Reviewer 1

The authors systematically introduce several state-of-the-art immunotherapies for the treatment of hepatocellular carcinoma, summarizing the perspectives for overcoming the limitations, and propose future prospects. My comments are as follows: 1. The limitations of vaccine therapy need to be clarified. 2. Simple conclusions and lack of unique insights. 3. Some references need to be cited, such as “The tumor microenvironment (TME) of HCC is the result of complex interactions between hepatic non-parenchymal resident cells, tumor cells, immune cells, and tumor-associated fibroblasts. The TME has important effects on all signaling molecules, such as cytokines and chemokines, as well as other paracrine factors” and “TGFβ is abundant in the HCC TME and is produced by tumor cells, TAM, or Treg cells”. 4. The citation format is incorrect in some places, such as “HCC cells sometimes overexpress some proteins relative to the surrounding healthy tissue; this is the case for glypican-3 (GPC3) [104]”. 5. Please provide the full name of MHC-II and CTL.

We thank the reviewer for his comments, we are sure they will improve the overall quality of the manuscript.

- We clarified the main limitation of the vaccine therapy: although first HCC vaccines were proved to be safe and have immunologic effects, their clinical efficacy is still deceiving, probably because of an immunological tolerance to self-antigens (not completely tumor-specific).
- We tried to enhance our personal point of view in the conclusions, trying to make them more original.
- We added and corrected the references where needed and indicated.
- The citation format was corrected.
- The full name of the MHC and CTL was provided.

Reviewer 2

In this well written manuscript, the authors review the available evidence concerning the use of immunotherapy treatemnts for patients affected by HCC. After resuming the physio-pathological mechanisms which regulate the liver immnue system and the development of HCC, the authors focus on different immunotherapy strategies for HCC patients, including targeted monoclonal antibodies, vaccine therapy, adoptive cell therapy, and combination of immunotherapy with existing oncologic strategies, including TACE, RFA, chemotherapy. I have only a comment, concenring the manuscript title: given that the majority of the studies cited in this manuscript concerns immunotherapy as a treatment strategy for advanced unresectable, not responding to chemotherapy, or not treateble by locoregional strategies HCC, I would suggest the authors to specify in the title that the manuscript focuses on advanced HCC.

- We really thank the reviewer for his comments. The title was corrected according to the reviewer suggestions.

Reviewer 3

The abstract is clear. The English language is excellent. I want to congratulate the authors on this work. I am impressed by the balanced structure and the detailed approach to such a complicated issue. The reference is up-to-date. I do suggest a high-priority publication. The only minor concern I have to indicate is that the tables are not informative enough and must be revised. Authors should also include further information (number of included patients, outcomes-survival, p-values) for each study.

- We really thank the reviewer for his comments and suggestions. We added the requested informations in the table. P-value were not added since the reported trials are actually ongoing.