

Response to reviewers' comments

Reviewer #1:

Comment: *The author has made a systematic review of immunotherapy for HCC and sorted out all the clinical trials of immunotherapy in HCC in recent years. Overall, this review has almost comprehensively reviewed all HCC immunotherapy, however, I think the present form review lacks following points. Authors should cover these in their manuscript.*

Response: Thank you for your comment and suggestions.

Concern 1: *The first part of the article elaborates on the characteristics of the tumor microenvironment of hepatocellular carcinoma, but this part is too long and lacks schematic diagrams. It is recommended that the author reduce the length or increase the schematic.*

Response: Thank you for your comment and suggestion. We have included schematic (Figure 1) in this section. We have not reduced the text because it may compromise the message of the text.

Concern 2: *When introduces each immunotherapy method, the author compiled the completed and ongoing clinical studies of HCC immunotherapy in recent years. However, the author simply piled up these clinical studies, and did not comment on the results and existing problems of these studies. It is recommended to add some comments on the problems that occurred in the clinical studies of these immunotherapies, for example, (1) Why the response rate of immune checkpoint inhibitors in the treatment of HCC is not high? (2) Why the clinical research of adoptive cell therapy for HCC is progressing slowly? (3) What are the problems with CAR-T or TCR-T therapy in the treatment of HCC and other solid tumors?*

Response: Thank you for your comments and insightful suggestions. We have included the text related to issues associated with limited response rate of immune checkpoint inhibitors, slow progression of adoptive cell therapy clinical research, and the problems with CAR-T or TCR-T therapy in the treatment of HCC in the respective section in the revised manuscript.

Concern 3: *The clinical trial NCT03434379 in Table 2 has already completed, and has reported its results (PMID: 32402160), please modify after confirmation.*

Response: Thank you for pointing out this. We have included the results of clinical trial NCT03434379 in Table 2 of the revised manuscript.

Concern 4: *The heading of the first column of Table 7 is immune checkpoint inhibitors, but the 9,10,11 line is about the clinical research of the HCC vaccine, please check and confirm.*

Response: Thank you for pointing out this and the suggestion. Line 9, 10, and 11 have been included in this table because HCC vaccines are being used in combination of other agents. To correct and ally it with the table title, we have change the column 1 heading.

Reviewer #2:

Comment: *The authors reviewed and discussed the recent status of the immunotherapy for hepatocellular carcinoma. According to the special circumstances of the tumor microenvironments, specific immunotherapeutic strategies should be considered in the liver cancer. The authors reviewed the current clinical trials of immunotherapy for HCC. This manuscript reviewed comprehensively almost all of the immunotherapy for HCC.*

Response: Thank you so much for your supportive comments.