E)	c.1421G>A	.	chr7:140481387	4.91%	NM_004333.6	missense	1997
BRAF	p.(S335F)	c.1004C>T	.	chr7:140494244	5.49%	NM_004333.6	missense	1638
MYC	p.(G123R)	c.367G>A	.	chr8:128750830	7.20%	NM_002467.6	missense	2000
MYC	p.(E367K)	c.1099G>A	.	chr8:128752938	22.15%	NM_002467.6	missense	2000
RET	p.(V882=)	c.2646A>G	.	chr10:43615567	4.66%	NM_020975.6	synonymous	687
FGFR2	p.(I383L)	c.1147A>T	.	chr10:123274771	4.45%	NM_000141.5	missense	1687
FGFR2	p.(A314=)	c.942C>T	.	chr10:123276975	4.97%	NM_000141.5	synonymous	684
CCND1	p.(E122*)	c.364G>T	.	chr11:69457964	17.77%	NM_053056.3	nonsense	1998
KRAS	p.(D33N)	c.97G>A	.	chr12:25398222	7.00%	NM_033360.4	missense	1999
KRAS	p.(N26=)	c.78T>C	.	chr12:25398241	5.40%	NM_033360.4	synonymous	2000
ERBB3	p.(P221S)	c.661C>T	.	chr12:56481626	21.43%	NM_001982.4	missense	1997
ERBB3	p.(N224=)	c.672C>T	.	chr12:56481637	31.20%	NM_001982.4	synonymous	2000
ERBB3	p.(G337E)	c.1010G>A	.	chr12:56482553	22.55%	NM_001982.4	missense	2000
ERBB3	p.(S346=)	c.1038C>T	.	chr12:56482581	6.35%	NM_001982.4	synonymous	2000
CDK4	p.(V39=)	c.117C>T	.	chr12:58145384	11.10%	NM_000075.4	synonymous	2000
CDK4	p.(A10T)	c.28G>A	.	chr12:58145473	31.00%	NM_000075.4	missense	2000
MAP2K1	p.(K64R)	c.191A>G	.	chr15:66727475	7.90%	NM_002755.4	missense	2000
MAP2K1	p.(Y134F)	c.401A>T	.	chr15:66729193	7.95%	NM_002755.4	missense	2000
MAP2K1	p.(G202=)	c.606G>A	.	chr15:66774130	51.15%	NM_002755.4	synonymous	2000
MAP2K1	p.(G210=)	c.630G>T	.	chr15:66774154	12.49%	NM_002755.4	synonymous	1994
NF1	p.(?)	c.-31C>T	.	chr17:29422297	17.30%	NM_001042492.3	unknown	341
ERBB2	p.(L726=)	c.2178T>A	.	chr17:37879883	4.40%	NM_004448.3	synonymous	2000
ERBB2	p.(H1044Q)	c.3132C>G	.	chr17:37883229	6.31%	NM_004448.3	missense	1997

Variant Details (continued)

DNA Sequence Variants (continued)

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
GNA11	p.(D195N)	c.583G>A	.	chr19:3115048	17.28%	NM_002067.5	missense	1059
JAK3	p.(L485=)	c.1453C>T	.	chr19:17949188	59.45%	NM_000215.4	synonymous	2000

Biomarker Descriptions

EGFR (epidermal growth factor receptor)

Background: The EGFR gene encodes the epidermal growth factor receptor (EGFR) tyrosine kinase, a member of the ERBB/human epidermal growth factor receptor (HER) family. In addition to EGFR/ERBB1/HER1, other members of the ERBB/HER family include ERBB2/HER2, ERBB3/HER3, and ERBB4/HER4[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]. In lung cancer containing EGFR exon 19 or 21 activating mutations, treatment with TKIs is eventually associated with the emergence of drug resistance[27]. 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[28] (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[27]. 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[29]. T790M and C797S can occur in either cis or trans allelic orientation[29]. 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[29]. 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[29,30]. However, C797S occurring in cis conformation with T790M, confers resistance to first- and third-generation TKIs[29]. Fourth-generation TKIs are in development to overcome acquired C797S and T790M resistance mutations after osimertinib treatment. EGFR targeting antibodies including cetuximab (2004), panitumumab (2006), and necitumumab (2016) are under investigation in combination with EGFR-targeting TKIs for efficacy against EGFR mutations. The bispecific antibody, JNJ-61186372[31], targeting EGFR and MET, and the TKI mobocertinib[32], each received a breakthrough designation from the FDA (2020) for NSCLC tumors harboring EGFR exon 20 insertion mutations. The Oncoprex immunogene therapy CNVN-202[33] 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[34] was granted a fast track designation (2020) for the treatment of solid tumors harboring an EGFR exon 20 insertion mutation.

