Author's response to reviews

Title: Durability of Stavudine, Lamivudine and Nevirapine among Advanced HIV-1 Infected Patients with/without Prior Co-administration of Rifampicin: A 144-week Prospective Study

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Author's response to reviews: see over
September 16, 2008

The Editor
BMC Infectious Diseases
Dear Editor,

Enclosed please find the attached file of a revised manuscript entitled “Durability of Stavudine, Lamivudine and Nevirapine among Advanced HIV-1 Infected Patients with/without Prior Co-administration of Rifampicin: A 144-week Prospective Study”, an original article for consideration to publish in *BMC Infectious Diseases*. The reviewers’ comments have been responded point by point.

The current information to authors has been read and followed. All authors have seen and approved the manuscript. This article has never been published elsewhere or submitted simultaneously for publication. There is no conflict of interest

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Yours sincerely,

Weerawat Manosuthi, M.D.
Response to reviewers’ comments

Reviewer 1

Reviewer's report

Title: Durability of Stavudine, Lamivudine and Nevirapine among Advanced HIV-1 Infected Patients with/without Prior Co-administration of Rifampicin: A 144-week Prospective Study

Version: 4 Date: 24 July 2008

Reviewer: Ploenchana Chetchotisakd

Reviewer's report:

1. There is no long-term metabolic complication of ART in the results as stated in the second objective.

“Long-term metabolic complication of ART” has been removed from the list of secondary objectives.

2. Did the patients in the TB group receive a lead-in when they initiated on nevirapine?

The patients in either TB group or control received a lead-in nevirapine for 14 days. The authors have added the following sentence in the method section.

“All patients received NVP 200-mg once-daily lead-in dose for 14 days, prior to the escalation to 200 mg twice daily.”

3. The authors should provide a figure of virological response over time between the 2 group to demonstrate the early response and the durability.

This figure has been added as figure 1.
The author also added figure 3 that shows the details of each mutation.
Reviewer 2

Reviewer’s report
Title: Durability of Stavudine, Lamivudine and Nevirapine among Advanced HIV-1 Infected Patients with/without Prior Co-administration of Rifampicin: A 144-week Prospective Study
Version: 4 Date: 18 August 2008
Reviewer: Elena Seoane

Minor Essential Revisions

1. RIFAMPICIN = (RFP) pag. 4

“RFP” has been changed to “rifampicin” in which is consistent along the manuscript.

2. IIT = INTENTION TO TREAT pag. 7

“ITT” has been changed to “intention-to-treat”.

Major Compulsory Revisions

Abstract

1. The purpose and design of the study is not defined, please include them

The following sentences had been added in the method section of the abstract.
“A prospective cohort study was conducted among 140 antiretroviral-naïve patients who were enrolled to initiate d4T, 3TC and NVP between November 2004 and March 2005. The objectives were to determine immunological and virological responses after 144 weeks of antiretroviral therapy.”

Material and methods

1. Which were Clinical, Immunological, and Virological characteristics of HIV-1–Infected Patients TB Group and Patients Control Group at the baseline; Please could you include a table with these characteristics? It is necessary for the correct understanding of this article

Table 1, which described baseline characteristic parameters, has been added.

2. If the most of patients had an important immunodeficiency. Why CD4 cell count < 350 was yours inclusion criteria?

Although this study was planned to enroll the patients who had CD4 cell count of less than 350 cell/mm3, almost all of our patients who were consecutively enrolled into the study had very low baseline CD4 cell counts (mean CD4 = 62 cells/mm3)

3. Why did you include patients who receiving Rifampicin > =1 month prior to
enrolment?

We enrolled the patients who received rifampicin-based anti-TB regimen for at least 1 month because we would like to decrease or avoid anti-TB-related side effects including skin rash and hepatitis that may occur after the first few weeks of TB treatment and overlap with nevirapine-related side effect.

4. All the patients were naive for antiretroviral treatment?

All patients in the present study were naïve to antiretroviral treatment as we had described in exclusion criteria #1.

Results

1. After 144 weeks of ART, 57 needed discontinues ART. how many were on TB group? Which were the reason to discontinues ART, were there any differences among groups?

The following sentences have been added in the results section to clarify this point. “Of all, 57 patients needed to discontinue ART after 144 weeks of ART, 27 patients were in TB group and 30 patients were in control group. There was no difference in term of ART discontinuation between the two groups (P=0.688).”

2. The following sentence seems difficult to understand “Among 13 patients with drug resistance, 5 (38%), 1(8%), and 7 (54%) patients had mutations contributed NRTI resistance, NNRTI resistance, and both NRTI and NNRTI resistance, respectively”.

This sentence has been revised as below. “Among 13 patients with drug resistance, 5 (38%) had mutations contributed to only NRTI resistance; 1 (8%) had mutations contributed to only NNRTI resistance; and 7 (54%) patients had mutations contributed to both NRTI and NNRTI resistance.”

3. Were there differences in NRTI and NNRTI resistance associated mutations between control group and TB group?

The sentence that mentioned these differences were at the last sentence in the 2nd paragraph of the result section. “There were no differences in terms of NRTI and NNRTI-resistance associated mutations between the two subgroups (P >0.05).”

4. This sentence “Of 70 patients in TB group, 31 (44.3%), 20 (28.6%), 14 (20%), 3 (4.3%), 2 (2.9%) patients were diagnosed pulmonary tuberculosis, disseminated tuberculosis, cervical tuberculous lymphadenitis, gastrointestinal tuberculosis and tuberculous meningitis, respectively” is not a result. These are the clinical characteristics of the TB group at baseline, please include it in
Material and Methods or include a table with baseline characteristic of patient as your table 1 of BMC Infectious Disease 2005, 5:67

We moved this sentence to the first paragraph of method section.

5. Levels of nevirapine are not included in this section

The author had added the sentence mentioned about this result in the discussion section as response to Discussion comment number 2 (below).

Discussion

1. The sentence “The present study has demonstrated that an antiretroviral regimen of stavudine, lamivudine and nevirapine showed sustainable and durable antiviral effectiveness in advanced HIV-1 infected patients. It is only partially, although improve CD4 cells count there is 40% of patients did not achieve HIV-1 RNA<50 copies/ml, Although this is considered favorable outcome when compared to the other NNRTI-based regimen

The authors have revised this sentence as below.
“The present study has demonstrated that an antiretroviral regimen of stavudine, lamivudine and nevirapine showed acceptable antiviral effectiveness in advanced HIV-1 infected patients

2. Authors include in Discussion a sentences of nevirapine levels, in results does not show these data

The authors have added this sentence that mentioned our previous results prior to discuss about nevirapine level.
“Average mean trough plasma nevirapine levels of week 8 and week 12 was 5.40 mg/l in the TB group and 6.56 mg/l in control group (p=0.048) [12]. Although minimum plasma concentration of nevirapine is somewhat different during the early period of ART between the two subgroup patients as mentioned, the long-term antiviral responses between these two groups were not different as demonstrated in the present study.”