

Reply to the comments and suggestions

Respond to Reviewer #1:

I truly appreciate all the hard work the study group invested in this review. The topic is a hot one and very much needed for patients with different types of GI cancer. The manuscript is clear, up-to-date and written with attention to details. The authors inserted a lot of data from recent studies.

1. However, in order to make it more useful and organized, I would suggest to summarize the mentioned studies in tables. Either tables for every type of cancer (gastric, colorectal, pancreatic, and hepatocellular carcinoma) or tables including all types of cancer, organized by "in vitro" studies and "in vivo" ones. Or, any other structure the authors would prefer. Just please summarize the data in tables. It is very important. Please also mention what databases were searched for articles and the period.

Answer: Thanks for your kind suggestion. We have added four more Tables, which were made according to the type of tumor. Thanks again.

2. Also, "Conclusion and Future directions" paragraph is way too long. Moreover, it contains data that was previously written. There is no point in repeating what was already written. Redundancy is not recommended. Conclusion should be short and crispy. Maybe this paragraph could be split in two: Future Directions and Conclusion. Usually, conclusion should not contain references...since they have already been used.

Answer: Thanks for your suggestion. We have decomposed the "Conclusion and Future directions" into "Future directions" and "Conclusion". And also, we have followed your advice and deleted the contents that are repeated with the previous ones. We also make sure that we won't cite the references that have been quoted in the previous

contents in the “Conclusion” section.

3. There are a few typos - minor correction of the English language is required; among them – very important – page 396 please replace “fetal” with “fatal”.

Answer: We apology for the mistake we make and we have polished our manuscript by AJE. Thanks again for the suggestion.

4. There are no «**Conflict-of-Interest Disclosure Form** » and « **Copyright License Agreement**». Please add the respective files. Please provide the Authors’ ORCID Numbers.

Answer: We added the files and all authors’ ORCID numbers. Thanks for you remind.

5. The format of the references is not the one requested by the journal. Please revise.

Answer: We have corrected the format of references as requested. Thanks for you remind.

Respond to Reviewer #2:

Dear Authors in your review article is very interesting and deserved attention. There is lack of literature search explanation, tables could contribute to the clarity of manuscript. Otherwise, it contains a lot of data about preclinical studies which are candidate for further clinical trials.

Answer: We have added four more Tables, which were made according

to the type of tumor. Thanks for you suggestion.