Taipei Veterans General Hospital

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## 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*<br>cyclin D1 | None | None | 4 |

**Public data sources included in relevant therapies: FDA**1, 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)

### 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:** Shin-Ying Lin 2020.08.25 17:03:05 +08'00'

**Laboratory Supervisor:**

2020.08.25
17:03:23 +08'00'

**Pathologist:**

2020.08.25
17:03:36 +08'00'

## References

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