

PEER-REPORT REPORT ANSWERS

First of all, we are grateful that the reviewer of this manuscript offered their suggestions and pointed out our mistakes. We have tried our best to revise the manuscript according to their comments. Here are the answers for the questions they have asked.

1. **Comment:** About language in this manuscript.

Answer :

- We have noticed that from the review report, reviewers have pointed out abundant grammatical and word choice errors in this manuscript.
- Therefore, we sent our manuscript to American Journal Experts (AJE) for professional language polishing and got the 'Non-Native Speakers of English Editing Certificate'. Language is not a problem in this manuscript now.

2. **Comment:** ORR is objective response rate. At one point in the manuscript it is defined as the overall survival rate. Also it does not need to be spelled out each time. After the first time it is spelled out, it is acceptable to use the abbreviated form throughout the manuscript.

Answer :

- During the carefully revision of this manuscript, we have changed according the advice from the reviewer.

3. **Comment:**

- i. The authors talk about PD-1/PD-L1 positivity as a biomarker for response to PD-1 blockade, however the authors need to discuss the discrepancies in how PD-1 is measured and the issues of cutoff values for "positive" and "negative".
- ii. Furthermore, given the uneven expression of PD-1 in tumor cell populations small needle biopsies may not give an accurate representation of true PD-1 density.
- iii. Lastly, the authors need to discuss that PD-1 negative patients can still respond to anti-PD-1/PD-L1 therapy and a substantial proportion of PD-1 positive tumors do not respond.

Answer:

- We also agree that discussion of the discrepancies in how PD-1 is measured and the issues of cutoff values for "positive" and "negative" is need,
 - In this review, we only discussed the role of PD-1/PD-L1 inhibitors in immunotherapy with gastric cancer. For other cancers, they may use small needle biopsies as a tool. However, we don't use small needle biopsies as a method to get the tissue from gastric cancer patients in the endoscopy center, we believe endoscopic multi-sites biopsy in gastric cancer is better, which provides more accuracy than small needle biopsies.
4. **Comment:** I would recommend expanding this paragraph to include concurrent checkpoint inhibitors and radiation as well.

Answer:

- We have included include concurrent checkpoint inhibitors and radiation in the revised manuscript and cited properly.
5. **Comment:** When mentioning chemotherapy for gastric cancer in 2019, one has to include paclitaxel. Please include this in your introduction.

Answer:

- We have included paclitaxel in the introduction part of revised manuscript.
6. **Comment:** The authors state PD-1 may be diagnostic. I think what is meant is predictive or response to therapy with anti-PD-1/PD-L1 therapy. The authors further suggest that because PD-1 expression is correlated with advanced stage that it could be used as for diagnosis of metastasis. This is not supported by the data. It may be a independent prognostic factor associated with advanced gastric cancer but would not really be a diagnostic test for metastasis.

Answer:

- From the previous data in Pubmed, we have noticed that increased PD-L1 and PD-1 expression are associated with nodal metastasis and a poor prognosis in oral squamous cell carcinoma.
 - So in this review, we read some literatures about the predictive role of diagnosis and metastasis in gastric cancer. It is supported by the data from pubmed and we have cited properly.
7. **Comment:**
- i. The title must show that this article is a review. Abbreviation of "PD-1/PD-L1" must be explained. Title: Recent progress of What? Progress of knowledge/therapy/... about the effects of PD-1/PD-L1 or ...?

- ii. Introduction: The first sentence needs a reference.
- iii. Immediately, after introduction, subtitles have been started, without any connecting sentences to explain the next subtitles.

Answer:

- We have searched pubmed, there are many review articles' name include the abbreviation of PD-1/PD-L1, we think this is not a problem that confuse the reader. Meanwhile, we have changed the title into *PD-1/PD-L1 antagonists in gastric cancer: current studies and perspectives*. We believe that this title is meet the requirements of the reviewer.
 - Already cited a reference in the revised manuscript.
 - Changed in the revised manuscript.
8. **Comment:** I would like the authors to emphasize the interpretation of the staining of gastric and OG junction cancers for the antibodies which are drug dependent. What antibodies should be used and how should the staining be scored in histologic slides?

Answer:

This review is mainly about the efficacy, safety, and possible combination treatment options of PD-1/PD-L1 inhibitors in gastric cancer in experimental and clinical settings. As for what antibodies should be used and how should the staining be scored in histologic slides? It's need professional answers from the department of pathology to further explain. We think this is deviate from the scope of this study.

9. **Comment:** In the text check the acronyms "PD-1/PD-L1" that are quite often alone. Please add the annotation "checkpoint", "checkpoint inhibitors" or "axis" to the acronyms when appropriate.

Answer:

- We addressed in the revised manuscript.