

#### Reviewer 1

The review manuscript, "Sorafenib-based combined molecule targeting in treatment of hepatocellular carcinoma" by Gao et al. is a timely review article summarizing the current status and rationale for clinical trials utilizing combined targeting with sorafenib and other candidate drugs. The review appears to be balanced and unbiased, discussing positive and negative aspects of each class of drugs and clinical trials. Suggest only to correct grammar/typos but otherwise the manuscript is well organized and presented.

Response: Thanks very much for your suggestions. The language of this manuscript has been improved by IAC Editing Support Organization (<http://www.iacmhr.com/iac-eso/support.php?lang=en>).

#### Reviewer 2

It is a well-written, comprehensive and useful review of the ongoing strategies on systemic treatments of HCC.

Response: Thanks very much for your encouraging comments.

#### Reviewer 3

Jian-Jun Gao et al summarized the emerging sorafenib-based combined molecule for the treatment of HCC and analysed the rationales of these combinations. The review is well written and interesting. I therefore have only minor comments.

1) I suggest to include a figure reporting graphically the main molecular pathways cited in the text.

Response: Thanks for your suggestions. We have added a figure for easy following the content of this article.

2) On page 5 line 2 from bottom just after references 34, I would suggest to include a recent review on VEGF and HCC (Scaggiante et al World J Gastroenterol 2014

February 7; 20(5): 1268-1288);

Response: Thanks for your suggestions. We have added this reference after ref. 34.

3) On page 9 line 5 from bottom, I suggest to include more details about the results of reference 64, in particular with regard to the improvements of time to progression and overall survival.

Response: Thanks for your suggestions. More details about the results of reference 64 were added.