

August 1st 2016

Dear Editors,

We thank referees for careful reading our manuscript and for giving useful comments.

In response to the Referees' comments, we have revised the manuscript

“Potassium-competitive acid blocker versus proton pump inhibitor for the healing of gastric ulcers induced by endoscopic submucosal dissection: a pilot prospective randomized controlled study”.

We look forward to a publication of our manuscript in *World Journal of Gastrointestinal Endoscopy*.

Sincerely,

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Our responses to the referees' reports are as follows.

Response for reviewer No.02441611

#1. The experiment still needs further improvement, because there is lack of the evidence of Vonoprazan and lansoprazole in the patients with extensive and poor metabolizers.

Although CYP2C19 polymorphism is important for the decisive conclusion, it was impossible to perform this examination at that time. It is the next assignment to investigate clinical effect of vonoprazan and lansoprazole for patients with extensive and poor metabolizers. This is the limitation of this study and I wrote this point in the discussion as follows: **“Third, we did not investigate the polymorphism of CYP2C19 in this study. This is important for making definitive conclusions.”**

#2. There were no complications such as bleeding in the enrolled patients in both group. Which is related to case screening or drug efficacy? It need to be further clarified.

We speculated that was related with the potent acid suppression of vonoprazan and lansoprazole and our careful hemostasis procedure during ESD. Therefore, we added the sentences in the discussion as follows: **“In our study, the delayed bleeding rate was 0% in both groups although our sample size was too small for the precise evaluation of the preventive effect on delayed bleeding. There are several reasons for this result. First, the acid suppression of both vonoprazan and lansoprazole was potent enough to prevent delayed bleeding. Second, we carefully coagulated thick blood vessels that might bleed afterward.”**

#3. Because vonoprazan did not show superiority to lansoprazole with regard to ulcer

healing after ESD and lansoprazole is more cost-effective, further study is needed to explore the necessity of using vonoprazan for the treatment of post ESD ulcers.

We totally agree with the reviewer and concluded as follows: **“Since vonoprazan theoretically has more potent acid-suppression and is not affected by CYP2C19 polymorphism, it could be more effective in the high risk groups or extensive metabolizers. A further prospective study with these patients is needed to make a definitive conclusion.”**

#4. This discussion indicates that vonoprazan might prove to be superior to PPIs in extensive metabolizers. Is this speculation or logic deduction? The results need further clarify.

Vonoprazan is not affected by CYP2C19 polymorphism and it was proved to have sustained, rapid, and more potent effect on acid suppression compared to PPIs.^[1-3]

Although vonoprazan could be more effective in the high risk groups or extensive metabolizers, we did not investigate these points in this study. Therefore, the conclusion was based on our speculation.

Response for reviewer No. 00069471

#1. Please explain how the sample size was decided.

This is a pilot study and we did not perform the formula calculation. Our sample size was relatively small compared to the previous same kind of studies.^[4,5] Therefore, we

wrote this limitation in the discussion as follows: **“the sample size was not large enough to obtain conclusive results.”**

#2. Please explain how to randomize the patients (e.g. envelope method).

We used permuted-block randomization. Therefore, we added the sentence in the study protocol as follows: **“Patients were prospectively and randomly assigned into either the vonoprazan or the lansoprazole group using permuted block randomization (Figure 1).”**

#3. Are authors planning to conduct a large-scale RCT in the future? In the present study it seems that P-CAB is not always necessary after ESD.

We concluded vonoprazan could be more effective in the high risk groups or extensive metabolizer. Therefore, we are planning to perform a prospective study with such patients.

Response for reviewer No.01469554

#1. Originally, anticoagulant, antiplatelet agents, and steroid user should be removed to arrange conditions without complications in comparing ulcer healing, but please add that it ended up in the study with combination of them to discussion.

We added it to the discussion as follows: **“Fourth, anticoagulant, antiplatelet agent,**

and steroid users should have been removed from the study to prevent their associated complications from affecting the comparison. However, they were included in the present study.

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