Taipei Veterans General Hospital

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

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

Table of Contents

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: FDA1, 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.

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

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
ALK	p.(=)	c.3600G>C	.	chr2:29443617	12.65%	NM_004304.4	synonymous	1961

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)

* 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 ✖ No evidence

PDGFRA amplification (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
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
14:10:46 +08'00'

Laboratory Supervisor:

2021.01.22
14:11:07 +08'00'

Pathologist:

2021.01.22
14:11:24 +08'00'

References

1. Ségaliny et al. Receptor tyrosine kinases: Characterisation, mechanism of action and therapeutic interests for bone cancers. J Bone Oncol. 2015 Mar;4(1):1-12. PMID: 26579483
2. Berenstein. Class III Receptor Tyrosine Kinases in Acute Leukemia - Biological Functions and Modern Laboratory Analysis. Biomark Insights. 2015;10(Suppl 3):1-14. PMID: 26309392
3. Donovan et al. Platelet-derived growth factor signaling in mesenchymal cells. Front Biosci (Landmark Ed). 2013 Jan 1;18:106-19. PMID: 23276912
4. Roskoski. The role of small molecule platelet-derived growth factor receptor (PDGFR) inhibitors in the treatment of neoplastic disorders. Pharmacol. Res. 2018 Mar;129:65-83. PMID: 29408302
5. Lasota et al. KIT and PDGFRA mutations in gastrointestinal stromal tumors (GISTs). Semin Diagn Pathol. 2006 May;23(2):91-102. PMID: 17193822
6. Corless et al. PDGFRA Mutations in Gastrointestinal Stromal Tumors: Frequency, Spectrum and In Vitro Sensitivity to Imatinib. J Clin Oncol. 2005 Aug 10;23(23):5357-64. Epub 2005 May 31. PMID: 15928335
7. Heinrich et al. PDGFRA activating mutations in gastrointestinal stromal tumors. Science. 2003 Jan 31;299(5607):708-10. Epub 2003 Jan 9. PMID: 12522257
8. Paugh et al. Novel oncogenic PDGFRA mutations in pediatric high-grade gliomas. Cancer Res. 2013 Oct 15;73(20):6219-29. PMID: 23970477
9. Brennan et al. The somatic genomic landscape of glioblastoma. Cell. 2013 Oct 10;155(2):462-77. PMID: 24120142
10. Weinstein et al. The Cancer Genome Atlas Pan-Cancer analysis project. Nat. Genet. 2013 Oct;45(10):1113-20. PMID: 24071849
11. Cerami et al. The cBio cancer genomics portal: an open platform for exploring multidimensional cancer genomics data. Cancer Discov. 2012 May;2(5):401-4. PMID: 22588877
12. Cools et al. Detection of the FIP1L1-PDGFRA fusion in idiopathic hypereosinophilic syndrome and chronic eosinophilic leukemia. Methods Mol. Med. 2006;125:177-87. PMID: 16502585
13. Cools. FIP1L1-PDGFR alpha, a therapeutic target for the treatment of chronic eosinophilic leukemia. Verh. K. Acad. Geneeskd. Belg. 2005;67(3):169-76. PMID: 16089297
14. Elling et al. Novel imatinib-sensitive PDGFRA-activating point mutations in hypereosinophilic syndrome induce growth factor independence and leukemia-like disease. Blood. 2011 Mar 10;117(10):2935-43. doi: 10.1182/blood-2010-05-286757. Epub 2011 Jan 11. PMID: 21224473
15. https://www.globenewswire.com/news-release/2017/12/01/1216122/0/en/Arog-Pharmaceuticals-Receives-FDA-Fast-Track-Designation-for-Crenolanib-in-Relapsed-or-Refractory-FLT3-Positive-AML.html
16. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/212608s000lbl.pdf
17. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/021588s056s057lbl.pdf
18. NCCN Guidelines® - NCCN-Soft Tissue Sarcoma [Version 1.2021]