Reviewer’s report

Title: Effects of highly active antiretroviral therapy with Nelfinavir in vertically HIV-1 infected children: 3 years of follow-up

Version: 1 Date: 23 May 2006

Reviewer: Marcelo Soares

Reviewer’s report:

General

The study by Resino and colleagues aimed to evaluate the use of HAART regimens containing nelfinavir (NFV) on virological and immunological outcomes of HIV-infected pediatric subjects in a 3yr follow-up. At the end of the study, the authors found that although a high number of patients (30/42) failed therapy, important increases in CD4 T cell counts and a rapid decline of VL occurred at the beginning of therapy in most cases. A low number of metabolic complications with the use of NFV were observed, leading the authors to conclude that this drug is safe and efficacious in HIV/AIDS pediatric settings.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Although some benefit of NFV-containing regimens are shown (only 27 out of 42 children remained on NFV at the end of the study!), there are several points of potential concern in interpreting the results shown by the authors.

1. The authors mentioned that there were multiple (non-uniform) previous treatment regimens with mono- or dual therapy in the children under study. There were no attempts to compare or discuss differences of those categories on the outcomes. The same can be applied to the non-uniformity of RTI-based backbones which were combined with NFV, which was also largely variable according to the authors.

2. There is no mention by the authors on the protocols to measure adherence to therapy by the subjects analyzed, what should be at least briefly discussed.

3. The authors attributed the improved CD4+ counts at the end of the study to the NFV-containing regimens used, but the change of therapy that was observed in high frequency in their patients could explain the observations. In other words, perhaps it is not the NFV that is benefiting the patients. The authors should clarify that issue.

4. This study is not an “intent-to-treat” one, as it should be. The authors should use the data from the patients that remained in NFV at the end of the follow-up study, but they rather included data from the patients that changed and/or failed NFV as well. This rather skews data toward better outcomes. It is not clear whether the Figures include all patients or only those which successfully remained on NFV.

5. Discussion is poor and could include comparison to others studies, with other drugs, in pediatric settings.

6. The study by the PACTG 377 cite by the authors (ref. 16) does not discuss dosage of nevirapine (NVP) on its pharmacokinetics in blood, but rather the effect of NVP on NFV pharmacokinetics. This should be corrected.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. English is poor throughout the manuscript. Authors should consider a professional language editing.

2. There are several abbreviations in the manuscript which are not previously defined (uVL, PI, ART, etc). Those turn reading by an average clinician or investigator into a difficult task.
3. Although the authors state that two Figures are included (Front page), only Figure 1 and its legend are included in the manuscript. Figure 1 is repeated afterwards.

4. The median baseline CD4+ T cell counts of the cohort as stated in Table 1 (25.8%) does not match the one presented at time point 0 of Figure 1A. This should be clarified.

5. Figure legends (graph codes) are confusing and should be simplified. There is no need for defining continuous X dotted lines AND distinct symbols in the same graphs.

6. The data presented in the manuscript text about the number of children that rebounded their HIV VL at the end of follow-up period (17/28) (line -2 of page 7) do not match the graph presented in Figure 1E.

Discretionary Revisions (which the author can choose to ignore)

1. Authors should briefly introduce their study in the introduction section, what was not done.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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: No

Declaration of competing interests:

I declare that I have no competing interests