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Sample Information

Patient Name: 楊惠敏 Gender: Female ID No.: U200683483 History No.: 47041612

Age: 69

Ordering Doctor: DOC8528A 劉思妤

Ordering REQ.: 0BHVHRJ Signing in Date: 2021/07/14

Path No.: S110-99090 **MP No.:** F21056

Assay: Oncomine Focus Assay

Sample Type: FFPE Block No.: S110-19195A Percentage of tumor cells: 20%

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

Note:

Sample Cancer Type: Non-Small Cell Lung Cancer

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Report Highlights

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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		

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Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IIC	MYC amplification MYC proto-oncogene, bHLH transcription factor	None	None	3

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 Variant Effect Coverage Frequency Transcript IDH1 p.(G105=)c.315C>T chr2:209113192 55.85% NM 005896.3 2000 synonymous **Copy Number Variations** Locus Gene **Copy Number** chr8·128748885 80.35 MYC

Biomarker Descriptions

MYC (MYC proto-oncogene, bHLH transcription factor)

<u>Background:</u> The MYC gene encodes the MYC proto-oncogene (c-MYC), a basic helix-loop-helix transcription factor that regulates the expression of numerous genes that control cell cycle progression, apoptosis, metabolic pathways, and cellular transformation^{1,2,3,4}. MYC is part of the MYC oncogene family that includes related transcription factors MYCN and MYCL that regulate transcription in 10-15% of promoter regions⁵. MYC functions as a heterodimer in complex with the transcription factor MAX^{2,6}.

Alterations and prevalence: Recurrent somatic alterations are observed in both solid and hematological cancers. Recurrent somatic mutations in MYC, including codon T58, are infrequent and hypothesized to increase the stability of the MYC protein^{7,8}. MYC gene amplification is particularly common in diverse solid tumors. MYC amplification is observed in 30% of serous ovarian cancer, 20% of uterine serous carcinoma, 15% of esophageal and breast cancers, and is common (1-10%) in numerous other cancer types^{9,10,11}. MYC is the target of the t(8;14)(q24;32) chromosomal translocation in Burkitt's lymphoma that places MYC coding sequences adjacent to immunoglobulin region regulatory sequences, which results in increased MYC expression^{12,13}.

<u>Potential relevance</u>: Currently, no therapies are approved for MYC aberrations. Due to the high frequency of somatic MYC alterations in cancer, many approaches are being investigated in clinical trials including strategies to disrupt complex formation with MAX, including inhibition of MYC expression and synthetic lethality associated with MYC overexpression^{1,14,15,16}.

Relevant Therapy Summary

In this cancer type	In this cancer type and other cancer types			X No evidence		
MYC amplificat	ion					
Relevant Therapy		FDA	NCCN	EMA	ESMO	Clinical Trials*
entinostat, nivolumak)	×	×	×	×	(1/11)

^{*} 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
O In other cancer type
O In this cancer type and other cancer types
X No evidence

MYC amplification (continued)					
Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
BMS-986158	×	×	×	×	(l)
KB-0742	×	×	×	×	(I)

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

Clinical Trials Summary

MYC amplification		
NCT ID	Title	Phase
NCT03838042	INFORM2 Exploratory Multinational Phase I/II Combination Study of Nivolumab and Entinostat in Children and Adolescents with Refractory High-risk Malignancies	1/11
NCT03936465	Phase I Study of the Bromodomain (BRD) and Extra-Terminal Domain (BET) Inhibitor BMS-986158 in Pediatric Cancer	I
NCT04718675	Phase I, First-in-human, Open-label Dose Escalation and Cohort Expansion Study of KB-0742 in Patients With Relapsed or Refractory Solid Tumors or Non-Hodgkin Lymphoma	I

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Signatures

Testing Personnel:

Laboratory Supervisor:

Pathologist:

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