

October 2, 2013

Dear Editor,

Please find enclosed our revised manuscript in Word format (file name: 5525-review.doc).

Title: Hepatitis B surface antigen seroconversion after HBV reactivation in non-Hodgkin's lymphoma

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Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 5525

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

1. The format has been updated
2. Revisions have been made according to the suggestions of the reviewers

Reviewer NO.00053556:

(1) INTRODUCTION:

It is short & informative.

In order to satisfy the reader, more details are advised to be added regarding Rituximab as an anti-CD20 monoclonal antibody that is successfully used in treatment of NHL and how, it may affect the immunity against HBV and thus increasing viral replication.

Response:

In the revised Introduction, we emphasized the effect of rituximab on the outcome of patients with NHL and added the hypothesis of HBV reactivation following rituximab-based treatment on page 5.

(2) CASE REPORT: Well presented however, the duration of the following is better to be clarified:

ETV treatment

ETV continuation after HBsAg seroconversion

Monitoring the sustained suppression of HBV DNA to ensure full recovery

Response:

In our revised Case Report, we added information as to the time of ETV initiation, the time of HBsAg clearance, the time of HBsAg seroconversion, and the duration of ETV therapy, which help to clarify the relationship between HBV recovery and ETV treatment.

Figure1 & 2: informative and descriptive, however, legends have to be written at the bottom of each figure.

Response:

We appreciate the reviewer's suggestion. Legends have been added at the bottom in the new figures (Figure 1 and Figure 2).

(3) DISCUSSION

Well organized, an overall theoretical analysis is given and conclusions are scientifically valuable. However, it is advisable to emphasize the optimal median duration of ETV therapy and HBV DNA monitoring after discontinuation of ETV in such group of patients.

Response:

In the Discussion of the revised manuscript, we discuss the optimal duration of ETV therapy and emphasize the significance of routine HBV DNA monitoring after discontinuation of ETV in our group of patients on page 8.

Third paragraph: 24,829 person-years of evaluation is better to be written as 24,829 person-years of follow-up

evaluation

Response:

Thank you for the reviewer's suggestion. The description of "24,829 person-years of evaluation" was revised to "24,829 person-years of **follow-up** evaluation" in the third paragraph.

(4) REFERENCES:

Finally, relevant and sufficient references, especially the most current literatures have been cited; 26/28 references were cited from publications within the last five years (≥ 2008);

The authors have to follow journal style in writing this section

Response:

In the revised Reference section, we reformatted the references according to the style of the Journal.

Reviewer NO.00502973:

(1) In "Case Report", the 2nd paragraph: I cannot understand the meaning of "No treatment with anticancer drugs or corticosteroid followed." Does the author mean that no other anti-cancer therapy or corticosteroid was adopted thereafter?

Response:

Yes, in accordance with the NCCN clinical practice guidelines for non-Hodgkin's lymphomas (http://www.nccn.org/professionals/physician_gls/f_guidelines.asp#nhl), the patient was observed without any additional anti-cancer therapy or corticosteroid treatment thereafter.

(2) In "Other reported cases in the literature", the 1st paragraph: I would suggest to change "...although there is limited experience[6]. However, there are few published studies examining the use of ETV for the treatment of HBV reactivation in lymphoma patients, despite data suggesting it is effective and safe[7-9]." to "...although experience is limited[6]. Several studies examined the use of ETV in the treatment of HBV reactivation in lymphoma patients suggestive of its effectiveness and safety[7-9]." Also in this paragraph, I would suggest to change "LAM prophylaxis was administered to prevent HBV reactivation in four cases from two different studies[7,14], among whom the three patients reported by Mimura, et al[14] developed HBV reactivation-related hepatitis 2-4 months after LAM cessation. One case of HBV reactivation occurred 8 months after cessation of LAM treatment in the report by Brost, et al[7]." to "LAM prophylaxis was administered to prevent HBV reactivation in four cases from two different studies[7,14], three of them[14] developed HBV reactivation-related hepatitis 2-4 months after LAM cessation. The remaining case of HBV reactivation occurred 8 months after cessation of LAM treatment[7]."

Response:

Thank you for the reviewer's suggestion. We have rewritten the paragraph in accordance with the recommendations mentioned above.

(3) In "Discussion", the 1st paragraph: I would change "However, HBV infection is associated with lymphoma and also hepatocellular carcinoma[20]." to "HBV infection is associated with lymphoma and hepatocellular carcinoma[20]."

Response:

Thank you for the reviewer's suggestion. We have changed the sentence as suggested.

(4) In "Discussion", the 2nd paragraph: The author stated "The rate of HBV reactivation after LAM withdrawal and the incidence of YMDD mutation in NHL patients have been reported to be 4% and 17%, respectively, ..."The YMDD mutation rate is increased upon the extension of LAM treatment. The author should clarify the duration of LAM application to reach a 17% YMDD mutation rate.

Response:

We have added the missing information as "17% of HBsAg-positive NHL patients developed YMDD mutation during LAM therapy (median duration: 11.5 months)".

Reviewer NO.01800545:

Thank you for your review.

Reviewer NO.01799105:

Thank you for your review.

3. References and typesetting have been corrected

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

Sincerely yours,

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