Peer Review File
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Reviewer A

Comment 1: The authors wrote that they assessed tumors at baseline using the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1, but generally, the main lesion of gastrointestinal tract cancers is difficult to evaluate using RESIST. For example, if a patient with cT2N0 disease, how did the authors evaluate this disease using RECIST criteria? The authors should explain details. How did the authors define as PR?

Reply 1: We thank the reviewer for this comment, and we would like to mention four major points in order to reply to this comment.

1、We are very sorry for our negligence of the clerical error in **Patients** part**.** According to 2023 CSCO, patients with cT2N0M0 disease are supposed to have surgery directly without neoadjuvant therapy (Strength of recommendation: 2A), so there were no patients with cT2N0M0 in our study.

2、As for Patients with cT3N0M0 disease, neoadjuvant therapy in combination with esophagectomy is the mainstay of treatment. (Strength of recommendation: 1A).

3、The CT measurements included lesion longest diameter (LLD, obtained at cross-sectional CT imaging), total number of clinically metastatic lymph nodes and the short diameter of the largest regional lymph node (SDL). The size of the lesion (based on the imaging and physical evaluations) will be used to compare the results based on RECIST v1.1 and the same imaging method should be used for the same subject during the trial. Other affected sites(such as PET-CT) should be examined based on the signs and symptoms of each subject. Radiological assessment will be conducted within 2 weeks before treatment initiation and again 4-6 weeks after the completion of the last nICT.

4、 The ORR was calculated according to the RECIST guidelines version 1.1 Complete response (CR) was declared when all the lesions (including scars) had disappeared radiologically or under gastroscope, partial response (PR) when there was a decrease in the size of target lesion (short diameter of LN >15 mm) ≥30%, stable disease (SD) when change in target lesions was within ±20%, progressive disease (PD) when the lesion enlarged by 20%.

Changes in the text: **see Page 6, line 121.**

Reviewer B

Comment 1: The low resection rate of 74.4% was commented to be due to refusal of surgery (23.3%). This would strongly affect the actual pathological outcome. Although in the discussion section, it was explained that most of the patients who refused have a clinical complete remission, we do not have an actual percentage. A high CR rate in drop-out may cause a falsely low pCR rate.

Reply 1: We thank the reviewer for this comment and agree with the fact that a high CR rate in drop-out may cause a falsely low pCR rate. We feel sorry that we did not provide enough information and we have checked our original data carefully. On the basis of our data, patients who had refused surgery(11 patients) most had significant improvement in QOL which means clinical symptoms were alleviated after tumor reduction. Among patients refusing surgery, 2 patients achieved a CR, 6 patients attained a PR, 2 patients got a SD and 1 patient experienced disease progression.

Comment 2: There is a rather large discrepancy between the Radiological CR rate (9.3%) and Pathological CR rate (28.1%), despite a "correlation" being found, signifying that the accuracy of radiological assessment alone for post-neoadjuvant assessment is inadequate. In your cohort, did you combine endoscopic (EUS/Upper endoscopy/Biopsy) assessment and radiological assessment in post-treatment assessment before surgery?

Reply 2：Thank the reviewer for the very constructive suggestion here. Radiological responses were assessed to confirm the efficacy of the neoadjuvant therapy by two independent central expert radiologists based on Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. CT is a commonly used imaging method for efficacy evaluation by measuring changes in tumor size or length in the treatment of ESCC. However, after treatment, significant fibrosis and edema often appear in the esophageal wall and surrounding tissues, which may interfere with the accuracy of CT measurement. Endoscopic (EUS/Upper endoscopy/Biopsy) assessment can't be evaluated with RECIST version 1.1. Moreover, there is no standard evaluation method for endoscopic (EUS/Upper endoscopy/Biopsy) assessment, so it's hard to combine endoscopic (EUS/Upper endoscopy/Biopsy) assessment and radiological assessment in post-treatment assessment before surgery. The discrepancy between the radiological CR rate and Pathological pCR rate also can be found in NIC-ESCC2019 study, SIN-ICE study, and other neoadjuvant trials of ESCC. We hope that there will be a standard protocol in the future.

Comment 3: The method section mentioned that overall survival and relapse-free survival were considered exploratory endpoints, but there was no data in the results section.
Reply 3：We thank the reviewer for this comment, as what we mentioned in DISSUCION, "A further limitation is that our study did not reach the exploratory endpoints RFS and OS because of the relatively short follow-up period. However, our study is still being followed up, and the long-term results will be reported after completion.", the follow up duration was short and there was no mature OS data so far, we all wish the long-term results will be reported after completion.

Comment 4: Pneumonia is one of the most common postoperative complications, which was not mentioned in the complication list. Consider using the ECCG complication definition list.
Reply 4: We sincerely appreciate the valuable comment. We have supplemented extra data and modified the **postoperative complications** part in the revised manuscript by referring to the ECCG complication definition list.
Changes in the text: **see Page 12, line 295-297**. A revised summary of the surgical findings is provided in *Table 6*, which is provided in a separate file named **Table 6**.

Comment 5: Please briefly discuss the difference between Sintilimab and other immune checkpoint inhibitors.

Reply 5: We are sorry that this part was not clear in the original manuscript. We should have explained that the difference between sintilimab and other immune checkpoint inhibitors. We have revised the contents of this part.

