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HEPATITIS

COMPLEXITIES OF HBV QUASISPECIES

New findings published in the *Journal of Viral Hepatitis* indicate that monitoring the dynamics of HBV quasispecies complexity during the first few weeks of antiviral therapy could enable treatment outcome to be predicted.

"We aimed to determine if the heterogeneity of HBV quasispecies—dynamic distributions of nonidentical, but closely related, viruses competing in a highly mutagenic environment—has an effect on antiviral treatment outcome, as has already been shown for HCV," explains Jan Peveling-Oberhag, from Goethe Universität, corresponding author of the study.

HBV quasispecies heterogeneity was calculated by cloning and sequencing the HBV reverse transcriptase region from 15 patients with chronic HBV who had received the low-to-moderate genetic barrier nucleoside analogues lamivudine or telbivudine for a minimum of 52 weeks.

Nine patients achieved complete virologic response (termed responders) by the study end point at 52 weeks. No difference was observed between baseline quasispecies complexity and diversity in responders and nonresponders. At week 4, however, the complexity of quasispecies was significantly higher in nonresponders versus responders at both the nucleotide ($P=0.01$) and amino acid ($P=0.04$) level. These findings indicate that HBV quasispecies complexity at week 4 of antiviral therapy with nucleoside analogues is associated with subsequent virologic response.

"A pressing issue in how best to use highly potent antiviral drugs with high genetic barriers is when continuous antiviral treatment can be stopped," states Peveling-Oberhag. Future studies on HBV quasispecies in this setting could provide helpful clues. Cost-effectiveness, however, is an important issue for future consideration. "Cloning and sequencing, as used in this study, is thought to be the gold standard for assessing quasispecies diversity, but such an intensive method might lack cost-effectiveness in clinical practice. Future methods will likely test the efficacy of next-generation sequencing in different therapeutic settings," Peveling-Oberhag concludes.

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Original article Peveling-Oberhag, J. *et al.* Dynamics of hepatitis B virus quasispecies heterogeneity and virologic response in patients receiving low-to-moderate genetic barrier nucleoside analogs. *J. Viral Hepat.* doi:10.1111/jvh.12013