Taipei Veterans General Hospital

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Sample Information

Patient Name: 郭淑月
Gender: Female
ID No.: Q200356067
History No.: 2795633
Age: 82

Ordering Doctor: DOC3160J 羅永鴻
Ordering REQ.: C32GFNH
Signing in Date: 2023/12/27

Path No.: M112-00338
MP No.: F23097
Assay: Oncomine Focus Assay
Sample Type: FFPE
Block No.: S112-62171A+B
Percentage of tumor cells: 40%

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

Note:

Sample Cancer Type: Non-Small Cell Lung Cancer

Report Highlights

0 Relevant Biomarkers
0 Therapies Available
0 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	***KRAS amplification***	ROS1	None detected
MET	None detected		

Relevant Biomarkers

No relevant biomarkers found in this sample.

Prevalent cancer biomarkers without relevant evidence based on included data sources
CDK4 amplification, KRAS amplification

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Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
ALK	p.(A1200=)	c.3600G>C	.	chr2:29443617	50.61%	NM_004304.5	synonymous	1974
FGFR4	p.(P136L)	c.407C>T	.	chr5:176517797	99.55%	NM_213647.3	missense	2000
EGFR	p.(Q787=)	c.2361G>A	.	chr7:55249063	98.80%	NM_005228.5	synonymous	1997
RET	p.(S904=)	c.2712C>G	.	chr10:43615633	36.65%	NM_020975.6	synonymous	1997

Copy Number Variations

Gene	Locus	Copy Number
KRAS	chr12:25364761	6.53
CDK4	chr12:58142052	6.68

Biomarker Descriptions

CDK4 (cyclin dependent kinase 4)

Background: The CDK4 gene encodes the cyclin-dependent kinase 4 protein, a homologue of CDK6. Both proteins are serine/threonine protein kinases that are involved in the regulation of the G1/S phase transition of the mitotic cell cycle[1,2]. CDK4 kinase is activated by complex formation with D-type cyclins (e.g., CCND1, CCND2, or CCND3), which leads to the phosphorylation of retinoblastoma protein (RB), followed by E2F activation, DNA replication, and cell-cycle progression[3]. Germline mutations in CDK4 are associated with familial melanoma[4,5,6].

Alterations and prevalence: Recurrent somatic mutations of CDK4 codon K22 and R24 are observed in melanoma (1-2%) and lung cancer (approximately 0.1%). Codons K22 and R24 are necessary for binding and inhibition by p16/CDKN2A[7,8,9]. CDK4 is recurrently amplified in several cancer types, most notably in sarcomas (15-20%), glioma (10-15%), adrenocortical carcinoma (5%), lung adenocarcinoma (5%), and melanoma (3%)[10,11,12,13].

Potential relevance: Currently, no therapies are approved for CDK4 aberrations. Amplification of region 12q14-15, which includes CDK4, is useful as an ancillary diagnostic marker of atypical lipomatous tumor/welldifferentiated liposarcoma (ALT/WDLS)[14]. Small molecule inhibitors targeting CDK4/6 including palbociclib (2015), abemaciclib (2017), and ribociclib (2017), are FDA approved in combination with an aromatase inhibitor or fulvestrant for the treatment of hormone receptor-positive, HER2-negative advanced or metastatic breast cancer.

KRAS (KRAS proto-oncogene, GTPase)

Background: The KRAS proto-oncogene encodes a GTPase that functions in signal transduction and is a member of the RAS superfamily which also includes NRAS and HRAS. RAS proteins mediate the transmission of growth signals from the cell surface to the nucleus via the PI3K/AKT/MTOR and RAS/RAF/MEK/ERK pathways, which regulate cell division, differentiation, and survival[15,16,17].

Alterations and prevalence: Recurrent mutations in RAS oncogenes cause constitutive activation and are found in 20-30% of cancers. KRAS mutations are observed in up to 10-20% of uterine cancer, 30-35% of lung adenocarcinoma and colorectal cancer, and about 60% of pancreatic cancer[11]. The majority of KRAS mutations consist of point mutations occurring at G12, G13, and Q61[11,18,19]. Mutations at A59, K117, and A146 have also been observed but are less frequent[10,20].

Potential relevance: The FDA has approved the small molecule inhibitors, sotorasib[21] (2021) and adagrasib[22] (2022), for the treatment of adult patients with KRAS G12C-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC). The FDA has also granted breakthrough therapy designation (2022) to the KRAS G12C inhibitor, GDC-6036[23], for KRAS G12C mutation in non-small cell lung cancer. The small molecular inhibitor, RO-5126766, was granted breakthrough designation (2021) alone for KRAS G12V mutant non-small cell lung cancer or in combination with defactinib, for KRAS mutant endometrial carcinoma and KRAS G12V mutant non-small cell lung cancer[24]. The PLK1 inhibitor, onvansertib[25], was granted fast track designation (2020) in combination with bevacizumab and FOLFIRI for second-line treatment of patients with KRAS-mutated metastatic colorectal cancer (mCRC). Additionally, the SHP2 inhibitor, BBP-398[26] was granted fast track designation (2022) in combination with sotorasib for previously treated patients with KRAS G12C-mutated metastatic NSCLC.The EGFR antagonists, cetuximab[27] and panitumumab[28], are contraindicated for treatment of

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Biomarker Descriptions (continued)

colorectal cancer patients with KRAS mutations in exon 2 (codons 12 and 13), exon 3 (codons 59 and 61), and exon 4 (codons 117 and 146)[20]. Additionally, KRAS mutations are associated with poor prognosis in NSCLC[29].

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Clinical Trials in Taiwan region:

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