

October 23rd, 2013

Dear Editor,

Please find the enclosed edited manuscript in Word Format (file 5552-review.doc)

Title: Then and Now: The Progress in Hepatitis B Treatment over the Past 20 years

Author: Dina Haleboua-DeMarzio, MD, Hie-Won Hann, MD

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 5552

The manuscript has been improved according to the suggestions of reviewers:

1. Format has been updated including the reference section
2. Revision has been made according to the suggestions of the reviewers

Reviewer #1

Comments:

1) It is stated in abstract that the ultimate goal of HBV treatment is HCC prevention. However, as the major guidelines point, prevention of disease progression, hepatic decompensation and improvement of patients QOL are major goals of the therapy and should be included in the manuscript.

- We agree with the reviewer and have modified this comment.

2) Section of "Progression of Hepatitis B treatment", second paragraph 5th line: Serial ALT and HBV-DNA monitoring every 3 months for 1 year...It should be discussed that this attitude is also useful to differentiate chronic active HBeAg negative hepatitis from inactive carriers in recently diagnosed HBV carriers.

- Noted and added to that section

3) Safety issues about potential bone and renal toxicity by nucleotide analogues are missing.

- A paragraph has been added to address these issues before the conclusion section

4) Effectiveness of modern analogues on decompensated cirrhosis are lacking. A discussion on potential benefit of modern analogues administration on the rate of liver transplantation should be added.

- This information has been noted and added to the conclusion

5) Discussion on the prevention of mother to child transmission by telbivudine should be discussed.

- Great Suggestion. This has been added to telbivudine section.

6) Reference 88 is a retrospective analysis of a database, limitations of these results should be stated.

- Noted in that section as requested

7) Risk of HCC development significantly lowers but not disappears with HBV-DNA suppression. Please, discuss potential mechanisms of HCC risk persistence.

- The mechanism of this is unclear and discussed under carcinogenesis in the manuscript.

8) Use of tables summarizing relevant information may improved readability of the MS.

- One figure and one table added in addition to the already present figure.

Minor Comments: 1) Abbreviation for Telbivudine should be LdT instead of TLV, which may be confused with telaprevir.—CHANGED 2) Truvda (Truvada) on p.17---CHANGED

Reviewer 2:

All suggestions added to manuscript.

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

Dina Halegoua-DeMarzio, MD
Hie-Won Hann, M.D.
1025 Walnut Street
Philadelphia, PA, 19107, USA
Email: dina.halegoua@gmail.com
hie-won.hann@jefferson.edu