



Yan-feng Liu, Dr

Professor

Department of Hepatobiliary
Qilu Hospital of Shandong University
107# Wenhua xi Road
Jinan, Shandong, P.R.China 250012
Email: liu19822012@163.com

November 10, 2021

Dear Editor,

Thank you for giving us the opportunity to revise our manuscript entitled “**High tumor mutation burden indicates a poor prognosis in patients with intrahepatic cholangiocarcinoma**”. We are grateful for your comments and suggestions. We addressed those comments by revising the related text, and providing more supporting materials. The following is a detailed list of our responses.

Reviewers 1#' Comments

1) I would suggest to change the Introductions section into Background as recommended by the journal.

Response: We appreciate the comment. We have changed the Introductions section into Background.

2) The authors have claimed in the Background section that no previous study has addressed the impact of TMB in ICC, however in the discussion section they cite Zhang et al. Please explain the reason for this.



Response: Thank you for your careful review. Our description in the Background section is not very accurate, and we have modified this part of the statement.

3) How were the training and test groups divided? If so please explain this in the methods section.

Response: Thank you for your careful review. The group division method was stated in the Result section and we have added it into the Method section.

4) In the discussion I believe the authors tried to mention the RAS gene instead of RARS. However, if I am wrong please explain what this acronym stands for.

Response: Thank you for your careful review. This is our mistake. We have made changes here.

Reviewers 1#' Comments

However, the patients includes various kinds of ICC, such as mass-forming type, hilar type ICC and so on. In the future, the authors should investigate the impact of TMB on the prognosis following several kinds of ICC.

Response: Thank you for your careful review. Our study was based on the ICC data of MSKCC. But no detailed information of the kinds ICC was contained in the patients clinical characters. In the future, we will continue to collect the clinical data of ICC patients and investigate the impact of TMB on the prognosis following several kinds of ICC.



Science editor' Comments

This study explored the prognostic role of TMB in ICC patients, found that TMB and CA19-9 were among the identified independent prognostic factors in ICC. But using a single data source will increase statistical error. It is necessary to make further larger-cohort studies to confirm the predictive value of TMB in the prognosis of ICC patients.

Response: We appreciate the comment. Using a single data source will increase statistical error. However, because of the relatively low incidence rate of cholangiocarcinoma, there is no other available ICC cohort with large sample size. Therefore, we are unable to make further larger-cohort studies. In the future, we will continue to collect the clinical data of ICC patients and consolidate our conclusions by expanding the present study's sample size.

Company editor-in-chief' Comments

I recommend the manuscript to be published in the World Journal of Clinical Cases.

Response: We appreciate the comment. We agreed to publish the manuscript in the World Journal of Clinical Cases.