

Dear Prof. Ma,

Re: Neoadjuvant chemotherapy for patients with resectable colorectal cancer liver metastases: A systematic review and meta-analysis

Thank you for your e-mail dated April 6, 2021. Here are my responses to the reviews' and Editorial office's comments.

#### Reviewer 1

Comment1; This meta-analysis tries to answer the question of usefulness of NAC in resectable colorectal liver metastasis, which remains controversial. This study concludes that NAC is useful in achieving better 5 year OS and DFS, without increasing the morbidity and mortality. The highly heterogeneous nature of the data from the studies included, renders the conclusion less authentic and emphasizes the need for further studies to provide a conclusive evidence.

Response1: Yes, our meta-analysis results showed that high heterogeneity in the pooled data for continuous variables and individual dichotomous variables, so subgroup analysis was conducted according to the different study regions and we performed a sensitivity analysis to explore their potential source and assess the robustness of the outcomes. After ignoring each included study in turn for each outcome, the results of those indicators were stable. These have been added into the paper.

#### Editorial office's comments

Issue 1: The "Author Contributions" section is missing. Please provide the author contributions;

Response1: These have been added into the paper.

Issue 2: 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);

Response 2: The approved funding application form and the copy of the funding agency's approval document have been updated in the manuscript and uploaded to the location of the document.

Issue 3: The authors did not provide original pictures. 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;

Response 3: These have been uploaded to the location of the file as required.

Issue 4: PMID and DOI numbers are missing 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;

Response 4: These have been modified and updated into the paper.

Issue 5: The "Article Highlights" section is missing. Please add the "Article Highlights" section at the end of the main text;

Response 4: These have been added into the paper.

I have revised the manuscript accordingly and the revised portion is marked in read bold. I hope this will make it more acceptable for publication.

Yours sincerely,

Hui Cai

### **Responses to the re-review comments**

Comment 1: The authors may include the limitations of the study in the conclusion itself instead of stating separately, (especially those limitations which may have influenced the quality and reliability of the conclusions).

**Response1: These have been modified and added into the paper.**

Comment 2: The authors may also explain why only NEC was discussed, whereas most of the studies included discuss peri-operative chemotherapy, which is the norm. The authors may include, in the discussion, points from the published guidelines (viz. NICE, ESMO, JSCCR, NCCN), on Perioperative chemotherapy.

**Response2: These have been modified and added into the paper. I have revised the manuscript accordingly and the revised portion is marked in read bold.**

I hope this will make it more acceptable for publication.

Yours sincerely, Hui Cai