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# Novel Anti-Hexokinase 1 Antibodies Are Associated With Poor Prognosis in Patients With Primary Biliary Cholangitis

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## Abstract

### OBJECTIVES:

Antibodies to hexokinase 1 (HK1) and kelch-like 12 (KLHL12) have been identified as potential biomarkers in primary biliary cholangitis (PBC), and this study assesses changes of these antibodies over time and if they are associated with clinical outcomes.

### METHODS:

Two hundred fifty-four PBC patients (93.3% female, 51 ± 12.3 years old) were tested for anti-HK1 and anti-KLHL12, antimitochondrial (AMA), anti-gp210, and anti-sp100 antibodies. One hundred sixty-nine patients were tested twice and 49 three times within 4.2 (0.8–10.0) years. Biochemistry and clinical features at diagnosis, response to therapy, events of decompensation, and liver-related death or transplantation were evaluated.

## RESULTS:

Anti-HK1 and anti-KLHL2 were detected in 46.1% and 22.8% patients, respectively. AMA were positive in 93.7%, anti-sp100 in 26.4%, and anti-gp210 in 21.3% of patients. Anti-HK1 and anti-KLHL12 positivity changed over time in 13.3% and 5.5% of patients, respectively. Anti-HK1 or anti-KLHL12 were present in 37.5% of AMA-negative patients, and in 40% of AMA, anti-gp210, and anti-sp100 negative. No significant differences were observed between those with or without HK1 and KLHL12 antibodies, but transplant-free survival and time to liver decompensation were significantly lower in patients anti-HK1 positive ( $P = 0.039$ ;  $P = 0.04$ ) and in those anti-sp100 positive ( $P = 0.01$ ;  $P = 0.007$ ). No changes in survival and events of liver decompensation were observed according to the positivity of AMA, anti-KLHL12, or anti-gp210 antibodies.

## DISCUSSION:

HK1 and KLHL12 antibodies are present in 40% of PBC patients who are seronegative by the conventional PBC-specific antibodies. The novel antibodies remain rather steady during the course of the disease, and HK1 antibodies are associated with unfavourable outcomes.

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