Taipei Veterans General Hospital

Department of Pathology and Laboratory Medicine
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Sample Information

Patient Name: 林俊宏
Gender: Male
ID No.: F124420153
History No.: 31756464
Age: 40

Ordering Doctor: DOC1878G 沈佳儀
Ordering REQ.: 0ALJEZT
Signing in Date: 2019/10/14

Path No.: S108-98613
MP No.: F1901
Assay: Oncomine Focus Assay
Sample Type: FFPE
Block No.: S108-25218B
Percentage of tumor cells: 50%
Note:

Sample Cancer Type: Non-Small Cell Lung Cancer

Report Highlights

3 Clinically Significant Biomarkers
7 Therapies Available
116 Clinical Trials

Clinically Significant Biomarkers

Indicated Contraindicated

Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
EGFR exon 19 deletion epidermal growth factor receptor Tier: IA Allele Frequency: 21.48%	osimertinib [1, 2] afatinib + cetuximab bevacizumab* + erlotinib [2] gefitinib + chemotherapy bevacizumab + gefitinib atezolizumab + bevacizumab + chemotherapy	None	93
EGFR p.(T790M) c.2369C>T epidermal growth factor receptor Tier: IA Allele Frequency: 7.20%	osimertinib [1, 2] afatinib + cetuximab gefitinib [2]	None	74
CDK4 amplification cyclin dependent kinase 4 Tier: IIC	None	None	6

Sources included in relevant therapies: FDA1, NCCN, EMA2, ESMO
*** Includes biosimilars**

Tier Criteria Met

Genomic Alteration	Tier Classification for Non-Small Cell Lung Cancer
EGFR exon 19 deletion Tier: IA	IA: Biomarker predicts response or resistance to FDA or EMA approved therapies in this cancer type IA: Biomarker is included in NCCN or ESMO guidelines that predict response or resistance to therapies in this cancer type IIC: Biomarker is an inclusion criteria for clinical trials
EGFR p.(T790M) c.2369C>T Tier: IA	IA: Biomarker predicts response or resistance to FDA or EMA approved therapies in this cancer type IA: Biomarker is included in NCCN or ESMO guidelines that predict response or resistance to therapies in this cancer type IIC: Biomarker is an inclusion criteria for clinical trials
CDK4 amplification Tier: IIC	IIC: Biomarker is an inclusion criteria for clinical trials

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 Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
EGFR	p.(E746_A750del)	c.2235_2249delGGAATTAAGAGAAGC	COSM6223	chr7:55242464	21.48%	NM_005228.4	nonframeshift Deletion	1951
EGFR	p.(T790M)	c.2369C>T	COSM6240	chr7:55249071	7.20%	NM_005228.4	missense	2000
ALK	p.(D1529E)	c.4587C>G	.	chr2:29416366	47.42%	NM_004304.4	missense	1997
ALK	p.(I1461V)	c.4381A>G	.	chr2:29416572	99.95%	NM_004304.4	missense	1998
ALK	p.(=)	c.3375C>A	.	chr2:29445458	43.15%	NM_004304.4	synonymous	1993
FGFR3	p.(=)	c.1953G>A	.	chr4:1807894	99.89%	NM_000142.4	synonymous	1752
PDGFRA	p.(=)	c.1701A>G	.	chr4:55141055	99.85%	NM_006206.5	synonymous	1998
FGFR4	p.(P136L)	c.407C>T	.	chr5:176517797	99.05%	NM_213647.2	missense	1375
FGFR4	p.(=)	c.483A>G	.	chr5:176517985	28.49%	NM_213647.2	synonymous	723
EGFR	p.(=)	c.2361G>A	.	chr7:55249063	47.82%	NM_005228.4	synonymous	1999
MET	p.(N375S)	c.1124A>G	.	chr7:116340262	49.17%	NM_001127500.2	missense	1999
RET	p.(=)	c.2307G>T	.	chr10:43613843	99.95%	NM_020975.4	synonymous	1993
RET	p.(=)	c.2712C>G	.	chr10:43615633	42.29%	NM_020975.4	synonymous	1972

