

December 16, 2013

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 6742-edited.doc).

**Title:** Optimization therapy for the treatment of chronic hepatitis B

**Author:** En-Qiang Chen, Hong Tang

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 6742

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

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

- (1) Review 1 (comment 1) noted that the subtitle under point 2.2 of primary manuscript should be changed. In our revised manuscript, it has been replaced by "Why optimization therapy should be considered?".
- (2) Review 1 (comment 2) noted some grammar errors in our manuscript. Thanks for this advice. The language of our manuscript had been edited by an English native speaker, and we believed those grammar errors had been corrected.
- (3) Review 1 (comment 3) want to know why HBsAg reponse was not focused instead of HBeAg response. Thanks for this professionally question. As we know, HBsAg loss or HBsAg/Anti-HBs seroconversion is very rare in real clinical practice, either in Nucleos (t) ide analogues or in interferon treated patients. So, to make this mini-review more readable and more practical, more attention was paid to HBeAg and HBV DNA.
- (4) Review 1 (comment 4) suggest us to add a flow chart to incorporate the major points in the optimization of personalized treatment of CHB. Thanks for this good advice. Considering the data of optimization therapy is still limited at present, and many views still lack strong evidence to support. So in this review, it is difficult for us to add a persuasive flow chart to guide optimization therapy according to current available clinical data. If possible, we would like to update this review several years later, and summariz a detailed and reliable flow chart to our clinicians.
- (5) Review 1 (comment 5) suggested us to provide evidence whether HBV DNA had been found to be an important predictor of other antiviral agents. In our revised manuscript, corresponding references had been added (reference 25-27).
- (6) Review 1 (comment 6) noted that he disagreed with recommendation of LAM as first line therapy of those CHB patients with HBV DNA<6.6 log 10 copies/mL. Thanks for

this comment. To a certain extent, we agreed with this comment. As we know, the efficacy of antiviral therapy was affected by many factors, and factors of host, viral and antiviral agents all influenced final responses of therapy. So, to make our suggestion more objective, we add following sentence "However, further studies are still needed to confirm that the baseline HBV DNA level of 6.6 log<sub>10</sub> copies/mL could be used as an ideal cutoff value in selecting the LAM initial treatment" in our revised manuscript.

- (7) Review 1 (comment 7) suggested us to add a reference for "rapidly decreasing HBV DNA to undetectable levels is significantly associated...". Thanks for this advice. Corresponding reference had been added in our revised manuscript (Reference 33 and 34).
- (8) Review 2 (comment 1) suggested us to add information on Tenofovir to make our review more comprehensive. Thanks for this kind suggestion. In our revised manuscript, related data of tenofovir had been added.
- (9) Review 2 (comment 2) noted that it would be more readable if a table of the response data and resistance rate of each treatment could be included. Thanks for this kind advice. Optimization therapy for CHB was a new treatment strategy, and the clinical data of this new treatment strategy was limited, which was not like combination therapy for HBV resistance (having lots of clinical data). So, in our revised manuscript, we finally gave up to add such a table. If possible, we would like to add a corresponding table in the up-date version of this review when there were lots of clinical data available.
- (10) Review 2 (comment 3) suggested us to revise the description of some sentences. Thanks for this advice. The language of our manuscript had been edited by an English native speaker, and we believed those issues had been resolved in our revised manuscript.
- (11) Review 3 (comment 1) suggested us to revise the language of our manuscript. Thanks for this advice. The language of our manuscript had been edited by an English native speaker.
- (12) Review 3 (comment 2) noted that the status of HBeAg also should be concerned for the considering of optimization therapy. We agree with this suggestion. In our revised manuscript, we have added corresponding clinical data. For example, we noted that ADV could be considered for HBeAg-negative patients with low baseline HBV DNA

3 References and typesetting were corrected

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

Sincerely yours,



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