In reference to the manuscript entitled "Safety and effectiveness of a PD-1 inhibitor combined with oxaliplatin plus S-1 in patients with Borrmann large type III and IV gastric cancers", this retrospective study is interesting and novel as it aims to compare two patient populations with Borrmann large type III or IV gastric cancers treated with oxaliplatin + S-1 with or without an unknown PD-1 inhibitor! The manuscript is of interest; however, minor and major issues must be addressed before any further consideration!

We thank you and the reviewers for the positive assessment and constructive comments and suggestions. We have now revised the manuscript accordingly. The major changes in the text are marked in red. The entire manuscript has been proofread and met the journal's guidelines.

Please revise in a point-by-point manner with the track changes so that the changes are visible to the reviewers!

Responses: We thank the reviewer for the positive assessment and constructive comments and suggestions, which have helped tremendously in the preparation of the revised manuscript. We have now revised the manuscript accordingly.

Please specify the PD-1 inhibitor in the abstract section. There are numerous typos and errors in the text which requires that it undergo a substantial English revision preferentially by a native speaker colleague experienced in this field or by a language-editing service provider. Sone tenses must also be revised.

Responses: Thank you for your suggestion.We are sorry about these faults, and we have modified all the mistakes.

One of the major gaps of this study is that there is no data of the assessment of the expression level of PD-1 or PD-L1? How do you think this might have affected the findings presented herein?

Responses: Thank you for your suggestion. Large Phase III randomized controlled studies such as ORIENT-16, CheckMate649, and KEYNOTE-811 have established the status of immunotherapy in the first-line treatment of advanced gastric cancer. Immunotherapy has not previously been a first-line treatment option for patients with advanced gastric cancer. We conducted a preliminary exploration of chemotherapy combined with immunotherapy in some advanced gastric cancer patients through an investigator-initiated clinical study. Our study retrospectively screened Borrmann III and IV patients and conducted a clinical study on whether chemotherapy combined with immunotherapy was used in these patients. Conclusion Borrmann major III and IV combined immunotherapy is superior to chemotherapy alone.

At the end of the introduction section, the nature of the PD-1 inhibitor is not elucidated yet. Please revise! The clinical trial registry number must be included both in abstract and main text alongside references to the original article(s).

Responses: Thank you for your suggestion. The clinical trial registration number has been added to the abstract and main text.

What is even this PD-1 mAb? Where is there no info of it? Are there more than one PD-1 inhibitor? Please specify all grading schemes with reference!

Responses: Thank you for your suggestion. A total of 28 immunotherapy patients were enrolled in our study, including 13 patients who were resistant to Sintilimab, 2 patients who were resistant to Carrilizumab, 4 patients who were resistant to Toripalimab, 2 patients who

were resistant to Pembrolizumab, 3 patients who were resistant to Tirelizumab, 3 patients who were resistant to Nivolumab, and 1 patient who was resistant to Cadonilimab.

Instead of using words such as discernible for reporting statistically significant difference, the authors must use "significant" throughout the text. There must be substantial revisions in the text wherever results are reported with statistical analysis.

Responses: Thank you for your suggestion.We are sorry about these faults, and we have modified all the mistakes

In section 3.6, results are compared based on the variates before and after treatment, rather than between the two study groups. However, the authors conclude that P-SOX is safer. How does this work?

Responses: Thank you for your suggestion. As shown in Table 6, there was a statistical difference between the SOX group, the leukocyte group, the red blood cell group and the lymphocyte group before and after blood images compared with the P-SOX group, and the reduction of blood images in the SOX group was more obvious than that before chemotherapy. The SOX group and the P-SOX group had statistical differences before and after treatment in the platelet group, but the P-SOX group showed a more obvious trend of overall blood image decline than the SOX group.

In the discussion section, please go deeper and give reader some details (in terms of CR, PD, SD, ORR, etc.) While discussing clinical findings!

