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INVITED EDITORIAL

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Editorial: biomarkers in HBV and prediction of treatment response

Hepatitis B cure is clinically defined as persistently undetectable HBsAg and hepatitis B virus (HBV) DNA in serum, with or without seroconversion to hepatitis B surface antibody (anti-HBs). Several definitions of HBV cure have been proposed, based on laboratory findings.[1,2] Prediction of treatment response is a key issue in HBV management. Baseline and on-treatment predictors are needed as stopping rules, especially for pegylated interferon (Peg-IFN). Several new biomarkers such as HBV RNA, quantitative HBsAg (qHBsAg) and quantitative HBV core-related antigen (qHBcrAg) have been evaluated to predict HBeAg and HBsAg loss and relapse after cessation of nucleos(t)ide analogues (NAs).[1,2]

Lim and colleagues recently described the role of these biomarkers in predicting HBsAg loss in HBeAg-negative patients treated with Peg-IFN with or without NAs.[3] The best predictor of HBsAg loss at 72 weeks was qHBsAg <70 IU/mL at week 8 of treatment. Interestingly, baseline characteristics and other biomarkers did not predict treatment response. Also, NA treatment before inclusion in the trial, regardless of type and duration, did not influence biomarker kinetics during or after Peg-IFN treatment.[3] After relapse, qHBsAg, HBV RNA and qHBcrAg did not follow HBV DNA dynamics.[3]

These results differ with others showing the predictive value of baseline and on NA treatment biomarkers. Baseline qHBsAg and rapid decrease in qHBsAg increase the likelihood of HBeAg seroconversion.[4] In NA-treated patients, the lower the level of baseline HBsAg, the greater the likelihood for HBsAg loss.[2,5] In HBeAg-positive patients, a ≥ log IU/mL reduction in qHBsAg is associated with HBsAg loss.[2,6-8] Also, patients achieving levels of qHBsAg below 100-200 IU/mL may be candidates for discontinuation of NAs.[2,9] According to current guidelines, qHBsAg at 12 or 24 weeks of treatment is used as stopping rule in HBeAg-positive and -negative Peg IFN-treated patients.[2,10]

In this study, qHBsAg <70 IU/mL at week 8 was the strongest predictor of HBsAg loss in HBeAg-negative patients.[3] Will this be used in clinical practice? We must be cautious when interpreting these results, since this study included a selected population: HBeAg-negative patients treated long term with different NAs and then treated with Peg-IFN.[3] Other studies, specifically designed, must confirm these results.

We need predictors to add Peg-IFN to boost antiviral response (increasing HBeAg and HBsAg loss), to stop it early if futile (besides HBsAg levels at week 12 or 24 of treatment) and to stop NAs in HBeAg-positive patients with seroconversion (since 40%-50% relapse) and to stop NAs in HBeAg-negative incidences. Even if baseline and on-treatment biomarkers (HBV DNA, HBV RNA, qHBsAg and HBcrAg) show some positive results, none has a clear impact in clinical practice. There are still many doubts about how to use the biomarkers and their potential role in clinical practice. More studies like this one are needed to better understand their potential role on HBV natural history and treatment response.

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LINKED CONTENT

This article is linked to Lim et al papers. To view these articles, visit https://doi.org/10.1111/apt.16149 and https://doi.org/10.1111/apt.16226

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