

Tel: 02-2875-7449

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Sample Information

Patient Name: 周海坤

Gender: Male **ID No.**: D101455183 **History No.**: 46318369

Age: 61

Ordering Doctor: DOC3064F 陳育民

Ordering REQ.: D57KH5G Signing in Date: 2020/07/08

Path No.: S109-99669 **MP No.:** F20041

Assay: Oncomine Focus Assay

Sample Type: FFPE Block No.: \$109-19775A Percentage of tumor cells: 20%

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 Findings

Gene	Finding	Gene	Finding	
ALK	Not detected	NTRK1	Not detected	
BRAF	Not detected	NTRK2	Not detected	
EGFR	EGFR p.(L861Q) c.2582T>A	NTRK3	Not detected	
ERBB2	Not detected	RET	Not detected	
KRAS	Not detected	ROS1	Not detected	
MET	Not detected			



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Indicated Contraindicated

Relevant Biomarkers

Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
EGFR p.(L861Q) c.2582T>A epidermal growth factor receptor Tier: IA Allele Frequency: 12.96%	afatinib 1, 2 dacomitinib erlotinib gefitinib 2 osimertinib bevacizumab + erlotinib erlotinib + ramucirumab afatinib + cetuximab gefitinib + chemotherapy bevacizumab + gefitinib	None	135

Public data sources included in relevant therapies: FDA1, NCCN, EMA2, 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.

Variant Details

DNA	Sequence Varia	ants						
Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
EGFR	p.(L861Q)	c.2582T>A	COSM6213	chr7:55259524	12.96%	NM_005228.4	missense	1999
JAK1	p.(=)	c.2199A>G		chr1:65310489	99.60%	NM_002227.3	synonymous	1985
ALK	p.(D1529E)	c.4587C>G		chr2:29416366	51.60%	NM_004304.4	missense	1998
ALK	p.(I1461V)	c.4381A>G		chr2:29416572	99.85%	NM_004304.4	missense	1999
ALK	p.(=)	c.3375C>A		chr2:29445458	50.90%	NM_004304.4	synonymous	1996
FGFR3	p.(=)	c.1953G>A		chr4:1807894	99.60%	NM_000142.4	synonymous	1997
PDGFRA	p.(=)	c.939T>G		chr4:55133726	99.55%	NM_006206.5	synonymous	1993
PDGFRA	p.(=)	c.1701A>G		chr4:55141055	99.90%	NM_006206.5	synonymous	1998
FGFR4	p.(P136L)	c.407C>T		chr5:176517797	99.25%	NM_213647.2	missense	2000
RET	p.(=)	c.2307G>T		chr10:43613843	100.00%	NM_020975.4	synonymous	1993

Biomarker Descriptions

EGFR (epidermal growth factor receptor)

<u>Background:</u> The EGFR gene encodes the epidermal growth factor receptor (EGFR) tyrosine kinase, a member of the human epidermal growth factor receptor (HER) family. Along with EGFR/ERBB1/HER1, ERBB2/HER2, ERBB3/HER3, and ERBB4/HER4 make up the HER protein family¹. EGFR ligand induced dimerization results in kinase activation and leads to stimulation of oncogenic signaling



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Biomarker Descriptions (continued)

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 of EGFR are observed in approximately 10-20% of lung adenocarcinoma and at higher frequencies in never-smoker, female, and in Asian populations with lung cancer^{4,5,6,7}. The most common mutations occur near the ATP-binding pocket of the kinase domain and include short in-frame deletions in exon 19 (EGFR exon 19 deletion) and the L858R amino acid substitution in exon 21⁸. These mutations constitutively activate the EGFR kinase resulting in downstream signaling and represent 80% of the EGFR mutations observed in lung cancer. A second group of recurrent activating mutations that are less common include E709K, G719X, S768I, L861Q, and short in-frame insertions in exon 20^{9,10,11,12}. EGFR activating mutations in lung cancer tend to be mutually exclusive to KRAS activating mutations¹³. Although these variants are common in lung cancer, they are rare in other cancer types. In glioblastoma, recurrent activating EGFR mutations in the extracellular domain include R108K, A289V and G598V^{8,14}. The recurrent focal amplification of the EGFR gene leads to an increase in expression in several cancer types. EGFR is amplified in up to 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 which is frequently observed in glioblastoma and has been shown to lead to lung cancer development as well as sensitivity to TKIs^{16,17,18}.

