Author’s response to reviews

Title: Pharmacokinetic and pharmacodynamic modelling of oral mitiglinide on glucose lowering in healthy Chinese volunteers

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Author’s response to reviews:

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To:
Editorial Office
Dear Editor:

Thank you very much for your careful review on our manuscript (PHAT-D-16-00190). I would like to appreciate the comments from you. We have revised the manuscript. Thanks for your interest in our work and we look forward to receiving your good news.

Sincerely yours

Shijia Liu

Editor Comments:

It does not appear that you have adequately addressed the initial comments made by Reviewer 1. For example, Reviewer 1 requested that you use median/IQR instead of mean/sd and using minutes instead of hours. Could you please re-address Reviewer 1’s comments and in your response indicate the line in the manuscript where you made the changes? If you disagree with one of the Reviewer’s comments please provide an explanation.

[Answer] I use mean and SD instead of median/IQR in the paper, as it’s more common to use mean and SD instead of median/IQR in the pharmacokinetic and pharmacodynamic modeling study. Most of this type of papers for PK-PD study the parameters for individual were presented as mean and SD. To make consistent with the whole paper, the unit of h for time was used. And I think it’s better to use hours instead of minutes to observe the data and the model intuitively.

Reviewer 2 has reviewed the manuscript and asked for further revisions.

Please correct the formatting of the manuscript to follow to the BMC Pulmonary Medicine formatting guidelines https://bmcpulmmed.biomedcentral.com/submission-guidelines/preparing-your-manuscript/research-article and correct the spelling of “modelling” in your Title to “modeling”

[Answer] We have corrected the spelling of “modelling” in the Title to “modeling”
There is significant text overlap in the manuscript, especially in the discussion. Please reduce text overlap. I have attached a document showing you where text overlap is of particular issue. Reuse of text is a violation of publication ethics and needs to be seriously addressed before acceptance of the manuscript.

[Answer] We have corrected text overlap in the manuscript thoroughly according to your suggestions.

Reviewer reports:

Melanie Felmlee, PhD (Reviewer 2): The authors made a number of the improvements suggested in the first review; however, I still have concerns that need to be addressed.

1) The English and grammar needs to be edited throughout.

[Answer] We have made the improvements to the English language in our manuscript. And the English and grammar have been edited throughout by a native English editor.

2) An explanation of the selection of the Biophase model needs to be included.

[Answer] An explanation of the selection of the Biophase model has been added according to the reviewer’s suggestions. Pharmacokinetic/pharmacodynamic model and data analysis section, line 6, page 8.

3) The statistical analysis section contains a description of the model. This should be moved to the model and data analysis section.

[Answer] A description of the model has been moved to the model and data analysis section. Pharmacokinetic/pharmacodynamic model and data analysis, line 14, page 6.

4) Methodology for selection of parameters that had population variability needs to be included.

[Answer] The inter-individual variation for parameters with high shrinkage value (>0.5) were not included in the model. Methods selection line 1, page 9.

5) For the table: non-compartmental and population modeling parameters should be separated into two tables.
[Answer] We separated the non-compartmental and population modeling parameters into two tables. Page 10.

6) Figure 1 should be revised and preferably generated outside of the Phoenix platform for clarity.

[Answer] Figure 1 have been revised. Fig 1.

7) The labels of figure 3 should be altered so that they are concentration versus time and effect versus time.

[Answer] Figure 1 have been revised. Fig 3.

8) The abstract still indicates that WinNonLin was used. Further the results section should include a description of the model development and fitting.

[Answer] We have corrected the abstract and a description of the model development and fitting in the results section according to the reviewer’s suggestions. Line 5, page 11.