Reviewer’s report

Title: Underestimated pyrazinamide resistance may compromise outcomes of pyrazinamide containing regimens for treatment of drug susceptible and multidrug-resistant tuberculosis in Tanzania

Version: 0 Date: 27 Feb 2018

Reviewer: Sarah Sengstake

Reviewer’s report:

Well designed study and comprehensively written paper. This study adds knowledge to the growing pool of data on PZA resistance associated with multidrug resistance and treatment outcome in the context of Tuberculosis.

Half of the MDR-TB patients presentend with PZA resistance as was analysed with the conventional culture based method. This is comparable to what has been published from other locations. In contrast, a higher than previously observed percentage of PZA resistance was found in non-MDR-TB patients. Respective strains were less likely to be M.bovis (which is intrinsically resistant to PZA) as the mutations differed from Mbovis related mutation. The underlying, possibly epidemiological cause, will be further studied. Treatment failure was high as 80% in PZA resistant MDR-TB however sample size is small (N=6) so if at all this observation shows a trend and needs to be confirmed in a larger data set. By combining the molecular pncA test with DST for PZA the two-by-two table (Table1) shows that in this setting the molecular test has a good NPV but a lower PPV. This highlights the culture based PZA test to still be the reference method that should be performed for the analysis of the PZA status.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?

Yes
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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Please indicate the quality of language in the manuscript:

Acceptable

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