Potential relevance: Erlotinib¹⁹ (2004), afatinib²⁰ (2013), gefitinib²¹ (2015), osimertinib²² (2015), and dacomitinib²³ (2018) are small molecule TKIs that are FDA approved for non-small cell lung cancer (NSCLC) patients with sensitizing exon 19 deletions and exon 21 L858R mutations. Acquired secondary mutations often confer resistance to first line TKI therapy with the T790M amino acid substitution accounting for 50-60% of cases⁸. Osimertinib is also indicated for NSCLC patients harboring EGFR T790M mutations whose disease has progressed on or after treatment with a first line TKI. EGFR targeting antibodies including cetuximab²⁴ (2004), panitumumab²⁵ (2006), and necitumumab²⁶ (2016) are also under investigation in combination with EGFR-targeting TKIs for efficacy against EGFR mutations. The use of cetuximab in combination with afatinib is currently recommended by the NCCN for patients who have progressed after receiving erlotinib, afatinib, dacomitinib, or gefitinib and chemotherapy²⁷.

In this cancer type and

other cancer types

Relevant Therapy Summary

In this cancer type \(\circ\) In other cancer

	туре	other cancer types	contraindicated			
EGFR p.(L861C) c.2582T>	·A				
Relevant Therapy		FDA	NCCN	EMA	ESMO	Clinical Trials*
afatinib		•	•	•	•	(IV)
gefitinib		×	•	•	•	(III)
bevacizumab + erlot	inib	×	•	×	•	(II)
erlotinib		×		×		(II)
osimertinib		×	•	×	•	(II)
dacomitinib		×	•	×	•	● (I)
erlotinib + ramucirun	nab	×	•	×	•	×
afatinib + cetuximab		×	•	×	×	×

Contraindicated

A Both for use and

contraindicated

X No evidence

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

Disclaimer: The data presented here is from a curated knowledgebase of publicly available information, but may not be exhaustive. The data version is 2020.03(007).



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Relevant Therapy Summary (continued)

In this cancer type In other cancer type

In this cancer type and other cancer types

Contraindicated

A Both for use and contraindicated

× No evidence

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
bevacizumab + gefitinib	×	×	×		×
gefitinib + carboplatin + pemetrexed	×	×	×		×
anlotinib hydrochloride, toripalimab	×	×	×	×	(IV)
apatinib + EGFR tyrosine kinase inhibitor	×	×	×	×	(IV)
apatinib + gefitinib	×	×	×	×	(IV)
bevacizumab + osimertinib, osimertinib	×	×	×	×	(IV)
EGFR tyrosine kinase inhibitor	×	×	×	×	(IV)
erlotinib, gefitinib, icotinib hydrochloride, chemotherapy	×	×	×	×	(IV)
gefitinib, radiation therapy	×	×	×	×	(IV)
icotinib hydrochloride	×	×	×	×	(IV)
icotinib hydrochloride, radiation therapy	×	×	×	×	(IV)
bevacizumab (Shanghai Hengrui Pharmaceutical) + chemotherapy, bevacizumab + chemotherapy	×	×	×	×	(III)
bevacizumab, atezolizumab, chemotherapy	×	×	×	×	(III)
bevacizumab, erlotinib	×	×	×	×	(III)
BPI-7711, gefitinib	×	×	×	×	(III)
durvalumab, chemotherapy	×	×	×	×	(III)
erlotinib, erlotinib + chemotherapy	×	×	×	×	(III)
gefitinib, apatinib	×	×	×	×	(III)
gefitinib, erlotinib	×	×	×	×	(III)
gefitinib, erlotinib, gefitinib + radiation therapy, erlotinib + radiation therapy	×	×	×	×	(III)
gefitinib, icotinib hydrochloride, erlotinib, gefitinib + radiation therapy, icotinib hydrochloride + radiation therapy, erlotinib + radiation therapy	×	×	×	×	(III)
HS-10296, gefitinib	×	×	×	×	(III)

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

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Relevant Therapy Summary (continued)

