Author’s response to reviews

**Title:** Clinical Experience with Tigecycline in the Treatment of Hospital-Acquired Pneumonia Caused by Multidrug Resistant Acinetobacter baumannii

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**Version:** 2  **Date:** 28 Jan 2019

**Author’s response to reviews:**

Dear editors,

Thank you very much for your feedback on “Clinical Experience with Tigecycline in the Treatment of Hospital-Acquired Pneumonia Caused by Multidrug Resistant Acinetobacter baumannii”, I am very appreciated about the suggestion you made. Here are the responses to the reviewers.

Stefanie Krick (Reviewer 1):

1. The whole manuscript needs to be edited for the English language due to multiple spelling and grammatical mistakes ("clinical experince" in the title, abstract double mentioning "treated with tigecycline line 30/31, lines 49, 62, 68, 140 etc.).

Response: Thank you for your feedback. Title has been corrected. Lines 30/49/62/68/140, as you mentioned have been revised and high lined in the revised manuscript, Line 31/46/60/68/133. A native English professor had reviewed the language, and revised the manuscript.
2. Procalcitonin is mentioned in the manuscript line 131, but it is not defined what the criteria directly are, same for the white blood cell count….the improvement of laboratory tests should be better defined.

Response: Although the criteria for procalcitonin was defined in general patient, it is defined in the the ICU patients. Since a majority of the patients in this study were ICU patients, the criteria applied. And since there are no unified criteria of the white blood cell count and CRP, so we just defined them as our experience. Methods part, Line 123-125.

3. Line 141/142, this method should have references.

Response:The reference of the strain sensitivities was added as reference 11, and high lined in Line 135.

4. Line 175…please rephrase "patients involving monoMDRAB.

Response: The sentence has been rephrased. Line 165

5. Discussion lines 243-249 is written very confusing, please clarify.

Response: The paragraph has been revised. Line 226-234.

6. Line 253: the authors did not find any difference between monotherapy and combination therapy - this is expected since sample size is too small to detect.

Response: We agreed with your opinion, and it has been revised.

7. It is problematic to state the efficacy of tigecycline, since most patients received a combination therapy…therefore, title is very speculative and should rather state that antibiotic therapies including tigecycline….this should be addressed throughout the manuscript.

Response:The reason why we use the statement of “the efficacy of tigecycline” instead of the “antibiotic therapies including tigecycline” is based on the followings: First, our study discussed the effect of tigecycline based treatment on the monomicromicrobial MDRAB HAP, although most patients received a combination therapy, the antibiotics used with tigecycline were almost all resistant to the MDRAB, we believe tigecycline is the key factor of the treatment. Second, one of the other important objectives of the study was to determine the predictors that affect the success of the tigecycline treatment. In addition, there were many studies that supported our results in combination therapy, such as Xu et al., Chemotherapy 2016.
8. The change of albumin is not addressed in the results but only in the discussion: is this relevant? It can be most likely omitted.

Response: We described the change of albumin to the clinical effect and 30-day mortality in Table 3 and 5, respectively. Since there were very few hypoproteinemia patients in this study, no significant correlation between albumin and the clinical effect and mortality, and the results are shown in the tables but not described it in the results section.

9. I recommend to include important references: 1. Wu et al., Biomed Res Int. 2016, Xu et al., Chemotherapy 2016.

Response: As you suggested, we added the literature of “Xu et al., Chemotherapy” in the introduction part as reference 9, Line 61; and the literature of “Wu et al., Biomed Res Int. 2016” in the discussion part as reference 18, Line 259.

Antonello Di Paolo, MD, PhD (Reviewer 2):

1. No results about strain sensitivity to other antibacterial drugs have been introduced within the text, whereas those findings could be interesting to further discuss the 30-day mortality rate.

Response: We added the strain sensitivity to other antibacterial drugs in the results section (Line 177-179) as you suggested. Since there was only 5 sensitive strains to sulbactam, and none of them was sensitive to carbapenems, fluoroquinolones or amikacin, it is expected that there was no significant differences between combination of the sensitive drug and non-sensitive drug because of the small sample size (data not show), as a result we didn’t discuss it in the 30-day mortality rate part.

2. The low number of patients severely limits the robustness of univariate and multivariate analysis (see for example Table 4, diabetes mellitus OR and wide interval).

Response: The low number is one of our limitations and the results showed that some of the univariate multivariate analyses were with wide intervals because of the small sample size. Since we want to focus on the monomicrobial MDRAB HAP patients, we have eliminated most of the subjects according to the strict inclusion criteria.

3. Bacterial strains were assessed for their sensitivity toward tigecycline (lines 144-147), then the emergence of resistance was further evaluated over the treatment (lines 151-153). Because a factor predictive of 30-day mortality was "higher resistance rate to tigecycline in the hospital" (lines 332-333), the Authors could further discuss the appropriateness of standard drug dosages when high dose regimens of tigecycline are advocated in the presence of resistant bacteria (see for example Cunha et al, Expert Rev Anti Infect Ther. 2017 Mar;15(3):257-267).
Response:

Thank you for your suggestion, we revised the discussion section of the risk factors of the mortality in Line 266-271.

4. The Authors should upload a revised text with track-changes option together with a point-to-point reply (showing exact queries and corresponding answers) for better clarity.

Response: Done.

5. A careful revision of English language is deemed to be necessary (i.e., sentences at lines 102-104, 177; line 193, elevator instead of elevation).

Response: Thank you for your feedback. Title has been corrected. Lines 102-104, 177, 193, as you mentioned have been revised and high lined in the revised manuscript, Line 97-99, 167, and 183. A native English professor had reviewed the language, and revised the manuscript.