

Response letter

Dear editors and reviewers:

We would like to thank the editors and reviewers once again for your professional comments and suggestions, which are very helpful in improving our manuscript. Our manuscript title is “Research progress regarding programmed cell death 1 /programmed cell death ligand 1 inhibitors combined with targeted therapy for treating hepatocellular carcinoma” [manuscript id: 63995]. We have carefully considered the comments and thoughtful suggestions by the reviewers, responded to these suggestions in a point-by-point manner, and revised the manuscript accordingly. A highlighted revised manuscript in which the revisions are marked in yellow has also been submitted.

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: The work is well conducted and the analysis of the data, both as regards the therapeutic efficacy and the adverse events of immunotherapy and targeted therapy and their association, confers a good knowledge of the state of the art in treatment perspectives and in assessing the risk of adverse events in patients with uHCC. In my opinion, the paper is accepted with minor revision. Minor revision: In the abstract Regorafenib is incorrectly referred as Regofinib English is poor, it should be made more fluent

Response: Thank you for your careful work. We are very sorry for our incorrect writing of “Regorafenib” (on page 3). We have corrected the spelling.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: The authors provide a detailed overview of the trials regarding immune checkpoints inhibitors and targeted therapy as well as their combination in the treatment of hepatocellular carcinoma. The current review provides an important information and conclusions for the scientists and clinicians. It is not clear whether the authors overview all trials in the field or there were any criterias for the trials that were chosen.

Response: Thank you for the thoughtful advice. **We outline most of the important trials in this field. The selection of targeted therapeutic drugs was successful in Phase III clinical trials of advanced HCC(on page 4). The selection of PD-1/PD-L1 inhibitors are the second-line drug treatments for HCC(on page 4),because the phase III clinical trials have often failed to reach the preset statistically significant thresholds for their main endpoints(on page 7).The combination of PD-1/PD-L1 inhibitors and targeted therapy was selected according to the results of the Phase III trials from the website for clinical trials (World Health Organization-International Clinical Trials Registry Platform (WHO-ICTRP) websites, and clinicaltrials) (on page 11).** If we do not understand your meaning correctly, please provide a more detailed explanation, and we will revise accordingly.

Reviewer #3:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: A good review on research progress regarding PD-1/PD-L1 inhibitors combined with targeted therapy for treating hepatocellular carcinoma.

Response: Thank you for your positive and constructive feedback.

Reviewer #4:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (High priority)

Specific Comments to Authors: No special comments.

Response: Thank you for the encouraging comment.

We appreciate for editors and reviewers' warm work earnestly, and we hope that the correction will meet with approval. Once again, thank you very much for your comments and thoughtful suggestions.

Sincerely,

Zhenglinlin, 13199935689