

## Answering Reviewers letter

Dear reviewers and editors:

Thank you for your efficient work in procession of our manuscript entitled 'Prolonged time interval to surgery following neoadjuvant concurrent chemoradiotherapy may improve disease-free survival and pathologic response in rectal cancer' ( Manuscript NO.: 57106). We also really appreciate our dear reviewers for giving us precious advices, which are important for us to improve the quality of our work.

In addition, we have carefully revised our paper based on the comments of reviewers, and the point-to-point responses to the reviewers' comments are presented below:

Reviewer #1:

Comments: 1. There is no information regarding radiation therapy technique (2D, 3D, IMRT?) in the method section. As well, there is no information and analysis regarding the total mean dose of radiation between groups.

Response 1: I'm glad you to put forward valuable opinion, this problem we at the time of draft manuscript was also discussed. Because all the patients enrolled in this study were received long-term radiation therapy, the dose and regime were the same, so there was no information list, but in the article "neoadjuvant therapy" part of the "methods" has carried on the brief description, the illustration was insufficient in this manuscript, and caused understanding deviation. As for radiation therapy technology application for locally advanced rectal cancer was IMRT technology in our center, and we have supplemented this in the manuscript.

Comment 2: Currently, oxaliplatin-containing chemoradiotherapy is generally not considered a standard approach for long-course chemoradiotherapy in rectal cancer, due to more treatment-related toxicity and no better outcomes compared with standard fluoropyrimidine-based chemoradiotherapy. What is your rationale for the selection of an oxaliplatin-containing regimen in your treatments?

Response: Many thanks for this point in manuscript. In reviewing these patients, we first truthfully recorded the use of neoadjuvant chemotherapy in these patients. These patients were screened through our central colorectal surgery case database. The chemotherapy regimen was formulated by the previous oncologist and we could not decide. Secondly, according to the

patient data, some patients have the risk factors of simultaneous metastasis, so oxaliplatin-containing is used for preventive treatment. Although such a regime does not meet the requirements of the guidelines, it has some positive significance from the perspective of individual treatment of patients, and this group of patients did not show grade 3 or higher adverse reactions in oxaliplatin-containing. Thirdly, our center receives a large number of patients with colorectal disease every year. Due to scheduling problems, some patients will actively choose preoperative routine chemotherapy to wait for surgery, so oxaliplatin-containing will be used.

Comment 3: There is no data about the cycles of induction chemotherapy before surgery? induction chemotherapy before and after CRT and before surgery can induce more tumor shrinkage and provide a higher response rate in group B.

Response: Thanks for this suggestion sincerely. In our revised article, as previous discussion, enrolled patients received concurrent chemotherapy during radiotherapy with a cycle of 3-4. There was still no difference between the two groups in terms of dose and duration of radiation therapy, as described earlier. When we were involved in the study, we had made no difference between the two factors that might influence tumor regression before surgery, so that the comparison of the effects of time interval would be more meaningful.

Comment 4: In table 2, there is a mistake and you missed patients with ypT0!

Response: Thanks for finding this “mistake”, It's our mistake not to explain why we didn't list ypT0.

Because pCR data are in the same as ypT0 in table2, we calculated that if ypT0 is repeatedly included, the original correct statistical results will be biased

Finally, we really appreciate your hard and efficient work, every piece of advice is truly precious for us to improve the quality of our work.

With kind regards,

Yours sincerely