

September 29, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 13312-review.doc).

**Title:** Role of anti-angiogenesis therapy in the management of hepatocellular carcinoma: The jury is still out

**Author:** Hong Sun, Man-Sheng Zhu, Wen-Rui Wu, Xiang-De Shi, Lei-Bo Xu

**Name of Journal:** *World Journal of Hepatology*

**ESPS Manuscript NO:** 13312

We thank the reviewers for their helpful and constructive comments. We thoroughly addressed all concerns and issues raised and revised our manuscript accordingly. All changes in the revised version are highlighted in yellow. Below you will find our point-by-point responses to the reviewers' comments.

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

(1) **Question:** The authors should have their manuscript proofread by a professional language editor to correct multiple typo, grammar, spelling, and language mistakes. For example, sorafenib need not be capitalized; molecular targeted should be molecularly targeted. By convention, the full name should be given first followed by its abbreviation in parentheses - in a few instances, the authors gave the abbreviation followed by full name in parentheses.

**Answer:** The revised manuscript has now been edited and corrected by an American native speaker of English.

(2) **Question:** The core tip section should be revised to summarize the most important points of the review. As it is written now, it is mostly a repeat of the introduction.

**Answer:** We accept the reviewers' critical comments and the core tip section were revised accordingly.

(3) **Question:** The review should be organized into different sections with appropriate headings to help orient the reader. For example, Introduction to liver cancer; Anti-angiogenic drugs used in HCC

treatment; Resistance to anti-angiogenic drugs in HCC; Future perspectives etc.

**Answer:** We thank the reviewer for this valuable comment, and we have made corrections according to the comment.

(4) **Question:** Although the title suggests that the review is about anti-angiogenesis therapy in general, much of the review is focused on sorafenib. The authors should try to include as much data as possible about other forms of anti-angiogenic drugs in use or under investigation.

**Answer:** The reviewer is correct, but sorafenib is the only molecular-targeted agent proven to have a positive effect on the survival rate of patients with advanced HCC. In addition, other forms of anti-angiogenic drugs such as brivanib and sunitinib have been discussed in the sixth paragraph.

(5) **Question:** In this review, both clinical studies and basic researches were introduced. It had better separate data into two categories more clearly. Also, authors had better add the summarized table.

**Answer:** The related data are summarized in Table 1 according to the reviewer's suggestion.

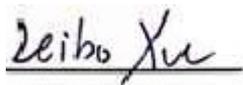
(6) **Question:** Authors mentioned 'in large-scale randomized phase 3 trials, unfortunately, none of them have shown survival benefits in the first-line, or second-line setting after Sorafenib progression.' However, I could not find the data about erlotinib in the referred papers 40, 41 and everolimus in the referred paper 42. Check them again.

**Answer:** We accept the reviewers' critical comments and related references were updated.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Hepatology*.

Sincerely yours,



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