

## AB048. P-16. Molecular profiling of intrahepatic cholangiocarcinoma in Taiwan using targeted next-generation sequencing

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**Background:** Intrahepatic cholangiocarcinoma (ICC) is the second most common malignancy arising from the liver, with increasing incidence globally in recent two decades. For unresectable locally advanced or metastatic disease, gemcitabine plus cisplatin is the standard of care in first-line setting. Recently, some actionable genomic alterations have been described, which lead to successful targeted therapies in a small fraction of ICC patients. However, the pattern of genomic alterations in ICC is somewhat geographic and etiology-dependent. Herein, we report the genomic profiling

of clinical ICC samples in Taiwan, an endemic area of HBV infection.

**Methods:** DNA sequencing of hybridization-captured libraries was performed. The Foundation Medicine T7 assay interrogates 395 genes for base substitutions, insertion-deletions and copy number changes, as well as introns of 31 genes involved in rearrangements. Sample DNA was isolated from 40 mm of 42 formalin-fixed paraffin-embedded ICC specimens and sequenced to high coverage.

**Results:** The most commonly observed alterations were TP53 (26%), TERT (21%), IDH1/2 (17%), BAP1 (17%), PTCH1 (17%), and MLL3 (17%). Twenty-seven cases (64%) harbored at least one potentially actionable alteration, including PTCH1 (17%), KRAS (14%), CDKN2A (12%), IDH2 (12%), MET (7%), PIK3CA (7%), FGFR2 (5%), IDH1 (5%), PTEN (5%), ERBB2 (5%), ERBB3 (5%), and TSC1 (5%). The incidence of TP53 mutation is lower than those of *O. viverrini*-related ICC (40–44%). Two cases harbored gene fusions involving the tyrosine kinases FGFR2 (FGFR2-BICC1 and FGFR2-CTNNA3). The most common involved signaling pathway is chromosome modification.

**Conclusions:** The results provide important background data for the incidence of common genetic alterations of ICC in Taiwan, which may facilitate more accurate estimation of potential patient enrollment in marker-drive industry-sponsored trials and the feasibility of investigator-initiated trials.

**Keywords:** Next-generation sequencing; intrahepatic cholangiocarcinoma (ICC); gene panel

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