

ANSWERING REVIEWERS

Name of journal: **World Journal of Clinical Cases**

Manuscript Number: **61380**

Type: Mini-Review

Title: **PROTON PUMP INHIBITORS AND COVID-19: A PARADOX RELATIONSHIP**

Authors: Maddalena Zippi, Sirio Fiorino, Roberta Budriesi, Matteo Micucci, Ivan Corazza, Roberta Pica, Dario de Biase, Giuseppe Claudio Gallo and Wandong Hong

Dear Editors and Reviewers,

Thank You for your precious time spent in reviewing the work and for allowing us to submit a revised version of our manuscript. We would also like to thank the reviewers for their pertinent and helpful comments. We have considered each of these in depth and have incorporated the appropriate changes in the revised version of the manuscript. We are confident that this revised manuscript will address the reviewers' concerns.

All changes we have made to address these comments are described below. In the revised manuscript, all changes in the text are highlighted in red.

Reviewer 05431343:

Comments To Authors: This review paper has used the currently available data to explore the relationship between the use of proton pump inhibitors (PPIs) and the Sars-CoV-2 infection and analyze the strengths and weaknesses of this relationship. Considering the ongoing pandemic situation, these data could be helpful for hospitals and treatment centres to handle the pandemic in a more effective fashion. In addition, please consider the following revision before the publication of the manuscript: 1- There are some grammatical and spell errors throughout the manuscript: "inhibitors" => "inhibitors" "... into lungs by by ..." => "into lungs by" "provided us few studies" => "provided us with few studies" "S2 subunit which in a second phase" => "which is" "the entire virus can entry into" => "can enter" "the disease COVI-19" => "COVID-19" 2- The following sentence requires citation: "Various reports in last decade have suggested that PPIs can favor the more severe course and mortality in patients suffering from conditions such as virosis by virtue of their side effects" 3- What are the inclusion and exclusion criteria of this review paper?

Answers:

1. We have revised the manuscript for grammatical and spell errors (using also the tool "grammarly.com").

2. We have added three references to the following sentence: "Various reports in last decade have suggested that PPIs can favor the more severe course and mortality in patients suffering from conditions such as virosis by virtue of their side effects" [**Savarino V**, Marabotto E, Furnari M, Zingone F, Zentilin P, Savarino E. Latest insights into the hot question of proton pump inhibitor safety - a narrative review. *Dig Liver Dis* 2020;**52**:842-52 [PMID: 32513631 DOI:

10.1016/j.dld.2020.04.020]//**Meijvis SC**, Cornips MC, Voorn GP, Souverein PC, Endeman H, Biesma DH, Leufkens HG, van de Garde EM. Microbial evaluation of proton-pump inhibitors and the risk of pneumonia. *EurRespir J* 2011;**38**:1165-72 [PMID: 21478217 DOI: 10.1183/09031936.00020811] //**Sasaki T**, Nakayama K, Yasuda H, Yamaya M. A new strategy with proton pump inhibitors for the prevention of acute exacerbations in COPD. *TherAdvRespir Dis* 2011;**5**:91-103 [PMID: 21285157 DOI: 10.1177/1753465810392264])

3- We have add the inclusion and exclusion criteria in the Section of “Available studies on this topic” in our review with the following words: “ Availing of Medline (PubMed) and Embase databases, we extrapolated all the studies led from January 1985 to November 2020 evaluating the relationship between COVID-19 and PPIs. Among their data two of them were extracted and pooled wherever possible: severe events, defined as the incidence of patients needing organ support or intensive care, and mortality, namely the death occurred during hospitalization. Some studies were excluded from the analysis if either the outcomes of interest were not mentioned or it was impossible to calculate them from the published results. Similarly, some other studies were ruled out in which sample size is less than ten and when focusing on animals.”

We thank You again for reviewing the article, your suggestions were very much appreciated.

Kind regards,

Maddalena Zippi, Sirio Fiorino, Roberta Budriesi, Matteo Micucci, Ivan Corazza, Roberta Pica, Dario de Biase, Giuseppe Claudio Gallo and Wandong Hong