

Format for ANSWERING REVIEWERS



Nov 25, 2014

Dear Editor,

Please find enclosed the edited "Current systemic treatment of hepatocellular carcinoma: A review of the literature" manuscript in Word Journal of Hepatology (file name: 13540-review.doc).

Title: Current systemic treatment of hepatocellular carcinoma: A review of the literature

Author: Kai-Wen Chen, Tzu-Ming Ou, Chin-Wen Hsu, Chi-Ting Horng, Ching-Chang Lee, Yuh-Yuan Tsai, Chi-Chang Tsai, Yi-Sheng Liou, Chen-Chieh Yang, Chao-Wen Hsueh, Wu-Hsien Kuo

Name of Journal: *World Journal of Hepatology*

ESPS Manuscript NO: 13540

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

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

- (1) Please consider to put the introduction of mechanisms of sorafenib in front of sorafenib clinical trials.

Reply: We thank the Reviewer for the instructive comments.

We have added an introduction of mechanisms of sorafenib in front of sorafenib clinical trial ([MOLECULARLY TARGETED THERAPY, Paragraph 2, Line 2-8](#)).

- (2) Some abbreviations such as CLIP-1, should be explained.

Reply: We thank the Reviewer for the instructive comments.

We have added explanation of CLIP-1 in the main text ([OTHER AGENTS UNDER STUDY FOR ADVANCED HCC - Hormone therapies - Tamoxifen and Megestrol, Paragraph 1, Line 5](#)).

- (3) In the abstract, the authors speak about "symptomatic" treatment; I suggest to better describe those strategy or to use the accurate terminology (i.e. "best supportive care") that are not only "symptomatic" treatments

Reply: We thank the Reviewer for the instructive comments.

We have revised the description in abstract about those treatment strategies ([Abstract, Paragraph 1, Line 11](#)).

- (4) In the abstract, the sentence "For example, the patients with BCLC stage 0 (very early stage) and stage A (early stage) HCC, the curable treatment modalities including resection, transplantation, radiofrequency ablation are taken into consideration" is not clear.

Reply: We thank the Reviewer for the instructive comments.

We have revised the description in abstract about those sentences. ([Abstract, Paragraph 1, Line 6-12](#))

- (5) The introduction comprises some unclear chapters; first, the authors cited the influence of HBV on the incidence of HCC, but they not gave any "conclusion" on the influence of viral factors or alcohol.

Reply: We thank the Reviewer for the instructive comments.

We have added reference with discussion of the influence of HBV and HCV on hepatocellular carcinoma. ([Introduction, Paragraph 1, Line 6-9](#))

- (6) The content of the abstract is inappropriate in regard to the declared aim of the review.

Reply: We thank the Reviewer for the instructive comments.

We have revised the description of the content of abstract. ([Abstract, Paragraph 1, Line 12-14](#))

- (7) Treatment strategies have to be described: why systemic therapy are indicated only for stage B

patients?

Reply: We thank the Reviewer for the instructive comments.

We have revised the description of the content of abstract. ([Abstract, Paragraph 1, Line 8-11](#))

(8) The first sentence of introduction is awkward.

Reply: We thank the Reviewer for the instructive comments.

We have deleted it.

(9) NEW DIRECTIONSThe Authors report several interesting observations. However, it is unclear whether these hypotheses led to new clinical studies.

Reply: We thank the Reviewer for the instructive comments.

We have deleted it.

(10) IMMUNOTHERAPY The Authors did not report the study on CTL4 blockade with tremelimumab (Sangro et al Journal of Hepatology 2013), which, to my knowledge, is the most significant clinical experience in this field. Why not mention CTLA-4.

Reply: We thank the Reviewer for the instructive comments.

We try to discuss this issue in Immunotherapy - CTLA-4 blockade. ([Immunotherapy, Paragraph 2](#))

3 References and typesetting were corrected.

4. Some important clinical trials were showed in the setting of tables.

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

Sincerely yours,

Wu-Hsien Kuo,



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