

# World Journal of Hepatology Manuscript NO: 81652 – Manuscript requires a revision

## **Responses to reviewers' comments**

Thanks a lot for providing us the chance for correcting our review entitled “*Current and Novel Modalities for Management of Chronic Hepatitis B Infection*”.

We highly appreciate the editor and the reviewers for their constructive comments and suggestions on our review. We have gone through the entire review again accordingly. We made red color changes to the original version during revision. The main corrections in the paper and our responses to the reviewer's comments are as follows:

*Responds to the reviewers' comments:*

### **Reviewer #1:**

There are no reference form the authors regarding the new treatments in this review, The organization of the article could have been more logic.

The manuscript was reorganized as requested. All modifications were written in red colour.

### **Reviewer #2:**

Title reflects the main subject/hypothesis of the manuscript. The manuscript interpret the findings adequately and appropriately, highlighting the key points concisely, clearly and logically. The findings and their applicability/relevance to the literature are stated in a clear and definite manner. The discussion is accurate and it discusses the paper's scientific significance and/or relevance to clinical practice sufficiently.

Thank You.

### **Reviewer #3:**

Hepatitis B virus infection is a major public health problem facing the world today. Chronic hepatitis B virus infection can cause chronic hepatitis, liver failure, cirrhosis and liver cancer. At present, there are two main types of drugs used in clinical treatment of chronic hepatitis B virus infection, including nucleos(t)ide analogues and IFN- $\alpha$  and Peg-IFN, but none of them can effectively remove the virus and cure chronic hepatitis B. It is a challenge for the medical community to completely eliminate hepatitis B virus infection. Chronic HBV infection is the result of the interaction between the virus and the host. The unique replication mode of HBV

plays a key role in the establishment and maintenance of continuous infection in hepatocytes. This manuscript expounds the current research progress of curing hepatitis B virus infection from the aspects of virus and host factors.

Thank you.

**Reviewer #4:**

This is a review that explains the current novelty in chronic HBV infection treatment. It mainly highlights the preclinical basis and mechanism of HBV drugs that are under investigation. There are some typos and English mistakes that should be corrected. I have only one commentary: in “author contribution” you state that some authors are responsible for HAV, HCV, HDV and HEV writing, but these topics are not present in the review. I think it is a mistake.

Authors' contribution was revised.

**Reviewer #5:**

The manuscript, submitted for publication by Salama et al., is a review article focused on treatment of chronic hepatitis B infection, as well as emphasized new treatment modalities. They have underlined new specific molecular treatments promising a new era for CHB. This paper can be used to guide the use of these new treatments and guide physicians in terms of further studies. However, there are some issues and questions that should be addressed in the study.

1- There are reviews quite a lot on this topic on this topic (doi: 10.3389/fmicb.2022.975584 , doi: 10.3390/ph14050417). In fact, recently published reviews contain almost the same information. The authors should clarify the aim of this study and difference from other reviews

Thank you. Done. Page 3.

2- I recommend using more up-to-date data when giving epidemiologic data about prevalence and incidence for hepatitis B infection.

Thank you. Done. Page 2.

3- Headlines and subheadings related to treatment modalities and new developments can be better organized.

Thank you. Done.

4- Please explain the particles associated with the HBV and their functions at the cellular level in more detail.

Thank you. Done. Pages 4 and 5.

All the molecular-based information should be collected under the introduction part all together or the subheadings related to the specific treatment.

Thank you. Done.

5- Authors could make more table and figure to explain better your points. I suggest improving the presentation and quality of figure and table. (Please summarize CHB treatments in tables for easy reading experience).

Thank you. Done. Table (1&2) in addition to Fig 1.

6- The discussion section is scarce, and they do not sufficiently highlight the originality and the significant contributions of the study. Therefore, they need to be rearranged.

Thank you. Done. All added parts are written in red color.

7- As an output of the study, what is the most recommending/promising therapy for CHB between all new treatments?

Thank you. We added in a section of combination of therapy. Pages 23 and 24.

Please define which treatment modalities is better for which patient group in detailed (please categorize specific treatments according to their side effects or benefits for specific patient groups, e.g. adults/children.)

Thank you. Done. Table (1).

8-The English language used throughout the manuscript needs some improvements in terms of style and grammar (for example Please rephrase this headline “Intoduction” and please spellcheck all text carefully)

Thank you. Language was revised.

9- Specify abbreviations where they are first mentioned in the text carefully.

Thank you. Done and List of abbreviation was added before reference section.