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: 邱寶華
Gender: Female
ID No.: P221196364
History No.: 49165073
Age: 57

Ordering Doctor: DOC3084A 陳胤之
Ordering REQ.: 0CDZYEW
Signing in Date: 2022/12/29

Path No.: M111-00036
MP No.: F22134
Assay: Oncomine Focus Assay
Sample Type: FFPE
Block No.: S22-11058A2 from En Chu Kong Hospital
Percentage of tumor cells: 70%

Reporting Doctor: DOC5466K 葉奕成 (Phone: 8#5466)

Note:

Sample Cancer Type: Breast Cancer

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Relevant Breast Cancer Variants

Gene	Finding
ERBB2	None detected
PIK3CA	***PIK3CA p.(V105_R108del) c.314_325delTAGGCAACCGTG***

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IIC	*PIK3CA p.(V105_R108del) c.314_325delTAGGCAACCGTG* phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha Allele Frequency: 38.64%	None	None	3

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
PIK3CA	p.(V105_R108del)	c.314_325delTAGGCAACCGTG	.	chr3:178916925	38.64%	NM_006218.4	nonframeshift Deletion	1972

Biomarker Descriptions

PIK3CA (phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha)

Background: The PIK3CA gene encodes the phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha of the class I phosphatidylinositol 3-kinase (PI3K) enzyme[1]. PI3K is a heterodimer that contains a p85 regulatory subunit, which couples one of four p110 catalytic subunits to activated tyrosine protein kinases[2,3]. The p110 catalytic subunits include p110α, β, δ, γ and are encoded by genes PIK3CA, PIK3CB, PIK3CD, and PIK3CG, respectively[2]. PI3K catalyzes the conversion of phosphatidylinositol (4,5)-bisphosphate (PI(4,5)P2) into phosphatidylinositol (3,4,5)-trisphosphate (PI(3,4,5)P3) while the phosphatase and tensin homolog (PTEN) catalyzes the reverse reaction[4,5]. The reversible phosphorylation of inositol lipids regulates diverse aspects of cell growth and metabolism[4,5,6,7]. Recurrent somatic alterations in PIK3CA are frequent in cancer and result in the activation of PI3K/AKT/MTOR pathway, which can influence several hallmarks of cancer including cell proliferation, apoptosis, cancer cell metabolism and invasion, and genetic instability[8,9,10].

Alterations and prevalence: Recurrent somatic activating mutations in PIK3CA are common in diverse cancers and are observed in 20-30% of breast, cervical, and uterine cancers and 10-20% of bladder, gastric, head and neck, and colorectal cancers[11,12]. Activating mutations in PIK3CA commonly occur in exons 10 and 21 (previously referred to as exons 9 and 20 due to exon 1 being untranslated)[13,14]. These mutations typically cluster in the exon 10 helical (codons E542/E545) and exon 21 kinase (codon H1047) domains, each having distinct mechanisms of activation[15,16,17]. PIK3CA resides in the 3q26 cytoband, a region frequently amplified (10-30%) in diverse cancers including squamous carcinomas of the lung, cervix, head and neck, and esophagus, and in serous ovarian and uterine cancers[11,12].

Potential relevance: The PI3K inhibitor, alpelisib[18], is FDA approved (2019) in combination with fulvestrant for the treatment of patients with PIK3CA-mutated, hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, advanced or metastatic breast cancer. Additionally, a phase Ib study of alpelisib with letrozole in patients with metastatic estrogen receptor (ER)-positive breast cancer, the clinical benefit rate, defined as lack of disease progression ≥ 6 months, was 44% (7/16) in PIK3CA-mutated tumors and 20% (2/20) in PIK3CA wild-type tumors[19]. Specifically, exon 20 H1047R mutations were associated with more durable clinical responses in comparison to exon 9 E545K mutations[19]. However, alpelisib did not improve response when administered with letrozole in patients with ER+ early breast cancer with PIK3CA mutations[20]. Case studies with MTOR inhibitors sirolimus and temsirolimus report isolated cases of clinical response in PIK3CA mutated refractory cancers[21,22].

Relevant Therapy Summary

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

PIK3CA p.(V105_R108del) c.314_325delTAGGCAACCGTG

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
inavolisib, palbociclib, hormone therapy	✖	✖	✖	✖	● (III)
inavolisib	✖	✖	✖	✖	● (II)
hormone therapy, alpelisib	✖	✖	✖	✖	● (I)

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

Clinical Trials in Taiwan region:

Clinical Trials Summary

PIK3CA p.(V105_R108del) c.314_325delTAGGCAACCGTG

NCT ID	Title	Phase
NCT04191499	A Phase III, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Efficacy and Safety of Inavolisib Plus Palbociclib and Fulvestrant Versus Placebo Plus Palbociclib and Fulvestrant in Patients With PIK3CA-Mutant, Hormone Receptor-Positive, Her2-Negative, Locally Advanced or Metastatic Breast Cancer	III
NCT04188548	EMBER: A Phase Ia/Ib Study of LY3484356 Administered as Monotherapy and in Combination With Anticancer Therapies for Patients With ER+ Locally Advanced or Metastatic Breast Cancer and Other Select Non-Breast Cancers	I
NCT04589845	Tumor-Agnostic Precision Immunooncology and Somatic Targeting Rational for You (TAPISTRY) Phase II Platform Trial	II

Signatures

Testing Personnel: Shu-Ying Wang 2022.12.30 15:01:21 +08'00'

Laboratory Supervisor: 2022.12.30 15:01:52 +08'00'

Pathologist: Yi-Chu Yeh 2022.12.30 15:02:32 +08'00'

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