Taipei Veterans General Hospital

Department of Pathology and Laboratory Medicine
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11217, R.O.C.
Tel: 02-2875-7449

Sample Information

Patient Name: 張文能
Gender: Male
ID No.: A122573941
History No.: 47893710
Age: 65

Ordering Doctor: DOC6382C 林開亮
Ordering REQ.: 0BVCGLZ
Signing in Date: 2022/05/13

Path No.: S111-99301
MP No.: F22042
Assay: Oncomine Focus Assay
Sample Type: FFPE
Block No.: S111-10774I
Percentage of tumor cells: 70%

Reporting Doctor: DOC5452C 周德盈 (Phone: 8#5452)

Note:

Sample Cancer Type: Non-Small Cell Lung Cancer

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Report Highlights

1 Relevant Biomarkers
1 Therapies Available
1 Clinical Trials

Relevant Non-Small Cell Lung Cancer Variants

Gene	Finding	Gene	Finding
ALK	None detected	NTRK1	None detected
BRAF	None detected	NTRK2	None detected
EGFR	None detected	NTRK3	None detected
ERBB2	None detected	RET	None detected
KRAS	None detected	ROS1	None detected
MET	None detected		

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IIC	*FGFR3-TACC3 fusion* fibroblast growth factor receptor 3 - transforming acidic coiled-coil containing protein 3	None	**erdafitinib** [1]	1

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)

Gene Fusions (RNA)

Genes	Variant ID	Locus	Read Count
FGFR3-TACC3	FGFR3-TACC3.F17T8.COSF1353	chr4:1808661 - chr4:1737458	48311

Biomarker Descriptions

FGFR3 (fibroblast growth factor receptor 3)

Background: The FGFR3 gene encodes fibroblast growth receptor 3, a member of the fibroblast growth-factor receptor (FGFR) family that also includes FGFR1, 2, 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: Aberrations most common to the FGFR family are amplifications, followed by mutations and fusions. The majority of these aberrations result in gain of function[4]. FGFR3 amplification is observed in up to 19% of uterine carcinoma, with somatic mutations occurring in 10-20% of bladder cancer[5,6,7]. Missense mutations that occur in the extracellular immunoglobulin-like and transmembrane domains of FGFR3, including S249C, R248C, and Y375C, cause ligand-independent dimerization and constitutive activation of FGFR3[8,9,10].

Potential relevance: The pan-FGFR inhibitor, erdafitinib[11], received FDA approval (2019) for the treatment of locally advanced or metastatic urothelial cancer that is positive for FGFR2 fusions, FGFR3 fusions including FGFR3-TACC3 and FGFR3-BAIAP2L1, and FGFR3 gene mutations including R248C, S249C, G370C, and Y373C. The FGFR3 monoclonal antibody, vofatamab[12] was granted fast-track designation (2019) by the FDA, for the treatment of advanced or metastatic bladder urothelial cell carcinoma that harbors FGFR3 mutations or fusions. The FDA also granted fast track designation (2018) to Debio 1347[13] for solid tumors harboring FGFR1, FGFR2, or FGFR3 aberrations. Unregulated activation of FGFR3 has been associated with resistance to tamoxifen in ER-positive breast cancer[14].

Relevant Therapy Summary

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

FGFR3-TACC3 fusion

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
erdafitinib	○	○	✖	○	● (II)

* 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

FDA information is current as of 2022-03-16. For the most up-to-date information, search www.fda.gov.

FGFR3-TACC3 fusion

○ erdafitinib

Cancer type: Bladder Urothelial Carcinoma **Label as of:** 2020-04-02 **Variant class:** FGFR3-TACC3 fusion

Indications and usage:

BALVERSA® is a kinase inhibitor indicated for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma that has

- susceptible FGFR3 or FGFR2 genetic alterations and
- progressed during or following at least one line of prior platinum-containing chemotherapy including within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy.

Select patients for therapy based on an FDA-approved companion diagnostic for BALVERSA®.

This indication is approved under accelerated approval based on tumor response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/212018s001lbl.pdf

Current NCCN Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types

NCCN information is current as of 2022-02-28. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

FGFR3-TACC3 fusion

○ erdafitinib

Cancer type: Bladder Cancer

Variant class: FGFR3-TACC3 fusion

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- Stage IV; Locally Advanced, Metastatic (Second-line therapy); Preferred intervention, Other recommended intervention
- Stage IV; Locally Advanced, Metastatic (Subsequent therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Bladder Cancer [Version 1.2022]

Current ESMO Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types

ESMO information is current as of 2022-02-28. For the most up-to-date information, search www.esmo.org.

FGFR3-TACC3 fusion

○ erdafitinib

Cancer type: Bladder Urothelial Carcinoma **Variant class:** FGFR3-TACC3 fusion

ESMO Level of Evidence/Grade of Recommendation: III / B

Population segment (Line of therapy):
- Relapsed, Advanced, Metastatic (Subsequent therapy)
- Advanced, Metastatic, Progression (Subsequent therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Bladder Cancer [Ann Oncol 2021; https://doi.org/10.1016/j.annonc.2021.11.012]

Clinical Trials in Taiwan region:

Clinical Trials Summary

FGFR3-TACC3 fusion

NCT ID	Title	Phase
NCT04083976	A Phase II Study of Erdafitinib in Subjects With Advanced Solid Tumors and FGFR Gene Alterations.	II

Alerts Informed By Public Data Sources

Current FDA Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

FDA information is current as of 2022-03-16. For the most up-to-date information, search www.fda.gov.

FGFR3-TACC3 fusion

Debio 1347

Cancer type: Solid Tumor

Variant class: FGFR3 aberration

Supporting Statement:
The FDA has granted Fast Track Designation to the FGFR 1-3 inhibitor, debio 1347, for FGFR1/2/3 alterations in unresectable or metastatic solid tumors.

Reference:

https://www.debiopharm.com/drug-development/press-releases/fda-grants-fast-track-designation-to-debiopharm-internationals-debio-1347-for-the-treatment-of-patients-with-unresectable-or-metastatic-tumors-with-a-specific-fgfr-gene-alteration/

vofatamab

Cancer type: Bladder Urothelial Carcinoma

Variant class: FGFR3 fusion

Supporting Statement:
The FDA has granted Fast Track Designation to the FGFR3-targeted monoclonal antibody, vofatamab, for FGFR3 mutations or fusions in advanced or metastatic urothelial carcinoma.

Reference:

https://www.healio.com/news/hematology-oncology/20190107/fda-grants-fast-track-designation-to-vofatamab-for-bladder-cancer-subset

Signatures

Testing Personnel:

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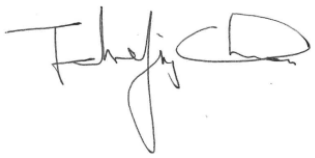
Laboratory Supervisor:

2022.05.16
15:05:57 +08'00'

Pathologist:



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References

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12. https://www.healio.com/news/hematology-oncology/20190107/fda-grants-fast-track-designation-to-vofatamab-for-bladder-cancer-subset
13. https://www.debiopharm.com/drug-development/press-releases/fda-grants-fast-track-designation-to-debiopharm-internationals-debio-1347-for-the-treatment-of-patients-with-unresectable-or-metastatic-tumors-with-a-specific-fgfr-gene-alteration/
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