Reviewer's report

Title: Efficacy and safety of thrice weekly DOTS in tuberculosis patients with and without HIV co-infection: an observational study

Version: 2 Date: 31 March 2013

Reviewer: Reinout R van Crevel

Reviewer's report:

The manuscript addresses an important topic. However, I feel there are some important limitations with regard to design and description of methods and results which make that the conclusions drawn are somewhat premature.

Major compulsory revisions:

1- the authors have used a large number of exclusion criteria which are likely to impact the results, including previous history of TB and diabetes. 38% of patients screened were excluded. Those excluded are likely to have a higher risk of treatment failure, and one may hypothesize that this is especially true for the HIV+ patients. I therefore feel that the conclusion "..outcomes in HIV co-infection were found to be similar to those reported previously with daily therapy, with no safety concerns." is premature

2- there may be a information collection bias. Culture results at baseline and during follow-up were missing for many patients. 'treatment completed' and 'cure' are combined, but these are clearly two very different endpoints. Based on the information provided I cannot conclude that treatment outcome is similar in HIV+ and HIV-.

dead is nog good endpoint to compare treatment results, as HIV+ patients are more likely to die from other causes. The ideal endpoint would be treatment failure and possible acquisition of drug resistance (which was not measured)

3- no DST was performed to exclude drug-resistance as an important confounding. This is not trivial; drug resistance may be overrepresented among HIV+ patients, for instance because of nosocomial exposure

4- the reporting of the data is somewhat confusing. what doe the authors mean by “Modified intention to treat analysis was applied to the population undergoing any treatment, within the 'end of treatment' groups (n=305) and to all excluding those still under regular follow-up in the 'follow-up' groups (n=211). On treatment analysis was applied to all those receiving any ATT in the context of adverse events (n=305).”?

5-“Follow-up included clinical assessment, monitoring for adverse events and opportunistic infections (in HIV- positive patients), routine blood investigations,
sputum smear and culture if appropriate and possible, and repeat imaging as at enrolment to monitor response to treatment.” Is rather vague and should be specified. Did the authors plan to sample sputum for culture monthly (smear is not very useful to monitor bacteriological response to treatment)? If not, why? The same for Chest X-ray, was it done / planned at specific time points (e.g. month 2 and 6.

Similarly, how was adherence monitored? Was a standardized questionnaire used?

The authors may not be able to correct some of these issues (related to the design of the study), but I feel that the data presented do not support the conclusion, and that because of limitations in the design one may not conclude that TB treatment outcome is not different among HIV+ individuals.

Minor:
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Table 1. gender in %, viral load in log.
Table 2. please add %
Tabel 3. Please combine ‘smear results’ with ‘smear bacuilliry load’. Under load: negative, scanty, 1+, 2+, 3+
Tables 1-4 may be combined (6 tables seems out of proportion to the amount of original data)

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
I declare that I have no competing interests