Taipei Veterans General Hospital

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Sample Information

Patient Name: 温秀美
Gender: Female
ID No.: U220632928
History No.: 45648359
Age: 50

Ordering Doctor: DOC3181E 徐大鈞
Ordering REQ.: 0BALTCG
Signing in Date: 2020/12/30

Path No.: S109-96877
MP No.: F20117
Assay: Oncomine Focus Assay
Sample Type: FFPE
Block No.: S109-36415A
Percentage of tumor cells: 60%
Note:

Sample Cancer Type: Non-Small Cell Lung Cancer

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Report Highlights

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Relevant Non-Small Cell Lung Cancer Variants

Gene	Finding	Gene	Finding
ALK	Not detected	NTRK1	Not detected
BRAF	Not detected	NTRK2	Not detected
EGFR	***EGFR p.(T790M) c.2369C>T, EGFR p.(G719S) c.2155G>A, EGFR amplification***	NTRK3	Not detected
ERBB2	Not detected	RET	Not detected
KRAS	Not detected	ROS1	Not detected
MET	Not detected		

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	*EGFR p.(T790M) c.2369C>T* epidermal growth factor receptor Allele Fraction: 0.618	**osimertinib** [1, 2]	None	62
IIC	*PIK3CA p.(H1047R) c.3140A>G* phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha Allele Fraction: 0.243	None	**alpelisib + hormone therapy** [1, 2]	13
IA	*EGFR p.(G719S) c.2155G>A* epidermal growth factor receptor Allele Fraction: 0.643	afatinib + cetuximab bevacizumab + erlotinib bevacizumab + gefitinib erlotinib + ramucirumab gefitinib + chemotherapy osimertinib	None	66
IIC	*EGFR amplification* epidermal growth factor receptor	None	None	4

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.
Although no fusion transcript can be detected, there is high imbalance of the number of 3' reads and 5' reads in the RET gene (3'/5' imbalance value: 25.86). A high 3'/5' imbalance value is suggestive of the presence of gene fusion. The possibility of RET fusion involving partners other than those targeted by the panel cannot be excluded. Further confirmation with other methodologies is suggested.

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

Variants (Exclude variant in Taiwan BioBank with >1% allele frequency)

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Fraction	Transcript	Variant Effect	Coverage
PIK3CA	p.(H1047R)	c.3140A>G	COSM775	chr3:178952085	0.243	NM_006218.3	missense	1999
EGFR	p.(G719S)	c.2155G>A	COSM6252	chr7:55241707	0.643	NM_005228.4	missense	1992
EGFR	p.(T790M)	c.2369C>T	COSM6240	chr7:55249071	0.618	NM_005228.4	missense	1999

Copy Number Variations

Gene	Locus	Copy Number
EGFR	chr7:55198956	6.57

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 EGFR exon 20 insertions confer resistance to the same therapies[23]. In lung cancer containing EGFR exon 19 or 21 activating mutations, treatment with TKIs is eventually associated with the emergence of drug resistance[24]. 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[25] (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[24]. 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[26]. T790M and C797S can occur in either cis or trans allelic orientation[26]. 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[26]. 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[26,27]. However, C797S occurring in cis conformation with T790M, confers resistance to first- and third-generation TKIs[26]. 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[28], targeting EGFR and MET, and the TKI mobocertinib[29], each received a breakthrough designation from the FDA (2020) for NSCLC tumors harboring EGFR exon 20 insertion mutations. The Oncoprex immunogene therapy CNVN-202[30] 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[31] was granted a fast track designation (2020) for the treatment of solid tumors harboring an EGFR exon 20 insertion mutation.

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

Background: The PIK3CA gene encodes the phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha of the class I phosphatidylinositol 3-kinase (PI3K) enzyme[32]. PI3K is a heterodimer that contains a p85 regulatory subunit, which couples one of four p110 catalytic subunits to activated tyrosine protein kinases[33,34]. The p110 catalytic subunits include p110α, β, δ, γ and are encoded by genes PIK3CA, PIK3CB, PIK3CD, and PIK3CG, respectively[33]. PI3K catalyzes the conversion of phosphatidylinositol (4,5)-bisphosphate (PI(4,5)P2) into phosphatidylinositol (3,4,5)-trisphosphate (PI(3,4,5)P3) while the phosphatase and tensin homolog

Biomarker Descriptions (continued)

(PTEN) catalyzes the reverse reaction[35,36]. The reversible phosphorylation of inositol lipids regulates diverse aspects of cell growth and metabolism[35,36,37,38]. Recurrent somatic alterations in PIK3CA are frequent in cancer and result in the activation of PI3K/AKT/MTOR pathway, which can influence several hallmarks of cancer including cell proliferation, apoptosis, cancer cell metabolism and invasion, and genetic instability[39,40,41].

Alterations and prevalence: Recurrent somatic activating mutations in PIK3CA are common in diverse cancers and are observed in 20-30% of breast, cervical, and uterine cancers and 10-20% of bladder, gastric, head and neck, and colorectal cancers[6,7]. Activating mutations in PIK3CA commonly cluster in two regions corresponding to the exon 9 helical (codons E542/E545) and exon 20 kinase (codon H1047) domains, each having distinct mechanisms of activation[42,43,44]. PIK3CA resides in the 3q26 cytoband, a region frequently amplified (10-30%) in diverse cancers including squamous carcinomas of the lung, cervix, head and neck, and esophagus, and in serous ovarian and uterine cancers[6,7].

Potential relevance: The PI3K inhibitor, alpelisib[45], is FDA approved (2019) in combination with fulvestrant for the treatment of patients with PIK3CA-mutated, hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, advanced or metastatic breast cancer. Additionally, a phase Ib study of alpelisib with letrozole in patients with metastatic estrogen receptor (ER)-positive breast cancer, the clinical benefit rate, defined as lack of disease progression ≥ 6 months, was 44% (7/16) in PIK3CA-mutated tumors and 20% (2/20) in PIK3CA wild-type tumors[46]. Specifically, exon 20 H1047R mutations were associated with more durable clinical responses in comparison to exon 9 E545K mutations[46]. However, alpelisib did not improve response when administered with letrozole in patients with ER+ early breast cancer with PIK3CA mutations[47]. Case studies with MTOR inhibitors sirolimus and temsirolimus report isolated cases of clinical response in PIK3CA mutated refractory cancers[48,49].