Multiple preclinical in vitro trials have demonstrated the ability of sintilimab to block the PD-1 pathway, such as the high binding affinity and low dissociation constant of sintilimab. The Orient-15 study showed that the overall survival advantage with sintilimab in combination with chemotherapy was not related to expression of PD-L1.

Changes in the text: **see Page 5, line 99-101**.

Comment 6: Most of the patients in the PreSANO/SANO study had adenocarcinoma, which may not be applicable or comparable to the patient population in this study.

Reply 6: Thanks for the constructive advice. As you suggested, we have added the relevant description to the article. The pre-SINO study was led by Professor Li Zhigang from Shanghai Thoracic Hospital, its aim was to assess the accuracy of response evaluations according to the preSANO trial outcome after nCRT in patients with ESCC, including PET-CT, endoscopy with bite-on-bite biopsies and endoscopic ultrasonography (EUS) with fine-needle aspiration (FNA) in patients with potentially curable ESCC. If the pre-SINO study shows that major locoregional residual disease (> 10% residual carcinoma or any residual nodal disease) can be accurately (i.e. with sensitivity of 80.5%) detected in patients with ESCC, a prospective trial will be conducted comparing active surveillance with standard esophagectomy in patients with a clinically complete response after nCRT (SINO trial).

Changes in the text: **see Page 15, line 381-384.**

Comment 7: Spelling mistake: Page 11, Line 270, "CORSS" study.

Reply 7：We are very sorry for our incorrect writing of "CROSS", and we have modified our text as advised.

Changes in the text: **see Page 13, line 321.**

Reviewer C

Comment 1: Abstract- expected pCR written once 30.4% and other place 30.5%

Reply 1：We are very sorry for our negligence of the expected pCR rate, and we have checked our original data which showed the expected pCR rate was 30.5% and modified our text as advised.

Changes in the text: **see Page 2, line 44.**

Comment 2: Methods- some confusion on the protocol- who got CT and Physical and who got PET/CT and EUS and when

Reply 2：We thank the reviewer for this comment. In our study, every patient underwent physical examination, CT and EUS for diagnosis and assessment within 2 weeks before treatment initiation and again 4-6 weeks after the completion of the last nICT. If indicated, positron emission tomography-computed tomography (PET-CT) was performed to exclude distant metastatic disease for initial staging.

Comment 3: L148- EGD - you probably mean Endoscopic Gastro Duodenoscopy and not Electronic.
Reply 3: We are very sorry for our incorrect writing of " Electronic", and we have modified our text as advised.
Changes in the text: **see Page 7, line158.**

Comment 4: Which "other staging examinations" you mean?
Reply 4: Thanks for the kind reminder. Other staging examinations included cranial magnetic resonance imaging (MRI), whole-body bone scanning. And for patients with suspected cervical lymph node involved, external ultrasonography of the neck with fine needle aspiration or PET-CT was required.
Changes in the text: **see Page 7, line 158-159.**

Reviewer D

Comment 1:、Could the authors explain what they are referring to when they say that patients undergoing nCRT have exhibited a higher recurrence rate (compared to?)
Reply 1: Thanks for the kind reminder. We apologize that “higher” may be a clerical error and it’s supposed to be “high”. What we refer to is the ten-year outcome of CROSS trial and some other references listed in the **REFERENCES** part.
With the publication of the results of the CROSS and NEOCRTEC5010 trials, nCRT combined with surgery has become the standard treatment for esophageal cancer. However, 40% to 50% of patients still experience tumor relapse, with distant metastasis being the most common. High recurrence and metastasis are still the main reasons for treatment failure. Therefore, there is an urgent demand for novel therapeutic strategies to address these challenges.
Changes in the text: **see Page 4, line 78.**
Comment 2: The authors should describe in more detail how the study was conducted: How the radiologic assessment was made: was only one radiologist? was the radiologist aware of the ongoing study? Was there only one surgeon or different surgeons involved? How the pathologic assessment was performed; was it only one pathologist? was he aware of the ongoing study? This information is pertinent for a better assessment of the presented outcomes.
Reply 2: We feel sorry that we did not provide enough information about how the study was conducted and we indeed thank you for your reminding. Your comment is of great importance to our article and have contributed a lot to improve the quality of this revision.
Radiologic responses were assessed to confirm the efficacy of the neoadjuvant therapy by two independent central expert radiologists based on RECIST v1.1. Pathological examination of the surgically resected specimens was performed independently by two senior pathologists using a standard protocol. All surgeries were performed by a professional and experienced thoracic surgeon at Lanzhou University Second Hospital, of whom performed more than 100 surgeries annually. All of the radiologist, pathologist and the surgeon are aware of the ongoing study priorly.
Changes in the text: **see Page 7, line 165-174.**

Comment 3:Discussion section line 284
Authors should elaborate or support better the assertion that the regimen did not affect the number of LNs resected during surgery.
Reply 3: Thanks for the constructive advice. As you suggested, we have added the relevant description to the article. It has been reported that the number of lymph nodes removed in the neoadjuvant immunotherapy group is significantly lower than that in the surgery alone group in NSCLC patients. However, the number of lymph node dissection in our study was comparable to that of the surgery alone group in Wang's research. These results demonstrated that this neoadjuvant therapy model can't affect the number of LNs resected during surgery and achieve satisfactory complete resection.
Changes in the text: Changes in the text: **see Page 13, line 335-338.**