In this cancer type O In other cancer

type

In this cancer type and other cancer types

Contraindicated

A Both for use and contraindicated

X No evidence

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
icotinib hydrochloride, chemotherapy	×	×	×	×	(III)
nivolumab, chemotherapy	×	×	×	×	(III)
AZD-3759, erlotinib, gefitinib	×	×	×	×	(II/III)
afatinib, bevacizumab	×	×	×	×	(II)
afatinib, chemotherapy, radiation therapy	×	×	×	×	(II)
bevacizumab + gefitinib + chemotherapy	×	×	×	×	(II)
bevacizumab, erlotinib, chemotherapy	×	×	×	×	(II)
bevacizumab, osimertinib	×	×	×	×	(II)
bintrafusp alfa, chemoradiation therapy, durvalumab	×	×	×	×	(II)
chemotherapy, atezolizumab, bevacizumab	×	×	×	×	(II)
chemotherapy, durvalumab	×	×	×	×	(II)
chemotherapy, ramucirumab	×	×	×	×	(II)
EGFR tyrosine kinase inhibitor + chemotherapy	×	×	×	×	(II)
EGFR tyrosine kinase inhibitor + chemotherapy, EGFR tyrosine kinase inhibitor	×	×	×	×	● (II)
EGFR tyrosine kinase inhibitor, radiation therapy	×	×	×	×	(II)
erlotinib + chemotherapy	×	×	×	×	(II)
erlotinib, gefitinib	×	×	×	×	(II)
erlotinib, gefitinib, icotinib hydrochloride, erlotinib + chemotherapy, gefitinib + chemotherapy, icotinib hydrochloride + chemotherapy	×	×	×	×	(II)
erlotinib, radiation therapy	×	×	×	×	(II)
famitinib, HS-10296	×	×	×	×	(II)
gefitinib + chemotherapy	×	×	×	×	● (II)
gefitinib + fulvestrant	×	×	×	×	● (II)
gefitinib + nazartinib	×	×	×	×	(II)

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



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Relevant Therapy Summary (continued)

In this cancer type O In other cancer

type

In this cancer type and other cancer types

Contraindicated

A Both for use and contraindicated

X No evidence

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials
gefitinib, chemotherapy	×	×	×	×	(II)
gefitinib, surgical intervention	×	×	×	×	(II)
icotinib hydrochloride + radiation therapy, icotinib hydrochloride	×	×	×	×	(II)
icotinib hydrochloride, icotinib hydrochloride + radiation therapy	×	×	×	×	(II)
nivolumab, ipilimumab	×	×	×	×	(II)
osimertinib + radiation therapy	×	×	×	×	(II)
osimertinib, bevacizumab	×	×	×	×	(II)
osimertinib, savolitinib	×	×	×	×	(II)
pembrolizumab + chemotherapy	×	×	×	×	(II)
poziotinib	×	×	×	×	(II)
sutetinib	×	×	×	×	(II)
targeted therapy, chemotherapy	×	×	×	×	(II)
tyrosine kinase inhibitors, radiation therapy	×	×	×	×	(II)
zoledronic acid, gefitinib	×	×	×	×	(II)
AZD-3759	×	×	×	×	(1/11)
bevacizumab + erlotinib + chemotherapy	×	×	×	×	(1/11)
CBT-502, anlotinib hydrochloride	×	×	×	×	(1/11)
DZD-9008	×	×	×	×	(1/11)
EMB01	×	×	×	×	(1/11)
erlotinib + trametinib	×	×	×	×	(1/11)
icotinib hydrochloride + chemotherapy + radiation therapy	×	×	×	×	(1/11)
KP-673	×	×	×	×	(I/II)
lazertinib	×	×	×	×	(I/II)

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



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Relevant Therapy Summary (continued)

In this cancer type O In other cancer

type

In this cancer type and other cancer types

Contraindicated

A Both for use and contraindicated

X No evidence

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
ningetinib, gefitinib	×	×	×	×	(1/11)
oleclumab + osimertinib	×	×	×	×	(1/11)
S-49076, gefitinib	×	×	×	×	(1/11)
U3-1402	×	×	×	×	(1/11)
afatinib, chemotherapy	×	×	×	×	(1)
afatinib, immunostimulant	×	×	×	×	(1)
afatinib, osimertinib	×	×	×	×	(l)
alisertib, osimertinib	×	×	×	×	(I)
dacomitinib, osimertinib	×	×	×	×	(1)
DS-1205c, gefitinib	×	×	×	×	(1)
DS-1205c, osimertinib	×	×	×	×	(1)
everolimus + neratinib, neratinib + palbociclib, neratinib + trametinib	×	×	×	×	(l)
genolimzumab, fruquintinib	×	×	×	×	(I)
JNJ-61186372	×	×	×	×	(1)
lazertinib, JNJ-61186372	×	×	×	×	(1)
maihuatinib	×	×	×	×	(1)
nazartinib + trametinib, nazartinib + ribociclib, LXH254 + nazartinib, capmatinib + nazartinib, gefitinib + nazartinib	×	×	×	×	(1)
niraparib, osimertinib	×	×	×	×	(I)
nivolumab, ipilimumab, radiation therapy	×	×	×	×	(I)
osimertinib + radiation therapy, osimertinib	×	×	×	×	(l)
osimertinib, necitumumab	×	×	×	×	(I)
osimertinib, sapanisertib	×	×	×	×	(I)
pirotinib	×	×	×	×	(I)

