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Reviewer#1

SPECIFIC COMMENTS TO AUTHORS

In this study, Borraccino AV et al. reviewed the application of Rifabutin as a salvage therapy for *H. pylori* eradication failure. They reported some combinations for *H. pylori* eradication, such as rifabutin with amoxicillin or tetracycline, added on novel acid suppressor drugs, vonoprazan. The side effects of rifabutin and the risk of drug resistance *Mycobacterium tuberculosis* were also reviewed when rifabutin-based regimens for *H. pylori* eradication. Their review was comprehensive and confluent for readers. I only have one comment: In view of gut microbiota change following *H. pylori* eradication antibiotic usage, the author may add some information about the change of gut bacterial diversity after rifabutin usage for *H. pylori* eradication.

We thank the reviewer for the comment. However, after searching on PubMed “*Helicobacter pylori* rifabutin microbiota”, only two articles were found and none of them investigated the changes of microbiota after rifabutin administration. Therefore there is no study investigating this topic. Nevertheless, we emphasized this aspect in revised manuscript (It is possible that rifabutin may induce changes in the intestinal microbiota even if there are no studies in the literature on this topic, to the best of our knowledge. Presumably, this can be explained by the limited use of this antibiotic in *H. pylori* infection therapy).

Minor correction: In page 5, the text “ Twenty-one studies were included, and the overall eradication rate was 70,4 by intent-to-treat (ITT) and 72.0% by per-protocol (PP) analyses.” “70,4” may be corrected into 70.4%.

We performed the requested change.



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Reviewer#2

SPECIFIC COMMENTS TO AUTHORS

Helicobacter pylori eradication has become a worldwide challenge for clinicians today due to increasing H. pylori antibiotic resistance. In this review, the authors summarized current evidence about traditional triple therapy containing amoxicillin and rifabutin as salvage therapy, based on the most recent meta-analyses. In addition, some other novelties regarding rifabutin based regimens have been described in detail. It is an interesting mini-review. in which the mechanism of action, pharmacodynamics and pharmacokinetics of rifambutin, H. pylori resistance to rifambutin, the efficacy and side effects of rifambutin based regimen have been detailed respectively. In addition, the precautions before and after starting a rifabutin-based eradication regimen were also detailed. However, there are still some flaws in this manuscript that need to be further improved:

1. The syntax of some sentences is not standard, such as the second paragraph of page 2.
2. Grammatical errors in some statements, such as paragraph 3 and paragraph 4 of the page 5.

Regarding point 1 and 2, the paper underwent a linguistic revision by a Native English speaker.

3. Abstract and conclusions are not concise enough.

Editorial guidelines require an Abstract containing at least 200 words, therefore an extensive shortening was not possible. Nevertheless, we cut short the conclusions by deleting a paragraph.