Peer Review File

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Review comments

The authors present an article entitled "Management of Autoimmune and Viral Hepatitis in the Setting of Immunotherapy" which aims to provide a narrative review of how immunotherapy treatments based on immune checkpoint inhibitors (ICI) influence the management, evolution and prognosis of autoimmune and viral liver diseases. The article is written in an orderly and well-structured manner that makes it easy to read, and it is also a very new topic on which there is not much information in the literature. Therefore, congratulations to the authors for the topic they chose to review, as it provides a new vision of a problem that is difficult to manage in clinical practice. I believe that the article could be very well received in the journal and therefore if several major and minor changes are made to the article I believe, from my point of view, that the article could be acceptable for publication.

The main problem I have found with the review is that it needs modification at certain points because it does not include all immunotherapy treatments for hepatocellular carcinoma (HCC) globally. It is likely that when the authors wrote the review the combination immunotherapy with Tremelimumab-Durvalumab (HIMALAYA Trial) had not yet been approved, however, it is essential that the review is done with the data provided by this new first-line therapy in HCC. Furthermore, the *Immune Checkpoint Inhibitors* section (line 78) does not include, for example, anti-LAG3 antibodies, whose molecule Relatlimab has already been approved for the treatment of metastatic melanoma by both the FDA and the EMA. Therefore, ICI in clinical practice go beyond PD-1, PD-L1 and CTLA-4 and this would also be important to update.

Regardless of the above problem, with the need for an update of the article, as I have already indicated the article is otherwise well structured, well written and the language is correct and, in my opinion, does not need any further changes. The objective set by the authors is clear and this is answered throughout the article, and the conclusion is very accurate, answering the questions that one thinks about while reading the manuscript. The figures and tables need some modification, but in general terms they are a good value of the article and are a welcome addition to the reading. The bibliographical references used are those that exist on the subject and except for a couple that are added below, and which would be convenient to include, all are up to date and deal well with the subject matter.

The changes I suggest for the article are as follows:

- Major changes

- Article update: as previously stated, it would be important to include data from the HIMALAYA Trial on the Durvalumab-Tremelimumab combination in first line (Abou-Alfa GK et al, *N Engl J Med*, 2022).
  HIMALAYA trial data included (lines 376-386)
- Discussion: there is no discussion section as such for the article. In this case, the previous data could be brought together, and an algorithm could be proposed for clinical practice on how to screen patients for these liver diseases and what the follow-up could be like. Also, a figure could be made on this point that would be of great interest to readers and the scientific community.
  Discussion added (lines 479-496). Additional figure added (Figure 5)

- Minor changes

- Title: include in the title that it is a narrative review.
  Included
- Keywords: add "immune checkpoint inhibitors".
  Added (lines 33-34)
- It would be useful to make a list of abbreviations given the large number of them in the article.
  Table created
- *Immune Checkpoint Inhibitors* section (line 78): as previously indicated, anti-LAG3 antibodies (Relatlimab) should be added.
  Added (line 74)
- Line 101: The first approval of ICI, which was Ipilimumab in melanoma, is rightly indicated at this point. However, given the importance of anti-PD1 antibodies compared to the rest, I think it would also be interesting to add some information on the first approval of an anti-PD1 antibody by the FDA, which was Pembrolizumab for metastatic melanoma in September 2014.
  Added (lines 94-99)
- Line 118: indicate that infusional reactions are very infrequent with this type of drug.
  Edited (new line 110)
- Line 161 paragraph: it would be very interesting to make a summary table on hepatotoxicity found in the main clinical trials conducted with ICI in HCC (CheckMate 040, KEYNOTE-224, IMbrave150 or HIMALAYA).
  Summary table created (Table 4)
- Line 292: the reference in Figure 2 is wrong. It is Figure 3.
  Edited
- Line 316: it would be useful to add some data on the following article that may be of interest to the review (Yoo S, et al. Risk of Hepatitis B Virus Reactivation in Patients Treated With Immunotherapy for Anti-cancer Treatment. *Clin Gastroenterol Hepatol*. 2022;20(4):898-907).
  Added (lines 305-307)
- Line 366: To emphasise that, although HBV and HCV testing in newly diagnosed cancer patients is not routine, guidelines generally recommend it in all patients.
  Added

- Line 395: correct the word “bevacizumabor” to “bevacizumab”.
  Corrected
- Figure 1: illustrate in the figure also the mechanism of action of anti-LAG3 antibodies.
  Added
- Figure 2: I think it would be advisable to modify this figure, enlarge it and indicate within each molecule which are its main approvals. Along with this, add Tremelimumab and Relatlimab.
  Modified

The review that the authors have carried out is undoubtedly of great value for publication and I believe that it is a very successful topic. In my opinion, the manuscript needs a series of changes that I have previously indicated, and if the authors make them correctly, it would be a paper of great interest for the journal.