Responses: We thank the reviewer for the positive assessment and constructive comments and suggestions.As mentioned above, this study describes the situation of cancer by evaluating pathological regression response. Relevant studies have pointed out that pathological regression response has highly similar prognostic evaluation results on tumors. Due to the short overall review time of this study, pathological regression response was adopted to judge the therapeutic effect of gastric cancer.

What do you this is or might be the underlying mechanism for less postoperative adverse events in the group that also underwent immunotherapy? is there a study that has investigated this?

Responses:Thank you for your comment. The adverse events in the P-SOX (with immunotherapy) group were generally similar to those in the no SOX (without immunotherapy) group, except for the difference in the amount of blood loss (decreased bleeding compared with the SOX group), which may be due to the obvious tumor regression, reduced degree of tumor invasion, and reduced difficulty of surgical resection after immunotherapy.

Review to the manuscript No. 89428 “Safety and effectiveness of a PD-1 inhibitor combined with oxaliplatin plus S-1 in patients with Borrmann large type III and IV gastric cancers” Unfortunately, late diagnosis of gastric cancer remains a serious problem in oncology. Patients with locally advanced GC require neoadjuvant chemotherapy, the effectiveness of which determines the prognosis of the disease. Unfortunately, existing neoadjuvant chemotherapy regimens for gastric cancer are often not effective enough. In this regard, the search for new treatment regimens may help improve long-term results of treatment of this

pathology. The authors note the advisability of including immune checkpoint inhibitors in standard neoadjuvant treatment regimens for patients with gastric cancer and substantiate the key predictors of response to this treatment. The results obtained are interesting from a clinical point of view. However, there are a number of issues and comments that the authors need to pay attention to.

We thank you and the reviewers for the positive assessment and constructive comments and suggestions. We have now revised the manuscript accordingly. The major changes in the text are marked in red. The entire manuscript has been proofread and met the journal ' s guidelines.

Abstract Give the correct definition of the abbreviation "TRG", namely, "tumor regression grade" Introduction 1. Page 4, line 3. Duplication of the expression "...chromosomal instability (CIN), and chromosomal instability (CIN)[9]." Define the abbreviations TCGA, MSS and ORR.

Responses: We thank the reviewer for the positive assessment and constructive comments and suggestions, which have helped tremendously in the preparation of the revised manuscript. We have now revised the manuscript accordingly.

Materials and methods Evaluation of the Treatment Effect It is advisable to provide specific criteria for assessing the effectiveness of neoadjuvant chemotherapy, which were followed by radiologists. In addition, the results obtained should be reflected in the appropriate section. Or authors must exclude assessment of the effectiveness of neoadjuvant chemotherapy using radiation methods. Results Given that the authors compare the frequency of ypN0 in the group of patients receiving P-SOX and SOX, it is advisable to provide cN0 values before treatment in these groups.

Responses: Thank you for your comment, we have defined TCGA, MSS and ORR, and added relevant values in Table 1. As shown in Table 1, cN0 in the two groups did not show statistical difference in the initial data, thus excluding the statistical difference between the two groups before treatment.

Clinical Characteristics Sentence: "At the time of the initial diagnosis, there was a statistically significant difference in CA125 (32.14% vs 14.75%, p = 0.034)." It is unclear from this sentence which group had higher CA125 levels. Discussion. Define the abbreviation "CPS" Tables The title "Demographic data..." is probably not the best title Supplement Table 2. Please note that for the PD-L1 marker you give RR = 1.356 and 95% CI = 0.090-0.740. It is incorrect. Either the RR must be less than 1 or both 95% CI values must be greater than one. There are quite a lot of stylistic errors and incorrect expressions in the manuscript. The manuscript requires language correction. In addition, it is advisable for authors to adhere to generally accepted terminology, for example, to use in the text the phrase "lymphovascular invasion" and not "vascular tumor thrombus"

Responses: Thank you for your suggestion.We are sorry about these faults, and we have modified all the mistakes.