

Dear reviewers:

Thank you for your comments for the manuscript. Those comments are all valuable and very helpful for revising and improving our paper. We have studied your comments carefully and have amended the relevant part in the manuscript, which we hope meet with approval. Revised portion are marked in yellow in the paper. Here below is our description on the main revisions and the responses to the your comments.

*Reviewer #1:*

*Scientific Quality: Grade C (Good)*

*Language Quality: Grade A (Priority publishing)*

*Conclusion: Major revision*

*Specific Comments to Authors: This manuscript was submitted as an META-ANALYSIS to the World Journal of Gastroenterology, first authored by Zi-Han Zhang. The authors review the relationship between Circulating Tumor Cells and prognosis of pancreatic cancer patients in the article "CTCs as Potential Prognostic Biomarkers for Early-Stage Pancreatic Cancer: A Systematic Review and Meta - Analysis". In my mind, this manuscript is well reviewed but partly insufficient for publication at this moment. As to the tumor stage of pancreatic cancer, pancreatic physicians recently focus on the three distinct dimensions: anatomical (A), biological (B), and conditional (C) [Pancreatology. 2018 Jan;18(1):2-11. PMID: 29191513 ]. CTCs is thought to be one of the biological markers (B). Basically, readers want to know the superiority as a biomarker of CTCs comparing to conventional tumor markers including CEA, CA19-9, Span-1, DUPAN II. This superiority should be reviewed and discussed.*

Response: Our meta-analysis only revealed the potential of CTCs as a prognostic marker and did not compare it with traditional tumor markers like CEA, CA19-9, Span-1 and DUPAN II. Given this, we have selected studies to compare the prognostic ability of CTCs with CA19-9 based on the existing included literature. After excluding the impact of sampling time, the pooled result showed that preoperative CA19-9 in the peripheral venous blood of early-stage pancreatic cancer patients is not an independent prognostic predictor for shorter time of recurrence after surgery compered to pre- and intra-operative CTCs.

*Reviewer #2:*

*Scientific Quality: Grade C (Good)*

*Language Quality: Grade B (Minor language polishing)*

*Conclusion: Minor revision*

*Specific Comments to Authors: This is a meta-analysis stating that measurement of CTCs in non-advanced pancreatic cancer may determine pancreatic cancer prognosis. If possible, you should evaluate in a meta-analysis of RCTs that measure CTCs preoperatively (or intraoperatively), as the method and timing of CTCs are different.*

Response: We are very sorry for our negligence of interference of sampling time differences in CTCs. Considering your suggestion, the sampling time of the included eight studies have been checked and confirmed that only pre- and intra-operative CTC data were included in this

meta-analysis. We have also stated this point in the manuscript.

We would like to express our great appreciation to you for comments on our paper. Looking forward to hearing from you.

Thank you and best regards.

Yours sincerely,

Jin-Tao Guo