



Sample Information

Patient Name: 葉佳綺
Gender: Female
ID No.: H221555368
History No.: 37103405
Age: 54

Ordering Doctor: DOC3127D_趙恆勝
Ordering REQ.: 0BZPWRM
Signing in Date: 2022/09/08

Path No.: S111-97875
MP No.: F22093
Assay: Oncomine Focus Assay
Sample Type: FFPE
Block No.: S111-29119A
Percentage of tumor cells: 60%

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

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	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	PIK3CA p.(N345K) c.1035T>A phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha Allele Frequency: 85.83%	None	None	1

Public data sources included in relevant therapies: FDA¹, NCCN, EMA², 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.(N345K)	c.1035T>A	COSM754	chr3:178921553	85.83%	NM_006218.4	missense	1997
JAK2	p.(D620=)	c.1860C>T	.	chr9:5073781	79.34%	NM_004972.4	synonymous	1999
HRAS	p.(Q70H)	c.210G>C	.	chr11:533846	34.60%	NM_001130442.2	missense	2000

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) enzyme¹. 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, respectively². 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 cluster in two regions corresponding to the exon 9 helical (codons E542/E545) and exon 20 kinase (codon H1047) domains, each having distinct mechanisms of activation^{13,14,15}. 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, alpelisib¹⁶, 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 tumors¹⁷. Specifically, exon 20 H1047R mutations were associated with more durable clinical responses in comparison to exon 9 E545K mutations¹⁷. However, alpelisib did not improve response when administered with letrozole in patients with ER+ early breast cancer with PIK3CA mutations¹⁸. Case studies with MTOR inhibitors sirolimus and temsirolimus report isolated cases of clinical response in PIK3CA mutated refractory cancers^{19,20}.

Relevant Therapy Summary

☒ In this cancer type ☐ In other cancer type ☒ In this cancer type and other cancer types ☒ No evidence

PIK3CA p.(N345K) c.1035T>A

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
inavolisib	×	×	×	×	<input checked="" type="radio"/> (II)

* 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.(N345K) c.1035T>A

NCT ID	Title	Phase
NCT04589845	Tumor-Agnostic Precision Immunooncology and Somatic Targeting Rational for You (TAPISTRY) Phase II Platform Trial	II

Signatures

Testing Personnel:

Laboratory Supervisor:

Pathologist:

References

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