Biomarker Descriptions (continued)

JAK3 (Janus kinase 3)

Background: The JAK3 gene encodes a non-receptor, membrane associated protein tyrosine kinase (PTK). JAK3 is a member of the Janus kinase (JAK) family that includes JAK1, JAK2, JAK3, and TYK2. Janus kinases are characterized by the presence of a second phosphotransferase-related or pseudokinase domain immediately N-terminal to the PTK domain[35]. JAK kinases function with signal transducer and activator of transcription (STAT) proteins to facilitate intracellular signal transduction required for cytokine receptor and interferon-alpha/beta/gamma signaling[35,36,37].

Alterations and prevalence: Recurrent somatic mutations in JAK3 have been observed in T-cell lymphomas and acute lymphoblastic leukemia (ALL)[38,39]. Mutations in the pseudokinase domain (M511I, A573V, R657W), and kinase domain (L857Q) activate the JAK/STAT pathway and transform hematopoietic cells in vitro[38]. These variants are infrequently observed in solid cancers[6].

Potential relevance: Currently, no therapies are approved for JAK3 aberrations. Tofacitinib (2012) is a JAK3 inhibitor FDA approved for rheumatoid and psoriatic arthritis. Activating mutations in JAK3, including the germline variant V722I, promoted increased expression of PD-L1 in lung cancer and were associated with durable benefit from tofacitinib PD-L1 blockade[40].

MAP2K1 (mitogen-activated protein kinase kinase 1)

Background: The MAP2K1 gene encodes the mitogen-activated protein kinase kinase 1, also known as MEK1. MAP2K1 is a member of the mitogen-activated protein kinase 2 (MAP2K) subfamily which also includes MAP2K2, MAP2K3, MAP2K4, MAP2K5, and MAP2K6[41]. MAP2K1 is involved in the ERK1/2 signaling pathway along with MAPK1, MAPK3, MAP2K2, BRAF, and RAF1[41,42]. Activation of MAPK proteins occurs through a kinase signaling cascade[41,43,44]. Specifically, MAP3Ks are responsible for phosphorylation of MAP2K family members[41,43,44]. Once activated, MAP2Ks are responsible for the phosphorylation of various MAPK proteins whose signaling is involved in several cellular processes including cell proliferation, differentiation, and inflammation[41,43,44]. MAP2K1 and MAP2K2 are 80% homologous, with 90% amino acid identity shared by their kinase domains[45].

Alterations and prevalence: MAP2K1 is activated by both gene amplification and somatic mutations. MAP2K1 mutations are found in 5-7% of melanoma, 4% of diffuse large B-cell lymphoma (DLBCL), 3% of uterine cancer and cholangiocarcinoma, and 1% of non-small cell lung cancer (NSCLC) associated with smoking[6,7,46,47]. The most common recurrent somatic mutations occur in the negative regulatory region at the F53, Q56, and K57 positions, and in the kinase domain positions P124 and E203. Amplifications occur in 4% of mesothelioma, and 2% of pancreatic and ovarian cancers[6,7,48,49].

Potential relevance: Since MEK1 is positioned downstream to BRAF and is known to form a high-affinity complex with BRAF, MEK inhibitors have demonstrated efficacy in cancers harboring BRAF mutations[50]. Several MEK inhibitors have been approved alone or in combination with BRAF inhibitors including trametinib[51] (2013) alone or in combination with dabrafenib in BRAF V600E/K mutant melanoma and BRAF V600E mutant NSCLC, cobimetinib[52] (2018) in combination with vemurafenib in BRAF V600E/K mutant melanoma, and binimetinib[53] (2018) in combination with encorafenib in BRAF V600E/K mutant melanoma. Although MAP2K1 mutations occur at multiple sites throughout the gene, recent studies have suggested that allele-specific mutations can be categorized based on mechanisms of activation, with one group leading to MEK inhibitor unresponsiveness due to RAF and phosphorylation independent mechanisms[54].

