

Manuscript ID: 65599

Title: Serum hepatitis B core-related antigen as a surrogate marker of hepatitis B e antigen seroconversion in chronic hepatitis B

Journal: World Journal of Gastroenterology

Response to Reviewer's Comments

Dear Professor Lian-Sheng Ma,

Thanks so much for the response about our manuscript entitled " Serum hepatitis B core-related antigen as a surrogate marker of hepatitis B e antigen seroconversion in chronic hepatitis B", submitted for publication in World Journal of Gastroenterology.

We are grateful to the Editor and Reviewers for the sound and constructive comments. By assessing these remarks, questions, and suggestions (see the point-by-point response below), we think we have substantially improved our manuscript.

We hope the current version would fulfill your editorial requirements. Please contact me if you have further questions.

Best wishes,

Dr Niu

POINT-BY-POINT RESPONSES TO THE COMMENTS OF REVIEWER #1

Comment 1: Many abbreviations in the abstract that were not explained in the first time of being written, and even in the (core tip).

Response: We thank the Reviewer. We verified the abbreviations in the Abstract and the core tip.

Comment 2: I think the authors should add a part about the pgRNA and its relation to cccDNA, as it is an important element of the study. Also they haven't mention its full name (pregenomic RNA) before abbreviation.

Response: We thank the Reviewer for the comment. We added a statement about the relationship between cccDNA and pgRNA, and we stated the description of pgRNA in the second paragraph of Introduction.

Comment 3: Could the authors please explain, why no correlation of HBcrAg with degree of inflammation or fibrosis in liver biopsy was presented? or any data about liver biopsy presented?

Response: We thank the Reviewer. This cohort study was based on the data from two randomized controlled trials. Therefore, the patients were selected according to the inclusion and exclusion criteria of the two trials, which might contribute to selection and information biases, resulting in no correlation. Table 1 presents the data about intrahepatic cccDNA and HBV DNA.

Comment 4: Could the authors please explain the absent correlation with clinical data and laboratory markers as liver enzymes and CBC?

Response: We thank the Reviewer for the comment. The purpose of this paper was to examine the predictive role of HBcrAg among the virological indicators. The liver enzymes and CBC are the quantification of liver function; therefore, they were not analyzed.

Comment 5: Discussion should include the studies done in the same aim (presented in the comment on the references). Some references important to mention as they presented the same aim of this study (literature review on the main topic), the discussion will benefit from their results presentation • Wang, L.; Cao, X.; Wang, Z.; Gao, Y.; Deng, J.; Liu, X.; Zhuang, H. Correlation of HBcrAg with Intrahepatic Hepatitis B Virus Total DNA and Covalently Closed Circular DNA in HBeAg-Positive Chronic Hepatitis B Patients. J. Clin. Microbiol. 2019, 57. [CrossRef] • Wong, D.K.; Seto, W.K.; Cheung, K.S.; Chong, C.K.; Huang, F.Y.; Fung, J.; Lai, C.L.; Yuen, M.F. Hepatitis B virus core-related antigen as a surrogate marker for covalently closed circular DNA. Liver Int. 2017, 37, 995–1001. [CrossRef] [PubMed] • Chen, E.Q.; Feng, S.; Wang, M.L.; Liang, L.B.; Zhou, L.Y.; Du, L.Y.; Yan, L.B.; Tao, C.M.; Tang, H. Serum hepatitis B core-related antigen is a satisfactory surrogate marker of intrahepatic covalently closed circular DNA in chronic hepatitis B. Sci. Rep. 2017, 7. [CrossRef] [PubMed]

Response: We thank the Reviewer for the references. We incorporated them to the second paragraph of the Discussion.

POINT-BY-POINT RESPONSES TO THE COMMENTS OF REVIEWER #2

Comment 1: All included patients with HBV are genotyp C and B, therefore study should be evaluated in the other genotype such as D.

Response: We thank the Reviewer for this fair comment. We agree that the study could benefit from a wider selection of patients. Unfortunately, HBV D is very rare in China and they were not included in the two randomized controlled trials that provided the data for the present study. Additional studies are necessary to examine this issue. It was added as a limitation.

POINT-BY-POINT RESPONSES TO THE COMMENTS OF EDITOR

Comment 1: Issues raised: (1) The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s).

Response: We are providing the document with this revision.

Comment 2: The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.

Response: We are now providing the original pictures.

Comment 3: The “Article Highlights” section is missing. Please add the “Article Highlights” section at the end of the main text.

Response: We now provide the Highlights.