Variant Details (continued)

Copy Number Variations

Gene	Locus	Copy Number
CDK4	chr12:58142052	7.14

Relevant Therapy Summary

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated ⚠ Both for use and contraindicated ✖ No evidence

EGFR exon 19 deletion

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
osimertinib	●	●	●	●	● (IV)
afatinib + cetuximab	✖	●	✖	✖	✖
bevacizumab + erlotinib	✖	✖	●	●	● (II)
bevacizumab (Allergan) + erlotinib	✖	✖	●	✖	✖
atezolizumab + bevacizumab + carboplatin + paclitaxel	✖	✖	✖	●	✖
bevacizumab + gefitinib	✖	✖	✖	●	✖
gefitinib + carboplatin + pemetrexed	✖	✖	✖	●	✖
apatinib + EGFR tyrosine kinase inhibitor	✖	✖	✖	✖	● (IV)
bevacizumab + osimertinib, osimertinib	✖	✖	✖	✖	● (IV)
EGFR tyrosine kinase inhibitor	✖	✖	✖	✖	● (IV)
icotinib hydrochloride	✖	✖	✖	✖	● (IV)
icotinib hydrochloride + radiation therapy	✖	✖	✖	✖	● (IV)
icotinib hydrochloride, icotinib hydrochloride + chemotherapy	✖	✖	✖	✖	● (IV)
atezolizumab + bevacizumab + chemotherapy, atezolizumab + chemotherapy	✖	✖	✖	✖	● (III)
bevacizumab + chemotherapy, bevacizumab (Shanghai Hengrui Pharmaceutical) + chemotherapy	✖	✖	✖	✖	● (III)
icotinib hydrochloride, icotinib hydrochloride + radiation therapy	✖	✖	✖	✖	● (III)
pembrolizumab + chemotherapy	✖	✖	✖	✖	● (III)

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

Relevant Therapy Summary (continued)

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated ⚠ Both for use and contraindicated ✖ No evidence

EGFR exon 19 deletion (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
tislelizumab, tislelizumab + chemoradiation therapy	✖	✖	✖	✖	● (III)
ado-trastuzumab emtansine + osimertinib	✖	✖	✖	✖	● (II)
alflutinib	✖	✖	✖	✖	● (II)
anlotinib hydrochloride + icotinib hydrochloride	✖	✖	✖	✖	● (II)
bevacizumab + osimertinib	✖	✖	✖	✖	● (II)
crizotinib + chemotherapy	✖	✖	✖	✖	● (II)
EGFR tyrosine kinase inhibitor + chemotherapy	✖	✖	✖	✖	● (II)
EGFR tyrosine kinase inhibitor, EGFR tyrosine kinase inhibitor + chemotherapy	✖	✖	✖	✖	● (II)
icotinib hydrochloride + chemotherapy	✖	✖	✖	✖	● (II)
ipilimumab + nivolumab, nivolumab	✖	✖	✖	✖	● (II)
ipilimumab + nivolumab, nivolumab + chemotherapy	✖	✖	✖	✖	● (II)
maihuatinib	✖	✖	✖	✖	● (II)
osimertinib + radiation therapy	✖	✖	✖	✖	● (II)
osimertinib + volitinib	✖	✖	✖	✖	● (II)
osimertinib, osimertinib + chemotherapy	✖	✖	✖	✖	● (II)
ramucirumab + chemotherapy + cytokine	✖	✖	✖	✖	● (II)
sunitinib	✖	✖	✖	✖	● (II)
tyrosine kinase inhibitors, tyrosine kinase inhibitors + radiation therapy	✖	✖	✖	✖	● (II)
AC0010MA	✖	✖	✖	✖	● (I/II)
ASK120067	✖	✖	✖	✖	● (I/II)
AZD4205, AZD4205 + osimertinib	✖	✖	✖	✖	● (I/II)
AZD4635 + oleclumab	✖	✖	✖	✖	● (I/II)
cetuximab, cetuximab + natural killer cell therapy	✖	✖	✖	✖	● (I/II)
CK-101	✖	✖	✖	✖	● (I/II)

