

Department of Pathology and Laboratory Medicine No.201, Sec. 2, Shipai Rd., Beitou District, Taipei City, Taiwan 11217, R.O.C. Tel: 02-2875-7449

Date: 29 Dec 2021 1 of 36

Sample Information

Patient Name: 陳玉秀 Gender: Female ID No.: Q201394374 History No.: 47970547

Age: 69

Ordering Doctor: DOC3183G 林昱廷 Ordering REQ.: 0BQGHCW Signing in Date: 2021/12/29

Path No.: S110-94995 **MP No.:** F21114

Assay: Oncomine Focus Assay

Sample Type: FFPE Block No.: S110-62348A Percentage of tumor cells: 80%

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

Note:

Sample Cancer Type: Non-Small Cell Lung Cancer

Table of Contents	Page
Variants (Exclude variant in Taiwan BioBank with >1% allele frequency)	2
Biomarker Descriptions	2
Relevant Therapy Summary	3
Relevant Therapy Details	4
Clinical Trials Summary	28
Alert Details	29

Report Highlights 2 Relevant Biomarkers 11 Therapies Available

8 Clinical Trials

Relevant Non-Small Cell Lung Cancer Variants

Gene	Finding	Gene	Finding
ALK	None detected	NTRK1	None detected
BRAF	None detected	NTRK2	None detected
EGFR	EGFR p.(G719S) c.2155G>A, EGFR p.(L861Q) c.2582T>A	NTRK3	None detected
ERBB2	None detected	RET	None detected
KRAS	None detected	ROS1	None detected
MET	None detected		

Date: 29 Dec 2021

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	EGFR p.(G719S) c.2155G>A, EGFR p.(L861Q) c.2582T>A epidermal growth factor receptor Allele Frequency: 53.94%, 63.08% (2 variants)	afatinib 1,2 gefitinib* 2 bevacizumab + erlotinib bevacizumab + gefitinib dacomitinib erlotinib + ramucirumab gefitinib + chemotherapy osimertinib osimertinib + chemotherapy	None	8
	Diagnostic significance: None			

Public data sources included in relevant therapies: FDA1, NCCN, EMA2, ESMO
Public data sources included in prognostic and diagnostic significance: NCCN, ESMO

Tier Reference: Li et al. Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists. J Mol Diagn. 2017 Jan;19(1):4-23.

* Includes biosimilars

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

DNA	Sequence Varia	ants						
Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
EGFR	p.(G719S)	c.2155G>A	COSM6252	chr7:55241707	53.94%	NM_005228.5	missense	1982
EGFR	p.(L861Q)	c.2582T>A	COSM6213	chr7:55259524	63.08%	NM_005228.5	missense	1999

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 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/HER4¹. 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 21⁸. 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 mutations¹³. 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 erlotinib¹⁹ (2004) and gefitinib²⁰ (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

Biomarker Descriptions (continued)

activating mutations. Second-generation TKIs afatinib21 (2013) and dacomitinib22 (2018) bind EGFR and other ERBB/HER gene family members irreversibly and were subsequently approved. First- and second-generation TKIs afatinib, dacomitinib, erlotinib, and gefitinib are recommended for the treatment NSCLC harboring EGFR exon 19 insertions, exon 19 deletions, point mutations L861Q, L858R, S768I, and codon 719 mutations, whereas most EGFR exon 20 insertions, except p.A763_Y764insFQEA, confer resistance to the same therapies^{23,24,25,26}. However, in 2021, the irreversible tyrosine kinase inhibitor, mobocertinib²⁷was FDA approved for the treatment of NSCLC with EGFR exon 20 insertion mutations. In lung cancer containing EGFR exon 19 or 21 activating mutations, treatment with TKIs is eventually associated with the emergence of drug resistance²⁸. The primary resistance mutation that emerges following treatment with first-generation TKI is T790M, accounting for 50-60% of resistant cases8. Third generation TKIs were developed to maintain sensitivity in the presence of T790M. Osimertinib²⁹ (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 cases²⁸. 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 versa³⁰. T790M and C797S can occur in either cis or trans allelic orientation³⁰. 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 TKIs30. 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^{30,31}. However, C797S occurring in cis conformation with T790M, confers resistance to first- and third-generation TKIs30. 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, amivantamab³², targeting EGFR and MET was approved (2021) NSCLC tumors harboring EGFR exon 20 insertion mutations. The Oncoprex immunogene therapy quaratusugene ozeplasmid³³ 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-18934 was granted a fast track designation (2020) for the treatment of solid tumors harboring an EGFR exon 20 insertion mutation.

