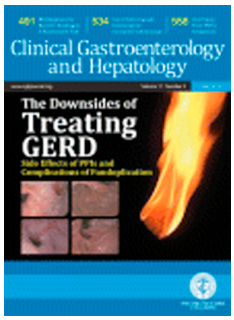
Accepted Manuscript



Occult Hepatitis B and Risk of Reactivation after Hepatitis C Treatment with Direct-Acting Antivirals-reply

Cheng Wang, Guofeng Chen, George Lau

PII: S1542-3565(16)31240-X
DOI: 10.1016/j.cgh.2016.12.016
Reference: YJCGH 55040

To appear in: *Clinical Gastroenterology and Hepatology*
Accepted Date: 20 December 2016

Please cite this article as: Wang C, Chen G, Lau G, Occult Hepatitis B and Risk of Reactivation after Hepatitis C Treatment with Direct-Acting Antivirals-reply, *Clinical Gastroenterology and Hepatology* (2017), doi: 10.1016/j.cgh.2016.12.016.

Title: Occult Hepatitis B and Risk of Reactivation after Hepatitis C Treatment with Direct-Acting Antivirals-reply

Authors:

Cheng Wang [1,2,3], Guofeng Chen[2], George Lau[2,4]

1. State Key Laboratory of Organ Failure Research, Guangdong Provincial Key Laboratory of Viral Hepatitis Research, Department of Infectious Diseases, Nanfang Hospital, Southern Medical University, Guangzhou, China

2. Beijing 302-Hong Kong Humanity and Health Hepatitis C Diagnosis and Treatment Center, Beijing, China

3. Humanity and Health Research Centre, Hong Kong SAR, China

4. Division of Gastroenterology and Hepatology, Humanity and Health Medical Centre, Hong Kong SAR, China

Corresponding author

George Lau, MBBS (HK), MRCP(UK), FHKCP, FHKAM (GI), MD(HK), FRCP (Edin, Lond), FAASLD (US)

Address: Division of Gastroenterology and Hepatology, Humanity and Health Medical Centre, Unit 2101, 21/F, No 9 Queen's Road Central, Hong Kong SAR, China

Email: gkklau@netvigator.com

Tele: 852-2861 3777

Conflict of Interest: None

Words counts-444

We read the comments by Ozaras et al with great interest[1] and would like to clarify a few issues raised on our post-marketing observational study on hepatitis due to hepatitis B virus (HBV) reactivation among Chinese with chronic hepatitis C (CHC) infection, treated with pan-oral direct-acting antivirals (DAAs) agents[2]. In our study, occult HBV infection (OBI) was defined as negative hepatitis B surface antigen but positive serum HBV DNA by nested polymerase chain reaction (PCR). To determine OBI, pre-treatment serum samples of all patients were tested by nested PCR for the pre-S/S (S), precore/core (Core), and X viral regions according to the methods previously described by our group[3]. Serum samples reactive by at least two of the three PCR assays were considered HBV DNA positive and diagnosed to have OBI. The sensitivity of this nested PCR assay was 10 copies/mL (approximately 1.8 IU/ml) as determined by serial 10-fold dilutions of cloned HBV DNA with known amount (10^8 copies/ml). There was no difference in sensitivity between S, Core, and X gene PCR. For those with OBI, serum HBV DNA levels were further quantified using the COBAS® AmpliPrep/COBAS® TaqMan® HBV Test, v2.0 (Roche Diagnostics, Branchburg, NJ), with a lower limit of detection of 6 IU/mL and a broad linear range from 20 – 1.7 x 10^8 IU/mL. Among 327 Chinese with CHC infection, 127 (40.0%) of the 317 hepatitis B surface (HBsAg) negative patients had OBI. None of the patients with OBI had quantifiable serum HBV DNA by COBAS® AmpliPrep/COBAS® TaqMan® HBV Test assay.

In our study, only those who developed hepatitis (defined as more than 2-fold increase of serum ALT on two consecutive determinations at least five days apart, from the nadir during direct-acting antiviral agents and follow-up till 12 weeks after end-of-treatment) were further tested for HBsAg and HBV DNA, from serial serum samples stored at -70^o C. Hence, not all serial samples of those with OBI was tested for HBV DNA and HBsAg. We agree that we cannot define the incidence of HBV reactivation among occult HBV infected CHC patients. In contrary to other reports that DAAs treatment can lead to hepatitis due to HBV reactivation in CHC patients with OBI, none of our patients with OBI suffered from hepatitis due to HBV reactivation[4,5]. Hence, we doubt whether there is any added value to test for HBV DNA from liver samples, which can only be obtained by invasive procedure[6]. Unlike our study which included only Chinese, all the reported cases of hepatitis due to HBV reactivation in CHC with OBI occurred in non-Chinese. It remains unclear whether host immunogenetic could be an important factor and further studies will be required to clarify this issue[7].

References

1. Ozaras R, Mete B, Tabak F. Clin Gastroenterol Hepatol. 2016 Dec 3. pii: S1542-3565(16)31129-6. doi: 10.1016/j.cgh.2016.11.030. [Epub ahead of print]
2. Wang C, Ji D, Chen J, et al. Clin Gastroenterol Hepatol. 2016 Jul 5. pii: S1542-3565(16)30370-6. doi: 10.1016/j.cgh.2016.06.023. [Epub ahead of print]
3. Hui CK, Cheung WW, Zhang HY, et al. Kinetics and risk of de novo hepatitis B infection in HBsAg-negative patients undergoing cytotoxic chemotherapy. Gastroenterology 2006;131(1):59-68.
4. Ende AR, Kim NH, Yeh MM, et al. Fulminant hepatitis B reactivation leading to liver transplantation in a patient with chronic hepatitis C treated with simeprevir and sofosbuvir: a case report. J Med Case Rep 2015;9:164.
5. Bersoff-Matcha SJ, et al. Program and abstracts of the 2016 Annual Meeting of the American Association for the Study of Liver Diseases; November 11-15, 2016; Boston, Massachusetts. Abstract LB-17.
6. Raimondo G, Allain JP, Brunetto MR, et al. Statements from the Taormina expert meeting on occult hepatitis B virus infection. J Hepatol 2008;49(4):652-7.
7. Heim MH, Bochud PY, George J. Host - hepatitis C viral interactions: The role of genetics. J Hepatol 2016;65 (1 Suppl):S22-32.