Response to Reviewers
(Reviewer comments in bold letters)
Reviewer #1

This meta-analysis by the authors investigated the long-term efficacy of neoadjuvant chemotherapy of XELOX (Xeloda + Oxaliplatin) targeting colorectal cancer. Although the analysis from various clinical cases is well presented, there are some questions that need to be compensated for.
Thank you for the careful review of our manuscript and the constructive comments.

1. In the part of the purpose (line 30-31), there is a description "The study of colon cancer alone is rare, and the impact of chemotherapy on long-term survival is not clear.". This reviewer can't agree to this. Many clinical studies for the long-term survival or efficacy of XELOX have already been published (J Cancer. 2018; 9(8): 1365–1370). The authors must provide correct information in the background.
We appreciate this reviewer's very important comment and apologize for the incorrect description. In the revised manuscript, we corrected this information and cited this reference (J Cancer. 2018; 9(8): 1365–1370). Many clinical studies for the long-term survival or efficacy of XELOX in colon cancer have already been studied [1-3], but its clinical benefit is controversial.

2. The reason why XELOX has been studied a lot in rectal cancer than colon cancer is that "XELOX + Radiation therapy (RT)" has been used as standard therapy (more usually Xeloda + rt). This clinical background was not described.
We agree with this reviewer's criticism and we added this information in the manuscript. "XELOX has been studied a lot in rectal cancer than colon cancer is that "XELOX + Radiation therapy (RT)" has been used as standard therapy."

3. As described in the background by the authors, FOLFOX (5-FU + folinic acid + Oxaliplatin) is usually the first choice for colorectal cancer treatment without RT. There is very a few information about the advantages of using XELOX as an alternative to FOLFOX.
We appreciate this useful comment for the improvement of our manuscript. In the revised manuscript, we added the advantage of using XELOX as an alternative to FOLFOX. "In the Loree JM[6] study, XELOX and FOLFOX were compared in the treatment of Colon Cancer. The results show that XELOX may be associated with improved disease-free survival despite greater toxicities, and reduce adjuvant chemotherapy duration to 3 months. In a safety analysis of adjuvant chemotherapy for stage III colon cancer after radical resection of stage III colon cancer, mFOLFOX6/XELOX regimens are acceptable[7]."
4. FOLFIRI (5-FU + LV + Irinotecan) is used as 2nd line standard therapy for treating colorectal cancer following the 1st line therapy, FOLFOX. Information on the major clinical implications of selecting XELOX instead of standard

primary and secondary treatment is missing.

We thanks this reviewer's very important comment. In the revised manuscript, we added Information on the major clinical implications of selecting XELOX instead of standard primary and secondary treatment. "A retrospective study on XELOX plus bevacizumab vs. FOLFIRI plus bevacizumab treatment for metastatic colon cancer reported that XELOX plus bevacizumabis more effective in response rate and overall survival compared with FOLFIRI plus bevacizumab [8]".

5. The inclusion and exclusion criteria for this meta-analysis have missed a critical description. If the author's meta-analysis has purpose to compare the long-term outcome of patients undergoing adjuvant treatment after stage 3 colon cancer surgery with neoadjuvant treatment such as FOLFOX and FOLFIRI, the author must investigate if he or she received neoadjuvant treatment prior to surgery. The search must include a distinction between patients who performed or did not perform neoadjuvant.

We really appreciate this comment for improvement. In the revised manuscript, we added this information.

Reviewer #2

This is a great study as is. I see no strong evidence of publication bias. Analyses are properly conducted in large part. I have just a few comments.

Thank you for the careful review of our manuscript and for your critical comments.

Now, tumor molecular pathology assessment is routine part of clinical practice. This information is missing. That should be discussed as a weakness. Treatment effect is unlikely uniform across different molecular subtypes. Related to the above point, the authors should discuss molecular pathological epidemiology (MPE) as a future direction. MPE is an integrative science to deal with molecular pathology in relation to clinical features and outcome in patients and populations. MPE references can be easily found by google search (eg, Gut 2011; Annu Rev Pathol 2019, etc.).

We appreciate this reviewer's very important and constructive comment for improvement. In the revised manuscript, we added this information as a weakness of current study in the discussion section.
Nowadays, tumor molecular pathology assessment serves as a regular part of clinical practice. Treatment effect is unlikely uniform across different molecular subtypes. Molecular pathological epidemiology (MPE) is an integrative science to deal with molecular pathology in relation to clinical features and outcome in patients and populations. MPE will be a future direction for personal treatment (eg, Gut 2011; Annu Rev Pathol 2019, etc.).