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ALT Levels and Risk of Hepatocellular Carcinoma (HCC) in Caucasian Chronic Hepatitis B (CHB) Patients Under Long-Term Therapy with Entecavir (ETV) or Tenofovir Disoproxil Fumarate (TDF)

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Abstract Text

Background: Recent reports have suggested that on-therapy ALT activity may be associated with the probability of HCC in CHB patients who receive long-term oral antiviral therapy. We evaluated whether ALT levels affect the incidence of HCC in Caucasian CHB patients treated with long-term ETV/TDF therapy in the multicenter, ongoing PAGE-B cohort study.

Methods: The PAGE-B cohort includes 1951 adult Caucasians with CHB with or without compensated cirrhosis (mean age 53±14 years, males:71%, HBeAg-positive:18%, compensated cirrhosis:27%). Mean follow-up has been 6.9±2.8 (median:7.3) years from ETV/TDF onset. The following upper normal limits (ULN) of ALT were considered: 30/19 IU/L for males/females (AASLD1-ULN), 35/25 IU/L for males/females (AASLD2-ULN) and 40 IU/L for all patients (EASL-ULN). The cumulative incidence rates of HCC derived from Kaplan-Meier estimates.

Results: HCC has been diagnosed in 103 cases within the first 5 years and another 33 cases after year 5 (until year 13). ALT was >AASLD1-ULN, >AASLD2-ULN and >EASL-ULN in 66.4%, 61.3% and 51.7% of 1843 patients at baseline, 45.1%, 29.7% and 15.7% of 1688 patients at year 1 and 33.9%, 18.6% and 9.3% of 1341 patients at year 5, respectively. In univariable analyses, elevated ALT at baseline by any definition and ALT >EASL-ULN at year 1 were associated with subsequent HCC development, but there was no association with ALT >AASLD1/2-ULN at year 1 or elevated ALT by any definition at year 5 or with ALT levels at any time point. After adjustment for age, sex, platelet counts and presence of cirrhosis, only ALT >EASL-ULN at year 1 was found to have an independent association with HCC development after year 1 (HR:1.9, 95% CI:1.2-3.1; P=0.010). ALT >EASL-ULN at year 1 was independently associated with HCC development in patients with baseline cirrhosis (adjusted HR:2.9, 95% CI:1.3-3.9; P=0.003), but not in non-cirrhotics (P=0.913). In 465 cirrhotics, the 3-, 5-, 10-year HCC incidence rates were 4%, 10%, 17% in 379 cases with ALT ≤EASL-ULN and 10%, 17%, 22% in 86 cases with ALT >EASL-ULN at year 1.

Conclusion: In ETV/TDF treated Caucasian CHB patients a) maintenance of elevated ALT at 1 year of therapy increases the subsequent HCC risk, particularly in patients with cirrhosis at baseline; b) the ULN of ALT recommended by EASL (40 IU/L), but not those by AASLD, at year 1 of therapy appears to offer independent clinically relevant predictability for HCC development.

Disclosures

George V. Papatheodoridis – Gilead: Advisory Committee or Review Panel; Gilead: Grant/Research Support; Gilead: Speaking and Teaching

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