Dear Editors of World Journal of Gastrointestinal Oncology,

We are sending you the revised manuscript entitled "ASSESSMENT OF PD-L1 EXPRESSION IN PRIMARY TUMORS AND PAIRED LYMPH NODE METASTASES OF GASTRIC ADENOCARCINOMA".

The manuscript was revised according to the reviewers' comments and responses to each question are provided below. Text modifications are highlighted in red.

We are glad for the opportunity to send the revised manuscript to this renowned journal.

Thank you in advance for your time.

Respectfully,

Marina Alessandra Pereira

Responses to reviewer comments

Reviewers' Comments to Author:

Reviewer #1:

Scientific Quality: Grade A (Excellent)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (High priority)

Specific Comments to Authors:

Dear Authors, I congratulate you for the work and for writing this manuscript. The manuscript is well written and complies with research and writing criteria. I would like you to make some clarifications regarding metastatic lymph nodes or sentinel lymph nodes, namely their location. They were peritumoral, or from the tumor basin or in places far from the primary tumor. Regarding the legend of figure 1, it would be appropriate to indicate the different stages with small arrows.

Response:

We appreciate your comment and review of our manuscript. The metastatic lymph nodes evaluated were all regional lymph nodes, located in the greater or lesser gastric curvature. The metastatic lymph nodes selected for analysis were those with the highest tumor burden. This information was added to the revised manuscript in the methods section.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Specific Comments to Authors:

This study has certain clinical significance and provides a new perspective for the diagnosis and treatment of PD-L1 in gastric cancer.

Response: Thank you for your comment and for reviewing our manuscript

Reviewer #3:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors:

Discussion of other cancer types rather than gastric cancer is redundant and lack of rationale or assumption for the study results

Response:

We appreciate the comment and, as mentioned, we improved the discussion of the revised manuscript by adding more information from studies that only address gastric cancer, and removed some references and studies in relation to other tumors.

In fact, the most interesting results to compare our findings would be those evaluating only gastric cancer. However, as the available literature on the evaluation of PD-L1 in the primary tumor and metastases is still scarce - and PD-L1 represents an "agnostic biomarker" used to select therapies regardless of the tumor type - we believe it is suitable and relevant to include studies regarding other tumor types to provide additional information on the expression pattern and heterogeneity of PD-L1 as a biomarker.

In relation to the justifications and assumptions of the study, we improved these topics in the discussion of the revised manuscript. In summary, the evaluation of PD-L1 in this context is justified by the need to verify the limitations of the biomarker's evaluation when comparing two sites (primary and metastasis). As mentioned in the introduction, immune checkpoints may express differently between primary and metastatic tumors, and this difference may have an impact on the selection of patients for therapy. Since combination of immunotherapy and chemotherapy is recommended for first line treatment of gastric adenocarcinoma patients with locally advanced unresectable disease or metastatic disease, data regarding the concordance rate between PD-L1 in primary GC and matched regional lymph node metastasis is required.

Therefore, knowing the heterogeneity of PD-L1 assessment as a biomarker may be important to predict whether the response in the primary and metastases will be the same, as we frequently observe different responses to therapy in PT and LNM. Furthermore, our findings can serve as a basis to verify the need to perform PD-L1 assessment not only in the primary tumor sample, but also in the metastasis - as a way of indicating therapy in cases of metastatic tumors.

EDITORIAL OFFICE'S COMMENTS

Science editor:

1 Conflict of interest statement: Academic Editor has no conflict of interest.

2 Manuscript's theme: The topic is within the scope of the journal.

3 Academic misconduct: No academic misconduct was found.

4 Scientific quality and comments: This study aims to compare programmed death-ligand 1 status in primary tumor and metastatic lymph nodes of gastric cancer patients and to determine the correlation between the programmed death-ligand 1 status and clinicopathological characteristics.

(1) Please add scale bar to the histopathological images if possible.

(2) Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

Response:

As requested, we adjusted the tables in the revised manuscript.

Unfortunately, it is not possible to add the scale bar to the figures. However, we describe in the caption the magnification size of the images: original magnification, 10x for C, D and F; and 20x for A, B and F).

5 Language evaluation: Grade A.

6 Recommendation: Conditional acceptance.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade C (Good)