

## Peer Review File

Article information: <https://dx.doi.org/10.21037/apm-21-2023>

### Responses to the comments of Reviewer #1

1. 107: “absence of a measurable target lesion” at baseline?

Response:

Thank you very much for your careful correction. Here I should write “without target lesions based on the Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 criteria” and have made corrections in the article. (Page 7, line 97-98)

2. 111-112: Write “hepatitis B virus (HBV) infection, hepatitis C virus (HCV) infection,” instead of “hepatitis C virus (HBV) infection, hepatitis V virus (HCV) infection,”

Response:

Thank you very much for your careful reading and suggestions. We are very sorry that we made this mistake. I have revised this sentence to “hepatitis C virus (HBV) infection, hepatitis V virus (HCV) infection” (Page 7, Line 102-103)

3. 112-113: Write circulating markers (neutrophil and lymphocyte counts)” instead of “blood routine (neutrophil and lymphocyte counts)”

Response:

We appreciate your correction. Blood routine is not a correct expression, and we think that circulating markers are more in line with the definition of neutrophils and lymphocytes. we have revied “blood routine (neutrophil and lymphocyte counts) to circulating markers (neutrophil and lymphocyte counts)” according to your suggestion. (Page 7, Line 103-104)

4. 131: In HCC terminology, PDX is well known as an abbreviation for Patient-derived xenografts term, while PD is well known as an abbreviation of Progression disease. In the text, the PDX is used as an abbreviation for Progression disease, which is confusing. PD is used in Figure 1 as an abbreviation of Progression disease. I would recommend using PD as an abbreviation of Progression disease everywhere.

Response:

Thanks for your correction. Your suggestions are very helpful. PD is a recognized abbreviation for progressive disease and PDX is well known as an abbreviation for Patient-derived xenografts term. It would be confusing that the PDX is used as an abbreviation for Progression disease. Therefore, this article will use PD as the abbreviation for progressive disease. According to your recommendation, we change all PDX to PD and mark it red. Thank you again for this very useful comment.

5. Discussion: “241 However, in our study, sex was associated with HPD, and primary liver cancer was 242 more likely to occur in male patients, although there were only a few female patients 243 in this study” should be reformulated as “this study shows that sex is not associated with HPD”

Response:

Thank you very much for your careful comment. Our logistics regression analysis shows that sex is not associated with HPD. So the original sentence is wrong and we have revised “However, in our study, sex was associated with HPD, and primary liver cancer was more likely to occur in male patients, although there were only a few female patients in this study” to “However, the present study shows that sex is not associated with HPD.” Thank you so much for your correction. (Page 13, Line 231-232)

6. Problematic of NLR is repeated two times in the discussion: Line 232-233: “Kim et al. reported that in patients with liver cancer receiving immunotherapy, NLR was related to HPD, and NLR >4.125 could predict HPD and a lower survival rate [22].” And Later again: Line 247-248: “Previous studies have reported that NLR may be a risk factor for HPD [22, 23].” This repetition should be avoided.

Response:

We appreciate your suggestions. In this article, I mentioned twice that NLR is related to progressive disease. To avoid repetition, we deleted this sentence: “Kim et al. reported that in patients with liver cancer receiving immunotherapy, NLR was related to HPD, and NLR >4.125 could predict HPD and a lower survival rate [22]” and retain “Previous studies have reported that NLR may be a risk factor for HPD [22, 23].” (Page 13, Line 236-267)

## Responses to the comments of Reviewer #2

1. English of this manuscript should be improved.

Response:

Thank you very much for your suggestion. We have carefully considered the expression of the article again and invited Editage to polish our article. The modification is marked as red. I'm sure that English of this manuscript has improved and I have attached our English polish certificate in the Email.

2. The risk factors can be added in the title and “A real-world study” is too vague.

Response:

Your suggestions were immensely valuable and we certainly appreciate it. It would be better to add risk factors in the title and I have modified the title to “Lung metastasis and lymph node metastasis are risk factors for hyperprogressive disease in primary liver cancer patients treated with immune checkpoint inhibitors”

3. In Abstract, some sentences are duplicated in the results and conclusions.

Response:

Thank you very much for your suggestions. I have carefully considered the results and conclusions in abstract and found that some sentences repeat as you said. I have revised the repetitive parts in the conclusions and results in the abstract. Thank you again for your careful correction.

### **Responses to the editor's comments**

**1. Please follow the attached “Submission Checklist for Authors” and revise your paper if needed. Here are some additional points:**

a. The article already followed a Checklist for reporting standards. Please place “Y” in the “Submission Checklist”.

Response:

Thank you very much for your suggestions. I have place “Y” in the “Submission Checklist” and filled out the checklist as requested.

b. “Data Sharing Statement” is a statement made by authors to confirm their willingness of sharing raw data/patient information related to the article with others. We attached a template for your reference.

Response:

Thank you for your advice to our article. I have I have read the contents of the template carefully and filled out the checklist“Data Sharing Statement”.

c. Conflict of Interest (COI) Form must be provided, as suggested by ICMJE: (<http://www.icmje.org/conflicts-of-interest/>). Each author should submit a separate form and is responsible for the accuracy and completeness of the submitted information. COI form download link: [https://cdn.amegroups.cn/static/public/coi\\_disclosure.docx](https://cdn.amegroups.cn/static/public/coi_disclosure.docx).

Response:

Thank you for your suggestion. As you requested, we have filled out the Conflict of Interest Form of all author.

d. Please indicate if any of the authors serves as a current Editorial Team member (such as Editors-in-Chief, Editorial Board Member, Section Editor) for this journal.

Response:

I declare that no authors served as members of the current editorial team of this journal.

e. Please confirm that all figures/tables/videos in this manuscript are original; if not, permission is needed from the copyright holder for the reproduction.

Response:

We confirm that all graphics and tables in this manuscript are original.

f. We are using the “Submission Checklist for Authors” to double-check your manuscript, place “Y” on blank space if you confirm your manuscript has followed the requirement. Place “N/A” if not applicable. If further explanation is needed on a certain item, you can copy the Item and write explanations down below. A filled “Submission Checklist for Authors” should be submitted to the editorial office, along with other required documents.

Response:

Thank you very much for your suggestions. I have place “Y” in the “Submission Checklist” and filled out the checklist. I will submit it to the editorial department along with other required documents.