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

Relevant Therapy Summary (continued)

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated ⚠ Both for use and contraindicated ✖ No evidence

EGFR exon 19 deletion (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
EMB01	✖	✖	✖	✖	● (I/II)
G1T38 + osimertinib	✖	✖	✖	✖	● (I/II)
icotinib hydrochloride + chemotherapy + radiation therapy	✖	✖	✖	✖	● (I/II)
itacitinib + osimertinib	✖	✖	✖	✖	● (I/II)
JNJ-63723283	✖	✖	✖	✖	● (I/II)
lazertinib	✖	✖	✖	✖	● (I/II)
TAK788	✖	✖	✖	✖	● (I/II)
U3-1402	✖	✖	✖	✖	● (I/II)
BPI-15086	✖	✖	✖	✖	● (I)
BPI-7711	✖	✖	✖	✖	● (I)
cetuximab + FATE-NK100	✖	✖	✖	✖	● (I)
durvalumab + oleclumab, oleclumab	✖	✖	✖	✖	● (I)
everolimus + neratinib, neratinib + palbociclib, neratinib + trametinib	✖	✖	✖	✖	● (I)
FCN-411	✖	✖	✖	✖	● (I)
JNJ-61186372	✖	✖	✖	✖	● (I)
LZM-009	✖	✖	✖	✖	● (I)
navitoclax + osimertinib	✖	✖	✖	✖	● (I)
nazartinib + trametinib	✖	✖	✖	✖	● (I)
necitumumab + osimertinib	✖	✖	✖	✖	● (I)
osimertinib + ramucirumab	✖	✖	✖	✖	● (I)
osimertinib, osimertinib + radiation therapy	✖	✖	✖	✖	● (I)
pirotinib	✖	✖	✖	✖	● (I)
SH-1028	✖	✖	✖	✖	● (I)
TNO-155	✖	✖	✖	✖	● (I)

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

Relevant Therapy Summary (continued)

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated ⚠ Both for use and contraindicated ✖ No evidence

EGFR exon 19 deletion (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
tyrosine kinase inhibitors, tyrosine kinase inhibitors + chemotherapy	✖	✖	✖	✖	● (I)
ZN-e4	✖	✖	✖	✖	● (I)

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

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
osimertinib	●	●	●	●	● (IV)
afatinib + cetuximab	✖	●	✖	✖	✖
gefitinib	✖	✖	⊘	✖	✖
apatinib + EGFR tyrosine kinase inhibitor	✖	✖	✖	✖	● (IV)
EGFR tyrosine kinase inhibitor	✖	✖	✖	✖	● (IV)
icotinib hydrochloride + radiation therapy	✖	✖	✖	✖	● (IV)
atezolizumab + bevacizumab + chemotherapy, atezolizumab + chemotherapy	✖	✖	✖	✖	● (III)
bevacizumab + chemotherapy, bevacizumab (Shanghai Hengrui Pharmaceutical) + chemotherapy	✖	✖	✖	✖	● (III)
tislelizumab, tislelizumab + chemoradiation therapy	✖	✖	✖	✖	● (III)
alflutinib	✖	✖	✖	✖	● (II)
anlotinib hydrochloride + sintilimab	✖	✖	✖	✖	● (II)
apatinib + chemotherapy	✖	✖	✖	✖	● (II)
avitinib	✖	✖	✖	✖	● (II)
bevacizumab + osimertinib	✖	✖	✖	✖	● (II)
EGFR tyrosine kinase inhibitor + chemotherapy	✖	✖	✖	✖	● (II)
EGFR tyrosine kinase inhibitor, EGFR tyrosine kinase inhibitor + chemotherapy	✖	✖	✖	✖	● (II)
ipilimumab + nivolumab, nivolumab	✖	✖	✖	✖	● (II)
ipilimumab + nivolumab, nivolumab + chemotherapy	✖	✖	✖	✖	● (II)

