Author's response to reviews

Title: Serological and parasitological response in chronic Chagas patients 3 years after nifurtimox treatment

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Author's response to reviews: see over
To the Editor

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RE: Manuscript: 8544569578052533 Immunological and parasitological response in chronic Chagas patients 3 years after nifurtimox treatment

Dear Editor and Reviewers

Thank you very much for the useful comments and suggestions. Please find below the point-by-point responses to your queries and the revised manuscript.

Wishing that you’ll find our responses and correction appropriate, we are looking forward to having your feedback soon.

Best regards,

Dr Yves Jackson
Point-by-point responses

Reviewer 1

Discretionary revisions
1. We agree with the reviewer, change has been made accordingly.
2. Change has been made in the text.
3. Acknowledging the reviewer point-of-view, we replaced “used” by “recommended”.
4. Change has been made in the text.

Minor essential revisions
1. Change has been made in the text.
2. Change has been made in the text.
3. Change has been made in the text.
4. Change has been made in the text.
5. In order to inform about the new technologies being developed, the work by Fernandez-Villegas et al. has been mentioned in the paragraph.
6. Change has been made in Table 2
7. The reference list has been corrected following the Journal’s recommendations

Major compulsory revisions
1. The reviewers is right in that sense that RDTs have not been officially recognised as first-line tools for diagnosis and have a lower sensitivity than most recent commercial serologies. Yet, given the recognised inoperability of recommendations in hard-to-reach populations, requesting two different serological techniques and hence access to full laboratory facilities, several authors, including us, have pragmatically suggested that RDT could be used in specific settings as first-line screening methods that need to be confirmed by more complex techniques. In order to respond to the reviewer concern, we modified the text as followed: They facilitate the screening of hard-to-reach populations such as rural communities or migrants in conditions where access to laboratory is difficult. Conventional serologies should be used to confirm the diagnosis.
2. Significance is used here in a statistical perspective, referring to the difference in OD values before and after treatment. The manufacturers – that we contacted for that specific topic – confirmed that ELISA results were primarily qualitative (POS/NEG) and that quantitative interpretation (ie. change in OD value) had to be used with great caution in absence of valid evidence-based information. In that sense, and given the very high variability of OD measurements between (and within) laboratories, we did not set a cut-off value for a “clinically” significant difference that would have appeared somewhat artificial and chose to present data as free of subjective interpretation. It is right that Viotti et al. (ref. 9) chose a 30% difference as significant but do not provide argument for that decision. As mentioned in the methods section, we tried our best to reduce the measurement bias by testing all samples (pre- and post-treatment) at the same time on the same machine.
   In order to fully respond to the query, we add a line in the methods section mentioning the lack of a cut-off for the interpretation of the quantitative difference.
3. The idea was to provide readers with the number and percentage of patients who had at least 30 days of treatment as recommendations for treatment duration widely vary between authors, institutions and across time. In order to make it simpler, we change the second category in 30-59.
4. In that paragraph, we took great care to claim that current recommendations about serological follow-up were not useful in a clinical context with adults treated with nifurtimox and did not claim that that extended to those treated with benznidazole (even if it probably does). Our clinical perspective – as opposed to a long-term epidemiological one – is further mentioned in subsequent paragraphs. In order to clarify, we added a line in the conclusions (p. 13, 2nd paragraph) that restricted our conclusions to nifurtimox.

Reviewer 2
Discretionary revision
1. The question is very pertinent in the sense that there is no absolute consensus on the optimal duration of nifurtimox treatment (cf references 4, 5 and 8). Historically, patients have received from 30 to 120 days therapies and no valid randomised comparison ever tested differences in outcome. In that sense, including patients with different treatment duration reflects real-life situation. In the present study, statistical analysis did not show a significant difference (P=0.69) between the three groups (60, 30-59 and < 30 days) as mentioned in the results section.