Taipei Veterans General Hospital

Department of Pathology and Laboratory Medicine
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Sample Information

Patient Name: 尤雲白
Gender: Male
ID No.: T101967725
History No.: 45460148
Age: 66

Ordering Doctor: DOC6250G 林淑馨
Ordering REQ.: 0AMGFWG
Signing in Date: 2019/11/18

Path No.: S108-98931
MP No.: F1905
Assay: Oncomine Focus Assay
Sample Type: FFPE
Block No.: S108-51175A
Percentage of tumor cells: 90%
Note:

Sample Cancer Type: Non-Small Cell Lung Cancer

Report Highlights

2 Clinically Significant Biomarkers
2 Therapies Available
67 Clinical Trials

Clinically Significant Biomarkers

Indicated Contraindicated

Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
PIK3CA p.(H1047L) c.3140A>T phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha Tier: IIC Allele Frequency: 27.35%	None	alpelisib + fulvestrant [1]	10
EGFR exon 20 insertion epidermal growth factor receptor Tier: IA Allele Frequency: 28.19%	osimertinib gefitinib [2]	None	58

Sources included in relevant therapies: FDA[1], NCCN, EMA[2], ESMO

Tier Criteria Met

Genomic Alteration	Tier Classification for Non-Small Cell Lung Cancer
PIK3CA p.(H1047L) c.3140A>T Tier: IIC	IIC: Biomarker predicts response or resistance to FDA or EMA approved therapies in other cancer types IIC: Biomarker is included in NCCN or ESMO guidelines that predict response or resistance to therapies in other cancer types IIC: Biomarker is an inclusion criteria for clinical trials
EGFR exon 20 insertion 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

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
PIK3CA	p.(H1047L)	c.3140A>T	COSM776	chr3:178952085	27.35%	NM_006218.3	missense	2000
EGFR	p.(A767_S768insSVD)	c.2311_2312insGCGTGGACA	COSM13428	chr7:55249002	28.19%	NM_005228.4	nonframeshift Insertion	1937
JAK1	p.(=)	c.2199A>G	.	chr1:65310489	99.65%	NM_002227.3	synonymous	1988
ALK	p.(D1529E)	c.4587C>G	.	chr2:29416366	99.95%	NM_004304.4	missense	1996
ALK	p.(I1461V)	c.4381A>G	.	chr2:29416572	99.75%	NM_004304.4	missense	2000
ALK	p.(=)	c.3375C>A	.	chr2:29445458	99.90%	NM_004304.4	synonymous	1990
FGFR3	p.(=)	c.1953G>A	.	chr4:1807894	99.84%	NM_000142.4	synonymous	1912
PDGFRA	p.(=)	c.939T>G	.	chr4:55133726	40.56%	NM_006206.5	synonymous	1997
PDGFRA	p.(=)	c.1701A>G	.	chr4:55141055	99.95%	NM_006206.5	synonymous	1998
PDGFRA	p.(=)	c.2472C>T	.	chr4:55152040	41.20%	NM_006206.5	synonymous	2000
FGFR4	p.(P136L)	c.407C>T	.	chr5:176517797	99.40%	NM_213647.2	missense	2000
FGFR4	p.(=)	c.483A>G	.	chr5:176517985	15.94%	NM_213647.2	synonymous	1650
EGFR	p.(=)	c.2361G>A	.	chr7:55249063	49.80%	NM_005228.4	synonymous	2000
RET	p.(=)	c.2307G>T	.	chr10:43613843	28.78%	NM_020975.4	synonymous	1998

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

PIK3CA p.(H1047L) c.3140A>T

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
alpelisib + fulvestrant	○	○	✖	✖	✖
capivasertib	✖	✖	✖	✖	● (II)
capivasertib, olaparib	✖	✖	✖	✖	● (II)
everolimus	✖	✖	✖	✖	● (II)
LY-3023414	✖	✖	✖	✖	● (II)
sirolimus	✖	✖	✖	✖	● (II)
temsirolimus	✖	✖	✖	✖	● (II)
atezolizumab + ipatasertib	✖	✖	✖	✖	● (I/II)
ARQ-751, chemotherapy, fulvestrant	✖	✖	✖	✖	● (I)
GDC-0077	✖	✖	✖	✖	● (I)
gedatolisib + palbociclib	✖	✖	✖	✖	● (I)

