Taipei Veterans General Hospital

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Sample Information

Patient Name: 詹弘吉
Gender: Male
ID No.: K120227883
History No.: 46657276
Age: 53

Ordering Doctor: DOC3153J 黃煦晴
Ordering REQ.: 0BBBSWF
Signing in Date: 2021/01/21

Path No.: S110-98094
MP No.: F21003
Assay: Oncomine Focus Assay
Sample Type: FFPE
Block No.: S110-01213A
Percentage of tumor cells: 80%
Note:

Sample Cancer Type: Non-Small Cell Lung Cancer

Report Highlights

1 Relevant Biomarkers
0 Therapies Available
5 Clinical Trials

Relevant Non-Small Cell Lung Cancer Variants

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	Not detected
KRAS	Not detected	ROS1	Not detected
MET	Not detected		

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IIC	*PDGFRA amplification* platelet derived growth factor receptor alpha	None	None	5

Public data sources included in relevant therapies: FDA[1], NCCN, **EMA**[2], 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	60.80%	NM_002227.3	synonymous	1977
ALK	p.(D1529E)	c.4587C>G	.	chr2:29416366	99.95%	NM_004304.4	missense	1996
ALK	p.(I1461V)	c.4381A>G	.	chr2:29416572	99.85%	NM_004304.4	missense	2000
ALK	p.(=)	c.3600G>C	.	chr2:29443617	12.65%	NM_004304.4	synonymous	1961
ALK	p.(=)	c.3375C>A	.	chr2:29445458	99.95%	NM_004304.4	synonymous	1994
FGFR3	p.(=)	c.1953G>A	.	chr4:1807894	99.75%	NM_000142.4	synonymous	1996
PDGFRA	p.(=)	c.1701A>G	.	chr4:55141055	100.00%	NM_006206.5	synonymous	1998
FGFR4	p.(P136L)	c.407C>T	.	chr5:176517797	99.05%	NM_213647.2	missense	2000
RET	p.(=)	c.2307G>T	.	chr10:43613843	99.95%	NM_020975.4	synonymous	1995

Copy Number Variations

Gene	Locus	Copy Number
PDGFRA	chr4:55097715	11.39

Biomarker Descriptions

PDGFRA (platelet derived growth factor receptor alpha)

Background: The PDGFRA gene encodes the platelet derived growth factor receptor alpha, a member of the PDGF receptor type III receptor tyrosine kinase family, which includes PDGFRB, CSF1R, FLT1, FLT3, FLT4, KDR, and KIT[1,2]. PDGFRA is a receptor for platelet derived growth factors, which are mitogens for cells of mesenchymal origin[3]. PDGFRA may function as a homodimer or heterodimer with PDGFRB depending on the ligand[4]. The PDGFRA gene is physically adjacent to KIT and KDR on chromosome 4q12. Ligand binding to PDGFRA results in kinase activation and stimulation of downstream pathways including the RAS/RAF/MEK/ERK and PI3K/AKT/MTOR pathways promoting cell proliferation and survival.

Alterations and prevalence: Recurrent somatic PDGFRA alterations are observed in both solid and hematological cancers and include activating mutations, gene amplification, and translocations generating PDGFRA gene fusions. Recurrent PDGFRA activating mutations, including D842V, V561D, N659K, and in-frame deletions in exon 18, are common in 30-40% of KIT negative gastrointestinal stromal tumors (GISTs) and approximately 7% overall[5,6,7,8]. PDGFRA recurrent mutations are also described in adult and pediatric glioblastoma and high-grade gliomas[8,9]. In these cases, PDGFRA amplification is common (about 10% of cases) and recurrent mutations frequently co-occur with gene amplification[10,11]. PDGFRA fusions are observed in gliomas and glioblastomas as well as eosinophilic leukemias, of which the FIP1L1-PDGFRA fusion defines approximately half of patients with hypereosinophilic syndrome[12,13,14].

Potential relevance: The FDA has granted fast track designation to crenolanib[15] (2017) for GISTs harboring PDGFRA D842V mutation. Avapritinib[16] is a tyrosine kinase inhibitor (TKI) that is approved (2020) by the FDA for metastatic or unresectable GIST harboring PDGFRA exon 18 mutations including PDGFRA D842V mutation. Another TKI, imatinib[17], is approved (2001) for patients diagnosed with chronic eosinophilic leukemia harboring FIP1L1-PDGFRA fusions. Additionally, imatinib is recommended for the treatment of GISTs harboring PDGFRA mutations with the exception of D842V[18]. The TKI, dasatinib, is also recommended for the treatment of GISTs harboring a PDGFRA D842V mutation following disease progression on imatinib, sunitinib, or regorafenib[18].

Relevant Therapy Summary

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ✖ No evidence

PDGFRA amplification

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
dasatinib, sunitinib	✖	✖	✖	✖	● (II)
nilotinib, pazopanib	✖	✖	✖	✖	● (II)
ponatinib	✖	✖	✖	✖	● (II)
sunitinib	✖	✖	✖	✖	● (II)
ripretinib	✖	✖	✖	✖	● (I)

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

Clinical Trials Summary

PDGFRA amplification

NCT ID	Title	Phase
NCT02029001	A Two-period, Multicenter, Randomized, Open-label, Phase II Study Evaluating the Clinical Benefit of a Maintenance Treatment Targeting Tumor Molecular Alterations in Patients With Progressive Locally-advanced or Metastatic Solid Tumors MOST: My own specific treatment	II
NCT03297606	Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR): A Phase II Basket Trial	II
NCT02272998	Phase II Study Of Ponatinib For Advanced Cancers With Genomic Alterations In Fibroblastic Growth Factor Receptor (FGFR) And Other Genomic Targets (KIT, Pdgfra, RET FLT3, ABL1)	II
NCT02693535	Targeted Agent and Profiling Utilization Registry (TAPUR) Study	II
NCT02571036	A Multicenter Phase I, Open-Label Study of DCC-2618 to Assess Safety,Tolerability, and Pharmacokinetics in Patients With Advanced Malignancies	I

Signatures

Testing Personnel:

2021.01.22
14:07:19 +08'00'

Laboratory Supervisor:

2021.01.22
14:07:31 +08'00'

Pathologist:

2021.01.22
14:07:45 +08'00'

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