Author’s response to reviews

Title: Virologic suppression in response to antiretroviral therapy despite extensive resistance within HIV-1 reverse transcriptase after the first virologic failure

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Author’s response to reviews:

Dear Dr. Antoinette C Van Der Kuyl
BMC Infectious Diseases

September 15, 2018

Subject: Revision and resubmission of manuscript entitled "Virologic suppression in response to antiretroviral therapy despite extensive resistance within HIV-1 reverse transcriptase after the first virologic failure" (INFD-D-18-00391R2)

Thank you for your letter and the opportunity to revise our paper entitled "Virologic suppression in response to antiretroviral therapy despite extensive resistance within HIV-1 reverse transcriptase after the first virologic failure" The suggestions offered by the reviewers have been immensely helpful, and we also appreciate your insightful comments on revising the abstract and other aspects of the paper.

I have included the reviewer comments immediately after this letter and responded to them individually, indicating exactly how we addressed each concern or problem and describing the changes we have made. The revisions have been approved by all authors and I have again been chosen as the corresponding author. The changes are marked in red in the paper as you requested, and the revised manuscript is attached.

Most of the revisions prompted by the reviewers’ comments are minor and require no further explanation than what appears in my responses below.
Regarding the remarks of reviewer 1:

Introduction. 5. Line 41: What is ITRN MAR(t) we explained it: I could not find any explanation, the abbreviation was replaced rather than explained, except for the use of it in the Tables. Please replace in Tables and Fig. 1 as well.

We explained it: mutations in bold red are associated with the highest levels of reduced susceptibility or virological response to the relevant NRTI. Mutations in bold reduce NRTI susceptibility or virological response. Mutations in plain text contribute to reduced susceptibility in combination with other NRTI-resistance mutations. It was replaced in Tables and Fig. 1 as well.

Methodology: 1. Less than 50% of records were included….. You answered: we showed it. But you did not, all I could find was a break-down of the numbers. Please clarify.

This sample is very representative, considering that it was a study carried out in limited resource scenario. It depicts a decade of genotyping in the first virological failure in Pernambuco, Northeast Brazil. Only in 2016, we can easily access this exam. Between 2006 and 2016, it was the therapeutic rescue happens without genotyping by the logistic difficulty of taking the exam in this region of Brazil. Therefore, more than 50% of the sample was excluded by changing the scheme without genotyping.

Results. 1. Why were there 59 records without MAR... You answered: we have included in the analysis. I hope you did not, as in the revised manuscript it has been explained that the 59 patients did not adhere to their ART regimen. Please make it clear that those 59 were not included in any analysis.

There was no selective pressure during genotyping. Therefore, the absence of mutation does not represent reality, so we chose to exclude from the statistical analysis the 59 exams without mutation of resistance.

Results. 2. Why did the authors use Poison-regression? You answered: ‘we explained it’, but there is no explanation at all. And yes, you can use this type of analysis for cross-sectional data. Please add to Methods.

We opted for poison-regression as it is an excellent alternative for estimating adjusted prevalence ratio for confounding variables in cross-sectional studies when compared with Cox and log-binominal logistic regression

Results. 3. The sub-heading “Factors associated...” was not revised to read what the authors answered here. Only the word ‘immuno-trophic’ has been replaced with ‘immunovirologic’.

I revised to " Factors associated with mutations associated, ...

Furthermore, I found many problems with the Tables, where numerous non-English words are used (Perdas, outros, Nao-B, sim, feminino, etc) and abbreviations are unclear. Please revise all tables carefully. Switch to English abbreviations in the Tables, such as PI for protease inhibitor, not IP. Table 3: it says RP in the column heading, but PR in the legend. Also: ‘viral subtype’, not ‘subtype viral’. What is ‘Viral charge’ in Table 4, also ‘SEM ITRN(t)’, ‘MAR’ and what is an ‘irrigation regimen’?
All words is in English.
We switched to English abbreviations in the Tables.

Figure 1, labelled ‘Graph 1’, is not referred to in the main text. There is also no legend to this figure.
Figure 1 has been referred to in the main text.
There is legend to this figure.

We hope the revised manuscript will better suit the BMC Infectious Diseases but are happy to consider further revisions, and we thank you for your continued interest in our research.

Sincerely,

Valter Romão de Souza Junior
Universidade Federal de Pernambuco