Reviewer's report

Title: Antiviral Resistance and Predictors of Virologic Failure in the first Cohort of HIV-Infected Children Gaining Access to Structured Antiretroviral Therapy in Lima, Peru: A Cross-Sectional Analysis

Version: 2 Date: 15 July 2012

Reviewer: Linda Wittkop

Reviewer's report:

Major comments:

1) The study design is not clear. In the first part of the method section the authors state that CD4 cell counts were determined every 3 months and viral load every 6 months. In the section “rates of clinical/immunological progression” – authors state that they computed rates of immunological and clinical progression between enrolment and several years of follow-up. Thus, the study is an observational cohort study and authors should carefully revise their manuscript using appropriate terminology.

However, later in the text the authors state that they performed a cross-sectional study. If the authors refer to the resistance testing data as the cross-sectional analysis, then this should be more precisely described. In the method section, it is not clearly stated at which time point the samples for resistance testing were drawn.

2) Definition of virological failure:
   - the authors state that virological failure was defined by two or more measurements of viral load >400 cp/mL. Did they mean two consecutive viral loads >400 cp/mL?

3) Statistical analyses are not described. The tests used to compare groups need to be described.

4) The term z-score may not be clear to all readers and should be defined.

5) The way clinical categories were defined should be reported in the method section and not in the result section.

6) Figure 1A is very difficult to read. Instead of presenting the trajectory for each child authors could present estimates of central tendency with a confidence interval to facilitate the reading of this figure.

7) Figure 1B shows the cumulative probability of virological failure. It is not described which method was used to determine these estimates. The numbers of patients at risk at each follow-up point need to be added.

8) How do authors consider treatment modifications, patients lost-to-follow-up or
patients who died in the analysis of time to virological failure?

9) After 3 years of follow-up only 19 children were still included. The fact that children still followed-up after three years have better immunological scores could also be explained by an attrition bias. What is the reason that after three years less than half of the children are followed-up? Authors should make sure that there was not an informative drop out.

10) What is the underlying method for figures 3A-3D? How is the blue arrow calculated?

11) All mutations detected by RNA-OLA, DNA-OLA and genotypic testing could be summarized in a table to see their frequencies overall and also according to patients failing and not failing therapy.

12) In the result section authors state that samples for resistance testing were drawn after treatment initiation and in the majority of cases after virological failure. Thus, authors should be very careful in using the term prediction (page 15/32 and also in the title)! To my understanding the authors can only state that mutations M184V, N88D and L90M were significantly more often found in patients with virological failure than in those not failing therapy.

13) Did authors any adjusted analyses for determining factors associated with virological failure? Which variables were tested? For example, when the analyses are adjusted for previous treatment exposure, age, sex etc. is the immunological classification still associated with virological failure?

Minor comments:

The following abbreviation was not defined:
- IRB

The sentence on page 19/23: “The DNA-OLA was very indicative .....in comparison to the DNA-OLA.” should be revised.

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, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests