Taipei Veterans General Hospital

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## Sample Information

**Patient Name:** 張鈺淇
**Gender:** Female
**ID No.:** N220474939
**History No.:** 45973704
**Age:** 48

**Ordering Doctor:** DOC8339B 劉松鈞
**Ordering REQ.:** 0ARLLFP
**Signing in Date:** 2020/04/30

**Path No.:** S109-99419
**MP No.:** F2018
**Assay:** Oncomine Focus Assay
**Sample Type:** FFPE
**Block No.:** C109-12279
**Percentage of tumor cells:** 60%
**Note:**

## Sample Cancer Type: Non-Small Cell Lung Cancer



### Report Highlights

1 Relevant Biomarkers
0 Therapies Available
12 Clinical Trials

## 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 | Not detected |
| 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 |
|---|---|---|---|
| *FGFR1 amplification*<br>fibroblast growth factor receptor 1<br>Tier: IIC | None | None | 12 |

**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 | 59.29% | NM_002227.3 | synonymous | 1997 |
| ALK | p.(D1529E) | c.4587C>G | . | chr2:29416366 | 99.90% | NM_004304.4 | missense | 1999 |
| ALK | p.(I1461V) | c.4381A>G | . | chr2:29416572 | 99.70% | NM_004304.4 | missense | 1997 |
| ALK | p.(=) | c.3375C>A | . | chr2:29445458 | 99.90% | NM_004304.4 | synonymous | 1992 |
| FGFR3 | p.(=) | c.1953G>A | . | chr4:1807894 | 99.90% | NM_000142.4 | synonymous | 1994 |
| PDGFRA | p.(=) | c.1701A>G | . | chr4:55141055 | 99.85% | NM_006206.5 | synonymous | 2000 |
| KIT | p.(=) | c.1638A>G | . | chr4:55593481 | 42.96% | NM_000222.2 | synonymous | 1997 |
| FGFR4 | p.(P136L) | c.407C>T | . | chr5:176517797 | 99.75% | NM_213647.2 | missense | 2000 |
| FGFR4 | p.(=) | c.483A>G | . | chr5:176517985 | 28.79% | NM_213647.2 | synonymous | 1997 |
| RET | p.(=) | c.2307G>T | . | chr10:43613843 | 99.70% | NM_020975.4 | synonymous | 1994 |
| RET | p.(=) | c.2712C>G | . | chr10:43615633 | 77.94% | NM_020975.4 | synonymous | 1999 |

## Copy Number Variations

| Gene | Locus | Copy Number |
|---|---|---|
| FGFR1 | chr8:38271445 | 5.88 |

# Biomarker Descriptions

**FGFR1 (fibroblast growth factor receptor 1)**

Background: The FGFR1 gene encodes fibroblast growth receptor 1, a member of the fibroblast growth factor receptor (FGFR) family that also includes FGFR2, 3, and 4. These proteins are single transmembrane receptors composed of three extracellular immunoglobulin (Ig)-type domains and an intracellular kinase domain. Upon FGF-mediated stimulation, FGFRs activate several oncogenic signaling pathways, including the RAS/RAF/MEK/ERK, PI3K/AKT/MTOR, PLC/PKC, and JAK/STAT pathways influencing cell proliferation, migration, and survival[1,2,3].

Alterations and prevalence: Recurrent somatic alterations common to the FGFR family include gene amplification, mutation, and chromosomal translocations leading to FGFR fusions[4]. Amplification of FGFR1 is observed in 15-20% of squamous lung cancer, 10-15% of breast cancer, 8% of bladder cancer, and 2-5% of uterine cancer cases[5,6,7,8,9,9]. The most common recurrent mutations, N546K and K656E, are relatively infrequent (<1%); they activate mutations in the kinase domain and are distributed in diverse cancer types[10]. FGFR1 translocations giving rise to expressed fusions are common in certain hematological cancers, but less common in solid tumors[11,12,13].

Potential relevance: The FDA has granted fast track designation to Debio 1347[14] (2018) for solid tumors harboring aberrations in FGFR1, FGFR2, or FGFR3. FDA has approved multi-kinase inhibitors, including regorafenib, ponatinib, lenvatinib, nintedanib, and pazopanib, that are known to inhibit FGFR family members. These inhibitors have demonstrated anti-tumor activity in select cancer types with FGFR alterations[15,16,17,18,19,20,21]. In a phase II clinical trial, dovitinib, a multi-tyrosine kinase inhibitor (TKI), exhibited an overall response rate (ORR) of 11.5% and a disease control rate (DCR) of 50% in patients with advanced squamous cell lung cancer

## Biomarker Descriptions (continued)

possessing FGFR1 amplification. The patients had a median overall survival (OS) of 5 months and progression-free survival (PFS) of 2.9 months[22]. Likewise, in a phase Ib study testing the FGFR inhibitor AZD4547, median OS was 4.9 months in patients with FGFR1-amplified advanced squamous cell lung cancer. One of 13 (8%) patients achieved a partial response, 4 (31%) exhibited stable disease, and 2 (13.3%) demonstrated PFS at 12 weeks[23].

## 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

### FGFR1 amplification

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|---|---|---|---|---|---|
| erdafitinib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| futibatinib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| nintedanib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| ponatinib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| sunitinib | ✖ | ✖ | ✖ | ✖ | ● (II) |
| pemigatinib, pembrolizumab, trastuzumab, chemotherapy, INCMGA00012 | ✖ | ✖ | ✖ | ✖ | ● (I/II) |
| CPL-304-110 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| Debio 1347 | ✖ | ✖ | ✖ | ✖ | ● (I) |
| pemigatinib | ✖ | ✖ | ✖ | ✖ | ● (I) |

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

## Signatures

**Testing Personnel:** Zih-Yu Liu 2020.04.30 14:03:57 +08'00'

**Laboratory Supervisor:** 2020.04.30 14:04:18 +08'00'

**Pathologist:** Yi-Chen Yeh 2020.04.30 14:04:35 +08'00'

## References

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