



Sample Information

Patient Name: 陳憲華

Gender: Female

ID No.: A210049503

History No.: 27885525

Age: 76

Ordering Doctor: DOC3109L 邱昭華

Ordering REQ.: D572GC5

Signing in Date: 2020/06/23

Path No.: S109-99625

MP No.: F20039

Assay: Oncomine Focus Assay

Sample Type: FFPE

Block No.: S109-76628A

Percentage of tumor cells: 20%

Note:

Sample Cancer Type: Non-Small Cell Lung Cancer

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Report Highlights

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Relevant Non-Small Cell Lung Cancer Findings

Gene	Finding	Gene	Finding
ALK	Not detected	NTRK1	Not detected
BRAF	Not detected	NTRK2	Not detected
EGFR	Not detected	NTRK3	Not detected
ERBB2	Not detected	RET	KIF5B-RET fusion
KRAS	Not detected	ROS1	Not detected
MET	Not detected		



Relevant Biomarkers

■ Indicated ■ Contraindicated

Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
KIF5B-RET fusion kinesin family member 5B - ret proto-oncogene Tier: IA	■ cabozantinib ■ vandetanib	None	18

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

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

Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
JAK1	p.(=)	c.2199A>G	.	chr1:65310489	44.77%	NM_002227.3	synonymous	1990
ALK	p.(D1529E)	c.4587C>G	.	chr2:29416366	99.80%	NM_004304.4	missense	1998
ALK	p.(I1461V)	c.4381A>G	.	chr2:29416572	99.65%	NM_004304.4	missense	1999
ALK	p.(=)	c.3375C>A	.	chr2:29445458	99.95%	NM_004304.4	synonymous	1995
FGFR3	p.(=)	c.1953G>A	.	chr4:1807894	99.39%	NM_000142.4	synonymous	991
PDGFRA	p.(=)	c.1701A>G	.	chr4:55141055	99.75%	NM_006206.5	synonymous	2000
FGFR4	p.(P136L)	c.407C>T	.	chr5:176517797	99.60%	NM_213647.2	missense	2000
FGFR4	p.(T179A)	c.535A>G	.	chr5:176518037	54.42%	NM_213647.2	missense	1764
RET	p.(=)	c.2307G>T	.	chr10:43613843	53.61%	NM_020975.4	synonymous	1996

Gene Fusions (RNA)

Genes	Variant ID	Locus
KIF5B-RET	KIF5B-RET.K15R12.COSF1232	chr10:32317356 - chr10:43612032

Biomarker Descriptions

RET (ret proto-oncogene)

Background: The RET gene encodes the RET receptor tyrosine kinase which is activated by a ligand family of glial cell line-derived neurotrophic factors (GDNF)¹. RET is the target of recurrent chromosomal rearrangements that generate fusion proteins containing the intact RET tyrosine kinase domain combined with several fusion partner genes. RET fusion kinases are constitutively activated and drive oncogenic transformation which can lead to activation of PI3K/AKT, RAS/RAF/MEK/ERK, and PLCγ/PKC pathways resulting in cell survival and proliferation².

Alterations and prevalence: RET fusions occur in approximately 55% of papillary thyroid carcinomas (PTC) with even higher frequencies observed in PTC patients with radiation exposure^{3,4,5}. RET rearrangement is also present in 1-2% of non-small cell lung cancer (NSCLC)⁶. Point mutations in RET are relatively common in sporadic medullary thyroid cancer (MTC), with 6% of patients found



Biomarker Descriptions (continued)

to contain germline mutations⁷. Somatic mutations (specifically at codon 918), which leads to increased kinase activity, have been observed in at least 25% of MTC cases⁷.

Potential relevance: Currently, no therapies are approved for RET aberrations. However, the RET inhibitor, pralsetinib^{8,9}, was granted breakthrough therapy designation for RET mutation-positive medullary thyroid cancer (2019) as well as for RET fusion-positive NSCLC (2020). The FDA approved small-molecule tyrosine kinase inhibitors, vandetanib (2011) and cabozantinib (2012), are recommended for treatment of NSCLC patients with RET rearrangements¹⁰. Cabozantinib has also demonstrated clinical benefit in RET mutated medullary thyroid cancer patients¹¹. Point mutations involving codons 804 and 806 have been shown to confer resistance to selective kinase inhibitors including vandetanib^{12,13}. RET mutations at codon 918 are associated with high risk and adverse prognosis in patients diagnosed with MTC¹⁴.

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

KIF5B-RET fusion

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
cabozantinib	✕	●	✕	✕	● (II)
vandetanib	✕	●	✕	✕	✕
alectinib	✕	✕	✕	✕	● (IV)
alectinib, crizotinib	✕	✕	✕	✕	● (III)
ipilimumab, nivolumab, radiation therapy, surgical intervention	✕	✕	✕	✕	● (III)
erdafitinib	✕	✕	✕	✕	● (II)
ponatinib	✕	✕	✕	✕	● (II)
sunitinib	✕	✕	✕	✕	● (II)
targeted therapy, chemotherapy	✕	✕	✕	✕	● (II)
pralsetinib	✕	✕	✕	✕	● (I/II)
selpercatinib	✕	✕	✕	✕	● (I/II)
TPX-0046	✕	✕	✕	✕	● (I/II)
BOS172738	✕	✕	✕	✕	● (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 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 2019-11-01. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

KIF5B-RET fusion

cabozantinib

Cancer type: Non-Small Cell Lung Cancer

Variant class: RET fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Non-Small Cell Lung Cancer; Emerging targeted agents

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

vandetanib

Cancer type: Non-Small Cell Lung Cancer

Variant class: RET fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Non-Small Cell Lung Cancer; Emerging targeted agents

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

Signatures

Testing Personnel:

Laboratory Supervisor:

Pathologist:



References

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8. <http://ir.blueprintmedicines.com/news-releases/news-release-details/blueprint-medicines-reports-first-quarter-2019-financial-results>
9. Blueprint Medicines Announces Top-line Data for Pralsetinib and Initiates Rolling NDA Submission to FDA for the Treatment of Patients with RET Fusion-Positive Non-Small Cell Lung Cancer. <http://ir.blueprintmedicines.com/news-releases/news-release-details/blueprint-medicines-announces-top-line-data-pralsetinib-and>
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