January 9, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 15824-review.doc).

Title: MET inhibitors for the treatment of advanced hepatocellular carcinoma: A review

Author: Xingshun Qi, Xiaozhong Guo, Guohong Han, Hongyu Li, Jiang Chen

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 15824

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 two reviewers.

We greatly appreciated the three reviewers' comments. The point-to-point response to comments were shown as follows.

Comment 1. This review manuscript extensively described and summarized the results of recent clinical trials related to mesenchymal epithelial transition tyrosine kinase inhibitors in the treatment of advanced hepatocellular carcinoma. The potential utility of these kinase inhibitors in hepatocellular carcinoma patients was also discussed. The manuscript can provide useful information to the readers. I recommend publishing this manuscript. Minor comment: The abbreviation of MET in section of abstract should be spelled in full in its first appearance.

Answer: Thank you very much for your review.
MET is also called as c-Met or hepatocyte growth factor receptor (HGFR). In humans, MET protein is encoded by the MET gene (i.e., MET proto-oncogene). MET gene has a total length of 125,982 bp, and it is located in the 7q31 locus of chromosome 7. MET gene is transcribed into a 6,641 bp mature mRNA, which is then translated into a 1,390 amino-acid MET protein. Because MET gene is firstly discovered in human osteosarcoma by Cooper in 1984, it is also called as the N-methyl-N'-nitroso-guanidine human osteosarcoma (MNNG HOS) transforming gene. Nowadays, MET is rarely spelt in full name in most of relevant articles because of its length. There are several excellent papers as follows. Indeed, in these papers, no full names of MET could be found.
1. Gherardi E, Birchmeier W, Birchmeier C, Vande Woude G. Targeting MET in cancer: rationale and progress. Nat Rev Cancer. 2012; 12(2): 89-103.
2. Blumenschein GR, Jr., Mills GB, Gonzalez-Angulo AM. Targeting the hepatocyte growth factor-cMET axis in cancer therapy. J Clin Oncol. 2012; 30(26): 3287-96.
3. Eder JP, Vande Woude GF, Boerner SA, LoRusso PM. Novel therapeutic inhibitors of the c-Met signaling pathway in cancer. Clin Cancer Res. 2009; 15(7): 2207-14.

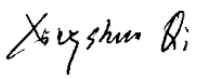
Comment 2. Xingshun Qi et described the studies about the use of MET inhibitors as potential novel treatments for the advanced stages of HCC reporting ongoing and completed clinical trials. The review is clearly written and gives a reasonable overview of the topic. I just suggest to slightly expanding, in the "Introduction" the biochemical pathway involved in MET inhibition. Finally, few words about the different chemical structures of the anti-MET molecules described may be useful.

Answer: Thank you for the reviewer's comments.
According to your comments, we added some words about the biochemical pathway involved in MET inhibition in the "Introduction" section (highlighted by yellow). We also highlighted some words about the targets of MET inhibitors by yellow.

3 References and typesetting were corrected.

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

Sincerely yours,



Xingshun Qi, MD
Department of Gastroenterology,
General Hospital of Shenyang Military Area,
No. 83 Wenhua Road, Shenyang, 110840 China.
Tel: 86-24-28897603; Fax: 86-24-28851113;
Email: xingshunqi@126.com