Feb 20, 2017

Dear Jing Yu,
Science Editor, World Journal of Gastroenterology

Thank you for your consideration of the manuscript entitled "**The safety and efficacy of Tenofovir in chronic hepatitis B-related decompensated cirrhosis"** for the publication in ***World Journal of Gastroenterology***.
We have carefully considered the suggestions by the reviewers. We fully agree with the opinions of the reviewers and have revised the manuscript accordingly. The responses to the reviewers are appended by point-to-point in the revised version and we hope that our explanations and revisions are satisfactory. Point-to-point answers are provided from the next page of this cover letter.

Point-by-Point Response to Reviewer I

1 Suggestion to express accurately: such as: "The 1-year complete virological response (CVR) and Hepatitis B e Antigen (HBeAg) seroconversion were seen in 70.2% (40/57) and 14.2% (14/28), respectively" in the Abstract should be described as "The 1-year complete virological response (CVR) and Hepatitis B e Antigen (HBeAg) seroconversion were seen in 70.2% and 14.2% in the decompensated cirrhosis group, respectively" more relevantly. "Chronic hepatitis B (CHB) infection" on the first line should be revised "Chronic hepatitis B virus (HBV) infection" better. The unit of measurement of "Albumin" in the Table 1 should be expressed. In title "Virological, biochemical and serological and responses", the word "and" should be removed.

➔ As you comment, we revised our manuscript.

2 The confounders of logistic regression analyses are not very appropriate.

➔ As you comment, we revised a statistical analysis by reclassifying the

confounders as continuous variables including age, ALT, and baseline HBV DNA.

Point-by-Point Response to Reviewer II

In the present manuscript the authors illustrated focus on when to treat, when to monitor, what patients should receive HBV therapy, and what drugs should be selected in HBV reactivations in cases of iatrogenic or natural IS. Although the information has been shown in some articles, the new developments in recent years are still not systemically reviewed. However, the article needs some minor correction before being published.

1. Patients disposition: as for all retrospective studies, a patient disposition figure is mandatory. How many treatment-naive patients with CHB-related cirrhosis were diagnosed between January 2013 to January 2014 and how many patients were on oral therapy and discontinued treatment. Or how many patients stopped oral therapy between 2013 and 2014?

➔ As you comment, we added a patient disposition figure in revision.

2. The upper limit of normal of ALT is defined as 40 IU/L in the present manuscript whatever the patient is male or female. But I suggest ULN of ALT is defined as 30 IU/L and 19 IU/L for male and female.

➔ We fully understand your comment. As the normal range of our laboratory department is 40 IU/L, we analyzed the cut off level of ALT normalization (40 IU/L). According to the change of ULN of ALT, ALT normalization status is significantly lower compared with previous normal ALT level (for example, ALT normalization at week 48 in total study group showed 33.3%). Therefore, we think the ULN of ALT is defined as 40 IU/L in this study.

3. There are some spelling and grammar mistakes need to be corrected before being published

➔ As you comment, we revised grammar and mistakes.

Point-by-Point Response to Reviewer III

The study investigated the Safety and efficacy of tenofovir in chronic hepatitis B-related decompensated cirrhosis and compared with compensated cirrhosis. The paper was well-written with good design and appropriate statistic method. But there are several limitations. 1.This is a retrospective study. 2.The case number is small. 3.Besides the tenofovir, the author should describe if the patients have taken any other treatments during follow-up period.

➔ As you comment, we revised the several limitations in the discussion paragraph. (See page 12, line 28-29, in revision)

➔ We added the sentence as follows; "All patients did not take any other antiviral agent except tenofovir during follow-up period." (See page 7, line5-6 in revision)

Point-by-Point Response to Reviewer IV

This is a nice retrospective study that reassures physicians with regard to the efficacy and renal safety of TDF in (Korean) patients with HBV-related cirrhosis. I have a few questions and comments –

1. Were there any decompensation events in either of the groups during the duration of the study?

➔ We fully understand your comment. In this study, there was decompensated event such as ascites in decompensated group. There was no decompensated events in compensated cirrhosis group.

2. Of the few patients who had a documented drop in GFR, did any have identifiable renal risk factors such as hypertension, diabetes, bacterial infections, or concomitant

use of nephrotoxic medications?

➔ We understand your comment. In few patients who had a documented drop in eGFR, we could not find significant identifiable renal risk factors. But we think that diabetes may be a renal risk factor in these patients.

3. Was Fanconi syndrome ruled out in patients with significant renal dysfunction on treatment?

➔ Yes, in this study, there was no Fanconi syndrome in patients with renal dysfunction on treatment.

4. on line 10 of the Result Section, the authors state that "The decompensated group had lower CTP and MELD scores" - it should state "higher".

➔ As, you comment, we revised the sentence.

Point-by-Point Response to Reviewer V

Overall, this is a clear and well-written manuscript. The introduction is relevant and theory based. The methods are appropriate and the results are clear. The authors make contribution to the research literature in this area of investigation.

➔ Thank you for your comments.

Our findings of treatment efficacy and safety in tenofovir therapy in chronic hepatitis B-related decompensated cirrhosis are worthy of publication in the ***World Journal of Gastroenterology***

We thank you for your time and efforts in dealing with our manuscript.

Sincerely yours,
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