Relevant Therapy Summary

In this cancer type	O In other cancer type	In this cancer type and other cancer types	No evidence
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FGFP n (G710S) c 2155G>A FGFP n (L8610) c 2582T>A

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
afatinib	•	•	•	•	×
gefitinib	×	•	•		×
bevacizumab + erlotinib	×	•	×	•	×
dacomitinib	×	•	×		×
erlotinib	×	•	×	•	×
erlotinib + ramucirumab	×	•	×	•	×
osimertinib	×	•	×	•	×
osimertinib + chemotherapy	×	•	×	×	×
gefitinib (Mylan)	×	×	•	×	×
bevacizumab + gefitinib	×	×	×	•	×
gefitinib + carboplatin + pemetrexed	×	×	×	•	×
durvalumab, chemotherapy	×	×	×	×	(III)

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

Date: 29 Dec 2021 4 of 36

Relevant Therapy Summary (continued)

■ In this cancer type
O In other cancer type
O In this cancer type and other cancer types
X No evidence

EGFR p.(G719S) c.2155G>A, EGFR p.(L861Q) c.2582T>A (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
atezolizumab, bevacizumab, chemotherapy	×	×	×	×	(II)
datopotamab deruxtecan	×	×	×	×	(II)
osimertinib, savolitinib	×	×	×	×	(II)
DZD-9008	×	×	×	×	(/)
amivantamab	×	×	×	×	(I)
lazertinib, amivantamab, chemotherapy	×	×	×	×	(I)
TNO-155, nazartinib	×	×	×	×	(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

FDA information is current as of 2021-11-17. For the most up-to-date information, search www.fda.gov.

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

afatinib

Cancer type: Non-Small Cell Lung Cancer Label as of: 2019-10-11 Variant class: EGFR G719 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

Reference:

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

Date: 29 Dec 2021 5 of 36

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

Reference:

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

Date: 29 Dec 2021 6 of 36

Current NCCN Information

In this cancer type

O In other cancer type

In this cancer type and other cancer types

NCCN information is current as of 2021-11-01. 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.(G719S) c.2155G>A

afatinib

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

NCCN Recommendation category: 1

Population segment (Line of therapy):

 Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2021]

dacomitinib

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

NCCN Recommendation category: 1

Population segment (Line of therapy):

 Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2021]

erlotinib

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

NCCN Recommendation category: 1

Population segment (Line of therapy):

 Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2021]

gefitinib

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

NCCN Recommendation category: 1

Population segment (Line of therapy):

 Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (First-line therapy); Other recommended intervention

Date: 29 Dec 2021 7 of 36

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

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, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (First-line therapy);
 Preferred intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2021]

afatinib

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2021]

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

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2021]

dacomitinib

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (Subsequent therapy)

Date: 29 Dec 2021 8 of 36

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

erlotinib

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2021]

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

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2021]

gefitinib

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

Adenocarcinoma, Large Cell, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2021]

osimertinib

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

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

osimertinib + chemotherapy

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

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

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2021]

afatinib

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

NCCN Recommendation category: 2B

Population segment (Line of therapy):

Brain Metastases (Line of therapy not specified)

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

gefitinib

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

NCCN Recommendation category: 2B

Population segment (Line of therapy):

■ Brain Metastases (Line of therapy not specified)

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

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, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (First-line therapy); Other recommended intervention

Date: 29 Dec 2021 10 of 36

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

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, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2021]

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, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2021]

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, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2021]

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, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (First-line therapy);
 Preferred intervention

Date: 29 Dec 2021 11 of 36

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

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, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2021]

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

Non-squamous Cell; Advanced, Metastatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2021]

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, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2021]

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, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (Subsequent therapy)

Date: 29 Dec 2021 12 of 36

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

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

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2021]

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, Squamous Cell, Not otherwise specified (NOS); Advanced, Metastatic (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2021]

osimertinib

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

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

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2021]

osimertinib + chemotherapy

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

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

Date: 29 Dec 2021 13 of 36

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

afatinib

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

NCCN Recommendation category: 2B

Population segment (Line of therapy):

Brain Metastases (Line of therapy not specified)

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

gefitinib

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

NCCN Recommendation category: 2B

Population segment (Line of therapy):

■ Brain Metastases (Line of therapy not specified)

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

Date: 29 Dec 2021 14 of 36

Current EMA Information

In this cancer type

O In other cancer type

In this cancer type and other cancer types

EMA information is current as of 2021-11-17. For the most up-to-date information, search www.ema.europa.eu/ema.