EGFR exon 20 insertion

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
osimertinib	✖	●	✖	✖	● (II)
gefitinib	✖	✖	⊘	✖	● (III)
apatinib + erlotinib, apatinib + gefitinib, apatinib + icotinib hydrochloride	✖	✖	✖	✖	● (IV)
apatinib + gefitinib	✖	✖	✖	✖	● (IV)
erlotinib + natural product, erlotinib + placebo, gefitinib + natural product, gefitinib + placebo, icotinib hydrochloride + natural product, icotinib hydrochloride + placebo	✖	✖	✖	✖	● (IV)
gefitinib, radiation therapy	✖	✖	✖	✖	● (IV)
icotinib hydrochloride, radiation therapy	✖	✖	✖	✖	● (IV)
atezolizumab, bevacizumab, 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 20 insertion (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
bevacizumab + chemotherapy, bevacizumab (Shanghai Hengrui Pharmaceutical) + chemotherapy	✖	✖	✖	✖	● (III)
chemotherapy, nivolumab	✖	✖	✖	✖	● (III)
erlotinib, gefitinib	✖	✖	✖	✖	● (III)
afatinib + bevacizumab	✖	✖	✖	✖	● (II)
afatinib + chemotherapy + radiation therapy + surgical intervention	✖	✖	✖	✖	● (II)
anlotinib hydrochloride + sintilimab	✖	✖	✖	✖	● (II)
apatinib + chemotherapy	✖	✖	✖	✖	● (II)
bevacizumab, osimertinib	✖	✖	✖	✖	● (II)
chemotherapy, ramucirumab	✖	✖	✖	✖	● (II)
erlotinib	✖	✖	✖	✖	● (II)
erlotinib + chemotherapy	✖	✖	✖	✖	● (II)
erlotinib + radiation therapy	✖	✖	✖	✖	● (II)
gefitinib + chemotherapy	✖	✖	✖	✖	● (II)
icotinib hydrochloride	✖	✖	✖	✖	● (II)
ipilimumab, nivolumab	✖	✖	✖	✖	● (II)
KN046	✖	✖	✖	✖	● (II)
poziotinib	✖	✖	✖	✖	● (II)
radiation therapy, tyrosine kinase inhibitors	✖	✖	✖	✖	● (II)
sintilimab	✖	✖	✖	✖	● (II)
sunitinib	✖	✖	✖	✖	● (II)
targeted therapy, targeted therapy + chemotherapy	✖	✖	✖	✖	● (II)
tarloxotinib	✖	✖	✖	✖	● (II)
afatinib + necitumumab	✖	✖	✖	✖	● (I/II)
bevacizumab + erlotinib + chemotherapy	✖	✖	✖	✖	● (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 20 insertion (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
cetuximab, cetuximab + natural killer cell therapy	✖	✖	✖	✖	● (I/II)
EMB01	✖	✖	✖	✖	● (I/II)
gefitinib + ningetinib	✖	✖	✖	✖	● (I/II)
icotinib hydrochloride + chemotherapy + radiation therapy	✖	✖	✖	✖	● (I/II)
oleclumab + osimertinib	✖	✖	✖	✖	● (I/II)
TAK788	✖	✖	✖	✖	● (I/II)
cetuximab + FATE-NK100	✖	✖	✖	✖	● (I)
durvalumab + oleclumab, oleclumab	✖	✖	✖	✖	● (I)
erlotinib + ixazomib	✖	✖	✖	✖	● (I)
everolimus + neratinib, neratinib + palbociclib, neratinib + trametinib	✖	✖	✖	✖	● (I)
JNJ-61186372	✖	✖	✖	✖	● (I)
necitumumab, osimertinib	✖	✖	✖	✖	● (I)
osimertinib, osimertinib + radiation therapy	✖	✖	✖	✖	● (I)
pirotinib	✖	✖	✖	✖	● (I)
TP-0903	✖	✖	✖	✖	● (I)
tyrosine kinase inhibitors, tyrosine kinase inhibitors + chemotherapy	✖	✖	✖	✖	● (I)

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

Relevant Therapy Details

Current FDA Information

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

FDA information is current as of 2019-08-23. For the most up-to-date information, search www.fda.gov.

PIK3CA p.(H1047L) c.3140A>T

○ alpelisib + fulvestrant

Cancer type: Breast Cancer **Label as of:** 2019-05-24 **Variant class:** PIK3CA mutation

Other criteria: ERBB2 negative, Hormone receptor positive

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

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/212526s000lbl.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 2019-05-15. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

PIK3CA p.(H1047L) c.3140A>T

○ alpelisib + fulvestrant

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

Other criteria: ERBB2 negative

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Recurrent or Stage IV Invasive Breast Cancer; No prior endocrine therapy within 1 year; Postmenopausal (First-line therapy) (Preferred)

Reference: NCCN Guidelines® - NCCN-Breast Cancer [Version 2.2019]

EGFR exon 20 insertion

● 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 1.2019]

👎 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%."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2019]

EGFR exon 20 insertion (continued)

EGFR tyrosine kinase inhibitor

Cancer type: Non-Small Cell Lung Cancer **Variant class:** EGFR exon 20 insertion

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Patients with EGFR exon 20 insertion mutations are usually resistant to TKIs, although there are rare exceptions."

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 5.2019]

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 2019-08-23. For the most up-to-date information, search www.ema.europa.eu/ema.

EGFR exon 20 insertion

gefitinib

Cancer type: Non-Small Cell Lung Cancer **Label as of:** 2019-05-28 **Variant class:** EGFR exon 20 insertion

Reference:

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

Signatures

Testing Personnel: Zih-Yu Liu 2019.11.22 08:32:24 +08'00'

Laboratory Supervisor: 2019.11.22 08:33:03 +08'00'

Pathologist: Yi-Chu Yeh 2019.11.22 08:33:55 +08'00'