Author’s response to reviews

Title: Safety and Efficacy of Prophylaxis for Pneumocystis jirovecii Pneumonia involving Trimethoprim-Sulfamethoxazole Dose Reduction in Kidney Transplantation

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Author’s response to reviews:

February 26, 2019

The Editor

BMC Infectious Diseases

Dear Editor,

Sub: Submission of revised manuscript to BMC Infectious Diseases
Ref: INFD-D-18-01658R1
Safety and Efficacy of Prophylaxis for Pneumocystis jiroveci Pneumonia involving Trimethoprim-Sulfamethoxazole Dose Reduction in Kidney Transplantation.

Thank you for your letter dated February 13, 2019 indicating the need for major revisions to the manuscript to enable potential acceptance of our manuscript for publication in BMC Infectious Diseases. We are most grateful for the opportunity to do so. We have addressed ALL of the comments of the learned reviewers, which we agree have significantly improved the manuscript. The changes are tracked in the document, but are also listed below for your convenience.

Reviewer 1

Thank you for your thoughtful consideration of our manuscript.

1. We agree that the focus of the paper should be on PcP prophylaxis and reduced dosage. To this end, the discussion on hyperkalemia and leukopenia has been shortened. We have also added the sentence that dosage reduction of TMP-SMX should be efficient enough to prevent PcP after solid organ transplantation (page 13, lines 5-6).

2. We have deleted Tables 2 and 3 as per your suggestion.

3. Thank you for your comment regarding Figure 1. We agree it would be very interesting to compare thrice weekly to twice weekly TMP-SMX as PcP prophylaxis. Unfortunately, there were only 4 patients who received twice weekly TMP-SMX. This small number precludes any comparison of patient characteristics. We have noted the twice weekly group in the legend to Figure 1.

4. Thank you for bringing to our attention the ECIL-5 guidelines, and especially thoughtfully providing us with the PMID. We have included this reference as reference 4. All other reference numbers have been adjusted accordingly.
5. PJP has been replaced by PcP throughout the manuscript.

Reviewer 2

Thank you for your thoughtful consideration of our manuscript.

1. We have changed PJP to PcP throughout the manuscript.

2. We agree that Pneumocystis colonization is a challenging problem in transplant recipients since reactivation can occur, besides person-to-person transmission, and therefore valuable to know. We do not have any clinical information on asymptomatic infection. This fact has been highlighted in the discussion section on page 13, lines 3-5.

3. We agree that it would be valuable to analyze further the breakdown of the reduced dose group into thrice weekly TMP-SMX, twice weekly TMP-SMX etc… The total number of patients who received less than thrice weekly TMP-SMX was extremely small. This critical point has been mentioned now on page 8, lines 15-17. The reduced dose period is illustrated in Figure 1. There were 12 dose reductions below thrice weekly. We have noted the twice weekly group in the legend to Figure 1.

4. We have corrected the SD regarding serum creatinine measurements (page 9, lines 1-2). Thank you for pointing this out.

5. Thank you for your insightful comment. We were unable to make any conclusions about TMP-SMX dose reductions below thrice weekly based on the small number of patients (N=12, Figure 1). Only 4 patients had a dose increased again after their dose was reduced to less than thrice weekly. Therefore, their data is not presented separately. We would not recommend considering a dose less than thrice weekly a priori in any kidney transplant recipient in the first post-transplant year.
6. Thank you for allowing us to improve Table 1. We have separated variables by line and also included (N, %) and SD where indicated.

We trust that all these changes have made the manuscript suitable for publication. We look forward to an early favorable decision.

Thank you.

Sincerely,

G. V. Ramesh Prasad

Corresponding Author