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

afatinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2021-04-21

Variant class: EGFR G719 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: 2021-03-05

Variant class: EGFR G719 mutation

Reference:

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

gefitinib (Mylan)

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2021-10-05

Variant class: EGFR G719 mutation

Reference:

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

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

afatinib

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2021-04-21

Variant class: EGFR L8610 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: 2021-03-05

Variant class: EGFR L861Q mutation

Reference:

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

gefitinib (Mylan)

Cancer type: Non-Small Cell Lung Cancer

Label as of: 2021-10-05

Variant class: EGFR L8610 mutation

Reference:

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

Date: 29 Dec 2021 15 of 36

Current ESMO Information

ESMO information is current as of 2021-11-01. For the most up-to-date information, search www.esmo.org.

EGFR p.(G719S) c.2155G>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 (First-line therapy)

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

erlotinib

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

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

Population segment (Line of therapy):

Advanced (First-line therapy)

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

gefitinib

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

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

Population segment (Line of therapy):

Advanced (First-line therapy)

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

osimertinib

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

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

Population segment (Line of therapy):

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

dacomitinib

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

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

Population segment (Line of therapy):

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

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

erlotinib

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

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

Population segment (Line of therapy):

■ Non-squamous Cell (Maintenance therapy)

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

afatinib

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

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

Population segment (Line of therapy):

Stage IV (First-line therapy)

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

bevacizumab + erlotinib

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

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

Population segment (Line of therapy):

■ Stage IV (First-line therapy)

bevacizumab + gefitinib

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

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

Population segment (Line of therapy):

■ Stage IV (First-line therapy)

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

dacomitinib

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

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

Population segment (Line of therapy):

■ Stage IV (First-line therapy)

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

erlotinib

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

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

Population segment (Line of therapy):

Stage IV (First-line therapy)

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

erlotinib + ramucirumab

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

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

Population segment (Line of therapy):

■ Stage IV (First-line therapy)

gefitinib

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

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

Population segment (Line of therapy):

■ Stage IV (First-line therapy)

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

gefitinib + carboplatin + pemetrexed

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

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

Population segment (Line of therapy):

■ Stage IV (First-line therapy)

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

bevacizumab + erlotinib

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

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

Population segment (Line of therapy):

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

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

bevacizumab + gefitinib

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

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

Population segment (Line of therapy):

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

erlotinib + ramucirumab

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

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

Population segment (Line of therapy):

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

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

gefitinib + carboplatin + pemetrexed

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

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

Population segment (Line of therapy):

Advanced (First-line therapy)

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

afatinib

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

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

Population segment (Line of therapy):

Stage IV (First-line therapy)

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

bevacizumab + erlotinib

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

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

Population segment (Line of therapy):

■ Stage IV (First-line therapy)

bevacizumab + gefitinib

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

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

Population segment (Line of therapy):

■ Stage IV (First-line therapy)

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

dacomitinib

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

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

Population segment (Line of therapy):

■ Stage IV (First-line therapy)

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

erlotinib

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

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

Population segment (Line of therapy):

Stage IV (First-line therapy)

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

erlotinib + ramucirumab

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

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

Population segment (Line of therapy):

■ Stage IV (First-line therapy)

Date: 29 Dec 2021 21 of 36

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

gefitinib

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

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

Population segment (Line of therapy):

■ Stage IV (First-line therapy)

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

gefitinib + carboplatin + pemetrexed

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

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

Population segment (Line of therapy):

■ Stage IV (First-line therapy)

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

EGFR p.(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 (First-line therapy)

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

erlotinib

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

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

Population segment (Line of therapy):

Advanced (First-line therapy)

gefitinib

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

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

Population segment (Line of therapy):

Advanced (First-line therapy)

