Taipei Veterans General Hospital

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Sample Information

Patient Name: 藍吳麗鈴
Gender: Female
ID No.: A224698738
History No.: 18826534
Age: 59

Ordering Doctor: DOC3109L 邱昭華
Ordering REQ.: C22P5EF
Signing in Date: 2021/02/24

Path No.: S110-98262
MP No.: F21017
Assay: Oncomine Focus Assay
Sample Type: FFPE
Block No.: S108-08399A
Percentage of tumor cells: 80%
Note:

Sample Cancer Type: Non-Small Cell Lung Cancer

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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	*ERBB3 p.(V104L) c.310G>C* erb-b2 receptor tyrosine kinase 3 Allele Frequency: 42.54%	None	None	4

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.

Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
ERBB3	p.(V104L)	c.310G>C	COSM160824	chr12:56478854	42.54%	NM_001982.3	missense	1998
JAK1	p.(=)	c.2199A>G	.	chr1:65310489	38.18%	NM_002227.3	synonymous	1980
ALK	p.(D1529E)	c.4587C>G	.	chr2:29416366	100.00%	NM_004304.4	missense	1994
ALK	p.(I1461V)	c.4381A>G	.	chr2:29416572	99.50%	NM_004304.4	missense	1996
ALK	p.(=)	c.3375C>A	.	chr2:29445458	100.00%	NM_004304.4	synonymous	1991
FGFR3	p.(=)	c.1953G>A	.	chr4:1807894	99.70%	NM_000142.4	synonymous	1994
PDGFRA	p.(=)	c.1701A>G	.	chr4:55141055	99.80%	NM_006206.5	synonymous	1998
FGFR4	p.(P136L)	c.407C>T	.	chr5:176517797	99.10%	NM_213647.2	missense	2000
RET	p.(=)	c.2307G>T	.	chr10:43613843	99.90%	NM_020975.4	synonymous	1995

Biomarker Descriptions

ERBB3 (erb-b2 receptor tyrosine kinase 3)

Background: The ERBB3 gene encodes the erb-b2 receptor tyrosine kinase 3, a member of the human epidermal growth factor receptor (HER) family. Along with ERBB3/HER3, EGFR/ERBB1/HER1, ERBB2/HER2, and ERBB4/HER4 make up the HER protein family[1]. ERBB3/HER3 binds to extracellular factors, such as neuregulins, but has an impaired kinase domain[2]. Upon ligand binding, ERBB3 forms hetero-dimers with other ERBB/HER family members, including ERBB2/HER2 resulting in activation of tyrosine kinase activity primarily through its dimerization partner.

Alterations and prevalence: ERBB3 gene amplification leading to an increase in expression occurs at low frequency (1-5%) in several cancer types including bladder, esophagus, lung adenocarcinoma, ovarian, pancreas, sarcoma, stomach, and uterine cancers[3,4,5,6,7,8,9]. ERBB3 is also the target of relatively frequent (5-10%) and recurrent somatic mutations in diverse cancer types including bladder, cervical, colorectal, and stomach cancers[3,6,8,9,10]. Recurrent ERBB3 mutations such as V104L/M, occur primarily in the extracellular domain.

Potential relevance: Currently, no therapies are approved for ERBB3 aberrations. Overexpression and activation of ERBB3/HER3 is one mechanism of acquired resistance to therapies targeting EGFR and ERBB2/HER2[11,12]. Preclinical and translational research studies have characterized the oncogenic potential of recurrent ERBB3 mutations and their sensitivity to anti-ERBB antibodies and small molecule inhibitors[13,14,15,16]. A phase I study exhibited progression-free survival (PFS) of 2.5 months and overall survival (OS) of 9 months in 25 patients with ERBB3 mutations treated by anti-ERBB antibodies or molecular-targeted agents[17].

Relevant Therapy Summary

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

ERBB3 p.(V104L) c.310G>C

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
afatinib	✖	✖	✖	✖	● (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

ERBB3 p.(V104L) c.310G>C (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
BDTX-189	✖	✖	✖	✖	● (I/II)
neratinib, palbociclib, everolimus, trametinib	✖	✖	✖	✖	● (I)
pirotinib	✖	✖	✖	✖	● (I)

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

Clinical Trials Summary

ERBB3 p.(V104L) c.310G>C

NCT ID	Title	Phase
NCT03810872	An Open Explorative Phase II, Open Label Study of Afatinib in the Treatment of Advanced Cancer Carrying an EGFR, a HER2 or a HER3 Mutation	II
NCT04209465	MasterKey-01: A Phase I/II, Open-label, Two-part, Multicenter Study to Assess the Safety, Tolerability, Pharmacokinetics & Antitumor Activity of BDTX-189, an Inhibitor of Allosteric ErbB Mutations, in Patients w/ Advanced Solid Malignancies	I/II
NCT03065387	Phase I Study of the Pan-ERBB Inhibitor Neratinib Given in Combination With Everolimus, Palbociclib, or Trametinib in Advanced Cancer Subjects With EGFR Mutation/Amplification, HER2 Mutation/ Amplification, or HER3/4 Mutation or KRAS Mutation	I
No NCT ID	Phase I Clinical Study With Advanced Solid Tumors KBP-5209 Treatment	I

Signatures

Testing Personnel:

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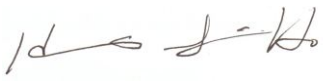
Laboratory Supervisor:



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Pathologist:

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