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)
erlotinib + ramucirumab	●	●	●	●	✖
bevacizumab + erlotinib	✖	●	●	●	✖
afatinib + cetuximab	✖	●	✖	✖	✖

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

Relevant Therapy Summary (continued)

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

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

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
osimertinib + chemotherapy	✖	●	✖	✖	✖
osimertinib + chemotherapy + surgical intervention	✖	●	✖	✖	✖
bevacizumab (Allergan) + erlotinib	✖	✖	●	✖	✖
bevacizumab (Fujifilm Kyowa Kirin Biologics) + erlotinib	✖	✖	●	✖	✖
bevacizumab (Mabxience) + erlotinib	✖	✖	●	✖	✖
bevacizumab (Pfizer) + erlotinib	✖	✖	●	✖	✖
bevacizumab (Samsung Bioepis) + erlotinib	✖	✖	●	✖	✖
atezolizumab + bevacizumab + carboplatin + paclitaxel	✖	✖	✖	●	✖
bevacizumab + gefitinib	✖	✖	✖	●	✖
gefitinib + carboplatin + pemetrexed	✖	✖	✖	●	✖
amivantamab, lazertinib, osimertinib	✖	✖	✖	✖	● (III)
osimertinib, chemotherapy	✖	✖	✖	✖	● (III)
bintrafusp alfa, chemoradiation therapy, durvalumab	✖	✖	✖	✖	● (II)
datopotamab deruxtecan	✖	✖	✖	✖	● (II)
durvalumab, tremelimumab, chemotherapy	✖	✖	✖	✖	● (II)
osimertinib, savolitinib	✖	✖	✖	✖	● (II)
patritumab deruxtecan	✖	✖	✖	✖	● (II)
DZD-9008	✖	✖	✖	✖	● (I/II)
amivantamab, lazertinib	✖	✖	✖	✖	● (I)
lazertinib, amivantamab	✖	✖	✖	✖	● (I)
telisotuzumab vedotin, osimertinib	✖	✖	✖	✖	● (I)
TNO-155, nazartinib	✖	✖	✖	✖	● (I)

EGFR p.(T790M) c.2369C>T

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
osimertinib	●	●	●	●	✖
osimertinib + chemotherapy	✖	●	✖	✖	✖
osimertinib + chemotherapy + surgical intervention	✖	●	✖	✖	✖

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

Relevant Therapy Summary (continued)

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

EGFR p.(T790M) c.2369C>T (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
osimertinib, chemotherapy	✖	✖	✖	✖	● (III)
durvalumab, tremelimumab, chemotherapy	✖	✖	✖	✖	● (II)
DZD-9008	✖	✖	✖	✖	● (I/II)
amivantamab	✖	✖	✖	✖	● (I)
lazertinib, amivantamab, chemotherapy	✖	✖	✖	✖	● (I)
telisotuzumab vedotin, osimertinib	✖	✖	✖	✖	● (I)

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

Relevant Therapy Details

Current FDA Information

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

FDA information is current as of 2021-07-14. For the most up-to-date information, search www.fda.gov.

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

● erlotinib + ramucirumab

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2021-06-15 **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/2021/125477s039lbl.pdf

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

osimertinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2020-12-18 **Variant class:** EGFR L858R mutation

Indications and usage:

TAGRISSO® is a kinase inhibitor indicated for:

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

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/208065s021lbl.pdf

EGFR p.(T790M) c.2369C>T

osimertinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2020-12-18 **Variant class:** EGFR T790M mutation

Indications and usage:

TAGRISSO® is a kinase inhibitor indicated for:

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

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/208065s021lbl.pdf

Current NCCN Information

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

NCCN information is current as of 2021-07-01. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

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

● osimertinib

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

NCCN Recommendation category: 1

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

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

● afatinib + cetuximab

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Progression (Subsequent therapy)

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

● bevacizumab + erlotinib

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

NCCN Recommendation category: 2A

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

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

● erlotinib + ramucirumab

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

NCCN Recommendation category: 2A

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

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

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

osimertinib

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

NCCN Recommendation category: 2A

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

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

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osimertinib + chemotherapy

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IIB, Stage IIIA, Stage IIIB (Adjuvant therapy)
- Stage IIIA; Resectable (Adjuvant therapy)

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

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osimertinib + chemotherapy + surgical intervention

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IIB (Adjuvant therapy)
- Stage IIIA; Resectable (Adjuvant therapy)

