Nov 23, 2023
Name of journal: *World Journal of Virology (WJV)*
Manuscript NO.: 88487
Title: **Hepatitis B virus (HBV) reactivation in patients treated with monoclonal antibodies**

Dear Editor-in-Chief of WJV,

I would like to extend my gratitude for the efforts and time spent reviewing the submission. The Reviewer makes excellent points and offer valuable suggestions to improve the manuscript. **Please find the responses in bold font under each of the comments made by the reviewer below, which can also be found in red font in the revised manuscript:**

Reviewer 1 (*number ID: 04382733)*

Dear authors, The article is well-written, there are a few minor orthographical problems and it should be revised. It appears appropriate as a mini-review, as it does not provide detailed data. Still a table or a figure summarizing recommendations and/or studies on the subject would be interesting.

Many thanks for the positive comment about our paper. The paper has been edited and corrected by a native English doctor. We have included a table, as suggested.

Table 1: Current literature

Author	Year	Type of Study	Conclusions
Baldo BA	2022	Review	Warning of adverse liver reactions after the initiation of mAbs. mAbs that are at high risk of HBV reactivation, TNF-α inhibitors are at moderate risk.
Evens AM	2011	Meta-Analysis	118 cases were reported to the US FDA in which rituximab was associated with HBV reactivation.
Dusheiko G	2023	Review	B-cell–depleting therapy with rituximab highlights the contribution of memory B cells to HBV control.
Nathan D	2006	Review	TNF inhibits hepatitis viral replication and stimulates HBV-specific T-cell responses to clear the virus from infected hepatocytes. TNF could cause increased expression of hepatitis B viral antigens.
Megna M	2022	Prospective cohort study	Highlights the risk of HBV reactivation in patients with latent infection treated with Secukinumab without prophylaxis
Chiu H-Y	2018	Multicenter Study	Without antiviral prophylaxis, 7 of 46 (15.2%) patients with HBV exhibited viral reactivation during therapy with secukinumab.
Chiu H-Y	2013	Clinical Trial	Among 11 patients positive for hepatitis B surface antigen (HBsAg), two out of the seven (29%) patients who did not receive antiviral prophylaxis exhibited HBV reactivation.
Ting S-W	2018	Prospective cohort study	Among the remaining 54 patients classified as inactive HBV carriers, resolved HBV infection, or isolated anti-HBc positivity, only 3 patients experienced virologic reactivation.

The valuable comments and assistance with the manuscript are greatly appreciated. I look forward to your final decision regarding our modifications, with the hopes that all concernshave been addressed appropriately.

Kind regards,
Marco Zeppieri

December 18, 2023
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Manuscript NO.: 88487
Title: **Hepatitis B virus (HBV) reactivation in patients treated with monoclonal antibodies**

Dear Editor-in-Chief of WJV,

I would like to extend my gratitude for the efforts and time spent reviewing the submission. The Editors makes excellent points and offer valuable suggestions to improve the manuscript. **Please find the responses in bold font under each of the comments made by the reviewer below, which can also be found with track changes in the revised manuscript:**

Executive Associate Editor-in-Chief (Dr. Yu-Chen Fan 05560823)

Please revise according to the journal chief editor's opinion, and don't forget to reply to the chief editor peer-to-peer.
Comment: 1. The minireview explores the complex relationship between monoclonal antibody therapy and HBV reactivation, drawing upon current literature and clinical case studies. It delves into the mechanisms underlying this phenomenon, highlighting the importance of risk assessment, monitoring, and prophylactic measures for patients at risk. The review was overall well organized and written.

Many thanks for the positive comments about our paper.

Executive Associate Editor-in-Chief (Dr.Shuai Gao 07821547)

3. In this manuscript, the authors briefly explored the complex relationship between monoclonal antibody therapy and HBV reactivation, drawing upon current literature and clinical case studies. Overall, the manuscript is well prepared. The reviews' comments have also been answered properly.