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



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Relevant Therapy Summary (continued)

In this cancer type \(\cap \) In other cancer tvpe

In this cancer type and other cancer types

Contraindicated

Both for use and contraindicated

X No evidence

EGFR p.(L861Q) c.2582T>A (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
SH-1028	×	×	×	×	(I)
telisotuzumab vedotin, osimertinib	×	×	×	×	(l)
TNO-155	×	×	×	×	(l)
TP-0903	×	×	×	×	(l)
tyrosine kinase inhibitors, tyrosine kinase inhibitors + chemotherapy	×	×	×	×	(1)

^{*} 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 O In other cancer type

In this cancer type and O Contraindicated other cancer types

Not recommended | Resistance

FDA information is current as of 2020-02-28. For the most up-to-date information, search www.fda.gov.

EGFR p.(L861Q) c.2582T>A

afatinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2019-10-11

Variant class: EGFR L861Q mutation

Indications and usage:

GILOTRIF® is a kinase inhibitor indicated for:

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

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

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

https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/201292s015lbl.pdf

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Current NCCN Information

In this cancer type and other cancer types

Contraindicated

Not recommended Resistance

NCCN information is current as of 2019-11-01. 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.(L861Q) c.2582T>A

afatinib

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L861Q mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Sensitizing EGFR mutation discovered prior to first-line systemic therapy (First-line therapy) (Other Recommended)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

dacomitinib

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L861Q mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Sensitizing EGFR mutation discovered prior to first-line systemic therapy (First-line therapy) (Other Recommended)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

erlotinib

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L861Q mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Sensitizing EGFR mutation discovered prior to first-line systemic therapy (First-line therapy) (Other Recommended)



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EGFR p.(L861Q) c.2582T>A (continued)

gefitinib

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L861Q mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

 Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Sensitizing EGFR mutation discovered prior to first-line systemic therapy (First-line therapy) (Other Recommended)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

osimertinib

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L861Q mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

 Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Sensitizing EGFR mutation discovered prior to first-line systemic therapy (First-line therapy) (Preferred)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

afatinib

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L861Q mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Sensitizing EGFR mutation discovered during first-line systemic therapy; Interrupt or complete planned systemic therapy, including maintenance therapy (First-line therapy)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Progression after first-line therapy (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L861Q mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

Non-Squamous Non-Small Cell Lung Cancer; Progression after first-line therapy (Subsequent therapy)



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EGFR p.(L861Q) c.2582T>A (continued)

dacomitinib

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L861Q mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Sensitizing EGFR mutation discovered during first-line systemic therapy; Interrupt or complete planned systemic therapy, including maintenance therapy (First-line therapy)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Progression after first-line therapy (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

erlotinib

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L861Q mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Sensitizing EGFR mutation discovered during first-line systemic therapy; Interrupt or complete planned systemic therapy, including maintenance therapy (First-line therapy)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Progression after first-line therapy (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

erlotinib + ramucirumab

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L861Q mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Sensitizing EGFR mutation discovered prior to first-line systemic therapy (First-line therapy) (Other Recommended)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Sensitizing EGFR mutation discovered during first-line systemic therapy (First-line therapy)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Progression after first-line therapy (Subsequent therapy)



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EGFR p.(L861Q) c.2582T>A (continued)

gefitinib

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L861Q mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Sensitizing EGFR mutation discovered during first-line systemic therapy; Interrupt or complete planned systemic therapy, including maintenance therapy (First-line therapy)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Progression after first-line therapy (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

osimertinib

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L861Q mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Sensitizing EGFR mutation discovered during first-line systemic therapy; Interrupt or complete planned systemic therapy, including maintenance therapy (First-line therapy) (Preferred)
- Progression on osimertinib (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

bevacizumab + erlotinib

Cancer type: Non-Small Cell Lung Cancer Variant class: EGFR L861Q mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- Non-Squamous Non-Small Cell Lung Cancer; Sensitizing EGFR mutation discovered prior to first-line systemic therapy (First-line therapy) (Useful in Certain Circumstances)
- Non-Squamous Non-Small Cell Lung Cancer; Sensitizing EGFR mutation discovered during first-line systemic therapy (First-line therapy)



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EGFR p.(L861Q) c.2582T>A (continued)

afatinib

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

Non-Small Cell Lung Cancer; Brain metastases; Recurrent disease; Use agents active against primary tumor (Not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 3.2019]

afatinib + cetuximab

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

Other criteria: EGFR T790M negative

NCCN Recommendation category: 2A

Population segment (Line of therapy):

