

## Response to Alectinib in ALK-positive Combined Hepatocellular Cholangiocarcinoma: A Case Report

연세대학교 의과대학 내과학교실<sup>1</sup>, 연세대학교 의과대학 병리학교실<sup>2</sup>, 연세대학교 의과대학 내과학교실 종양내과<sup>3</sup>

홍문기<sup>1</sup>, 김선일<sup>2</sup>, 김민환<sup>3</sup>, 심효섭<sup>2</sup>, 최혜진<sup>3</sup>, 이충근<sup>3</sup>

**Introduction:** Anaplastic lymphoma kinase (ALK)-rearrangement is a well-known target in non-small cell lung cancer (NSCLC). Here, we report a rare case of combined hepatocellular cholangiocarcinoma (HCC-CCC) with HOOK3-ALK fusion that showed a good response to Alectinib.

**Case presentation:** A 26-year-old female patient with no known medical history and a paternal family history of gastric cancer presented with 3 months of right upper quadrant pain. Initial AFP, PIVKA-II, CEA and CA 19-9 levels were 458.2ng/mL, 113mAU/mL, 0.71ng/mL and 68U/mL respectively. Abdominopelvic CT showed a 10cm sized tumor of the right hepatic lobe with hepatic capsular retraction and multiple intrahepatic and lung metastases. Pathology reports based on liver biopsy and its immune profile suggested either HCC-CCC or AFP producing cholangiocarcinoma. Despite immediate initiation of systemic chemotherapy, Tumor progressed after 1st line Gemcitabine/Cisplatin and 2nd line Cisplatin/Capecitabine regimen, resulting in lung and liver progression in less than two months. Since HCC tumor markers (AFP and PIVKA-II) were elevated, Lenvatinib was chosen as the 3rd line therapy. Lenvatinib showed response for 5 months, however metastatic lung nodules progressed afterward. Meanwhile, NGS panels (Illumina TSO 500) of the primary tumor liver biopsy showed a rare HOOK3-ALK fusion and SRGAP2/NOTCH2 fusion gene. CT-guided lung biopsy targeting the metastatic lesion was done, which showed an ALK-positive immunohistochemistry result via ALK VENTANA assay (Figure 1A). Another NGS panels (Foundation Medicine) of the metastatic lung tissue also showed HOOK3-ALK fusion and ZNF217 amplification. Based on this result, Alectinib was added to Lenvatinib. 1 month later, Alectinib showed a dramatic response to not only the lung lesions but also the hepatic lesions (Figure 1B). An impressive decline of tumor markers was also noted. The patient is on the treatment with partial response for 2 months.

**Discussion:** This case presents a possible benefit of Alectinib in ALK-positive cancer other than NSCLC. Routine NGS for poor-prognostic cancer with limited treatment options such as HCC-CCC is warranted.

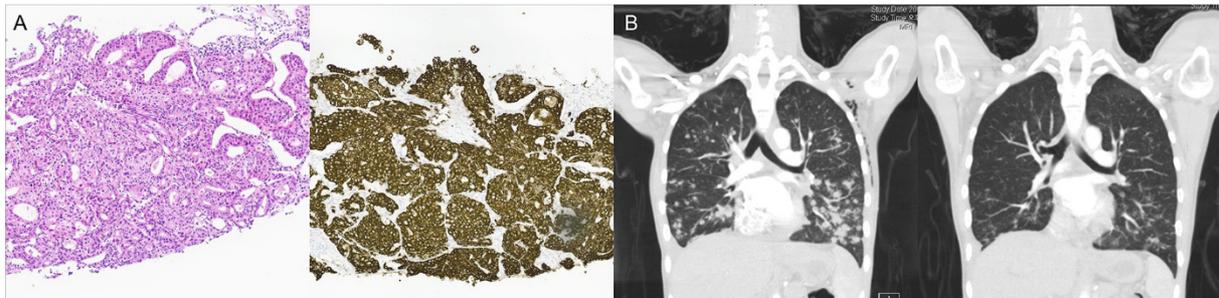


Figure 1. Response to Alectinib in ALK positive HCC-CCC  
 (A) Lung metastatic tissue showing positive expression of ALK.  
 (B) Chest CT images showing lung metastatic lesions before (left) and after 1 month Alectinib treatment (right).