We are grateful for the efforts and comments by the Executive Associate Editor-in-Chief.

Editorial Board (Dr. Mina T Kelleni 05431771)

2. The manuscript must be edited by an academic professional, as the native English doctor who assisted you has used informal language that is not acceptable for publication in this Journal. For examples phrases like "we remember", and "we talk" should be revised. In some cases, this has even led to scientific errors such as the mention of "liver decompensation and even liver failure" The manuscript should be checked for similarities with other previously published ones to ensure that this is kept to the minimum. The iTheticate report identified significant sections that need to be rewritten.

The text has been thoroughly checked and modified to enhance the scientific quality of the manuscript, improve the formality of the writing style, and reduce the similarity index, as requested. All specific comments mentioned have been modified accordingly. Further modifications can be made upon request, if needed.

The role of each author must be explicitly stated especially for those who specialize in medical subjects unrelated to the topic being reviewed.

The following modifications have been made to describe the author contribution:
"Author contributions: Grando M, De Pauli S and Zeppieri M wrote the outline; Grando M and De Pauli S did the research and writing of the manuscript together as co-authors; Grando M, De Pauli S, Miotti G, and Zeppieri M assisted in the writing of the paper; Zeppieri M was responsible for the conception and design of the study and completed the English and scientific editing; Grando M, De Pauli S, Miotti G and Zeppieri M assisted in the editing and making critical revisions of the manuscript. Although authors are from different areas of

specialization, all authors provided general information and details regarding Hepatitis B virus reactivation based on the literature review. Each author participated in the research and writing of the paper, even if not directly pertinent to the area of study, considering the multidisciplinary approach in managing these patients. All authors provided the final approval of the article."

Certain scientific data should be presented more effectively. For example, the phrase "reverse HBsAg seroconversion OR reappearance of HBsAg", there's no "OR", they're the same thing. Similarly, the sentence "any dose corticosteroid therapy lasting less than a week" needs to be refined in language and its cited paper doesn't support "any dose". Numerous other papers argue against the inclusion of very high doses of corticosteroids.

The specific sections mentioned here have been modified and/or deleted accordingly to address the issues raised.

In the conclusion, the statement "we still can't accurately assess the risk of a new class of drugs prior to its clinical application" is scientifically inaccurate and there's nothing in the discussion that supports it.

In accordance with the suggestion made, this sentence has been deleted.

Lastly, a section explaining the updates regarding the mechanisms of HBV reactivation should be added to enrich the discussion.

The following section has been added in the Discussion section regarding possible updates in this field of research:

"Future and ongoing research on the reactivation of the hepatitis B virus (HBV) must evaluate the complexity of this illness. The risk of HBV reactivation can be associated with immunosuppressive therapy and reactivation. These drugs include those used to treat autoimmune illnesses, organ transplants, and specific types of cancer. Research may look into how these treatments impact the host immune system and help latent HBV reactivate. Molecular processes and viral components may also be significant. One of the main areas of research is understanding the molecular processes of HBV reactivation. This entails investigating how the virus endures in the liver and how certain circumstances can cause it to reactivate.

Innovative studies might concentrate on factors related to viruses, like modifications in the expression of viral genes, mutations, or adjustments in the life cycle of the virus that support reactivation. Genetic predisposition and host variables may also be significant. Studies may look at host variables that make people more vulnerable to HBV reactivation. This includes genetic variants that could impact the virus's ability to withstand immunological responses or maintain viral latency. Predicting which individuals are more likely to experience reactivation can be aided by identifying particular host variables. Antiviral prophylaxis, timing of therapies, and monitoring techniques are all part of clinical care and prevention. There is also continuing research being done on the creation and assessment of preventive interventions such immunization and antiviral medications."

The valuable comments and assistance with the manuscript are greatly appreciated. I look forward to your final decision regarding our modifications, with the hopes that all concernshave been addressed appropriately.

Kind regards,
Marco Zeppieri