

Reviewer(s)' Comments to Author:

Reviewer #1

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: In this review, the synergistic therapy of anti-angiogenesis and immunotherapy for HCC is described in detail, the mechanism and application of this therapy are comprehensively explained, and the author's own original opinions are put forward. I think it is very valuable. However, there are still some parts that need to be modified.

1. The development of drugs targeting VEGFR was introduced in detail with a large space, but the introduction of drugs blocking VEGF was relatively brief. If the author can introduce the drug development of VEGF blocking in more detail, the structure of the article will become more perfect.

Response: We do appreciate the reviewer's suggestion. According to your advice, we added several current studies on inhibitors and small molecules that targeting VEGF in the second paragraph of the part of "Vascular normalization measures in HCC and targeting of the VEGF/VEGFR axis" to make the structure of the whole review more comprehensive.

2. Of the 57 articles cited by the author, only 7 are from the last three years. It is hoped that the proportion of citations of published literatures in the past three years can be increased to reflect the latest progress in relevant fields.

Response: We thank the reviewer for the comment, and this point is important. We added several literatures that published in the past three years as references to make this review better reflect the research progress in the field of synergistic therapy of anti-angiogenesis and immunotherapy for HCC.

3. The author can introduce the mechanism of treating HCC with ICB in

more detail, so as to make it easier to understand the synergistic effect of ICB and anti-angiogenesis. It can also make the structure of the article more reasonable.

Response: This point has been well taken. We added the detailed introduced of the mechanism of ICB in HCC on the first paragraph of the part of “IMMUNOTHERAPY IN HCC”, which made the paper better understand.

Reviewer #2

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: Very well conceptualised and written manuscript. Suggestions: Table 1 can included survival data from the cited study. Incidence and toxicities (numerical or percentage) should also be added. Table2: Current status of the trial to be added uniform referencing style to be used. Informative review, recommended for publication.

Response: We do appreciate the reviewer's suggestion. These points have been well taken and modified accordingly in the paper.

Reviewer #3

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: This is a well-written manuscript covering the topic of HCC immunotherapy with special emphasis on the role of VEGF as a modulator of anti-tumor immunity and target for combination immunotherapy of advanced HCC. The article is relatively up to date and reasonably comprehensive. Figures and tables add to the presentation. An article on HCC immunotherapy from the perspective of VEGF adds novelty and may distinguish this article from many other recent articles on the mechanisms of immunotherapy response in HCC.

Response: We appreciate your comments.

Editorial Comments:

Response: The editorial recommendations have been well taken. Appropriate modifications have been made to the revised manuscript.