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INVITED EDITORIAL

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Editorial: only steps away from primetime? Hepatitis B virus RNA as a routine marker to guide HBV treatment decisions—authors' reply

We thank Drs Wehmeyer and Schulze zur Wiesch for their interest in our paper. Their comments underlined the potential of quantitative hepatitis B viral RNA (HBV RNA) testing in the management of chronic hepatitis B virus (HBV) infection.[1,2]

They pointed out that HBV RNA measurements should be compared with other proposed predictive markers for biochemical relapse. However, while we found that the hepatitis B surface antigen (HBsAg) was significantly associated with biochemical relapse in the univariable analysis, the association was not statistically significant in the multivariable model adjusted for HBV RNA level. This suggests that HBV RNA level may be a stronger predictor than HBsAg level. This is in line with another study of Asian patients with chronic hepatitis B (CHB).[3] In patients with CHB who are treated with long-term nucleos(t)ide analogues (NA), the serum HBsAg mainly derives from the integrated HBV genome rather than covalently closed circular DNA (cccDNA),[4] while the serum HBV RNA is transcribed from cccDNA.[5] Therefore, HBV RNA may be a more direct marker for cccDNA activity. Other promising biomarkers are hepatitis B core-related antigen (HBcrAg) and serum level of antibodies against hepatitis B core protein.[6,7] However, most studies usually investigate only one biomarker in a relatively small patient population. We agree that larger heterogeneous cohorts and investigation of multiple biomarkers are needed to support guidelines.

Wehmeyer et al also noted that characterisation of NA therapy and HBV genotypes were not included in our study. More than half of the patients were treated with entecavir or tenofovir. As we stated, the specific NA was not associated with relapse. HBV genotype data was not available in most patients; this remains a limitation of our study. Since all patients were Asian, genotypes B and C are presumed to have been most prevalent.[7] A previous study suggested that HBV genotype D was associated with higher HBV RNA levels, followed by genotypes B, A and C.[8] Additionally, 71.1% of patients in our study were HBeAg-positive at the start of treatment, and 28.9% were HBeAg-negative. Among patients with biochemical relapse, 12 finally developed HBe reversion (six were HBeAg-positive and six were HBeAg-negative). No association was found between the start of treatment HBeAg status and biochemical relapse.

A recently published study underlines the utility of HBcrAg and HBsAg levels in the prediction of sustained response after NA withdrawal in a heterogenous patient population.[6] HBV RNA assay is an up-and-coming biomarker, and more laboratories are becoming experienced in its testing. Also, theoretically, it may reflect HBV "presence" better than other established biomarkers. Our study, together with several others, underlines the potential of HBV RNA assay in the management of treatment cessation.[3,9,10] We agree with Wehmeyer et al that HBV RNA assay needs to be validated in a large heterogenous cohort; thereafter, it will be ready for primetime.

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The authors' declarations of personal and financial interests are unchanged from those in the original article.[2]

LINKED CONTENT

This article is linked to Xia et al and Wehmeyer & Schulze zur Wiesch papers. To view these articles, visit https://doi.org/10.1111/apt.16538 and https://doi.org/10.1111/apt.16560

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This article is linked to Muye Xia et al and Malte H. Wehmeyer and Julian Schulze zur Wiesch papers. To view this article, visit http://doi.org/10.1111/apt.16538. The Malte H. Wehmeyer and Julian Schulze zur Wiesch paper is now under press.

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