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Cover letter

RE - Invited editorial article: Epidermal growth factor receptor and metastatic colorectal cancer: insights into target therapies (ID = 02494908)

Dear Dr. Lian-Sheng Ma,

We would greatly appreciate if you could reconsider a revised version of the above invited editorial article (ID = 02494908) for publication in *World Journal of Gastroenterology*. The manuscript has been reviewed according to the referees' suggestions. Below please find a detailed 'point-by-point' response to the reviewers' comments.

1. Reviewer I (00289406): *"There are several spelling errors in the script that need to be corrected. Otherwise a table with study results, effects and side effects would be helpful, however it might not be appropriate for an editorial article"*

    a. **REPLY**: Thank you very much for this comments. The manuscript was submitted for a new language revision and spelling errors was corrected. We created a table with the main clinical trials discussed in this article, as the reviewer suggested. Also, we believe that this article is much appropriated for an editorial, because it brings current discussion concerning anti-EGFR therapies and biomarkers in mCRC. In additional, we make a synthesis of the main clinical trials in the field and give future perspectives in this regard.

2. Reviewer II (02456377): *"This paper summarized the efficacy and safety of anti-EGFR therapies (cetuximab or panitumumab) for colorectal cancer. Meanwhile, the author also discussed the efficacy of these therapies in conjunction with conventional chemotherapy. The conclusion was that the*

choice to use cetuximab or panitumumab in association with standard chemotherapy for mCRC according to patients fitness, acceptable toxicities profile, survival outcome and mainly pharmaco-economic evaluation of those drugs in this setting."

i. *Major concerns*:

1. *"The topic is not so innovative, because the therapy method has been used in clinic for many years."*

    a. **REPLY**: indeed cetuximab and panitumumab drugs are cornerstone for mCRC treatment. Thus, our paper was written in order to give readers briefly insights and summarize key points in this regard.

2. *"Could the authors augment the context in how to treat those patients with mutant-type KRAS, which will make the review become more integrated and acceptable."*

3. **REPLY**: thank you for this comment. We also inserted some concerns regarding KRAS mutant treatment in the text: … please see … "…with mCRC or maintenance therapies in chemorrefractory tumors (table 1). In overall, current guidelines advocate the use of the following regimens as initial standard chemotherapy for mCRC: fluorouracil, leucovorin, and oxaliplatin-based chemotherapy (FOLFOX), fluorouracil, leucovorin, and irinotecan-based chemotherapy (FOLFIRI), capecitabine plus oxaliplatin (CapeOx or XELOX) [12, 13], and fluorouracil, leucovorin, oxaliplatin…"

3. We also change the title and other issues requested by the editing staff.

We hope we have satisfactory clarified the issues the reviewers raised. Enclosed please find a revised version of the manuscript. Should any further information be required, please do not hesitate to contact me.

Many thanks for your attention. I look forward to hearing from you in due course.

Yours sincerely, on behalf of all authors:

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