Taipei Veterans General Hospital

Department of Pathology and Laboratory Medicine
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## Sample Information

**Patient Name:** 林家祥
**Gender:** Male
**ID No.:** A110515279
**History No.:** 32696643
**Age:** 65

**Ordering Doctor:** DOC1322F 趙毅
**Ordering REQ.:** H3LMM45
**Signing in Date:** 2021/12/03

**Path No.:** S110-94702
**MP No.:** F21100
**Assay:** Oncomine Focus Assay
**Sample Type:** FFPE
**Block No.:** S110-77291B
**Percentage of tumor cells:** 80%

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

**Note:**

## Sample Cancer Type: Cholangiocarcinoma

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### Report Highlights

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## Relevant Biomarkers

| Tier | Genomic Alteration | Relevant Therapies (In this cancer type) | Relevant Therapies (In other cancer type) | Clinical Trials |
|---|---|---|---|---|
| IA | *IDH1 p.(R132H) c.395G>A*<br>isocitrate dehydrogenase (NADP(+)) 1<br>Allele Frequency: 23.33%<br>**Prognostic significance:** NCCN: Poor<br>**Diagnostic significance:** None | ivosidenib | None | 1 |

**Public data sources included in relevant therapies: FDA**1, NCCN, **EMA**2, ESMO
**Public data sources included in prognostic and diagnostic significance:** NCCN, 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 |
|---|---|---|---|---|---|---|---|---|
| IDH1 | p.(R132H) | c.395G>A | COSM28746 | chr2:209113112 | 23.33% | NM_005896.3 | missense | 1997 |

# Biomarker Descriptions

**IDH1 (isocitrate dehydrogenase (NADP(+)) 1)**

Background: The IDH1 and IDH2 genes encode homologous isocitrate dehydrogenase enzymes that catalyze the conversion of isocitrate to α-ketoglutarate (α-KG)[1]. The IDH1 gene encodes the NADP+ dependent cytoplasmic isocitrate dehydrogenase enzyme; IDH2 encodes the mitochondrial isoform.

Alterations and prevalence: Recurrent somatic mutations in IDH1 and IDH2 are mutually exclusive and observed in several malignancies including glioma, chondrosarcoma, intrahepatic cholangiocarcinoma, acute myeloid leukemia (AML), and myelodysplastic syndrome (MDS)[2]. Recurrent IDH1 variants include predominately R132H/C plus other substitutions at lower frequencies. These gain of function variants confer neomorphic enzyme activity[3]. Although wild-type enzymatic activity is ablated, recurrent IDH1 variants catalyze the conversion of α-KG to D-2-hydroxyglutarate, an oncometabolite with diverse effects on cellular metabolism, epigenetic regulation, redox states, and DNA repair[1,4]. Recurrent IDH1 mutations are present in 5-10% of patients with AML and 5% of patients with MDS[5,6,7]. Recurrent IDH1 mutations are present in nearly 80% of lower grade diffuse gliomas[8,9].

Potential relevance: Ivosidenib[10] is FDA approved (2018) for the treatment of AML patients with IDH1 R132C/G/H/L/S variants[11]. Ivosidenib has also been granted breakthrough designation (2020) for IDH1 mutated relapsed or refractory myelodysplastic syndrome (MDS)[12]. IDH1 mutations are associated with inferior leukemia-free survival in primary myelofibrosis (PMF) and inferior overall survival in polycythemia vera (PV) but have been shown to confer improved prognosis in lower grade gliomas[13,14,15].

# Relevant Therapy Summary

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ✖ No evidence

## IDH1 p.(R132H) c.395G>A

| Relevant Therapy | FDA | NCCN | EMA | ESMO | Clinical Trials* |
|---|---|---|---|---|---|
| ivosidenib | ✖ | ● | ✖ | ✖ | ✖ |
| LY-3410738 | ✖ | ✖ | ✖ | ✖ | ● (I) |

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

# Relevant Therapy Details

## Current NCCN Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types

NCCN information is current as of 2021-08-02. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

## IDH1 p.(R132H) c.395G>A

### ● ivosidenib

**Cancer type:** Extrahepatic Cholangiocarcinoma, Intrahepatic Cholangiocarcinoma

**Variant class:** IDH1 mutation

**NCCN Recommendation category:** 2A

**Population segment (Line of therapy):**
- Unresectable, Metastatic, Progression (Subsequent therapy); Useful in certain circumstances

**Reference:** NCCN Guidelines® - NCCN-Hepatobiliary Cancers [Version 3.2021]

# Prognostic Details

## Current NCCN Information

NCCN information is current as of 2021-08-02. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

## IDH1 p.(R132H) c.395G>A

### Prognostic significance: NCCN: Poor

**Cancer type:** Extrahepatic Cholangiocarcinoma **Variant class:** IDH1 mutation

**NCCN Recommendation category:** 2A

**Summary:**
- NCCN® associates the biomarker with poor prognosis

**Reference:** NCCN Guidelines® - NCCN-Hepatobiliary Cancers [Version 3.2021]

## Clinical Trials in Taiwan region:

## Clinical Trials Summary

### IDH1 p.(R132H) c.395G>A

| NCT ID | Title | Phase |
|---|---|---|
| NCT04521686 | Study of LY3410738 Administered to Patients With Advanced Solid Tumors With IDH1 Mutations. | I |

## Signatures

**Testing Personnel:**


2021.12.08
11:01:09 +08'00'

**Laboratory Supervisor:**

2021.12.08
11:01:26 +08'00'

**Pathologist:**

2021.12.08
11:01:36 +08'00'

## References


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