

Dear Esteemed Reviewers,

Thank you very much for your thoughtful comments. They have indeed been useful in finetuning our manuscript and increasing its scientific value. We have included our replies as follows.

Reviewer #1: This study presents a literature review of data regarding management of patients with isolated hepatitis B core antibody receiving immunosuppression. Whilst the review is well presented, a number of amendments could be made to increase the clarity and quality of the manuscript. Suggestions:

- HBV literature is confounded by confusion regarding terminology, as the authors note. However, although it is stated that the AASLD terms will be used, the title includes "previous hepatitis B exposure" which is not one of the AASLD definitions. The title may benefit from using serological definitions i.e. hepatitis B surface antigen negative, core antibody positive
- The abstract does not state the type of study performed, nor the aim of the study
- No keywords were listed
- In the introduction the term serological clearance needs to be defined
- No methods for how the review was performed are described (were PRISMA guidelines followed, was this a narrative synthesis?)
- Summary of the data in a table with a treatment algorithm (definitely treat / consider treating / do not treat) would be helpful for clinicians
- Discussions regarding cost efficacy should be separate from the medical evidence about reactivation. Now that entecavir is off patent, is cost less of an issue? were the studies conducted when it was still patented?
- The authors need to outline how their data contributes to the pre existing guidelines, including Perrillo (Gastroenterology 2015)
- Guidelines have recently been published in Australia, they are attached below.

Thank you very much for your detailed suggestions. We have changed the title to make it more consistent with the AASLD definition, included keywords, and expounded further on the type and aims of this narrative review. We believe that our manuscripts would help synthesize the large amount of literature available on this topic to help fellow clinicians manage such patients better. Entecavir remains patented in various parts of the world, including Singapore. Cost unfortunately remains a major issue in these parts of the world, and our manuscript aims to help fellow clinicians make a clinically sound and cost-effective treatment decision.

Reviewer #2: The review is good, interesting. Two major points must be underlined:

- The lack of helpful diagrams or "take home" messages. For example, a table targeting the treatments associated with risks and which corresponding strategy is the best...
- The lack of originality: reviews were performed concerning the subjects. There are no important difference (maybe the immune treatment.) with them.

Thank you very much for your comments. Our review article aims to synthesize the vast amount of available knowledge in this field to help clinicians make a treatment decision. All patients with previous Hepatitis B exposure in Hepatitis B endemic countries must be assessed for risk of Hepatitis B reactivation. We have incorporated your suggestions in the latest edition of our manuscript.

Reviewer #3: In this manuscript, Clement Chun-Ho Wu et al performed a review of the literature pertaining to screening, treatment and follow-up strategies in patients with previous Hepatitis B exposure who are planned for immunosuppression. This review is detailed, and it will be helpful for the treatment of HBV reactivation prevention in immunosuppressed patients with previous HBV exposure.

Thank you very much for your kind comments. It is our hope that our manuscript will help clinicians make a clinically sound and cost-effective treatment decision to attenuate Hepatitis B reactivation risk in patients who are HBsAg-negative and anti-HBc positive.

Reviewer #4: In this review, the authors mainly reviewed the risk factors and management of HBV reactivation in immunosuppressed patients. Compared with the published reviews (1.Semin Liver Dis. 2013 ay;33(2):167-77. doi: 10.1055/s-0033-1345722. 2. World J Gastroenterol. 2011 Mar 28;17(12):1531-7. 3. World J Gastroenterol. 2016 Jul 28;22(28):6484-500.), there are not many updates on the content. Furthermore, there are still some conceptual problems in the text, such as: in introduction part: "HBV is a common disease.." "HBV cccDNA persist in host genome"...

Thank you very much for your detailed suggestions. We have incorporated your suggestions in our manuscript. HBV is a common infection, and HBV cccDNA persists in the host hepatocyte nucleus.

Reviewer #5: This is a nice review. However, it is advisable to include a few diagrams for clarity. like a flow chart to handle reactivation.

Thank you for your kind comments. We have added in a flowchart to aid our readers.

Yours Faithfully,

Clement Chun-Ho Wu and Rajneesh Kumar