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

osimertinib

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

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

Population segment (Line of therapy):

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

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

dacomitinib

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

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

Population segment (Line of therapy):

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

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

erlotinib

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

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

Population segment (Line of therapy):

■ Non-squamous Cell (Maintenance therapy)

afatinib

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

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

Population segment (Line of therapy):

■ Stage IV (First-line therapy)

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

bevacizumab + erlotinib

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

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

Population segment (Line of therapy):

■ Stage IV (First-line therapy)

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

bevacizumab + gefitinib

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

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

Population segment (Line of therapy):

Stage IV (First-line therapy)

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

dacomitinib

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

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

Population segment (Line of therapy):

■ Stage IV (First-line therapy)

erlotinib

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

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

Population segment (Line of therapy):

■ Stage IV (First-line therapy)

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

erlotinib + ramucirumab

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

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

Population segment (Line of therapy):

■ Stage IV (First-line therapy)

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

gefitinib

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

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

Population segment (Line of therapy):

Stage IV (First-line therapy)

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

gefitinib + carboplatin + pemetrexed

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

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

Population segment (Line of therapy):

■ Stage IV (First-line therapy)

bevacizumab + erlotinib

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

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

Population segment (Line of therapy):

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

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

bevacizumab + gefitinib

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

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

Population segment (Line of therapy):

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

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

erlotinib + ramucirumab

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

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

Population segment (Line of therapy):

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

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

gefitinib + carboplatin + pemetrexed

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

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

Population segment (Line of therapy):

Advanced (First-line therapy)

afatinib

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

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

Population segment (Line of therapy):

■ Stage IV (First-line therapy)

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

bevacizumab + erlotinib

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

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

Population segment (Line of therapy):

■ Stage IV (First-line therapy)

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

bevacizumab + gefitinib

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

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

Population segment (Line of therapy):

Stage IV (First-line therapy)

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

dacomitinib

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

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

Population segment (Line of therapy):

■ Stage IV (First-line therapy)

Date: 29 Dec 2021 27 of 36

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 (First-line therapy)

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

erlotinib + ramucirumab

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

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

Population segment (Line of therapy):

■ Stage IV (First-line therapy)

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

gefitinib

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

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

Population segment (Line of therapy):

Stage IV (First-line therapy)

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

gefitinib + carboplatin + pemetrexed

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

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

Population segment (Line of therapy):

■ Stage IV (First-line therapy)

Date: 29 Dec 2021 28 of 36

Clinical Trials in Taiwan region:

Clinical Trials Summary

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

NCT ID	Title	Phase
NCT04147351	A Phase II Study of Atezolizumab in Combination With Bevacizumab, Carboplatin or Cisplatin, and Pemetrexed for EGFR-mutant Metastatic Non-small Cell Lung Cancer Patients After Failure of EGFR Tyrosine Kinase Inhibitors.	II
NCT03778229	A Phase II, Single Arm Study Assessing Efficacy of Osimertinib With Savolitinib in Patients With EGFRm + MET+, Locally Advanced or Metastatic Non Small Cell Lung Cancer Who Have Progressed Following Osimertinib Treatment (SAVANNAH Study)	II
NCT02609776	A Phase I, First-in-Human, Open-Label, Dose Escalation Study of JNJ-61186372, a Human Bispecific EGFR and cMet Antibody, in Subjects With Advanced Non-Small Cell Lung Cancer.	I
NCT04484142	Phase II, Single-arm, Open-label Study of DS-1062a in Advanced or Metastatic Non-small Cell Lung Cancer With Actionable Genomic Alterations and Progressed On or After Applicable Targeted Therapy and Platinum Based Chemotherapy (TROPION-Lung05)	II
NCT03114319	An Open-label, Multi-center, Phase I, Dose Finding Study of Oral TNO155 in Adult Patients With Advanced Solid Tumors.	I
NCT03974022	A Phase I/II, Open-Label, Multicenter Study to Assess the Safety, Tolerability, Pharmacokinetics and Anti-tumor Efficacy of DZD9008 in Patients With Advanced Non-Small Cell Lung Cancer (NSCLC) With EGFR or HER2 Mutation	I/II
NCT04077463	An Open-label Phase I/Ib Study to Evaluate the Safety and Pharmacokinetics of JNJ-73841937 (Lazertinib), a Third Generation EGFR-TKI, as Monotherapy or in Combinations With JNJ-61186372, a Human Bispecific EGFR and cMet Antibody in Participants With Advanced Non-Small Cell Lung Cancer	I
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