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

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osimertinib

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

NCCN Recommendation category: 2A

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

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

EGFR p.(T790M) c.2369C>T

osimertinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR T790M mutation

NCCN Recommendation category: 1

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

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

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osimertinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR T790M mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Brain Metastases (Line of therapy not specified)

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

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osimertinib + chemotherapy

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR T790M mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IIB, Stage IIIA, Stage IIIB (Adjuvant therapy)
- Stage IIIA; Resectable (Adjuvant therapy)

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

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osimertinib + chemotherapy + surgical intervention

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR T790M mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Stage IIB (Adjuvant therapy)
- Stage IIIA; Resectable (Adjuvant therapy)

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

EGFR p.(T790M) c.2369C>T (continued)

osimertinib

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

NCCN Recommendation category: 2A

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

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

Current EMA Information

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

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

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

● bevacizumab (Allergan) + erlotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2021-05-21 **Variant class:** EGFR L858R mutation

Reference:

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 L858R mutation

Reference:

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

● bevacizumab (Mabxience) + erlotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2021-04-26 **Variant class:** EGFR L858R mutation

Reference:

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

● bevacizumab (Pfizer) + erlotinib

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

Reference:

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

● bevacizumab (Samsung Bioepis) + erlotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2021-05-18 **Variant class:** EGFR L858R mutation

Reference:

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

● bevacizumab (Samsung Bioepis) + erlotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2021-06-21 **Variant class:** EGFR L858R mutation

Reference:

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

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

bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2021-01-28 **Variant class:** EGFR L858R mutation

Reference:

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

erlotinib + ramucirumab

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2020-07-02 **Variant class:** EGFR L858R mutation

Reference:

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

osimertinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2021-07-01 **Variant class:** EGFR L858R mutation

Reference:

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

EGFR p.(T790M) c.2369C>T

osimertinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2021-07-01 **Variant class:** EGFR T790M 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 2021-07-01. For the most up-to-date information, search www.esmo.org.

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

● atezolizumab + bevacizumab + carboplatin + paclitaxel

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

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

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

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

● 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.]

● bevacizumab + erlotinib

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

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

Population segment (Line of therapy):
- Stage IV (First-line therapy)

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

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

bevacizumab + gefitinib

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

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

Population segment (Line of therapy):
- Stage IV (First-line therapy)

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

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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.]

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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.]

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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.]

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

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.]

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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.]

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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.]

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bevacizumab + erlotinib

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

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

Population segment (Line of therapy):
- Stage IV (First-line therapy)

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

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

bevacizumab + gefitinib

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

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

Population segment (Line of therapy):
- Stage IV (First-line therapy)

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

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 + 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.]

EGFR p.(T790M) c.2369C>T

osimertinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR T790M mutation

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

Population segment (Line of therapy):
- Stage IV (Second-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.]

Clinical Trials in Taiwan region:

Clinical Trials Summary

EGFR p.(L858R) c.2573T>G + EGFR p.(T790M) c.2369C>T

NCT ID	Title	Phase
NCT04035486	A Phase III, Open-label, Randomized Study of Osimertinib With or Without Platinum Plus Pemetrexed Chemo, as First-line Treatment in Patients With Epidermal Growth Factor Receptor (EGFR) Mutation Positive, Locally Advanced or Metastatic Non-small Cell Lung Cancer (FLAURA2)	III
NCT04351555	A Phase III, Randomised, Controlled, Multi-center, 3-Arm Study of Neoadjuvant Osimertinib as Monotherapy or in Combination With Chemotherapy Versus Standard of Care Chemotherapy Alone for the Treatment of Patients With Epidermal Growth Factor Receptor Mutation Positive, Resectable Non-small Cell Lung Cancer	III
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
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

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

NCT ID	Title	Phase
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
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
NCT04619004	HERTHENA-Lung01: A Phase II Randomized Open-Label Study of Patritumab Deruxtecan (U3-1402) in Subjects With Previously Treated Metastatic or Locally Advanced EGFR-mutated Non-Small Cell Lung Cancer (NSCLC)	II
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
NCT03840902	A Multicenter, Double Blind, Randomized, Controlled Study of M7824 With Concurrent Chemoradiation Followed by M7824 Versus Concurrent Chemoradiation Plus Placebo Followed by Durvalumab in Participants With Unresectable Stage III Non-small Cell Lung Cancer	II
NCT04484142	Phase II, Single-arm, Open-label Study of DS-1062a in Advanced or Metastatic Non-small Cell Lung Cancer With Actionable Genomic Alterations and Progressed on or After Kinase Inhibitor Therapy and Platinum Based Chemotherapy (TROPION-Lung05)	II
NCT03114319	An Open-label, Multi-center, Phase I, Dose Finding Study of Oral TNO155 in Adult Patients With Advanced Solid Tumors.	I

Clinical Trials Summary (continued)

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

NCT ID	Title	Phase
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

EGFR p.(T790M) c.2369C>T

NCT ID	Title	Phase
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
NCT03974022	A Phase I/II, Open-Label, Multicenter Study to Assess the Safety, Tolerability, Pharmacokinetics and Anti-tumor Efficacy of DZD9008 in Patients With Advanced Non-Small Cell Lung Cancer (NSCLC) With EGFR or HER2 Mutation	I/II
NCT04077463	An Open-label Phase I/Ib Study to Evaluate the Safety and Pharmacokinetics of JNJ-73841937 (Lazertinib), a Third Generation EGFR-TKI, as Monotherapy or in Combinations With JNJ-61186372, a Human Bispecific EGFR and cMet Antibody in Participants With Advanced Non-Small Cell Lung Cancer	I

Alerts Informed By Public Data Sources

Current FDA Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

FDA information is current as of 2021-07-14. For the most up-to-date information, search www.fda.gov.

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

osimertinib + quaratusugene ozeplasmid

Cancer type: Non-Small Cell Lung Cancer

Variant class: EGFR mutation

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

Reference:

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

EGFR p.(T790M) c.2369C>T

osimertinib + quaratusugene ozeplasmid

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

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

Reference:

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

Current NCCN Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

NCCN information is current as of 2021-07-01. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

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

alectinib

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

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended as subsequent therapy for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

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

brigatinib

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

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended as subsequent therapy for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

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

ceritinib

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

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended as subsequent therapy for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

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

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

crizotinib

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

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended as subsequent therapy for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

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

lorlatinib

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

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended as subsequent therapy for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

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

atezolizumab

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

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "subsequent therapy with pembrolizumab, nivolumab, or atezolizumab is not recommended in patients with EGFR mutations or ALK fusions."

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

nivolumab

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

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "subsequent therapy with pembrolizumab, nivolumab, or atezolizumab is not recommended in patients with EGFR mutations or ALK fusions."

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

pembrolizumab

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

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "subsequent therapy with pembrolizumab, nivolumab, or atezolizumab is not recommended in patients with EGFR mutations or ALK fusions."

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

EGFR p.(T790M) c.2369C>T

atezolizumab

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

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "subsequent therapy with pembrolizumab, nivolumab, or atezolizumab is not recommended in patients with EGFR mutations or ALK fusions."

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

nivolumab

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

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "subsequent therapy with pembrolizumab, nivolumab, or atezolizumab is not recommended in patients with EGFR mutations or ALK fusions."

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

pembrolizumab

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

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "subsequent therapy with pembrolizumab, nivolumab, or atezolizumab is not recommended in patients with EGFR mutations or ALK fusions."

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

afatinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR T790M mutation

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "The most common known mechanism is the acquisition of T790M (which is a secondary mutation in EGFR), which renders the kinase resistant to erlotinib, gefitinib, dacomitinib, or afatinib."

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

dacomitinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR T790M mutation

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "The most common known mechanism is the acquisition of T790M (which is a secondary mutation in EGFR), which renders the kinase resistant to erlotinib, gefitinib, dacomitinib, or afatinib."

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

EGFR p.(T790M) c.2369C>T (continued)

erlotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR T790M mutation

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "The most common known mechanism is the acquisition of T790M (which is a secondary mutation in EGFR), which renders the kinase resistant to erlotinib, gefitinib, dacomitinib, or afatinib."

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

gefitinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR T790M mutation

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "The most common known mechanism is the acquisition of T790M (which is a secondary mutation in EGFR), which renders the kinase resistant to erlotinib, gefitinib, dacomitinib, or afatinib."

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

Current EMA Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

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

EGFR p.(T790M) c.2369C>T

gefitinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2021-03-05 **Variant class:** EGFR T790M mutation

Reference:

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

Signatures

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