Relevant Therapy Summary

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

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

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
osimertinib	●	●	●	●	● (II)
anlotinib hydrochloride, osimertinib	✖	✖	✖	✖	● (IV)
apatinib + EGFR tyrosine kinase inhibitor	✖	✖	✖	✖	● (IV)
icotinib hydrochloride, radiation therapy	✖	✖	✖	✖	● (IV)
durvalumab, chemotherapy	✖	✖	✖	✖	● (III)
icotinib hydrochloride, chemotherapy	✖	✖	✖	✖	● (III)
sintilimab, bevacizumab (Innovent Biologics), chemotherapy	✖	✖	✖	✖	● (III)
toripalimab, chemotherapy	✖	✖	✖	✖	● (III)
abivertinib	✖	✖	✖	✖	● (II)
apatinib, chemotherapy	✖	✖	✖	✖	● (II)
atezolizumab, bevacizumab	✖	✖	✖	✖	● (II)

* 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*
avitinib	✖	✖	✖	✖	● (II)
bevacizumab, osimertinib	✖	✖	✖	✖	● (II)
D-0316	✖	✖	✖	✖	● (II)
EGFR tyrosine kinase inhibitor + chemotherapy, EGFR tyrosine kinase inhibitor	✖	✖	✖	✖	● (II)
EGFR tyrosine kinase inhibitor, apatinib	✖	✖	✖	✖	● (II)
EGFR tyrosine kinase inhibitor, chemotherapy	✖	✖	✖	✖	● (II)
EGFR tyrosine kinase inhibitor, radiation therapy	✖	✖	✖	✖	● (II)
famitinib, almonertinib	✖	✖	✖	✖	● (II)
icotinib hydrochloride	✖	✖	✖	✖	● (II)
KN046	✖	✖	✖	✖	● (II)
nivolumab, ipilimumab	✖	✖	✖	✖	● (II)
osimertinib, bevacizumab	✖	✖	✖	✖	● (II)
osimertinib, radiation therapy	✖	✖	✖	✖	● (II)
ramucirumab, chemotherapy, cytokine	✖	✖	✖	✖	● (II)
SH-1028	✖	✖	✖	✖	● (II)
targeted therapy, chemotherapy	✖	✖	✖	✖	● (II)
toripalimab, anlotinib hydrochloride, chemotherapy	✖	✖	✖	✖	● (II)
tyrosine kinase inhibitors, radiation therapy	✖	✖	✖	✖	● (II)
ASK120067	✖	✖	✖	✖	● (I/II)
DZD-9008	✖	✖	✖	✖	● (I/II)
EMB01	✖	✖	✖	✖	● (I/II)
KP-673	✖	✖	✖	✖	● (I/II)
alisertib, osimertinib	✖	✖	✖	✖	● (I)
alisertib, sapanisertib, osimertinib	✖	✖	✖	✖	● (I)
amivantamab	✖	✖	✖	✖	● (I)

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

Relevant Therapy Summary (continued)

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

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

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
BCA101	✖	✖	✖	✖	● (I)
CK-101	✖	✖	✖	✖	● (I)
lazertinib, amivantamab	✖	✖	✖	✖	● (I)
neratinib, palbociclib, everolimus, trametinib	✖	✖	✖	✖	● (I)
osimertinib, necitumumab	✖	✖	✖	✖	● (I)
Palcitoclax, osimertinib	✖	✖	✖	✖	● (I)
pirotinib	✖	✖	✖	✖	● (I)
TQB 3804	✖	✖	✖	✖	● (I)
TQB3456	✖	✖	✖	✖	● (I)
TY-9591	✖	✖	✖	✖	● (I)
U3-1402	✖	✖	✖	✖	● (I)
YK-029A	✖	✖	✖	✖	● (I)
YZJ-0318	✖	✖	✖	✖	● (I)

PIK3CA p.(H1047R) c.3140A>G

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
alpelisib + fulvestrant	○	○	○	○	✖
EGFR tyrosine kinase inhibitor, chemotherapy	✖	✖	✖	✖	● (II)
everolimus	✖	✖	✖	✖	● (II)
paxalisib	✖	✖	✖	✖	● (II)
samotolisib	✖	✖	✖	✖	● (II)
sirolimus	✖	✖	✖	✖	● (II)
temsirolimus	✖	✖	✖	✖	● (II)
copanlisib, nivolumab, ipilimumab	✖	✖	✖	✖	● (I/II)
TAS-117, futibatinib	✖	✖	✖	✖	● (I/II)
copanlisib, olaparib, durvalumab	✖	✖	✖	✖	● (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

PIK3CA p.(H1047R) c.3140A>G (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
GDC-0077	✖	✖	✖	✖	● (I)
gedatolisib + palbociclib	✖	✖	✖	✖	● (I)
paxalisib, radiation therapy	✖	✖	✖	✖	● (I)

EGFR p.(G719S) c.2155G>A

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
osimertinib	✖	●	✖	●	● (II)
bevacizumab + erlotinib	✖	●	✖	●	✖
erlotinib + ramucirumab	✖	●	✖	●	✖
afatinib + cetuximab	✖	●	✖	✖	✖
bevacizumab + gefitinib	✖	✖	✖	●	✖
gefitinib + carboplatin + pemetrexed	✖	✖	✖	●	✖
apatinib + EGFR tyrosine kinase inhibitor	✖	✖	✖	✖	● (IV)
bevacizumab + osimertinib, osimertinib	✖	✖	✖	✖	● (IV)
EGFR tyrosine kinase inhibitor	✖	✖	✖	✖	● (IV)
icotinib hydrochloride, radiation therapy	✖	✖	✖	✖	● (IV)
atezolizumab, bevacizumab, chemotherapy	✖	✖	✖	✖	● (III)
durvalumab, chemotherapy	✖	✖	✖	✖	● (III)
icotinib hydrochloride, chemotherapy	✖	✖	✖	✖	● (III)
anlotinib hydrochloride, osimertinib	✖	✖	✖	✖	● (II)
atezolizumab, bevacizumab	✖	✖	✖	✖	● (II)
avitinib, AZD-3759	✖	✖	✖	✖	● (II)
bevacizumab, atezolizumab, chemotherapy	✖	✖	✖	✖	● (II)
bevacizumab, osimertinib	✖	✖	✖	✖	● (II)
bintrafusp alfa, chemoradiation therapy, durvalumab	✖	✖	✖	✖	● (II)

