

Ying Dou

Science Editor, Editorial Office

World Journal of Meta-Analysis

4 June 2019

Dear Ying Dou,

Re: resubmission of manuscript reference No: 48225

Please find attached a revised version of our manuscript originally entitled "Adjuvant and Neoadjuvant Treatment versus Surgery Alone for Resectable Pancreatic Cancer: A Network Meta-analysis", which we would like to resubmit for consideration for publication in *World Journal of Meta-Analysis*.

The reviewer's comments were highly insightful and enabled us to greatly improve the quality of our manuscript. In the following pages are our point-by-point responses to each of the comments.

Revisions in the manuscript are shown as red text. and the entire manuscript has undergone substantial English editing.

We hope that the revisions in the manuscript and our accompanying answers will be sufficient to make our manuscript suitable for publication in the *World Journal of Meta-Analysis*.

Yours sincerely,

Zhang Tao, M.D., Professor

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the First Affiliated Hospital, Sun Yat-sen University

E-mail: 11139398@qq.com

Reviewer 1#

Reviewer's code: 00034177

Reviewer's country: Japan

SPECIFIC COMMENTS TO AUTHORS

This paper ignores the historical evidence of pancreatic cancer treatment. Historical evidence is very important to mention about chemotherapies. I am so sorry to reject your paper.

Answer:

Thank you for your kindly review. We are agreed with your opinion that historical evidence is very important to mention about chemotherapies. However, we include studies about pancreatic cancer treatment from 1985 - 2015, historical evidence is an important point in our network meta-analysis.

Reviewer 2#

Reviewer's code: 02541859

Reviewer's country: United States

SPECIFIC COMMENTS TO AUTHORS

Short meta-analysis. I have only suggestion to mention some of the chemotherapeutic agents used in the study.

Answer:

Thank you for your kindly review. We have discussed the chemotherapeutic agents used in the discussion part of the study (Page 16, Lines 419–430).

Reviewer 3#**Reviewer's code:** 02551692**Reviewer's country:** Italy**SPECIFIC COMMENTS TO AUTHORS**

The work is well done. Pancreatic cancer is one of the most common and lethal malignancies worldwide. However, the optimal treatment is still controversial. The authors, using network meta-analysis (which includes 13 high quality trials with 1591 participants), identify the most effective approach for pancreatic cancer: surgery with adjuvant CT. The work is very interesting because this is the first network meta-analysis comparing surgery alone, neoadjuvant chemotherapy (CT), neoadjuvant chemoradiotherapy (CRT), adjuvant CT and adjuvant CRT. Surgery with adjuvant CT has better survival compared with surgery alone and surgery with adjuvant CRT. The authors should give more details about figure 1 and figure 3. Results are exhaustively described. English language is overall good. Minor revision of the article is need.

Answer:

Thank you for your kindly review. Your suggestion is rational and we have added some detail information about figure 1 and figure 3 (Page 29, 31).

Reviewer 4#**Reviewer's code:** 00053888**Reviewer's country:** United Kingdom**SPECIFIC COMMENTS TO AUTHORS**

This is a large and powerful meta-analysis of adjuvant/neoadjuvant chemotherapy & chemoradiotherapy in the treatment of pancreatic cancer. There have been differing views expressed and demonstrated over recent years as to the best approach but this meta-analysis has allowed a certain degree of clarity to be applied. It appears that adjuvant chemotherapy is better than alternate approaches and this should allow researchers to concentrate on the best adjuvant chemotherapy regimes rather than continue to muddy the water with further neoadjuvant approaches and additional radiotherapy. There are a few things that are not made clear in the study and that should be addressed. This study refers only to 'resectable' pancreatic adenocarcinoma and borderline of conventionally irresectable but downstaging therapies are not addressed. Also the included studies are largely external beam radiotherapy and not some of the more highly targeted radiotherapy that are now available. the authors should clarify these points. In addition there are some grammatical errors that would need editorial input before final publication.

Answer:

Thank you for your kindly review. We are agreed with your opinion. This study refers only to resectable pancreatic adenocarcinoma, and we draw a conclusion that adjuvant chemotherapy is better than alternate approaches. Borderline pancreatic cancer is recently emerged as a category clinically distinct from resectable or locally advanced disease. We have discussed this topic in the discussion part and it is an interesting topic in further studies (Page 16-17, Lines 431-449).

It is a fact that the included studies are largely external beam radiotherapy. In

this network meta-analysis, only RCTs comparing the efficiency of neoadjuvant/adjuvant therapy and surgery alone are included. Highly targeted radiotherapy is now available and widely used. However, no RCTs comparing the efficiency of highly targeted radiotherapy can be found nowadays. We will discuss this situation in the discussion part. (Page 16, Lines 409–413)