

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 7240-review.doc).

Title: Efficacy of tailored *Helicobacter pylori* eradication therapy based on antibiotic susceptibility and CYP2C19 genotype

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Name of Journal: *World Journal of Gastroenterology*

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The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

Reviewer 1.

- 1> There are some writing errors (i.e; " eradication" in line 88, ..10 mg q.d.s.. in Line 280 and etc).

Response:

According to Reviewer's comments, we carefully check and edit any writing errors in revised version.

- 2> In Lines 141-145 " The Maastricht IV consensus report recommends first-line eradication treatment using a CAM-based regimen (PPI-CAM-AMPC or -metronidazole [MNZ]), a bismuth-containing quadruple treatment in areas where prevalence of CAM-resistant strains is low, and a bismuth-containing quadruple treatment in areas of high resistance.1" should be corrected. Because in the Maastricht IV consensus report; in the in areas of low clarithromycin resistance, clarithromycin- containing treatments are recommended for first-line empirical treatment and bismuth-containing quadruple treatment is proposed as an alternative treatment regimen.

Response:

Thank you for your suggestion. This was our mistake. Therefore, we edit these sentences about the Maastricht IV consensus report in revised version.

- 3> When we use rabeprazole q.i.d. for all patients (the authors' proposal; Lines 340-342) irrespective of patients' CYP2C19 genotype, it will take a huge cost because not all patients are rapid metabolizer (RM). This proposal may be applicable to patients with first ± second eradication failure.

Response:

Thank you for your comments. As your suggestion, this tailored treatment may be applicable third-line treatment, because not all patients are RM of CYP2C19. However, I think that benefits of this tailored treatment are to save a cost of

genotyping test and to prevent increased CAM-resistant *H. pylori* strain.

According to your suggestion, we add any explanations as limitations of this tailored treatment (e.g., cost) in revised version.

Reviewer 2.

- 1> In terms of genotyping, although the authors propose a way that can save the cost of CYP2C19 genotyping, there are other genetic factors (Table 1) to be considered to implement a tailored therapy. This will be time consuming and the cost-effectiveness needs to be evaluated. Besides, the impact of genotyping can be improved by increasing the doses and/or frequency of PPIs. The antimicrobial resistance of *H. pylori* can only be improved by giving suitable antibiotics.

Response:

Thank you for your suggestions. As your comments, there are other genetic factors to influence in eradication rate. This fact suggests that it is better to consider effects of genetic factors for optimal tailored treatment. Of those, we think that acid inhibition and antimicrobial resistance are major influenced factors for eradication rate. Therefore, we focused in this study. We mention about this point in revised version.

- 2> Since this is a review article, some descriptions in the introduction section needs to be elaborated to help general readers (e.g., Evidence level 1a, Grade A....etc). Also, although data in Japan have been cited in a number places, relevant data from other areas should also be included.

Response:

Thank you for your recommendation. According to your suggestion, we add any explanations to help general readers, especially in Introduction section. In addition, we delete any parts of data from Japan and add data from other areas in revised version.

- 3> Section VII seems to be irrelevant to this topic.

Response:

As your suggestion, any part of section VII may be irrelevant to this review article. However, we think that part of "efficacy of divided dosing of AMPC for *H. pylori* eradication" is a key point for our tailored treatment. Therefore, most of part of section VII is deleted and we change a title of section VII as efficacy of divided dosing with AMPC.

- 4> More evidences should be provided for the role of ABCB1 polymorphism on *H. pylori* treatment.

Response:

As your recommendation, we added the role of ABCB1 polymorphism on *H. pylori* treatment in revised version.

- 3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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