AUTHOR REPLY


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We appreciate the interest of Professors Urbina and McKerrow in our recent paper (1) and welcome the opportunity to discuss the work further. In our study, we found that benznidazole consistently cured both acute and chronic Trypanosoma cruzi infections in mice, whereas posaconazole was much less effective, data consistent with the results of a recent clinical trial (2).

In response to specific comments by our colleagues, we point out the following. (i) Contrary to what is stated in the letter from Professors Urbina and McKerrow, our paper does not include experiments where mice in the acute stage of T. cruzi infection were treated with benznidazole for 5 or 10 days. (ii) Previous studies on the efficacy of 20 days of benznidazole treatment against infections with the T. cruzi CL strain (see references 7 to 10 in the letter from Professors Urbina and McKerrow) have produced a range of results, which may reflect the differing mouse models, timing of treatment start points, and choice of drug vehicle. Indeed, we notice in a paper by Professor Urbina that treatment of Swiss mice with 100 mg/kg orally for 20 days resulted in a 100% cure (see Table 1 in reference 8 of the letter from Professors Urbina and McKerrow). (iii) The bioluminescent CL clone used in our study was not “hypersusceptible to benznidazole.” We would have been careless not to test for this. The 50% inhibitory concentration for intracellular amastigote forms was 1.2 μM (unpublished data), not significantly different from that for the wild type and well within the normal range reported elsewhere for T. cruzi CL and other diverse strains (3). (iv) Our treatment data are consistent with findings reported in a recent paper (4). Using PCR to assess drug efficacy, these authors find that treatment of T. cruzi CL-infected mice with 100 mg/kg benznidazole for 20 days results in a complete cure. Furthermore, they also find that posaconazole has a limited curative effect, even when treatment is extended to 40 days.

Investigating whether subcurative treatment with posaconazole leads to improved clinical outcomes is a complex issue and was not an objective of our study. However, it is unlikely that any new treatment for T. cruzi infection will be licensed unless it can achieve a sterile cure. Unfortunately, based on in vitro studies (3), in vivo assessment (1, 4), and a clinical trial (2), posaconazole does not seem to meet this benchmark.

As outlined by Professors Urbina and McKerrow, benznidazole is far from an ideal drug and the search for more effective alternatives must remain a research priority.

REFERENCES


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This is a response to a letter by Urbina and McKerrow (doi:10.1128/AAC.01714-15).

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