represents a current challenge for the aetiological treatment of Chagas' disease.

Transparency declarations

None to declare.

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Benznidazole treatment safety: the Médecins Sans Frontières experience in a large cohort of Bolivian patients with Chagas' disease—authors' response

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Sir,

We thank Novaes and Gonçalves[1] for their thoughtful comments on our paper.[2]

We would like to further clarify the characteristics of our study population. We included subjects from rural areas in Bolivia whose serological screening for Chagas' disease was positive. Therefore, our focus was on patients in the chronic phase of Chagas' disease; however, as this disease is endemic to rural areas in Bolivia,[3] we cannot rule out recent reinfection. Thus, patients positive for *Trypanosoma cruzi* infection were treated with benznidazole based on the assumption of a possible recent chronic phase, as recommended by a recent consensus.[4] We are aware of the results of the BENEFIT trial,[5] but we considered that most of our population was not composed of patients in the advanced stages of the cardiac form of the disease as among patients with available ECG data, 73.3% presented a normal ECG.[2] However, as we have already published,[2] information on ECG changes was limited and we could not properly classify patients with ECG changes into indeterminate or cardiac form and therefore we could not evaluate if the form of Chagas' disease influenced the likelihood of developing adverse drug reactions (ADRs) during benznidazole treatment.

We agree with the authors that the clinical efficacy of benznidazole in chronic cases is still under debate, but unfortunately our study[2] did not evaluate the clinical or parasitological efficacy of benznidazole treatment as the study was run in a rural area with a

retrospective design. Therefore, we cannot contribute any data on the relationship between ADRs and the clinical or parasitological efficacy of benznidazole treatment.

We agree with Novaes and Gonçalves[1] that studies on new treatment protocols are welcome, but at this point we cannot recommend protocols with shorter benznidazole treatment duration or using lower or intermittent doses until these new regimens are proved safe and effective in double-blind, randomized, prospective, controlled trials. Furthermore, the dose of benznidazole does not appear to be associated with ADRs causing treatment interruption ($P = 0.27$, $P = 0.780$),[6,7] and ADRs that require treatment interruption occur mostly in the first 30 days of treatment ($P < 0.001$).[6] Additionally, our recent results suggest that skin disorders were significantly associated with permanent suspension of benznidazole treatment,[2] and allergic dermatitis due to benznidazole is not dose related.[8] Moreover, skin reactions are the main side effect of benznidazole and begin around the 10th day of treatment.[8] These reactions are responsible for benznidazole treatment suspension on average by the 28th day of benznidazole treatment,[2] suggesting that a 30 day long protocol would not be enough to avoid benznidazole treatment interruption. On the contrary, the Médecins Sans Frontières protocol described in our paper proved very interesting as up to 89.8% of the patients were able to complete the proposed treatment even though 56% of the patients experienced some kind of ADR.[2] We attributed this success to the close follow-up surveillance together with patient counselling and reassurance, which prompted an earlier identification of ADRs and their treatment with a consequent lower abandonment rate.

Regarding the authors' comments on individual resistance to ADRs, we agree that individual characteristics and resistance to ADRs may be an alternative explanatory variable for adherence rates. In fact, we have reported that educational level was able to predict overall ADRs.[7] However, in the present study the retrospective design and the unavailability of data regarding educational level precluded some variables from being entered in the analysis, as already discussed in the published paper.[2]

Transparency declarations

None to declare.

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