**Author’s response to reviews**

**Title:** In vitro Activities of Eravacycline against 336 Isolates Collected from 2012 to 2016 from 11 Teaching Hospitals in China

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Dear editor

First of all, we would like to acknowledge your work and reviewer’s comments to make this manuscript better. We took these comments very seriously and revised our manuscript according to reviewer’s comments one by one.

The newly added parts were highlighted in light green. We also invited an English-speaking language editor to revise the sentences and grammar to make the article more fluent. This version of manuscript is the final clean file, so that the marks of the tracked changes were not displayed.

The following below is our detailed point to point revision.
First reviewer's comment:

1- The methods are not clear and details are missing and its need improvement. The authors should provide more primary data.

Response:

We rewrote this section and described the specific steps of the experiment, and clarified the quality control strains used in the experiment. At end of the manuscript, specifically in the Availability of data and materials section, we have declared that the data can be obtain from the corresponding author on reasonable request.

2- Please added PCR section and then please added amounts of each substance in RT-PCR reaction.

Response:

In fact, PCR amplification of the drug resistance genes was not performed in this experiment. The results of drug resistance genes are derived from our previous research data. The data source has been declared in the methods section.

3- Result section is very long and needs much work to improve it.

Response:

We have modified this section. Make the whole part more concise and coherent.

4- The conclusions are supported by their data; however, the paper is not focused and needs much work to improve it.

Response:

We have modified this section to make it more explicit and objective.

5- No limitations of the study are indicated. Please add "limitation and suggestion in end of paper.

Response:
The recommended Limitation and Suggestion section was added above the conclusion section.

Second reviewer's comment:

1. No quality control has been performed in the AST, or at least it is not explained in the Material and Methods section.

Response:

We rewrote this section and described the specific steps of the experiment, and clarified the quality control strains used in the experiment.

2. It is not clear to me the meaning of the sentence "Considering the relative small number of each organism with certain resistance mechanism, sampling error is inevitable, and additional studies are needed to clarify the potential application of eravacycline as substitutes for carbapenems and tigecycline in the treatment for some infection caused by resistant strains and to reduce the dissemination of resistant strains in the future." What is the meaning of "sampling error" in the sentence? Why eravacycline should substitute carbapenem or tigecycline?

Response:

This sentence was indeed easy to cause ambiguity. The previous sentence was indeed apt to cause ambiguity. The incidence of CRE in some parts of China is high and has become an important threat to clinical treatment. The emergence of eravacycline could be used as an alternative option to treat CRE strains rather than replacing carbapenems and tigecycline. The previous statement is not very accurate. Considering the 4th comment of this reviewer that we should focus on the in vitro activity against the tested bacteria rather than in concluding about its clinical efficacy, we revised the whole sentence as below.

"Considering the relatively small number of each organism and limited types of resistant phenotypes, the result of this study only partially represent the resistant phenotype encountered in real clinical practice, and additional studies are needed for a more comprehensive assessment of the antibacterial activity of eravacycline."

3. Not clear to me the sentence "In addition, the total number of Staphylococcus. sp strains is relatively small, which may be caused by random errors and need to be clarified in subsequent studies with more study objects" Why random errors may affect the total number of staphylococci?
Response:

The structure of this sentence is wrong. We have made the following changes. We have replaced it with the correct sentence in the manuscript.

The sentence was revised as below:

“In addition, the total number of Staphylococcus spp strains which were successfully treated was relatively small, which may be caused by random errors in the antibacterial activity of eravacycline. Thus, further validation utilizing different bacterial isolates is required.”

4. In general, some sentences in the discussion section point out that the results obtained in the study indicate that eravacycline could be the treatment of choice for infections caused by multidrug resistant bacteria. However, this assertion cannot be taken from the results of this study. Authors should focus on the in vitro activity against the tested bacteria rather than in concluding about its clinical efficacy. Additional studies are needed to determine its role in the treatment of infectious diseases.

Response:

This is a good comment. We have made some revision to focus on the result of the study itself and we deleted the sentences referred to clinical efficacy of eravacycline. We have modified this section to make it more explicit and objective.

The above is the point to point revision. Once again, thanks to the hard work of editor and reviewers, we also learned a great deal of Eravacycline from the process of revising this manuscript.

Best regards

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