

Manuscript ID: 60219, Case report

Title: Prolonged use of bedaquiline in two patients with pulmonary extensively drug-resistant tuberculosis: A case report

Journal: World Journal of Clinical Cases

Response to Reviewers' comments

Dear Dr. Ma,

We thank you for your careful consideration of our manuscript. We appreciated your response and overall positive initial feedback and made modifications to improve the manuscript. After carefully reviewing the comments made by the Reviewers, we have modified the manuscript to improve the presentation of our results and discussion, therefore providing a complete context for the research that may be of interest to your readers.

We hope that you will find the revised paper suitable for publication, and we look forward to contributing to your journal. Please do not hesitate to contact us with other questions or concerns regarding the manuscript.

Best regards,
Jingtao Gao

Reviewer #1

Please emphasize more detail the recommendation for future study in combination bedaquiline with other second line anti TB, based on this case report

Response: We thank the Reviewer for the comment. We revised the recommendation for future studies. “Future studies could be focused on exploring the effectiveness including sputum culture conversion and final treatment outcomes and safety of prolonged use of bedaquiline for 36 weeks versus standard 24 weeks in the treatment of MDR/XDR-TB, or further exploring the biomarker and criteria indicative for extension of bedaquiline to facilitate clinical use of this novel drug. Moreover, studies on shortened regimens composed of 36-week use of bedaquiline and other second line anti-TB drugs are ongoing. We expected rapid increase in the evidence supporting the prolonged use of bedaquiline will provide additional treatment options for MDR/XDR-TB patients.” You can refer to the revised Discussion.

Scientific Editor

1 Scientific quality: The manuscript describes two case report of the prolonged use of bedaquiline in patients with pulmonary extensively drug-resistant tuberculosis. The topic is within the scope of the WJCC. (1) Classification: Grade A; (2) Summary of the Peer-Review Report: Please emphasize more detail the recommendation for future study in combination bedaquiline with other second line anti TB, based on this case report. The questions raised by the reviewers should be answered; and (3) Format: There are 2 figures. A total of 9 references are cited, including 3 references published in the last 3 years. There are no self-citations. 2 Language evaluation: Classification: Grade A. A language editing certificate was provided. 3 Academic norms and rules: The authors provided the signed Conflict-of-Interest Disclosure Form, Copyright License Agreement, Written informed consent and CARE Checklist–2016. No academic misconduct was found in the CrossCheck detection and Bing search. 4 Supplementary comments: This is an unsolicited manuscript. The study was supported by “Thirteenth Five-Year” Major National Science and Technology Project. The topic has not previously been published in the WJCC. The corresponding author has not published articles in the BPG.

Response: We thank the Scientific Editor for the comment. We revised the recommendation for future studies. “Future studies could be focused on exploring the effectiveness including sputum culture conversion and final treatment outcomes and safety of prolonged use of bedaquiline for 36 weeks versus standard 24 weeks in the treatment of MDR/XDR-TB, or further exploring the biomarker and criteria indicative for extension of bedaquiline to facilitate clinical use of this novel drug. Moreover, studies on shortened regimens composed of 36-week use of bedaquiline and other second line anti-TB drugs are ongoing. We expected rapid increase in the evidence supporting the prolonged use of bedaquiline will provide additional treatment options for MDR/XDR-TB patients.”

5 Issues raised: (1) I found the “Abstract” did not meet our requirements. Please re-

write the “Abstract” section, including “BACKGROUND”, “CASE SUMMARY”, and “CONCLUSION” section;

Response: We thank the Scientific Editor. The Abstract was revised accordingly.

(2) I found no “Core Tip” section. Please provide the core tip;

Response: We thank the Editor. We added the Core Tip.

(3) I found no “INTRODUCTION” section. Please provide the introduction;

Response: We are sorry for this. It was misnamed as Background. Now it was corrected.

(4) I found the authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s);

Response: We are sorry for this. We now provided the electronic approval document for funding and please review the pdf format.

(5) I found the authors did not provide the original figures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;

Response: We thank the Scientific Editor. We now provide the original figures.

(6) I found the authors did not add the PMID and DOI in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout;

Response: We now provided the DOIs and PMIDs when available.

and (7) I found the “Case Presentation” did not meet our requirements. Please re-write the “Case Presentation” section, and add “FINAL DIAGNOSIS”, “TREATMENT”, and “OUTCOME AND FOLLOW-UP” section to the main text, according to the Guidelines and Requirements for Manuscript Revision.

Response: We thank the Reviewer. The Case Presentation section was revised.

Round-2:

bedaquiline has several side effects, including cough and chest pain. in the 1st case, patient complained cough, was the cough reduced or got worse? please add more side effect information.

Response: We are grateful for the reviewer’s comments of our manuscript and have modified the manuscript to add the improvement of cough with treatment on line 136-137 in red with the sentence “Cough was relieved and gradually disappeared after 24-week anti-TB treatment with bedaquiline”. Cough is presumably attributed to bronchial TB. After 24-week of treatment with bedaquiline-containing regimen, focus of both

lung and bronchus turned much better and accordingly cough is relieved and controlled. Cough is not evaluated as the side effect of bedaquiline or combined background drugs. Patients were strictly monitored during treatment and no more adverse effects occurred except the prolongation of QT interval increase more than 60ms compared to that at baseline of case 1. Please do not hesitate to contact us with other questions or concerns regarding the manuscript. Best regards, Jingtao Gao

Reviewer bedaquiline has several side effects, including cough and chest pain. in the 1st case, patient complained cough, was the cough reduced or got worse? please add more side effect information.

Response: We thank the Reviewer for the comment. We have modified the manuscript to add the improvement of cough with treatment. As described in the manuscript, she had a cough and expectoration for 7 months and the symptoms were relieved after cephalosporin treatment before she came to our hospital. Then In May 2018, she was diagnosed with pulmonary and bronchial TB. Starting on June 1, 2018, MDR-TB treatment was given but she still had a cough and expectoration. Since August 1, bedaquiline- containing MDR-TB regimen was provided and cough was relieved and gradually disappeared after 24-week anti-TB treatment with bedaquiline. (The text in red has been added into the revised manuscript.) Cough is presumably attributed to bronchial TB. After 24-week of treatment with bedaquiline-containing regimen, focus of both lung and bronchus turned much better and accordingly cough is relieved and controlled. Cough is not evaluated as the side effect of bedaquiline or combined background drugs. Patients were strictly monitored and no more adverse effects occurred during treatment except the prolongation of QT interval increase more than 60ms compared to that at baseline of the case 1.