* 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.(G719S) c.2155G>A (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
EGFR tyrosine kinase inhibitor + chemotherapy, EGFR tyrosine kinase inhibitor	✖	✖	✖	✖	● (II)
EGFR tyrosine kinase inhibitor, apatinib	✖	✖	✖	✖	● (II)
EGFR tyrosine kinase inhibitor, chemotherapy	✖	✖	✖	✖	● (II)
EGFR tyrosine kinase inhibitor, radiation therapy	✖	✖	✖	✖	● (II)
famitinib, almonertinib	✖	✖	✖	✖	● (II)
icotinib hydrochloride	✖	✖	✖	✖	● (II)
maihuatinib	✖	✖	✖	✖	● (II)
neratinib	✖	✖	✖	✖	● (II)
nivolumab, ipilimumab	✖	✖	✖	✖	● (II)
osimertinib, bevacizumab	✖	✖	✖	✖	● (II)
osimertinib, chemotherapy	✖	✖	✖	✖	● (II)
osimertinib, necitumumab	✖	✖	✖	✖	● (II)
osimertinib, radiation therapy	✖	✖	✖	✖	● (II)
osimertinib, savolitinib	✖	✖	✖	✖	● (II)
pembrolizumab, chemotherapy	✖	✖	✖	✖	● (II)
ramucirumab, chemotherapy, cytokine	✖	✖	✖	✖	● (II)
SH-1028	✖	✖	✖	✖	● (II)
targeted therapy, chemotherapy	✖	✖	✖	✖	● (II)
tyrosine kinase inhibitors, radiation therapy	✖	✖	✖	✖	● (II)
ASK120067	✖	✖	✖	✖	● (I/II)
CBT-502, anlotinib hydrochloride	✖	✖	✖	✖	● (I/II)
DZD-9008	✖	✖	✖	✖	● (I/II)
EMB01	✖	✖	✖	✖	● (I/II)
KP-673	✖	✖	✖	✖	● (I/II)
AB-928, zimberelimab, chemotherapy	✖	✖	✖	✖	● (I)

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

Relevant Therapy Summary (continued)

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

EGFR p.(G719S) c.2155G>A (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
alisertib, osimertinib	✖	✖	✖	✖	● (I)
amivantamab	✖	✖	✖	✖	● (I)
BCA101	✖	✖	✖	✖	● (I)
genolimzumab, fruquintinib	✖	✖	✖	✖	● (I)
lazertinib, amivantamab	✖	✖	✖	✖	● (I)
neratinib, palbociclib, everolimus, trametinib	✖	✖	✖	✖	● (I)
niraparib, osimertinib	✖	✖	✖	✖	● (I)
osimertinib, ipilimumab	✖	✖	✖	✖	● (I)
pirotinib	✖	✖	✖	✖	● (I)
telaglenastat, sapanisertib	✖	✖	✖	✖	● (I)
telisotuzumab vedotin, osimertinib	✖	✖	✖	✖	● (I)
TNO-155, nazartinib	✖	✖	✖	✖	● (I)
TQB 3804	✖	✖	✖	✖	● (I)
TY-9591	✖	✖	✖	✖	● (I)
U3-1402	✖	✖	✖	✖	● (I)
WSD-0922	✖	✖	✖	✖	● (I)

EGFR amplification

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
nimotuzumab + chemotherapy	✖	✖	✖	✖	● (II)
osimertinib, necitumumab	✖	✖	✖	✖	● (II)
BCA101	✖	✖	✖	✖	● (I)
neratinib, palbociclib, everolimus, trametinib	✖	✖	✖	✖	● (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 2020-10-14. For the most up-to-date information, search www.fda.gov.

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

● osimertinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2020-05-23 **Variant class:** EGFR T790M mutation

Indications and usage:

TAGRISSO® is a kinase inhibitor indicated for

- the first-line treatment of patients with metastatic 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 treatment of 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/2020/208065s016lbl.pdf

PIK3CA p.(H1047R) c.3140A>G

○ alpelisib + fulvestrant

Cancer type: Breast Cancer **Label as of:** 2020-09-01 **Variant class:** PIK3CA H1047R mutation

Other criteria: ERBB2 negative, Hormone receptor positive

Indications and usage:
PIQRAY® is a kinase inhibitor indicated in combination with fulvestrant for the treatment of postmenopausal women, and men, with hormone receptor (HR)- positive, human epidermal growth factor receptor 2 (HER2)-negative, PIK3CA-mutated, advanced or metastatic breast cancer as detected by an FDA-approved test following progression on or after an endocrine-based regimen.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/212526s001lbl.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 2020-10-01. 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.(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, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Progression on erlotinib +/- (ramucirumab or bevacizumab), afatinib, gefitinib, or dacomitinib; Asymptomatic or symptomatic brain metastases (Subsequent therapy)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Progression on erlotinib +/- (ramucirumab or bevacizumab), afatinib, gefitinib, or dacomitinib; Systemic multiple lesions; If not previously given (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 8.2020]

● osimertinib

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Non-Small Cell Lung Cancer; Brain metastases; Use active agents against primary tumor (Not specified)
- Non-Small Cell Lung Cancer; Leptomeningeal and spine metastases (Not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 3.2020]

● osimertinib

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Non-Small Cell Lung Cancer; Leptomeningeal and spine metastases (Not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 3.2020]

PIK3CA p.(H1047R) c.3140A>G

alpelisib + fulvestrant

Cancer type: Breast Cancer **Variant class:** PIK3CA mutation

Other criteria: ERBB2 negative, ER positive, PR positive

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Recurrent or Stage IV Invasive Breast Cancer; Postmenopausal or Premenopausal receiving ovarian ablation or suppression (Second-line or subsequent therapy) (Preferred)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 6.2020]

EGFR p.(G719S) c.2155G>A, EGFR amplification

osimertinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR G719 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; EGFR sensitizing mutation discovered prior to first-line systemic therapy (First-line therapy) (Preferred)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 8.2020]

afatinib + cetuximab

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR G719 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Non-Small Cell Lung Cancer; Progression on erlotinib, afatinib, dacomitinib, gefitinib, chemotherapy, or osimertinib; Systemic multiple lesions (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 8.2020]

EGFR p.(G719S) c.2155G>A, EGFR amplification (continued)

bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR G719 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Non-Squamous Non-Small Cell Lung Cancer; Advanced or metastatic disease; No recent history of hemoptysis; Progression on erlotinib +/- (ramucirumab or bevacizumab), afatinib, gefitinib, or dacomitinib; Asymptomatic or symptomatic with brain metastases or isolated lesions (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 8.2020]

erlotinib + ramucirumab

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR G719 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Sensitizing EGFR mutation discovered prior to or during first-line systemic therapy (First-line therapy) (Other Recommended)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Progression on erlotinib +/- (ramucirumab or bevacizumab), afatinib, gefitinib, or dacomitinib; Asymptomatic or symptomatic with brain metastases or isolated lesions (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 8.2020]

osimertinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR G719 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Sensitizing EGFR mutation discovered during first-line systemic therapy; Interrupt or complete planned systemic therapy, including maintenance therapy (First-line therapy) (Preferred)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Advanced or metastatic disease; Progression on osimertinib; Asymptomatic or symptomatic with brain or isolated lesions (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 8.2020]

EGFR p.(G719S) c.2155G>A, EGFR amplification (continued)

bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR G719 mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):
- Non-Squamous Non-Small Cell Lung Cancer; Advanced or metastatic disease; No recent history of hemoptysis; Sensitizing EGFR mutation discovered prior to or during first-line systemic therapy (First-line therapy) (Useful in Certain Circumstances)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 8.2020]

osimertinib

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Non-Small Cell Lung Cancer; Leptomeningeal and spine metastases (Not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 3.2020]

Current EMA Information

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

EMA information is current as of 2020-10-14. For the most up-to-date information, search www.ema.europa.eu/ema.

