September 8, 2015

Manuscript NO.: 21031

Title: Neoadjuvant Treatment for Resectable Pancreatic Adenocarcinoma

Authors: John Wong, Naveen Solomon and Chung-Tsen Hsueh

Dear Dr. Jin-Xin Kong,

We have summarized our responses to reviewers' comment as below. Please let us know for any question or issue. Thank you for considering our paper as a publication in World Journal of Clinical Oncology.

1. Reviewer # 02544379: This is a well written comprehensive and detailed overview of neoadjuvant trials in pancreatic cancer. I would suggest adding the radiation dosages that were used in the different studies to make comparison easier.

We have added radiation dosages in table I and II, highlighted in yellow, as suggested by reviewer for easier comparison.

2. Reviewer # 20150727: I agree that this review is very informative and contains a lot of references. This manuscript needs some reconsideration. Among the descriptions, the information of ACOSOG Z5041 is very exciting. The authors say that this phase II study will announce the benefit of erlotinib as an adjunct to gemcitabin as an neoadjuvant. Are there any publications to show the evidence that this phase II study demonstrates the future possibility of addition of erlotinib to the neoadjuvant therapy for resectable pancreatic cancers? In NIH website for NCT00733746, I could find no study results posted. The authors seem to cite reference 25 as an evidence of the above conclusion, but reference 25 was published in 2007 and deals patients with advanced pancreatic cancer. In this phase II study, one of eligibility criteria is localized, potentially resectable tumors. Thus, please provide information sources, like publications or personal communications, to say 'The ACOSOG Z5041 will address the benefit of erlotinib as an adjunct to gemcitabine given perioperatively in resectable settings'. In addition, there are no comments on ecadherin in the biomarker section. It look more persuasive if more publications are included to explain why ecadherin is used for the biomarker of erlotinib, like ecadherin for erlotinib usage in patients with non-small cell lung cancer. Please explain the role of ecadherin as a biomarker for erlotinib in the biomarker section.

In responding to this reviewer's comments, we have made the following changes.

1. In page 8, we have the result of ACOSOG Z5041 study is "expected to be announced at end of 2015″ to "highly anticipated" since we do not have a confirmed time when the result will be announced.

2. In page 8, we have added reference 26 to support the statement of "The ACOSOG Z5041 will address the benefit of erlotinib as an adjunct to gemcitabine given perioperatively in resectable setting".

3. In page 12, we have added a new section to describe the utility of E-cadherin as a biomarker for pancreatic cancer.

All the changes are highlighted in yellow.

Sincerely,

Chung-Tsen Hsueh, M.D., Ph.D.