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

Relevant Therapy Summary (continued)

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated ⚠ Both for use and contraindicated ✖ No evidence

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

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
osimertinib, osimertinib + chemotherapy	✖	✖	✖	✖	● (II)
ramucirumab + chemotherapy + cytokine	✖	✖	✖	✖	● (II)
sunitinib	✖	✖	✖	✖	● (II)
tyrosine kinase inhibitors, tyrosine kinase inhibitors + radiation therapy	✖	✖	✖	✖	● (II)
AC0010MA	✖	✖	✖	✖	● (I/II)
ASK120067	✖	✖	✖	✖	● (I/II)
AZD4635 + oleclumab	✖	✖	✖	✖	● (I/II)
cetuximab, cetuximab + natural killer cell therapy	✖	✖	✖	✖	● (I/II)
CK-101	✖	✖	✖	✖	● (I/II)
EMB01	✖	✖	✖	✖	● (I/II)
G1T38 + osimertinib, osimertinib	✖	✖	✖	✖	● (I/II)
icotinib hydrochloride + chemotherapy + radiation therapy	✖	✖	✖	✖	● (I/II)
itacitinib + osimertinib	✖	✖	✖	✖	● (I/II)
JNJ-63723283	✖	✖	✖	✖	● (I/II)
lazertinib	✖	✖	✖	✖	● (I/II)
TAK788	✖	✖	✖	✖	● (I/II)
BPI-15086	✖	✖	✖	✖	● (I)
BPI-7711	✖	✖	✖	✖	● (I)
cetuximab + FATE-NK100	✖	✖	✖	✖	● (I)
D-0316	✖	✖	✖	✖	● (I)
durvalumab + oleclumab, oleclumab	✖	✖	✖	✖	● (I)
ES-072	✖	✖	✖	✖	● (I)
everolimus + neratinib, neratinib + palbociclib, neratinib + trametinib	✖	✖	✖	✖	● (I)

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

Relevant Therapy Summary (continued)

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated ⚠ Both for use and contraindicated ✖ No evidence

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

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
FCN-411	✖	✖	✖	✖	● (I)
navitoclax + osimertinib	✖	✖	✖	✖	● (I)
nazartinib + trametinib	✖	✖	✖	✖	● (I)
necitumumab + osimertinib	✖	✖	✖	✖	● (I)
osimertinib + ramucirumab	✖	✖	✖	✖	● (I)
osimertinib, osimertinib + radiation therapy	✖	✖	✖	✖	● (I)
pirotinib	✖	✖	✖	✖	● (I)
SH-1028	✖	✖	✖	✖	● (I)
TQB3456	✖	✖	✖	✖	● (I)
tyrosine kinase inhibitors, tyrosine kinase inhibitors + chemotherapy	✖	✖	✖	✖	● (I)
YK-029A	✖	✖	✖	✖	● (I)
ZN-e4	✖	✖	✖	✖	● (I)

CDK4 amplification

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
abemaciclib	✖	✖	✖	✖	● (II)
palbociclib	✖	✖	✖	✖	● (II)

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

Relevant Therapy Details

EGFR exon 19 deletion

Current FDA Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated 👎 Not recommended 🛡 Resistance

FDA information is current as of 2019-05-29. For the most up-to-date information, search www.fda.gov.

● osimertinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2018-08-28 **Variant class:** EGFR exon 19 deletion

Indications and usage:

TAGRISSO® is a kinase inhibitor indicated for

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

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/208065s011lbl.pdf

Current NCCN Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated 👎 Not recommended 🛡 Resistance

NCCN information is current as of 2019-02-14. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

● afatinib + cetuximab

Cancer type: Non-Small Cell Lung Cancer **Variant classes:** EGFR T790M mutation & EGFRi sensitizing mutation

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 3.2019]

EGFR exon 19 deletion (continued)

osimertinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

NCCN Recommendation category: 1

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

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2019]

osimertinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 19 deletion

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 (First-line) (Preferred)
- Progression on osimertinib (Subsequent Therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [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 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 3.2019]

EGFR exon 19 deletion (continued)

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 3.2019]

ceritinib

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 3.2019]

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 3.2019]

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 3.2019]

EGFR exon 19 deletion (continued)

Current EMA Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated 👎 Not recommended 🛡 Resistance

EMA information is current as of 2019-05-29. For the most up-to-date information, search www.ema.europa.eu/ema.