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

● osimertinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2020-07-31 **Variant class:** EGFR T790M mutation

Reference:

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

PIK3CA p.(H1047R) c.3140A>G

○ alpelisib + fulvestrant

Cancer type: Breast Cancer **Label as of:** 2020-07-30 **Variant class:** PIK3CA mutation

Other criteria: ERBB2 mutation negative, Hormone receptor positive

Reference:

https://www.ema.europa.eu/en/documents/product-information/piqray-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 2020-10-01. For the most up-to-date information, search www.esmo.org.

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; Resistance to first-/second generation EGFR TKI; If not received previously; ESMO-Magnitude of Clinical Benefit Scale Version 1.1 Score: 4 (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.]

PIK3CA p.(H1047R) c.3140A>G

○ alpelisib + fulvestrant

Cancer type: Breast Cancer **Variant class:** PIK3CA exon 20 mutation

Other criteria: ERBB2 negative, ER positive

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

Population segment (Line of therapy):
- Luminal Advanced Breast Cancer; ESMO-MCBS v1.1 score: 3 (Not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-ESO-ESMO Advanced Breast Cancer [Annals of Oncology (2020), doi: https://doi.org/10.1016/j.annonc.2020.09.010 (ABC 5)]

EGFR p.(G719S) c.2155G>A, EGFR amplification

● 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 stage; ESMO-Magnitude of Clinical Benefit Scale Version 1.1 Score: 4 (First-line therapy) (Preferred)

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.(G719S) c.2155G>A, EGFR amplification (continued)

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; PS 0-2 (First-line therapy)

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

bevacizumab + gefitinib

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

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

Population segment (Line of therapy):
- Stage IV; PS 0-2 (First-line therapy)

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

erlotinib + ramucirumab

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

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

Population segment (Line of therapy):
- Stage IV; PS 0-2 (First-line therapy)

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

gefitinib + carboplatin + pemetrexed

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

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

Population segment (Line of therapy):
- Stage IV; PS 0-2 (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.(G719S) c.2155G>A, EGFR amplification (continued)

bevacizumab + erlotinib

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

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

Population segment (Line of therapy):
- Stage IV; ESMO-Magnitude of Clinical Benefit Scale Version 1.1 Score: 3 (First-line therapy)

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

bevacizumab + gefitinib

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

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

Population segment (Line of therapy):
- Stage IV; ESMO-Magnitude of Clinical Benefit Scale Version 1.1 Score: 3 (First-line therapy)

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

erlotinib + ramucirumab

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

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

Population segment (Line of therapy):
- Stage IV; ESMO-Magnitude of Clinical Benefit Scale Version 1.1 Score: 3 (First-line therapy)

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

gefitinib + carboplatin + pemetrexed

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

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

Population segment (Line of therapy):
- Advanced stage (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.(G719S) c.2155G>A, EGFR amplification (continued)

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; PS 3-4 (First-line therapy)

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

bevacizumab + gefitinib

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

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

Population segment (Line of therapy):
- Stage IV; PS 3-4 (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; PS 3-4 (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; PS 3-4 (First-line therapy)

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

Clinical Trials Summary

EGFR p.(T790M) c.2369C>T + PIK3CA p.(H1047R) c.3140A>G + EGFR p.(G719S) c.2155G>A

NCT ID	Title	Phase
NCT04552613	Study on the Efficacy of Targeted Therapy of EGFR-sensitive Mutation in Patients With Non-sensitive Lung Cancer Based on Molecular Typing	II

EGFR p.(T790M) c.2369C>T + EGFR p.(G719S) c.2155G>A

NCT ID	Title	Phase
NCT04029350	A Multi-center, One-arm, Phase II Trial of Anlotinib Combined With Osimertinib as the Second-line Treatment in Stage IIIb-IV NSCLC With Confirmed EGFRm and T790M.	II
NCT04426825	A Single Arm, Phase II Study of Atezolizumab (MPDL3280A, Anti-PD-L1 Antibody) in Combination With Bevacizumab in Patients With EGFR Mutation Positive Stage IIIB/IV Non-Squamous Non-Small Cell Lung Cancer Pretreated With Epidermal Growth Factor Receptor Tyrosine-Kinase Inhibitors	II
NCT02824952	Neo-adjuvant Trial With AZD9291 in EGFRm+ Stage IIIA/B NSCLC - a Phase II Open-label Study	II
NCT04233021	A Phase II, Multi-centre Study, to Evaluate the Efficacy and Safety of Osimertinib Treatment for Patients With EGFR-mutated Non-small Cell Lung Cancer (NSCLC) With Brain or Leptomeningeal Metastases	II
NCT03823807	A Multicenter, Open-label, Phase II Study to Evaluate the Safety and Efficacy of SH-1028 in Locally Advanced or Metastatic NSCLC	II
NCT03502850	A Phase I/II Study to Assess the Safety,Tolerability, Pharmacokinetics and Anti-tumour Activity of ASK120067 in Patients With Locally Advanced or Metastatic T790M Mutation-positive Non-Small Cell Lung Cancer Who Have Progressed Following Prior Therapy With an Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor Agent	I/II
NCT02496663	A Phase I Trial of AZD9291 and Necitumumab in EGFR-Mutant Non-small Cell Lung Cancer After Progression on a Previous EGFR Tyrosine Kinase Inhibitor	I
NCT03618043	A Phase I, Open-label Study to Assess the Safety and Tolerability of Ascending Doses of SH-1028 Tablets in Patients With Advanced Solid Cancer	I
NCT04204473	Phase I, Open-label, Single-arm Study to Evaluate the Safety, Tolerance, Pharmacokinetics and Preliminary Efficacy of TY-9591 Tablets in Advanced NSCLC Patients With Epidermal Growth Factor Receptor(EGFR) Positive Mutation	I
NCT03260491	A Multicenter, Open-Label Phase 1 Study of U3-1402 in Subjects With Metastatic or Unresectable Non-small Cell Lung Cancer	I

EGFR p.(G719S) c.2155G>A + EGFR amplification

NCT ID	Title	Phase
NCT03944772	A Biomarker-directed Phase II Platform Study in Patients With Advanced Non-Small Lung Cancer Whose Disease Has Progressed on First-Line Osimertinib Therapy	II

Clinical Trials Summary (continued)

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

NCT ID	Title	Phase
No NCT ID	Clinical Study Anlotinib Combined with Osimertinib in the Treatment of Advanced Non-Squamous Non-Small Cell Lung Cancer with 1st Generation and 2nd Generation EGFR-TKI Resistance with T790M Mutation	IV
No NCT ID	Apatinib Combined With EGFR-TKI For Patients With EGFR Mutation Who Failed EGFR-TKI: A Prospective Study	IV
No NCT ID	Clinical Study Of Combined Action Of Icotinib And Brain Radiotherapy On EGFR-Mutated Non-Small-Cell Lung Cancer Patients With Brain Metastasis	IV
NCT03802240	A Randomized, Double-blind, Multi-center, Phase III Clinical Study Assessing the Efficacy and Safety of Sintilimab ± IBI305 Combined With Pemetrexed and Cisplatin in Patients With EGFR-mutant Locally Advanced or Metastatic Non-squamous Non-small Cell Lung Cancer Who Have Failed Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor (EGFR-TKI) Treatment (ORIENT-31)	III
NCT03924050	A Randomized, Double-Blind, Placebo-Controlled, Multicenter, Phase III Study of Pemetrexed + Platinum Chemotherapy With or Without Toripalimab (JS001) in Advanced Non-small Cell Lung Cancer (NSCLC) Participants With TKI-resistant EGFR-mutated Tumors	III
NCT03800134	A Phase III, Double-blind, Placebo-controlled, Multi-center International Study of Neoadjuvant/Adjuvant Durvalumab for the Treatment of Patients With Resectable Stages II and III Non-small Cell Lung Cancer (AEGEAN)	III
NCT03992885	Combination Therapy With Icotinib, Pemetrexed and Platinum in Patients With Metastatic Non-squamous Non-small Cell Lung Cancer With EGFR Mutations Who Did Not Progress After Pemetrexed in Combination With Platinum-based Chemotherapy:a Single-arm, Open, Multicenter Clinical Study.	III
NCT03300115	Single-arm,Multi-center,Phase II Clinical Trial of the Efficacy and Safety of AC0010 in the Treatment of EGFR T790M Mutation-positive Patients With Advanded NSCLC	II
NCT03574402	An Open-label, Multi-center, Phase II Umbrella Study to Assess Efficacy of Targeted Therapy or Immunotherapy Directed by Next Generation Sequencing (NGS) in Chinese Patients With Advanced NSCLC (TRUMP)	II
NCT03861156	A Phase II Study to Assess the Safety and Efficacy of D0316 in Patients With Locally Advanced/ Metastatic Non Small Cell Lung Cancer Whose Tumors Are Epidermal Growth Factor Receptor Mutation Positive	II
No NCT ID	An Evaluation of Tumor Response to Osimertinib by Early FDG-PET Finding In Patients with T790M Positive EGFR Mutated Non-Small Cell Lung Cancer	II
No NCT ID	Phase II Study of Osimertinib in Patients with Non-Small Cell Lung Cancer Who Acquired Resistance to Afatinib (ALCSG-04)	II
NCT03433469	A Phase II Study to Evaluate Neoadjuvant Osimertinib Therapy in Patients with Surgically Resectable, EGFR-Mutant Non-Small Cell Lung Cancer	II
NCT03497767	A Randomised Phase II Trial of Osimertinib With or Without Stereotactic Radiosurgery for EGFR Mutated Non-Small Cell Lung Cancer (NSCLC) With Brain Metastases	II
NCT04316351	Efficacy and Safety of Toripalimab (JS001) Combined With Pemetrexed and Anlotinib for Patients With T790M Positive Non-Small Cell Lung Cancer After Osimertinib Resistance: a Phase II, Muti-center, Single Arm Study	II

Clinical Trials Summary (continued)

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

NCT ID	Title	Phase
NCT03376737	A Single-Arm Phase II Clinical Trial of Apatinib as the Maintenance Therapy in Advanced Lung Adenocarcinoma	II
NCT03838848	A Phase II Study to Evaluate the Efficacy, Safety, and Tolerability of KN046 in Patients With Advanced Non-small Cell Lung Cancer	II
NCT03804580	First-Line Treatment With Osimertinib In EGFR-Mutated Non-Small Cell Lung Cancer, Coupled To Extensive Translational Studies	II
No NCT ID	Osimertinib Combined Bevacizumab in Untreated Epidermal Growth Factor Receptor Mutated Non-small-cell Lung Cancer Patients with Malignant Pleural And/Or Pericardial Effusion -phase II Trial	II
No NCT ID	Randomized Controlled Trial for EGFR-TKIs Plus S-1 or EGFR-TKIs as the First-Line Therapy for Patients with Advanced Non-small Cell Lung Cancer Harboring EGFR Mutations	II
No NCT ID	Single arm, Exploratory Study for Apatinib mesylate Combined with EGFR-TKI in Patients with EGFR Mutation-positive Advanced Non-squamous Non–small-cell Lung Cancer	II
No NCT ID	EGFR-TKI Combined With Stereotactic Body Radiation Therapy Versus TKI alone for Stage IV Oncogene-Driven Non-Small Cell Lung Cancer.	II
NCT03904823	An Open, Single-arm, Multi-center, Phase II Clinical Trial of Famitinib Combined With Epidermal Growth Factor Receptor (EGFR) Inhibitor HS-10296 in Patients With Advanced EGFR-mutant Non-Small Cell Lung Cancer (NSCLC)	II
NCT02960607	A Phase II Study of High-dose Icotinib in Previously Treated Non-small Cell Lung Cancer Patients With Epidermal Growth Factor Receptor Mutation	II
NCT02961270	Clinical Activity of Icotinib in Patients With Advanced Non-small-cell Lung Cancer Harbouring Uncommon EGFR Mutations: a Single-arm, Prospective, Phase II Study	II
NCT03091491	Randomised Phase II Study of Nivolumab Versus Nivolumab and Ipilimumab Combination in EGFR Mutant Non-small Cell Lung Cancer	II
NCT03460275	Osimertinib as First-line Therapy for Patients With EGFR Mutation-positive Locally Advanced or Metastatic Non-squamous Non-Small Cell Lung Cancer(NSCLC), a Single-Arm, Open-Label, Prospective, Multicenter, Phase II Clinical Trial	II
NCT04425681	Phase II Study of Osimertinib With Bevacizumab for Leptomeningeal Metastasis From EGFR-mutation Non-Small Cell Lung Cancer	II
No NCT ID	Phase II Trial Of Docetaxel Plus Ramucirumab Combination Therapy In Patients With Advanced EGFR Gene Mutation Positive Advanced Stage Non-Squamous Cell Non small Cell Lung Cancer	II
No NCT ID	A Single-center, Open-label , Non-randomized Control Clinical Trial On Clinical Features and Medical Treatment of Advanced NSCLC With Rare Gene Mutations	II
No NCT ID	Clinical Study of Combined Action of the First Generation of TKIs and Brain Radiotherapy on EGFR-Mutated Non-Small-Cell Lung Cancer Patients with Brain Metastasis	II
NCT03446417	A Phase 1/2 Open Label, Multicenter Study to Assess the Safety, Tolerability, Pharmacokinetics, and Anti-tumor Activity of ZN-e4 (KP-673) in Patients With Advanced Non-Small Cell Lung Cancer With Activating Epidermal Growth Factor Receptor (EGFR) Mutations	I/II

Clinical Trials Summary (continued)

EGFR p.(T790M) c.2369C>T (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
NCT03797391	First-in-human, Phase I/II, Multicenter, Open-Label Study of EMB-01 in Patients With Advanced/ Metastatic Solid Tumors	I/II
NCT04085315	A Phase I/Ib Study of Alisertib in Combination With Osimertinib in Metastatic EGFR-mutant Lung Cancer	I
NCT04479306	A Ph Ib Study of Osimertinib + Alisertib or Sapanisertib for Osimertinib-Resistant EGFR Mutant Non-Small Cell Lung Cancer (NSCLC) (Crossover Study)	I
No NCT ID	Phase I Clinical Study of Safety, Tolerability, Pharmacokinetics and Initial Efficacy of RX518 in Patients with Advanced Non-small Cell Lung Cancer	I
NCT03754244	A Phase I Study of TQ-B3456 on Tolerance and Pharmacokinetics	I
No NCT ID	Evaluation Of The Phase I Clinical Trial Of Safety, Tolerability, Pharmacokinetic Characteristics, And Preliminary Efficacy Of YK-029A Tablets In Patients With Advanced Non-Small Cell Lung Cancer (NSCLC)	I
No NCT ID	A Multicenter, Open and Dose Escalation Phase I Study of YZJ-0318 Maleate Tablets in Patients with Advanced Non-Small Cell Lung Cancer with Positive Epidermal Growth Factor Receptor T790M Mutation.	I
NCT02609776	A Phase I, First-in-Human, Open-Label, Dose Escalation Study of JNJ-61186372, a Human Bispecific EGFR and cMet Antibody, in Subjects With Advanced Non-Small Cell Lung Cancer	I
NCT04001777	A Phase Ib Study of Safety and Efficacy of APG-1252 in Combination With Osimertinib (AZD9291) in EGFR TKI Resistant NSCLC Patients	I
No NCT ID	Phase I Study of DZD9008 in EGFR or HER2 Mutant NSCLC Chinese Patients	I
NCT04077463	An Open-label Phase 1/1b 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
No NCT ID	Study Of Immunologic Factor In Re-Biopsy Specimen, Peritumoral BALF, And The Peripheral Blood For Predicting Response To Osimertinib In NSCLC Patients	I
No NCT ID	Pharmacokinetic and dose finding study of osimertinib in patients with impaired renal function and low body weight	I
NCT03535363	Phase I Trial of Osimertinib With Stereotactic Radiosurgery (SRS) in Patients With Brain Metastases From EGFR Positive Non-Small-Cell Lung Cancer (NSCLC)	I
No NCT ID	Phase I Clinical Study With Advanced Solid Tumors KBP-5209 Treatment	I
NCT03065387	Phase I Study of the Pan-ERBB Inhibitor Neratinib Given in Combination With Everolimus, Palbociclib, or Trametinib in Advanced Cancer Subjects With EGFR Mutation/Amplification, HER2 Mutation/ Amplification, or HER3/4 Mutation or KRAS Mutation	I
NCT04128085	A Phase I, Open-label, Multicenter, Dose Escalation and Expansion Study to Evaluate the Tolerance and Pharmacokinetics of TQB3804 in Subjects With Advanced Malignant Tumors	I

Clinical Trials Summary (continued)

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

NCT ID	Title	Phase
NCT04429542	First-in-Human, Phase I/Ib, Open-label, Multicenter Study of Bifunctional EGFR/TGFß Fusion Protein BCA101 Alone and in Combination With Pembrolizumab in Patients With EGFR-Driven Advanced Solid Tumors	I

PIK3CA p.(H1047R) c.3140A>G

NCT ID	Title	Phase
NCT03994796	Genomically-Guided Treatment Trial in Brain Metastases	II
NCT03065062	Phase I Study of the CDK4/6 Inhibitor Palbociclib (PD-0332991) in Combination With the PI3K/mTOR Inhibitor Gedatolisib (PF-05212384) for Patients With Advanced Squamous Cell Lung, Pancreatic, Head & Neck and Other Solid Tumors	I
NCT02688881	Study to Evaluate the Safety and Efficacy of Sirolimus, in Subject With Refractory Solid Tumors	II
NCT03239015	Efficacy and Safety of Targeted Precision Therapy in Refractory Tumor With Druggable Molecular Event	II
NCT03155620	NCI-COG Pediatric MATCH (Molecular Analysis for Therapy Choice) Screening Protocol	II
NCT03213678	NCI-COG Pediatric MATCH (Molecular Analysis for Therapy Choice)- Phase II Subprotocol of LY3023414 in Patients With Solid Tumors	II
NCT03297606	Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR): A Phase II Basket Trial	II
NCT04317105	A Phase I/II Biomarker Driven Combination Trial of Copanlisib and Immune Checkpoint Inhibitors in Patients With Advanced Solid Tumors	I/II
No NCT ID	Phase I/II Study of TAS-117 In Combination With TAS-120 In Patients With Advanced Solid Tumors	I/II
NCT03842228	A Phase Ib Biomarker-Driven Combination Trial of Copanlisib, Olaparib, and MEDI4736 (Durvalumab) in Patients With Advanced Solid Tumors	I
NCT03006172	A Phase I, Open-Label, Dose-Escalation Study Evaluating the Safety, Tolerability, and Pharmacokinetics of GDC-0077 as a Single Agent in Patients With Locally Advanced or Metastatic PIK3CA-Mutant Solid Tumors and in Combination With Endocrine and Targeted Therapies in Patients With Locally Advanced or Metastatic PIK3CA-Mutant Hormone-Receptor Positive Breast Cancer	I
NCT04192981	A Phase I Study With Expansion Cohort of Concurrent GDC-0084 With Radiation Therapy for Patients With Solid Tumor Brain Metastases or Leptomeningeal Metastases Harboring PI3K Pathway Mutations	I

EGFR p.(G719S) c.2155G>A, EGFR amplification

NCT ID	Title	Phase
No NCT ID	The Efficacy and Safety of Osimertinib Combined with Bevacizumab in the Treatment of SD Patients with Non-Squamous Cell Lung Cancer	IV
No NCT ID	The Continuous Evaluation of EGFR Mutation in EGFR-mutation Positive Lung Cancer Patients During EGFR TKI Treatment	IV

Clinical Trials Summary (continued)

EGFR p.(G719S) c.2155G>A, EGFR amplification (continued)