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

NCT ID	Title	Phase
NCT04147351	A Phase II Study of Atezolizumab in Combination With Bevacizumab, Carboplatin or Cisplatin, and Pemetrexed for EGFR-mutant Metastatic Non-small Cell Lung Cancer Patients After Failure of EGFR Tyrosine Kinase Inhibitors.	II
NCT03778229	A Phase II, Single Arm Study Assessing Efficacy of Osimertinib With Savolitinib in Patients With EGFRm + MET+, Locally Advanced or Metastatic Non Small Cell Lung Cancer Who Have Progressed Following Osimertinib Treatment (SAVANNAH Study)	II
NCT02609776	A Phase I, First-in-Human, Open-Label, Dose Escalation Study of JNJ-61186372, a Human Bispecific EGFR and cMet Antibody, in Subjects With Advanced Non-Small Cell Lung Cancer.	I
NCT04484142	Phase II, Single-arm, Open-label Study of DS-1062a in Advanced or Metastatic Non-small Cell Lung Cancer With Actionable Genomic Alterations and Progressed On or After Applicable Targeted Therapy and Platinum Based Chemotherapy (TROPION-Lung05)	II
NCT03114319	An Open-label, Multi-center, Phase I, Dose Finding Study of Oral TNO155 in Adult Patients With Advanced Solid Tumors.	1

Date: 29 Dec 2021 29 of 36

Clinical Trials Summary (continued)

EGFR p.(L861Q) c.2582T>A (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	1/11
NCT04077463	An Open-label Phase I/Ib Study to Evaluate the Safety and Pharmacokinetics of JNJ-73841937 (Lazertinib), a Third Generation EGFR-TKI, as Monotherapy or in Combinations With JNJ-61186372, a Human Bispecific EGFR and cMet Antibody in Participants With Advanced Non-Small Cell Lung Cancer	I
NCT03800134	A Phase III, Double-blind, Placebo-controlled, Multi-center International Study of Neoadjuvant/Adjuvant Durvalumab for the Treatment of Patients With Resectable Stages II and III Non-small Cell Lung Cancer (AEGEAN)	III

Alerts Informed By Public Data Sources

Current FDA Information





Not recommended



Resistance





A Fast Track

Variant class: EGFR mutation

Variant class: EGFR mutation

FDA information is current as of 2021-11-17. For the most up-to-date information, search www.fda.gov.

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

osimertinib + quaratusugene ozeplasmid

Cancer type: Non-Small Cell Lung Cancer

Supporting Statement:

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

Reference:

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

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

A osimertinib + quaratusugene ozeplasmid

Cancer type: Non-Small Cell Lung Cancer

Supporting Statement:

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

Reference:

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

Date: 29 Dec 2021 30 of 36

Current NCCN Information

Contraindicated

Not recommended

Resistance

Breakthrough

Fast Track

NCCN information is current as of 2021-11-01. 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.(G719S) c.2155G>A

alectinib

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

Summary:

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

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

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2021]

brigatinib

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

Summary:

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

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

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2021]

ceritinib

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

Summary:

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

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

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2021]

crizotinib

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

Summary:

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

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

Date: 29 Dec 2021 31 of 36

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

lorlatinib

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

Summary:

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

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

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2021]

atezolizumab

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

Summary:

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

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

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2021]

nivolumab

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

Summary:

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

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

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2021]

pembrolizumab

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

Summary

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

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

Date: 29 Dec 2021 32 of 36

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

alectinib

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

Summary:

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

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

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2021]

brigatinib

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

Summary:

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

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

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2021]

ceritinib

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

Summary:

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

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

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2021]

crizotinib

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

Summary:

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

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

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2021]

lorlatinib

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

Summary:

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

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

Date: 29 Dec 2021 33 of 36

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

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 7.2021]

nivolumab

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

Summary:

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

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

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2021]

pembrolizumab

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

Summary:

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

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

Date: 29 Dec 2021 34 of 36

Signatures

Testing Personnel:

Laboratory Supervisor:

Pathologist:

Date: 29 Dec 2021

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