Author's response to reviews

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

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Dear Editor,

We would like to submit a manuscript entitled “Immunological and parasitological response in chronic Chagas patients 3 years after nifurtimox treatment” for publication as an article in *BMC Infectious Diseases*.

The distribution of Chagas disease has recently become global in the context of international migration. Clinicians, laboratories, blood banks and public health officers in Europe, North America, and Western Pacific Region are now facing an emerging health problem due to imported cases and local transmission (vertically, by blood transfusion or organ transplant).

In 2010, we published the largest epidemiological study of *Trypanosoma cruzi* infection in Latin American migrants in Europe. At that time, we also reported the largest study on tolerability and safety of nifurtimox in adult patients. We found overall poor tolerance and concerns about nifurtimox, one of the two drug registered against *T. cruzi* infection. Here we report the serological and parasitological follow-up of the same group of patients. This is, to our knowledge, the largest follow-up study with nifurtimox in adults conducted to date and the first in an area where patients are not at risk of vectorial reinfection.

Three years after treatment, we still found positive serological and rapid immunochromatographic results in all patients. All conventional PCR results were negative but one patient had a positive Real-Time PCR. Therefore, in this cohort, 97.3% participants could not be adequately informed about their current status, with a single patient conclusively found to be still infected. The positive serological test results could either indicate treatment failure or simply reflect the window period of persistent humoral response despite potential treatment efficacy. This highlights the lack of clinical utility in adults of the current WHO recommendation for treatment follow-up that stipulate serial serological tests over long periods. Our results also allow for discarding rapid immunochromatographic tests as an accurate early post-treatment test of cure.

These results are of importance regarding the number of adult patients eligible for treatment according to recent recommendations. Clinicians and patients are both affected by the lack of an appropriate test of cure. Moreover, treated patients are denied the opportunity to donate blood and organs for many years until these tests may eventually become negative. This is unfortunate in a period of shortage of donors. We believe that discovering more efficient and safer treatments and accurate and early responding tests of cure are the priorities in the modern management of Chagas disease both in endemic and non-endemic areas.
We chose to submit our manuscript to *BMC Infectious diseases* as this Journal has shown commitment to publishing on Chagas disease, a global yet neglected infection, and we believe that our results will be of interest to its unrestricted readership.

All authors have participated in the writing of the manuscript and have approved its content. They declare no conflict of interest.

We hope that this manuscript will be of interest to you.

With best regards,

Dr Yves Jackson