

Reply: we have revised the author contributions section based on your comment.

All the changes can be followed by track changes

Reviewer A:

Recommendation: Revisions Required

1. Relevance of the title to the content of the article

Good

Remarks

2. Summary: Presents the general idea of the topic, objectives, research methods, results and conclusions, written in an objective and concise manner; and are found according to the maximum number of words per section.

Good

Remarks

3. Introduction: Presentation of the subject, justification of the problem, objectives, hypotheses and methodological foundation, exposing the subject in an orderly and detailed manner

Regular

Remarks

In terms of previous publications, there is a lack of information about EBM indications for COVID regarding the drugs involved in the study.

Reply: we have revised the introduction section to address your comment.

4. Methodology: Describes the procedure, methods and techniques used in data collection and analysis.

Remarks

Authors need to explain, in detail, the random process of participant selections, with particular care to explain the allocation. On the other hand, the way authors calculated sample size needs to be explained. May be useful to calculate power, assuming the sample size is correct.

Reply: We have revised the methods section. Randomization process and blinding are now added to the manuscript. Moreover, we have improved the statistical analysis part. Explanation of sample size calculation was included in the manuscript.

How many days did the participants have at the hospital when they were allocated to one of the study groups?

Reply: they received the medication after admission. After assessment of the eligibility criteria, enrolment was performed. These explanations are added to the manuscript.

5. Ethical aspects. Does the manuscript have a paragraph on ethical aspects, where it mentions approval by the ethics committee, informed consent, and strict compliance with research ethics?

Yes

6. Results: They are presented adequately and it is not redundant with tables or graphs shown.

Regular

Remarks

How were P values calculated for categorical variables?

Reply: Now they are assessed using logistic regression models. We have revised the statistical analysis and results section and performed much more analysis to improve the paper. All the statistical methods are explained in the statistical analysis section.

7. Discussion: They present a level of critical analysis in correspondence with the problem presented. Purposes of the article, scope, support theory and proposed methodological design.

Regular

Remarks

Discuss how limitations could affect conclusions. A discussion about risk of bias is needed.

Reply: We have revised the discussion section based on your comment. All the changes can be followed by "track changes".

8. Conclusions: Presents the author's inferences and teachings in relation to the investigated topic, it must correspond to the objectives of the study.

Regular

Remarks

9. References. Quality of bibliographic references and if they are in accordance with the Vancouver format.

Good

Remarks

10. Redaction. Is the manuscript correctly written? Does it contain any spelling or grammar mistakes?

Needs some language corrections.

[Reply: we have revised the manuscript.](#)

11. Contributions. What are the main weaknesses of the manuscript and how the author can do to improve it

[Reply: we have improved the limitation section along with recommendations for future trials.](#)

Reviewer B:

Recommendation: Revisions Required

1. Relevance of the title to the content of the article

Poor

Remarks

2. Summary: Presents the general idea of the topic, objectives, research methods, results and conclusions, written in an objective and concise manner; and are found according to the maximum number of words per section.

Poor

Remarks

3. Introduction: Presentation of the subject, justification of the problem, objectives, hypotheses and methodological foundation, exposing the subject in an orderly and detailed manner

Poor

Remarks

4. Methodology: Describes the procedure, methods and techniques used in data collection and analysis.

Poor

Remarks

5. Ethical aspects. Does the manuscript have a paragraph on ethical aspects, where it mentions approval by the ethics committee, informed consent, and strict compliance with research ethics?

Yes

6. Results: They are presented adequately and it is not redundant with tables or graphs shown.

Poor

Remarks

7. Discussion: They present a level of critical analysis in correspondence with the problem presented. Purposes of the article, scope, support theory and proposed methodological design.

Poor

Remarks

8. Conclusions: Presents the author's inferences and teachings in relation to the investigated topic, it must correspond to the objectives of the study.

Poor

Remarks

9. References. Quality of bibliographic references and if they are in accordance with the Vancouver format.

Poor

Remarks

10. Redaction. Is the manuscript correctly written? Does it contain any spelling or grammar mistakes?

Needs some language corrections

11. Contributions. What are the main weaknesses of the manuscript and how the author can do to improve it

The critical point is that they do not explicitly establish whether the groups to be compared are different in severity at the beginning of the study.

Also, an almost significant age difference between the groups could have affected the final result and was not considered in the analysis. The umifenovir group was younger.

The longer hospitalization time in umifenovir may have been caused by being an analysis of survivors compared to the other group that has more deaths (and therefore a shorter hospitalization time due to earlier death). It is not clear if this was considered in the analysis or not.

Reply: thanks for your informative comment. We have now performed much analysis based on logistic regressions and controlled for age. Moreover, we re-designed the format of Table 1 completely.

Reviewer D:
Recommendation: Decline Submission

-It is estimated that manuscript does not contrast the efficacy presented in the title and not present sufficient consistency with respect to the Randomized Clinical Trial.

Reply: we have revised the title to address your comment.

-It is considered that the article does not follow the specific protocol of a randomized clinical trial and its description does not allow replicating or understanding the procedure.

-We have revised the manuscript and added lots of information to the introduction and methods section. Moreover, we have performed much new analysis based on regression models to improve the paper.

The abstract is not descriptive enough.

Reply: we have revised the abstract section.

3. Introduction: Presentation of the subject, justification of the problem, objectives, hypotheses and methodological foundation, exposing the subject in an orderly and detailed manner

Too short. Inadequate.

Reply: We have revised the introduction section to improve the paper

-Methodology is not sufficiently described.

Reply: we have revised the methods section and included a paragraph in terms of the randomization and blinding process. Moreover, statistical analysis section is revised.

- Results are not correctly detailed.

Reply: we have revised the results section and performed much new analyses to improve the paper.

7. Discussion: They present a level of critical analysis in correspondence with the problem presented. Purposes of the article, scope, support theory and proposed methodological design.

Poor

Remarks

Too short. Inadequate.

-Reply: we have revised the Discussion section now.

8. Conclusions: Presents the author's inferences and teachings in relation to the investigated topic, it must correspond to the objectives of the study.

Poor

Remarks

They are not representative of the study that is intended to be presented.

Reply: we have revised the Tables and presentation of the results

9. References. Quality of bibliographic references and if they are in accordance with the Vancouver format.

Reply: We have revised the references.

Regular

Remarks

Presentation of journals is not uniform or adjusted to Vancouver.

10. Redaction. Is the manuscript correctly written? Does it contain any spelling or grammar mistakes?

Acceptable

11. Contributions. What are the main weaknesses of the manuscript and how the author can do to improve it

Reply: we have included study limitations in the discussion

The article requires general changes and an optimal description of the randomized clinical trial.

Reply: We have revised the manuscript based on your comment.