NCT ID	Title	Phase
No NCT ID	Apatinib Combined With EGFR-TKI For Patients With EGFR Mutation Who Failed EGFR-TKI: A Prospective Study	IV
No NCT ID	Clinical Study Of Combined Action Of Icotinib And Brain Radiotherapy On EGFR-Mutated Non-Small-Cell Lung Cancer Patients With Brain Metastasis	IV
NCT03991403	Study of Atezolizumab in Combination With Carboplatin + Paclitaxel +Bevacizumab vs With Pemetrexed + Cisplatin or Carboplatin With Stage IV NON-SQUAMOUS NON-SMALL CELL LUNG CANCER With EGFR(+) or ALK(+)	III
NCT03800134	A Phase III, Double-blind, Placebo-controlled, Multi-center International Study of Neoadjuvant/Adjuvant Durvalumab for the Treatment of Patients With Resectable Stages II and III Non-small Cell Lung Cancer (AEGEAN)	III
NCT03992885	Combination Therapy With Icotinib, Pemetrexed and Platinum in Patients With Metastatic Non-squamous Non-small Cell Lung Cancer With EGFR Mutations Who Did Not Progress After Pemetrexed in Combination With Platinum-based Chemotherapy:a Single-arm, Open, Multicenter Clinical Study.	III
No NCT ID	A Phase II Trial for Mefatinib (MET-306) in the Treatment of EGFR Rare Mutations (g719x, l861q, s768i) in Patients With Advanced Non-small Cell Lung Cancer	II
NCT03497767	A Randomised Phase II Trial of Osimertinib With or Without Stereotactic Radiosurgery for EGFR Mutated Non-Small Cell Lung Cancer (NSCLC) With Brain Metastases	II
NCT03242915	Phase II Multi-center Study of Pembrolizumab in Combination With Platinum-based Doublet Chemotherapy in NSCLC (Non-small Cell Lung Cancer) Patients With Targetable Genetic Alterations in Their Tumor Previously Treated With Appropriate Targeted Agents With Progressive Disease	II
NCT03574402	An Open-label, Multi-center, Phase II Umbrella Study to Assess Efficacy of Targeted Therapy or Immunotherapy Directed by Next Generation Sequencing (NGS) in Chinese Patients With Advanced NSCLC (TRUMP)	II
NCT04042558	A Multicentre Phase II, Open-label, Non-randomized Study Evaluating Platinum-Pemetrexed-Atezolizumab (+/- Bevacizumab) for Patients With Stage IIIB/IV Non-squamous Non-small Cell Lung Cancer With EGFR Mutations, ALK Rearrangement or ROS1 Fusion Progressing After Targeted Therapies	II
NCT03840902	A Multicenter, Double Blind, Randomized, Controlled Study of M7824 With Concurrent Chemoradiation Followed by M7824 Versus Concurrent Chemoradiation Plus Placebo Followed by Durvalumab in Participants With Unresectable Stage III Non-small Cell Lung Cancer	II
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
NCT03804580	First-Line Treatment With Osimertinib In EGFR-Mutated Non-Small Cell Lung Cancer, Coupled To Extensive Translational Studies	II
NCT04410796	A Phase 2 Randomized Study of Osimertinib Versus Osimertinib Plus Chemotherapy for Patients With Metastatic EGFR-Mutant Lung Cancers That Have Detectable EGFR-Mutant cfDNA in Plasma After Initiation of Osimertinib	II
No NCT ID	Osimertinib Combined Bevacizumab in Untreated Epidermal Growth Factor Receptor Mutated Non-small-cell Lung Cancer Patients with Malignant Pleural And/Or Pericardial Effusion -phase II Trial	II

Clinical Trials Summary (continued)

EGFR p.(G719S) c.2155G>A, EGFR amplification (continued)

NCT ID	Title	Phase
No NCT ID	Randomized Controlled Trial for EGFR-TKIs Plus S-1 or EGFR-TKIs as the First-Line Therapy for Patients with Advanced Non-small Cell Lung Cancer Harboring EGFR Mutations	II
No NCT ID	Single arm, Exploratory Study for Apatinib mesylate Combined with EGFR-TKI in Patients with EGFR Mutation-positive Advanced Non-squamous Non–small-cell Lung Cancer	II
No NCT ID	EGFR-TKI Combined With Stereotactic Body Radiation Therapy Versus TKI alone for Stage IV Oncogene-Driven Non-Small Cell Lung Cancer.	II
NCT03904823	An Open, Single-arm, Multi-center, Phase II Clinical Trial of Famitinib Combined With Epidermal Growth Factor Receptor (EGFR) Inhibitor HS-10296 in Patients With Advanced EGFR-mutant Non-Small Cell Lung Cancer (NSCLC)	II
NCT02960607	A Phase II Study of High-dose Icotinib in Previously Treated Non-small Cell Lung Cancer Patients With Epidermal Growth Factor Receptor Mutation	II
NCT02961270	Clinical Activity of Icotinib in Patients With Advanced Non-small-cell Lung Cancer Harbouring Uncommon EGFR Mutations: a Single-arm, Prospective, Phase II Study	II
NCT03091491	Randomised Phase II Study of Nivolumab Versus Nivolumab and Ipilimumab Combination in EGFR Mutant Non-small Cell Lung Cancer	II
NCT03460275	Osimertinib as First-line Therapy for Patients With EGFR Mutation-positive Locally Advanced or Metastatic Non-squamous Non-Small Cell Lung Cancer(NSCLC), a Single-Arm, Open-Label, Prospective, Multicenter, Phase II Clinical Trial	II
NCT04425681	Phase II Study of Osimertinib With Bevacizumab for Leptomeningeal Metastasis From EGFR-mutation Non-Small Cell Lung Cancer	II
No NCT ID	Phase II Trial Of Docetaxel Plus Ramucirumab Combination Therapy In Patients With Advanced EGFR Gene Mutation Positive Advanced Stage Non-Squamous Cell Non small Cell Lung Cancer	II
No NCT ID	A Single-center, Open-label , Non-randomized Control Clinical Trial On Clinical Features and Medical Treatment of Advanced NSCLC With Rare Gene Mutations	II
No NCT ID	Clinical Study of Combined Action of the First Generation of TKIs and Brain Radiotherapy on EGFR-Mutated Non-Small-Cell Lung Cancer Patients with Brain Metastasis	II
NCT03446417	A Phase 1/2 Open Label, Multicenter Study to Assess the Safety, Tolerability, Pharmacokinetics, and Anti-tumor Activity of ZN-e4 (KP-673) in Patients With Advanced Non-Small Cell Lung Cancer With Activating Epidermal Growth Factor Receptor (EGFR) Mutations	I/II
NCT03983928	A Phase Ib, Open-label, Single Center, Non-randomized Study for Safety and Efficacy of TQB2450 Combined With Anlotinib in Subjects With Advanced Mutation Positive Non-Small Cell Lung Cancer	I/II
NCT03974022	A Phase I/II, Open-Label, Multicenter Study to Assess the Safety, Tolerability, Pharmacokinetics and Anti-tumor Efficacy of DZD9008 in Patients With Advanced Non-Small Cell Lung Cancer (NSCLC) With EGFR or HER2 Mutation	I/II
NCT03797391	First-in-human, Phase I/II, Multicenter, Open-Label Study of EMB-01 in Patients With Advanced/ Metastatic Solid Tumors	I/II
NCT04085315	A Phase I/Ib Study of Alisertib in Combination With Osimertinib in Metastatic EGFR-mutant Lung Cancer	I

