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Dear professor Hsin-Chen Lee,

This letter pertains to our submission of the revised manuscript entitled: "Impact of duration of adjuvant chemotherapy in radically resected patients with T4bN1-3M0/TxN3bM0 gastric cancer" (Manuscript NO.: 36031).
We would like to thank you for giving us an opportunity to revise our manuscript. We thank the reviewers for their constructive and insightful comments, which helped us to improve the manuscript. As requested, we have corrected the mistakes in our manuscript and attached our point by point responses to the reviewer's comments.
We hope that the revised manuscript is satisfactory and acceptable for publication in *World Journal of Gastroenterology Oncology*. We look forward to your response regarding the revised manuscript.

Yours sincerely,

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Reviewer 1（Number ID：00505438）

Comment 1: The authors note 12 patients who declined chemotherapy. It was unclear what the outcome of these patients were. Were they excluded from analysis or were they included in the patients who had chemotherapy less than 6 mths. They should be recorded as a separate group in terms of outcome as if there any survivors from this group it could raise so questions as to the conclusions.

Response: Thank you for your comments. The survival data of the 12 patients who had declined postoperative chemotherapy was recorded as a separate group in **Table 5**， the median OS of theses patients was 18.6 months. They were excluded from the analysis of the patients who had chemotherapy less than 6 months. The Table 5 was also shown as below:

Comment 2: The authors rightly note the heterogeneous group particularly with chemo regimes but by categorizing them into mono, bi and tri therapy groups they overcome some of these issues. It is unclear however how they deal with patients who had recurrence and then moved onto further regimes. Were these patients included in the study and if so what were the outcomes.

Response: Thank you very much for your suggestions. More than half of the patients received palliative chemotherapy after relapse, but the specific treatment regimen was unknown due to the retrospective analysis. Therefore this study failed to make a correlation analysis.

Comment 3: The authors concentrate on outcomes with korean and japanese studies not unnaturally as these deal with adjuvent therapies. However the screening programmes used in these countries mean that they do not have the bulk of experience in advanced gastric cancers and the authors should reference the european and australasian literature where this is far more commonly seen and compare their outcomes. Similarly the gold standard for treatment of these stages of gastric cancer in europe, Australasia, and US is neoadjuvent therapy followed by surgery then adjuven t therapy. The authors should discuss these regimes and the associated clinical studies more comprehensively in their discussion perhaps looking at geographical differences in terms of treatments. Similarly the gold standard for treatment of these stages of gastric cancer in europe, Australasia, and US is neoadjuvent therapy followed by surgery then adjuvent therapy. The authors should discuss these regimes and the associated clinical studies more comprehensively in their discussion perhaps looking at geographical differences in terms of treatments.

Response: Thank you for your useful suggestions There are great differences with gastric cancer between Eastern and Western countries in the primary site, biological behavior，

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therapeutic approaches and other aspects, so this study of China discussed the data in Japan and South Korea, did not involve more data from European and American. With the changes in treatment philosophy, the treatment of these stages of gastric cancer in china is also neoadjuvent therapy followed by surgery then adjuvent therapy in recent years. However, due to limited evidence and a lack of gold standard for treatment, T4bN1-3M0/TxN3bM0 gastric cancer remains a challenging clinical problem. Our retrospective study analyzed the adjuvent therapy for patients with T4bN1-3M0/TxN3bM0 gastric cancer, which were impossible to received adjuvent therapy alone now in clinical practice. This study is complementary to large-scale phase III prospective trials in the adjuvant chemotherapy in Asia.

Comment 4: The authors rightly acknowledge the limitations of their preoperative staging regimes in terms of identifying metastatic disease and thus the ability in avoiding futile surgery. The authors should discuss the staging investigations which were used and the fact that those patients who had a laparotomy only and recurrence within 1 month undoubtedly had preoperative metastatic disease accounting for their demise which with modern staging would not have had a laparotomy. This should be more fully discussed.

Response: In this study, the staging investigations included physical examination, routine laboratory tests, abdominal computed tomography (CT) scan, endoscopy, and chest X-ray. New diagnostic modalities such as endoscopic ultrasound (EUS), positron emission tomography/computed tomography (PET/CT), magnetic resonance imaging (MRI), and laparoscopic staging, were not used for preoperative staging of patients treated during the early part of the study, which may have reduced the accuracy of staging and led to the advanced gastric cancer be treated as resectable gastric cancer improperly [12-14]. Therefore, patients included in this study may be mixed with advanced patients actually, and these errors can be avoided using new staging approach. We have discussed it in the manuscript.

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Reviewer 2（Number ID：02534438）

Comment 1: Authors state from 326 patients with T4bN1-3M0/TxN3bM0 stage there were 18+48 patients with distant metastases ? M0 excludes distant metastases. Btw., what were those distant meatstases ? Liver ? Lungs ? Also, from 326 patients who underwent R0 resection 21 had positive resection margin ?

Response: Thank you for your useful suggestions. We screened patients with T4bN1-3M0 / TxN3bM0 GC from the postoperative pathology reports, and during preoperative imaging data 18 of these patients had confirmed distant metastases, mostly peritoneal metastasis and liver metastases. The metastatic lesions and the primary lesions did not reported in one report clinically，led to imperfect pathological M-staging. Thus, we checked the integrated medical records and then excluded these patients. In addition, 21 patients with surgery without R0 resection were confirmed to be R1 excision in the postoperative pathology reports, we also excluded out these patients（Fig. 1）.

Comment 2: What do authors mean by D2 lymphadenectomy ? By the book, it involves splenectomy, but many surgeons call spleen presevring gastrectomy D2. Actually it is in between D1 and D2, depending on how well the splenic nodes were harvested (usually not sufficiently in Europe).

Response: Thank you for your comments. According to the NCCN Clinical Practice Guidelines in Oncology-Gastric Cancer（Version 4.2017）, D2 dissection is a D1 plus all the nodes along the left gastric artery, common hepatic artery, celiac artery, splenic hilum, and splenic artery. Routine or prophylactic splenectomy is not required. Splenectomy is acceptable when the spleen or the hilum is involved. The D2 lymphadenectomy mentioned in this study was the standard D2 lymphadenectomy with non-essential splenectomy, according to the NCCN Clinical Practice Guidelines. We added this note in the manuscript.

Comment 3: Do outcomes differ between different regimens of doublet and triplet chemotherapy ?

Response: Thank you for your comments. As a result of the retrospective analysis, a variety of regimens of doublet and triplet chemotherapy, including capecitabine/S1/5-FU, FOLFOX, XELOX, SOX, capecitabine/S1+cisplatin, paclitaxel+capecitabine, paclitaxel+cisplatin/oxaliplatin and triplet chemotherapy based on 5-FU, were involved in this study. Due to fewer cases in each group, we failed to make a difference in prognosis among the patients with different regimens.

Comment 4: Was intraperitoneal perfusion performed in a HIPEC setting with peritonectomy ?

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Response: Thank you for your comments. In this study, only fourteen patients received intra- or postoperative intraperitoneal perfusion, not in a HIPEC setting.

Comment 5: Why was stage included in multivariate analysis when it was not significant in univariate analysis ?
Response: Thank you for your comments. Although there were no statistically significant differences in the univariate analysis, the 5-year survival rate was considered to be in magnitudes of difference among the patients with different stage. In order to avoid missing the important factor due to the presence of confounding factors in the univariate analysis, the stage was involved in the multivariate analysis.

Comment 6: How many patients had bone metastases without liver or lung metastases ?
Response: Eight of ten patients had bone metastases as the first recurrence site without liver or lung metastases. We added this note in the manuscript.