

The Pattern and Predictors of Serum HBsAg Decline in Chronic Hepatitis B Patients Receiving Up to Five Years of Entecavir Therapy

Abstract

Background: The decline in quantitative serum hepatitis B surface antigen (qHBsAg) level and its predictors in chronic hepatitis B (CHB) patients undergoing long-term entecavir (ETV) therapy remain unclear.

Patients and Methods: 419 treatment-naïve (370 compensated and 49 acutely decompensated) CHB patients had been treated with ETV for at least 1 year. Serum HBsAg and HBV DNA levels were measured with the Abbott Architect HBsAg QT assay and the Cobas AmpliCor HBV Monitor Test throughout treatment, respectively.

Results: At baseline: median age: 49 years, 74.7% men, 38% HBeAg-positive (N=159), 62.6% genotype B infection, median ALT: 84 IU/L, HBV DNA: 6.60 log₁₀copies/mL, and qHBsAg: 3.27 log₁₀IU/mL. Among them, 298, 218 and 157 patients had received ETV therapy for ≥ 3 , 4 and 5 years, respectively (mean duration: 50.7 \pm 20.1 months (M)). At 3 and 12M of therapy, 5.5% (HBeAg-positive:3.5% vs -negative: 8.8%) and 16.5% (HBeAg-positive: 11.5% vs -negative: 24.5%) of patients had qHBsAg decline from baseline of $\geq 75\%$, respectively. For HBeAg-positive patients, there were significant declines in qHBsAg level between baseline and 3M ($P<0.0001$), 12 and 24M ($P=0.0123$), 36 and 48M, and 48 and 60M (both $P<0.0001$). For HBeAg-negative patients, there were significant declines in qHBsAg level between baseline and 3M ($P=0.0451$), 6 and 12M ($P=0.0012$), 12 and 24M, 24 and 36M, 36 and 48M, and 48 and 60M (all four $P<0.0001$). Patients were categorized in three subgroups according to the pattern of qHBsAg decline from baseline: $\geq 75\%$ at 3M, $\geq 75\%$ at 12M, and $<75\%$ at 12M. For HBeAg-positive patients, the subgroup with qHBsAg decline from baseline of $\geq 75\%$ at 3M of therapy had significantly lower qHBsAg levels than the other two subgroups up to 3 years of treatment. Multivariate logistic regression analyses identified genotype B (OR=3.642, $P=0.0117$), ALT ≥ 120 IU/L (OR=9.514, $P<0.0001$) and baseline qHBsAg ≥ 5000 IU/mL (OR=12.985, $P<0.0001$) as predictors of qHBsAg decline from baseline of $\geq 75\%$ at 3M of therapy. For HBeAg-negative patients, the qHBsAg levels between the subgroups with qHBsAg decline from baseline of $\geq 75\%$ at 3 or 12M of therapy were similar but was significantly lower than the subgroup with qHBsAg decline from baseline of $<75\%$ at 12M of therapy up to 3 years of treatment. Multivariate logistic regression analyses identified ALT ≥ 120 IU/L (OR=11.284, $P<0.0001$) and baseline qHBsAg ≥ 5000 log₁₀ IU/mL (OR=15.873, $P<0.0001$) as predictors of qHBsAg decline from baseline of $\geq 75\%$ at 12M of therapy. **Conclusion:** Higher baseline serum qHBsAg and ALT levels are predictors of qHBsAg decline from baseline of $\geq 75\%$ for both HBeAg-positive and -negative patients undergoing ETV therapy.