 Non-Small Cell Lung Cancer; Progression after receiving erlotinib, afatinib, dacomitinib, or gefitinib and systemic therapy (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

erlotinib

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

Non-Small Cell Lung Cancer; Brain metastases; Recurrent disease; Use agents active against primary tumor (Not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 3.2019]

gefitinib

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

Non-Small Cell Lung Cancer; Brain metastases; Recurrent disease; Use agents active against primary tumor (Not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 3.2019]



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EGFR p.(L861Q) c.2582T>A (continued)

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; Brain metastases; Newly diagnosed (Not specified)
- Non-Small Cell Lung Cancer; Leptomeningeal and Spine metastases (Not specified)

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 3.2019]

alectinib

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

Summary:

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

"Likewise, crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

brigatinib

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

Summary:

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

"Likewise, crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

eritinib 🖷

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

Summary:

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

"Likewise, crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."



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EGFR p.(L861Q) c.2582T>A (continued)

1

crizotinib

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

Summary:

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

"Likewise, crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

lorlatinib

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

Summary:

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

"Likewise, crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib are not recommended for patients with sensitizing EGFR mutations who relapse on EGFR TKI therapy."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 2.2020]

pembrolizumab

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

Other criteria: CD274 overexpression

Summary:

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

"A small study suggests that single-agent pembrolizumab is not effective as first-line therapy in patients with metastatic NSCLC and EGFR mutations, even those with PD-L1 levels more than 50%."

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Current EMA Information

EMA information is current as of 2020-02-28. For the most up-to-date information, search www.ema.europa.eu/ema.

EGFR p.(L861Q) c.2582T>A

afatinib

Cancer type: Non-Small Cell Lung Cancer Label as of: 2020-02-13 Variant class: EGFR L861Q mutation

Reference

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

gefitinib

Cancer type: Non-Small Cell Lung Cancer Label as of: 2019-05-28 Variant class: EGFR L861Q mutation

Reference:

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

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Current ESMO Information

In this cancer type O In other cancer type

In this cancer type and other cancer types

Contraindicated

Not recommended Resistance

ESMO information is current as of 2019-11-01. For the most up-to-date information, search www.esmo.org.

EGFR p.(L861Q) c.2582T>A

afatinib

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

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

Population segment (Line of therapy):

Advanced stage (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192-iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

erlotinib

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

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

Population segment (Line of therapy):

Advanced stage (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): $iv192-iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer \cite{Continuous} and the continuous of the cont$

gefitinib

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

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

Population segment (Line of therapy):

Advanced stage (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192-iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]



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EGFR p.(L861Q) c.2582T>A (continued)

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)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192-iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

dacomitinib

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

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

Population segment (Line of therapy):

Stage IV; Magnitude of Clinical Benefit Scale Version v1.1 Score: 3 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192-iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

erlotinib

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

ESMO Level of Evidence/Grade of Recommendation: III / ${\sf B}$

Population segment (Line of therapy):

Non-Squamous (Maintenance therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192-iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

afatinib

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

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

Population segment (Line of therapy):

Stage IV; PS 0-2 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192-iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]



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EGFR p.(L861Q) c.2582T>A (continued)

erlotinib

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

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

Population segment (Line of therapy):

Stage IV; PS 0-2 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192-iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

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 [Ann Oncol (2018) 29 (suppl 4): iv192-iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

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 [Ann Oncol (2018) 29 (suppl 4): iv192-iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

bevacizumab + erlotinib

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

ESMO Level of Evidence/Grade of Recommendation: II / 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 [Ann Oncol (2018) 29 (suppl 4): iv192-iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]



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EGFR p.(L861Q) c.2582T>A (continued)

bevacizumab + gefitinib

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

ESMO Level of Evidence/Grade of Recommendation: II / 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 [Ann Oncol (2018) 29 (suppl 4): iv192-iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

erlotinib + ramucirumab

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

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

Population segment (Line of therapy):

Stage IV (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192-iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

afatinib

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

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

Population segment (Line of therapy):

Stage IV; PS 3-4 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192-iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

dacomitinib

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

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

Population segment (Line of therapy):

Stage IV; PS 3-4 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192-iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

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EGFR p.(L861Q) c.2582T>A (continued)

erlotinib

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

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

Population segment (Line of therapy):

■ Stage IV; PS 3-4 (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192-iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

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 [Ann Oncol (2018) 29 (suppl 4): iv192-iv237; https://www.esmo.org/Guidelines/Lung-and-Chest-Tumours/Metastatic-Non-Small-Cell-Lung-Cancer]

Signatures	
Testing Personnel:	
Laboratory Supervisor:	
Pathologist:	



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