Reviewer's report

Title: High T-cell immune activation and immune exhaustion among ART-treated patients with suboptimal CD4 recovery despite long-term viral suppression in an African cohort

Version: 2 Date: 24 September 2010

Reviewer: Susanne Dam Nielsen

Reviewer's report:

The manuscript by Nakanjako et al aims at describing the association between immune activation/immune exhaustion and immunological recovery in HIV-infected individuals 4 years after initiating HAART in an African setting.

The aim of the study is well defined.
The number of patients included is 128 which seems to be adequate.
The methods used to determine immune activation/exhaustion are appropriate.
There is a clear and concise presentation of data. Language is fine.
The authors conclude that immune activation/exhaustion is found in HIV-infected patients even after 4 years of HAART. The level of immune activation is associated with the degree of immune recovery. This is adequately supported by data.
The abstract clearly reflects the findings in the manuscript.

Conclusion: This manuscript adds to the growing pool of knowledge regarding persistent immune activation in some HIV-infected individuals despite fully suppressed viral load, and it is performed in an African setting. Furthermore, it demonstrates an association between residual immune activation and the degree of immune recovery.

Following needs to be considered:
The authors chose to divide the cohort into 3 groups based on the current CD4 count. However, in the remaining manuscript only increase in CD4 count from baseline is used. Most studies choose to define immunological non responders as persons with CD4 counts less than 200 and responders as persons with CD4 counts > 500. Using the increase in CD4 count actually results in groups that overlap (suboptimal with increase 94-298, optimal 94-435). It is fine to present data on increase in CD4 count, it would provide additional information though to present the association between immune activation/exhaustion and the actual CD4 count. This would also make comparison with previous findings easier.

The patients included are not very well described. The authors provide information on age, sex, and antiretroviral treatment. Did any of the patients have AIDS-defining illness? The patients with poor immune recovery and immune
activation - could that be due to co-infections such as TB or HCV? Were any of the patients actually treated for TB during the 4 years of HAART?

Patients are tested for concurrent infections. Surprisingly few patients were found HBsAg positive. Even more surprisingly is the finding of no intestinal parasitic infections in the entire cohort. These findings need to be discussed.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare I have no competing interests