

## Answering Reviewers

**Manuscript NO:** 59868

**Title:** Elevated levels of alpha-fetoprotein (AFP) and cancer antigen 125 (CA125) are risk factors for the development of intraocular metastasis in diabetic patients with primary liver cancer

Dear Dr. editors

Thank you very much for your letter inviting us to submit a revised version of the above-mentioned manuscript. We are very grateful to the reviewers for their affirmation and suggestions. We have revised the paper according to the reviewer's suggestions. In addition to this reply, we have attached a manuscript with a revised record and the original manuscript.

Below are our specific responses to the reviewers' comments.

### REVIEWER EVALUATION

Q1: The contents of introduction should be concise focusing on the background and aims.

RE1: Done, thanks.

Q2: In Table 1 Clinical features of diabetic patients, no data of diabetes, BMI, HbA1c, smoking, and complications are provided, although the authors mentioned that diabetes have greater risk of developing certain cancers, especially primary hepatic cancer [5]. (Line 83). These information are informative for the readers.

RE2: We supplemented the patient's HbA1c information. Data on BMI, smoking and other complications are incomplete and have been added to the limitations. Thanks.

Q3: In Table 3, the odds ratios are very low, almost close to 1. I wonder such results have no clinical relevance, even though statistical significance was observed. In addition, were the background factors such as age, sex, BMI, and HbA1c adjusted in the model? The authors should mention the results of Table 3 in the results section.

RE3: We supplemented the patient's HbA1c information. Data on BMI, smoking and other complications are incomplete and have been added to the limitations. I have added the contents of Table 3 in the result section. The possible reason for the OR value close to 1 is that the sample content is too small to make the estimated result unstable, resulting in large standard errors and making the otherwise meaningful variables look meaningless. The solution is

to increase the sample size. According to some experts, if the sample is less than 100, there may be some risks in the results of Logistic regression, while if the sample is more than 500, it is more appropriate. However, the number of patients with eye metastases in our patients is small, and larger sample size collection may make the results seem more meaningful. Thanks!

Q4: The clinical relevance of Figure 5 showing lipids in terms of cancer is unclear. Is the figure truly necessary? If necessary, please add some explanations.

RE4: Done, thanks.

Q5: The number of case for IOM is very low (n = 13), which may reflect low reliability of the results. Please mention this limitation.

RE5: Done, thanks.

Science editor:

Q1: I found the title was more than 18 words. The title should be no more than 18 words

RE: Done, thanks.

Q2: I found no "Author contribution" section. Please provide the author contributions;

RE: Done, thanks.

Q3: I found the authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s);

RE: Done, thanks.

Q4: I found the authors did not provide the original figures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;

RE: Done, thanks.

Q5: I found the authors did not add the PMID and DOI in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout.

RE: Done, thanks.

Q6: I found the authors did not write the "article highlight" section. Please write the "article highlights" section at the end of the main text.

RE: Done, thanks.

Best regards

Yi Shao