Clinical Trials Summary (continued)

EGFR p.(G719S) c.2155G>A, EGFR amplification (continued)

NCT ID	Title	Phase
NCT03976856	A Phase Ib Clinical Study With Extension Phase to Evaluate Safety and Efficacy of Genolimzumab (GB226) in Combination With Fruquintinib in the Treatment of Relapsed or Metastatic NSCLC Patients	I
No NCT ID	Phase I Open, One-arm, Multi-center Clinical trial of Mefatinib in the Treatment of Advanced Non-Small Cell Lung Cancer with EGFR Rare Mutations (G719X, L861Q, S768I)	I
NCT02099058	A Multicenter, Phase I/Ib, Open-Label, Dose-Escalation Study of ABBV-399, an Antibody Drug Conjugate, in Subjects With Advanced Solid Tumors	I
NCT03846310	A Phase I/Ib Study to Evaluate the Safety and Tolerability of Immunotherapy Combinations in Participants With Lung Cancer	I
NCT02609776	A Phase I, First-in-Human, Open-Label, Dose Escalation Study of JNJ-61186372, a Human Bispecific EGFR and cMet Antibody, in Subjects With Advanced Non-Small Cell Lung Cancer	I
NCT04141644	A Phase Ib Study to Evaluate the Safety and Efficacy of Osimertinib in Combination With Ipilimumab in Patients With EGFR Mutated Non-Small-Cell Lung Cancer Tumors	I
NCT03891615	Phase I Study of Niraparib in Combination With Osimertinib in EGFR-Mutated Advanced Lung Cancer	I
NCT04250545	A Phase I Trial of MLN0128 (Sapanisertib) and CB-839 HCl (Telaglenastat) in Advanced NSCLC Patients	I
NCT03114319	An Open-label, Multi-center, Phase I, Dose Finding Study of Oral TNO155 in Adult Patients With Advanced Solid Tumors	I
NCT04197934	Phase I Study to Evaluate Safety, Tolerability, Pharmacokinetics and Anti-Tumor Activity of WSD0922-FUFU	I
No NCT ID	Phase I Study of DZD9008 in EGFR or HER2 Mutant NSCLC Chinese Patients	I
NCT04077463	An Open-label Phase 1/1b 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
No NCT ID	Study Of Immunologic Factor In Re-Biopsy Specimen, Peritumoral BALF, And The Peripheral Blood For Predicting Response To Osimertinib In NSCLC Patients	I
No NCT ID	Pharmacokinetic and dose finding study of osimertinib in patients with impaired renal function and low body weight	I
NCT03535363	Phase I Trial of Osimertinib With Stereotactic Radiosurgery (SRS) in Patients With Brain Metastases From EGFR Positive Non-Small-Cell Lung Cancer (NSCLC)	I
No NCT ID	Phase I Clinical Study With Advanced Solid Tumors KBP-5209 Treatment	I
NCT01953926	An Open-Label, Phase II Basket Study of Neratinib in Patients With Solid Tumors With Somatic Activating HER Mutations	II
NCT03065387	Phase I Study of the Pan-ERBB Inhibitor Neratinib Given in Combination With Everolimus, Palbociclib, or Trametinib in Advanced Cancer Subjects With EGFR Mutation/Amplification, HER2 Mutation/ Amplification, or HER3/4 Mutation or KRAS Mutation	I
NCT04128085	A Phase I, Open-label, Multicenter, Dose Escalation and Expansion Study to Evaluate the Tolerance and Pharmacokinetics of TQB3804 in Subjects With Advanced Malignant Tumors	I

Clinical Trials Summary (continued)

EGFR p.(G719S) c.2155G>A, EGFR amplification (continued)

NCT ID	Title	Phase
NCT04429542	First-in-Human, Phase I/Ib, Open-label, Multicenter Study of Bifunctional EGFR/TGFß Fusion Protein BCA101 Alone and in Combination With Pembrolizumab in Patients With EGFR-Driven Advanced Solid Tumors	I

Alerts Informed By Public Data Sources

Current NCCN Information

Contraindicated Not recommended Resistance

NCCN information is current as of 2020-10-01. 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.(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 8.2020]

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 8.2020]

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

pembrolizumab

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

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

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 8.2020]

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."
- "EGFR p.Thr790Met (T790M) is a mutation associated with acquired resistance to EGFR TKI therapy and has been reported in about 60% of patients with disease progression after initial response to erlotinib, gefitinib, or afatinib."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 8.2020]

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."
- "EGFR p.Thr790Met (T790M) is a mutation associated with acquired resistance to EGFR TKI therapy and has been reported in about 60% of patients with disease progression after initial response to erlotinib, gefitinib, or afatinib."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 8.2020]

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."
- "EGFR p.Thr790Met (T790M) is a mutation associated with acquired resistance to EGFR TKI therapy and has been reported in about 60% of patients with disease progression after initial response to erlotinib, gefitinib, or afatinib."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 8.2020]

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

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."
- "EGFR p.Thr790Met (T790M) is a mutation associated with acquired resistance to EGFR TKI therapy and has been reported in about 60% of patients with disease progression after initial response to erlotinib, gefitinib, or afatinib."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 8.2020]

EGFR p.(G719S) c.2155G>A, EGFR amplification

alectinib

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

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Thus, 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 8.2020]

brigatinib

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

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Thus, 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 8.2020]

ceritinib

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

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Thus, 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 8.2020]

EGFR p.(G719S) c.2155G>A, EGFR amplification (continued)

crizotinib

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

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Thus, 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 8.2020]

lorlatinib

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

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Thus, 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 8.2020]

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 8.2020]

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 8.2020]

EGFR p.(G719S) c.2155G>A, EGFR amplification (continued)

pembrolizumab

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

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

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 8.2020]

Current EMA Information

Contraindicated Not recommended Resistance

EMA information is current as of 2020-10-14. 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:** 2019-05-28 **Variant class:** EGFR T790M mutation

Reference:

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

Signatures

Testing Personnel:

2020.12.31
08:25:31 +08'00'

Laboratory Supervisor:

2020.12.31
08:25:46 +08'00'

Pathologist:

2020.12.31
08:26:03 +08'00'

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