

Dear Editors and Reviewers,

Thank you for your letter and reviewers' comments concerning our manuscript entitled "**LTEVB₁₂ initial and celecoxib rescue therapy reverse intestinal metaplasia and atrophy of chronic gastritis: a retrospective cohort study (Manuscript NO: 65281)**". These comments are very valuable and helpful for improving and revising our paper. We have studied comments carefully and have made revision which we hope meet with approval. Revised parts are highlighted in line numbers and pages. The main corrections in the paper and the responses to the editors and reviewers' comments are as follows:

Comment: Major i) Some papers[1, 2] have shown that H. pylori eradication improves AG and IM, and I think that its effect in this study should be discussed. In addition, since there has been some discussion on the post-eradication period, it is recommended that this period be described if possible. 1. Kong YJ, Yi HG, Dai JC, et al. Histological changes of gastric mucosa after Helicobacter pylori eradication: a systematic review and meta-analysis. World J Gastroenterol 2014;20:5903-11. 2. Kodama M, Murakami K, Okimoto T, et al. Ten-year prospective follow-up of histological changes at five points on the gastric mucosa as recommended by the updated Sydney system after Helicobacter pylori eradication. J Gastroenterol 2012;47:394-403.

Response: We really appreciated your comments which is important to our study. We conducted extra literature review to provide some evidence about reversibility of IM to enrich the content of the article. The revision lied from line 16, page 14 to line 2 page 15.

Comment: Major ii) From line 28, page 9 to lines 1-2, page 10 The authors found that higher stages of the disease (stages III and IV) using the Operative Link on Gastric Intestinal Metaplasia Assessment (OLGIM) and Operative Link on Gastritis Assessment (OLGA) systems responded well to monotherapy compared to the lower stages. This is an important result, since it implies that that the benefit of this therapy is greater for those who are at higher risk. Therefore, a discussion on why the effect is more pronounced in higher stages would be more useful to the readers.

Response: We sincerely appreciate your significant comment. We conducted more discussion on why the effect is more pronounced in higher stages would be more useful. However, because of the stages of IM were related to many factors from

individual and study design. We provide our ideas for readers to discuss. The revision lied from line 23, page 13 to line 29 page 23.

Comment: Minor i) Lines 17-18, page 6 Is this 35 an error in the description? This is different from the number given in sup1.

Response: We sincerely appreciate your significant comment. We have rechecked our manuscript to correct the error. We delete the “35”.

Comment: Minor ii) Lines 14-15, page 8 This study did not compare LTEVB₁₂ alone or celecoxib alone with LTEVB₁₂ initial and celecoxib rescue therapy. Rather than saying that the combination was more effective, it would be better to state that the addition of celecoxib rescue therapy further increased the regression rate of IM.

Response: Thank you for your prudence. Based on your suggestion, we have changed the better expression in the manuscript. The revision lied from line 23, page 11 to line 25 page 11.

Comment: Minor iii) Lines 26-27, page 8 The COX-2 inhibitor celecoxib has been suggested to cause H. pylori-related gastric lesions through various mechanisms, and a description of the definition of high-risk clinical risk factors is needed. This sentence seems to be contradictory in the context of the preceding and following sentences; if celecoxib works as a tumor suppressor, it should be rewritten. If celecoxib is involved in gastric lesions, it would be better to cite the literature.

Response: We really appreciated your comments which is important to our study. That is a clerical error. We carelessly used “The COX-2 inhibitor celecoxib” instead of the correct expression “COX-2”. The expression of COX-2 has been suggested to associated with the development of GC. So that the COX-2 inhibitor celecoxib was found to inhibit tumor-promoting effect of COX-2. In manuscript, we have been illustrated. The revision lied from line 10, page 12 to line 15 page 12.

Comment: iv) Table 2, page 22 The table footnote listed PP = per-protocol, but it seems unnecessary because PP is not used in the table in the first place.

Response: Thanks a lot for your important suggestion. We have deleted the “PP = per-protocol” in the footnote of Table 2.