



Sample Information

Patient Name: 李水音
Gender: Male
ID No.: L100970909
History No.: 21185342
Age: 70

Ordering Doctor: DOC3016D 江起陸
Ordering REQ.: 0AVARSE
Signing in Date: 2020/08/20

Path No.: S109-99892
MP No.: F20063
Assay: Oncomine Focus Assay
Sample Type: FFPE
Block No.: S109-25970A
Percentage of tumor cells: 70%
Note:

Sample Cancer Type: Non-Small Cell Lung Cancer

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Relevant Non-Small Cell Lung Cancer Findings

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	CCND1 amplification cyclin D1	None	None	4

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.



Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
JAK1	p.(=)	c.2199A>G	.	chr1:65310489	38.30%	NM_002227.3	synonymous	1987
ALK	p.(D1529E)	c.4587C>G	.	chr2:29416366	50.28%	NM_004304.4	missense	1999
ALK	p.(I1461V)	c.4381A>G	.	chr2:29416572	99.85%	NM_004304.4	missense	1997
ALK	p.(=)	c.3375C>A	.	chr2:29445458	48.67%	NM_004304.4	synonymous	1993
FGFR3	p.(=)	c.1953G>A	.	chr4:1807894	99.80%	NM_000142.4	synonymous	1996
PDGFRA	p.(=)	c.1701A>G	.	chr4:55141055	99.90%	NM_006206.5	synonymous	1997
FGFR4	p.(P136L)	c.407C>T	.	chr5:176517797	99.20%	NM_213647.2	missense	2000
EGFR	p.(=)	c.2361G>A	.	chr7:55249063	62.89%	NM_005228.4	synonymous	1997
RET	p.(=)	c.2307G>T	.	chr10:43613843	99.75%	NM_020975.4	synonymous	1994

Copy Number Variations

Gene	Locus	Copy Number
CCND1	chr11:69456942	6.89

Biomarker Descriptions

CCND1 (cyclin D1)

Background: The CCND1 gene encodes the cyclin D1 protein, a member of the highly conserved D-cyclin family that also includes CCND2 and CCND3^{1,2,3}. D-type cyclins are known to regulate cell cycle progression by binding to and activating cyclin dependent kinases (CDKs), specifically CDK4 and CDK6, which leads to the phosphorylation and inactivation of the retinoblastoma (RB1) protein^{1,2}. Consequently, RB1 inactivation results in E2F transcription factor activation and cellular G1/S phase transition thereby resulting in cell cycle progression, a common event observed in tumorigenesis^{1,2,4}. Aberrations in the D-type cyclins have been observed to promote tumor progression suggesting an oncogenic role for CCND1^{3,5}.

Alterations and prevalence: Recurrent somatic alterations to CCND1, including mutations, amplifications, and chromosomal translocations, are observed in many cancer types. A common mechanism of these alterations is to increase the expression and nuclear localization of the cyclin D1 protein. Recurrent somatic mutations include missense mutations at codons T286 and P287 and c-terminal truncating mutations that are enriched in about 33% of uterine cancer, and missense mutations at Y44 that are enriched in about 50% of Mantle cell lymphoma (MCL)^{6,7,8,9}. These mutations block phosphorylation-dependent nuclear export and proteolysis^{10,11,12,13}. CCND1 is recurrently amplified in many cancer types, including up to 35% of esophageal cancer, 20-30% of head and neck cancer, and 10-20% of breast, squamous lung, and bladder cancers^{6,8,14}. MCL is genetically characterized by the t(11;14) (q13;q13) translocation, a rearrangement that juxtaposes CCND1 to the immunoglobulin heavy (IgH) chain gene. This rearrangement leads to constitutive expression of cyclin D1 and plays an important role in MCL pathogenesis^{15,16}.

Potential relevance: Currently, no therapies are approved for CCND1 aberrations.



Relevant Therapy Summary

☒ In this cancer type
 ☐ In other cancer type
 ☒ In this cancer type and other cancer types
 ☒ Contraindicated
 ☒ Both for use and contraindicated
 ☒ No evidence

CCND1 amplification

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
abemaciclib	×	×	×	×	● (II)
palbociclib	×	×	×	×	● (II)
siremadlin, ribociclib	×	×	×	×	● (II)

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

Signatures

Testing Personnel:

Laboratory Supervisor:

Pathologist:



References

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