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Letter: Lessons from the "real-world" entecavir therapy in chronic hepatitis B patients - authors' reply

J. Ahn[1,*], M. H. Nguyen[2], J. K. Lim[3], H. M. Lee[4], C. Q. Pan[5] and A. S. Lok[6]

[1] Division of Gastroenterology & Hepatology, Oregon Health & Science University, Portland, OR, USA

[2] Division of Gastroenterology & Hepatology, Stanford University, Stanford, CA, USA

[3] Digestive Diseases, Yale University, New Haven, CT, USA

[4] Gastroenterology/Hepatology Division, Tufts Medical Center, Boston, MA, USA

[5] Department of Medicine, NYU Langone, New York, NY, USA

[6] Division of Gastroenterology and Hepatology, University of Michigan, Ann Arbor, MI, USA

Correspondence to:

Dr Joseph Ahn – email: ahnj@ohsu.edu

To the Editor:

We appreciate the interest and comments from Drs. Liaw and Chang on our recent report on the safety and effectiveness of entecavir (ETV) in "real-world" patients with chronic hepatitis B (CHB) in the United States (US). (1,2) The comments highlighted the impact and importance of "real-world" challenges in maintaining long-term therapy in patients with CHB infection.

As they pointed out, our study had lower 3-year HBV DNA complete suppression rates and 5-year HBeAg seroconversion rates than reported in previous international studies from Argentina, Europe, and Asia. (3,4) The majority of our patients were also Asian (83%), and 61% were born outside the US. Thus, demographic or presumed transmission route differences cannot account fully for the differences in virologic outcomes from the Asian studies, though they may provide some basis for the observed differences from the Argentinian and European studies. The more likely reason for our lower response rates, as also suggested by Drs. Liaw and Chang, is the "real-world" outcomes in this US study of 26 individual sites and their associated heterogeneity in patient population, provider practices, and laboratory testing. Lower HBeAg seroconversion rates have also been reported by a number of smaller studies from the US and elsewhere. (5)

Of the four patients with cirrhosis who developed new hepatic decompensation while on ETV, 3 were alive at last follow up and one had died after being listed for liver transplantation. The relatively small number of patients with cirrhosis (n=66) limits our ability to generalize our findings regarding hepatic decompensation while on ETV therapy. Furthermore, we do not have data whether these four patients had other causes of liver disease such as alcohol or nonalcoholic steatohepatitis.

With regard to the comparison of patients who self-discontinued therapy versus those who did so by provider recommendation, reliable comparison of outcomes cannot be made as patients who self-discontinued were generally lost to follow up or lacked sufficient follow-up data due to the lack of regular monitoring. Therefore, we cannot confirm the concern that there could be

worse outcomes for those who self-discontinued ETV versus those whose ETV was stopped by their providers. However, we fully agree that maintenance of adherence to long-term treatment is critical but remains a challenge in "real-world" practice, as previously discussed in our paper. Furthermore, we concur that strategies to maintain adherence and to identify those patients who may be eligible for a "stop and watch" approach, to reduce the risk of self-discontinuation, will also be safer and critical to optimize "real-world" treatment outcomes in patients with CHB.

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

1. Chang M-L, Liaw Y-F. Letter: Lessons from the "real-world" entecavir therapy in chronic hepatitis B patients. Aliment Pharmacol Ther 2016; in press.
2. Ahn J, Lee HM, Lim JK, Pan CQ, Nguyen MH, Ray Kim W, Mannalithara A, Trinh H, Chu D, Tran T, Min A, Do S, Te H, Reddy KR, Lok AS. Entecavir safety and effectiveness in a national cohort of treatment-naïve chronic hepatitis B patients in the US- the ENUMERATE study. Aliment Pharmacol Ther. 2016; 43: 134-44.
3. Zoutendijk R, Reijnders JG, Zoulim F, et al. Virological response to entecavir is associated with a better clinical outcome in chronic hepatitis B patients with cirrhosis Gut 2013; 62:760-5.
4. Yuen MF, Seto WK, Fung J, et al. Three years of continuous entecavir therapy in treatment-naive chronic hepatitis B patients: VIRAL suppression, viral resistance, and clinical safety. Am J Gastroenterol 2011; 106: 1264–71.
5. Liu A, Ha N, Lin B, et al. Low hepatitis B envelope antigen seroconversion rate in chronic hepatitis B patients on long-term entecavir 0.5 mg daily in routine clinical practice. Eur J Gastroenterol Hepatol 2013; 25: 338-43.