Reviewer's report

Title: Local Phylogenetic Analysis Identifies Distinct Trends in Transmitted HIV Drug Resistance: Implications for Public Health Interventions

Version: 1 Date: 26 April 2013

Reviewer: Dineke Frentz

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- Major Compulsory Revisions

1. In order to avoid the possible bias coming from convergent evolution due to treatment experience on the phylogenetic analysis, all sites associated with major antiretroviral drug resistance should be excluded.

2. In the method section about phylogenetic analysis, the authors don’t mention the use of an out-group. The use of an out-group is extremely important in phylogenetic inference as it allows you to determine the polarity of direction of evolution.

- Minor Essential Revisions

3. The abbreviation ‘OCR’ below the headline ‘Digitization of Nucleotide Sequences’ is not written out.

4. For the interquartile range, the authors use one number. It would be more clear if the authors would give the lower and the upper bound for the interquartile range, which gives a better idea of how the data is distributed.

5. For the CD4 cell count a mean is given. CD4 cell counts tend to be not normally distributed. Therefore a median with an interquartile range would be preferred.

6. Following the mean CD4 count of 326 cells/ul a ‘(23%)’ is given. It is not clear what this percentage stands for.

7. The text in the result section in paragraph ‘drug resistance’ is in contrast with Table 2. Table 2 shows 15 out of 19 patients with NRTI resistance only, while the text mentions 14 out of 19 patients. Furthermore, Table 2 shows 1 patient with NNRTI resistance only, 1 patient with a 2-class resistance of NRTI and PI resistance. One patient shows a 2-class resistance of NRTI and NNRTI resistance and 1 patient shows resistance to the three classes of antiretrovirals.

8. In the results section in the paragraph ‘phylogenetic analysis’ Table 3 is being referred to. This should be changed into Table 2.

9. In the paragraph just before the discussion ‘Table 5’ should be changed into ‘Table 4’.
10. In Table 1, the superscript symbols are not explained.

- Discretionary Revisions

11. In my view, Table 3 should be arranged differently, to be able to extrapolate the resistance percentages more easy. In the text, resistance prevalence are given for different groups of HIV patients. In order to see these resistance proportions in the table, the percentages in the table should be given in a vertical direction instead of the horizontal direction. So the percentages should sum up to 100% within a row instead of within the column.

12. Table 4 does not give more additional information as compared to the column of patients with TDR in table 3. It only differs for 4 patients. I would suggest to delete table 4 and give the characteristics of the cluster in the text, so for example: ‘patients within the monophyletic cluster were all male, infected with a subtype B virus and either have MSM as their risk factor or it is not reported’.

13. In the discussion the authors state ‘as is the case for antibacterial therapy in the ICU, treating physicians are best served by drug resistance data that most accurately represents the local ecology’. As in HIV-care baseline resistant testing is the standard of care, I assume the authors were referring to HIV treatment as prevention. As both the Ontario study and this study do not show the mutations associated with resistance to tenofovir or emtricitabine, the question is whether this study is needed to change treatment as prevention guidelines for this local region.

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests