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Prediction and Need for Surveillance of Hepatocellular Carcinoma (HCC) Development after the First 5 Years of Entecavir (ETV) or Tenofovir Disoproxil Fumarate (TDF) Therapy in Caucasian Chronic Hepatitis B (CHB) Patients of the PAGE-B Cohort

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Abstract Text

Background: We recently showed that the HCC incidence is decreasing after 5 years of ETV/TDF, but HCC may still develop and cannot be easily predicted. We assessed predictors and need for HCC surveillance beyond year 5 of ETV/TDF in CHB patients.

Methods: Of 1951 adult Caucasians with CHB±compensated cirrhosis included in the PAGE-B cohort, 1427 (73%) have completed follow-up >5 years without HCC until year 5 (age at year 5:57±13 years, males:70%, baseline cirrhosis:26%). Mean follow-up has been 8.1±1.6 (median:8.3) years from ETV/TDF onset. The cumulative HCC incidence rates derived from Kaplan-Meier estimates.

Results: In years 5-13, HCC has been diagnosed in 33/1427 (2.3%) patients with cumulative incidence 0.7%,1.8%,2.4%,3.2%,3.8% at year 6,7,8,10,13, respectively. In multivariable Cox regression analysis, only age [RH:1.08 (1.04-1.13), P<0.001] and presence of cirrhosis at baseline [RH:2.45 (1.03-5.86), P=0.043] or year 5 [RH:2.90 (1.21-7.41), P=0.018] were independently associated with HCC development in years 5-13. After year 5, HCC developed only in cases >50 years old (33/992, 3.3%) and in none of 435 cases ≤50 years old at year 5 (P<0.001). Cirrhosis at baseline or year 5 was present in 62/429 (15%) or 8/254 (3%) of patients aged ≤50 and 308/963 (32%) or 70/676 (10%) of patients >50 years at year 5 and available data (P<0.001). The 6,8,10-year HCC incidence was lower in 658 non-cirrhotics at baseline (0.6%,1.7%,2.0%) than 206 patients with cirrhosis reversion (stiffness <12 kPa) at year 5 (1.0%,5.1%,8.0%; P=0.001) or 66 patients who maintained cirrhosis (1.5%,7.0%,7.0%; P=0.005); HCC incidence did not differ in the latter two subgroups (P=0.657). If cirrhosis was not considered, HCC development was associated with age and platelets <150x10^9/L at year 5 [RH:2.28 (1.07-4.85), P=0.032]. In patients >50 years old, the 6,8,10-year HCC incidence was 1.3%,5%,8.9% and 0.8%,3.1%,3.8% in cases with platelets <150 and ≥150x10^9/L (P=0.037).

Conclusion: HCC after the first 5 years of ETV/TDF therapy seems to develop exclusively in patients older than 50 years. Elastographic reversion of cirrhosis at 5 years does not appear to decrease the HCC risk. Platelets are not useful for excluding patients from HCC surveillance after year 5, as the annual HCC risk in any platelet subgroup is >0.2%, the threshold for cost-effective HCC surveillance. Thus, HCC surveillance should continue in all patients >50 years old and probably in the few cirrhotics ≤50 years old.

Disclosures

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