● **bevacizumab (Allergan) + erlotinib**

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2019-04-10 **Variant class:** EGFR exon 19 deletion

Reference:

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

● **bevacizumab + erlotinib**

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2018-08-31 **Variant class:** EGFR exon 19 deletion

Reference:

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

● **osimertinib**

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2018-09-07 **Variant class:** EGFR exon 19 deletion

Reference:

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

Current ESMO Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated 👎 Not recommended 🛡 Resistance

ESMO information is current as of 2019-02-14. For the most up-to-date information, search www.esmo.org.

● **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):

- Stage IV Non-Squamous Cell Carcinoma; ESMO-Magnitude of Clinical Benefit Scale score v1.1 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.]

EGFR exon 19 deletion (continued)

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 Non-Small Cell Lung Cancer (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-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: II / B

Population segment (Line of therapy):
- Stage IV Non-Squamous Cell Carcinoma; 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.]

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 Non-Squamous Cell Carcinoma; 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.]

atezolizumab + bevacizumab + carboplatin + paclitaxel

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):
- Metastatic Non-Squamous Non Small Cell Lung Cancer; Without contraindications to use immunotherapy after targeted therapies have been exploited (Second-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

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

Current FDA Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated 👎 Not recommended 🛡 Resistance

FDA information is current as of 2019-05-29. For the most up-to-date information, search www.fda.gov.

● osimertinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2018-08-28 **Variant class:** EGFR T790M mutation

Indications and usage:

TAGRISSO® is a kinase inhibitor indicated for

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

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/208065s011lbl.pdf

Current NCCN Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated 👎 Not recommended 🛡 Resistance

NCCN information is current as of 2019-02-14. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

● afatinib + cetuximab

Cancer type: Non-Small Cell Lung Cancer **Variant classes:** EGFR T790M mutation & EGFRi sensitizing mutation

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 3.2019]

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

osimertinib

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

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Progression on erlotinib, afatinib, gefitinib or dacomitinib (Subsequent therapy)
- Adenocarcinoma, Large Cell, Non-Small Cell Lung Cancer (NOS), Squamous Cell Carcinoma; Progression with symptomatic brain metastases (Subsequent therapy)

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2019]

osimertinib

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Central Nervous System Cancers [Version 2.2018]

afatinib

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

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

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2019]

dacomitinib

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

Summary:

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

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2019]

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

erlotinib

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

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

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2019]

gefitinib

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

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

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 3.2019]

Current EMA Information

In this cancer type | In other cancer type | In this cancer type and other cancer types | Contraindicated | Not recommended | Resistance

EMA information is current as of 2019-05-29. For the most up-to-date information, search www.ema.europa.eu/ema.

osimertinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2018-09-07 **Variant class:** EGFR T790M mutation

Reference:

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

gefitinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2019-05-28 **Variant class:** EGFR T790M mutation

Reference:

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

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

Current ESMO Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated 👎 Not recommended 🛡 Resistance

ESMO information is current as of 2019-02-14. For the most up-to-date information, search www.esmo.org.

● **osimertinib**

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

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

Population segment (Line of therapy):

- Stage IV Non-Squamous Cell Carcinoma; Resistance to first/second generation EGFR TKI and T790M positive; If not received previously; ESMO-Magnitude of Clinical Benefit Scale Version 1.1 Score: 4 (Second-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237.]

Signatures

Testing Personnel:

Laboratory Supervisor:

Pathologist: