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:** 2 November 2010

**Reviewer:** David DM Meya

**Reviewer’s report:**

Minor Essential Revisions

Overall the paper presents interesting data especially from a resource limited setting. Studies of this nature enhance the role of basic science in resource limited settings, contributing to the body of knowledge.

1. Although the authors looked across controls and cases, it would have been interesting to have a comparison group with on going viral replication (VL > 400 copies/ml) to compare the persistence of PD-1 and T cell activation. This should be highlighted as a limitation.

2. The authors conclude well about the relevance of their findings to the argument regarding early initiation of ART especially in settings where patients show up with Stage IV disease. Although this is explicitly mentioned in the conclusion, it is not clear whether this was a question that they had posed in the introduction. Namely, would the findings in this study be of use in contributing to the immunological argument for early initiation of ART.

3. The authors also should note which facility was used for the analyses in this study. Otherwise methods used were appropriate.

4. The authors in reporting the results should have included a figure showing the actual fluorescence.

5. In the discussion, the authors should include more detail on PD-1 and a reference to look at and include would be Michelle D'Souza et al Programmed Death 1 expression on HIV Specific CD4T cells is driven by viral replication and associated with T cell dysfunction. Journal of Immunology 2007; 179:1979-1987

6. Second paragraph under discussion should be under the limitations section of the discussion.

7. Perhaps the authors could report on any important clinical outcomes for the sub optimal responders e.g OIs/hospitalizations during the 4 years of ART.

8. Suggest changing title to "High T-cell immune activation and immune exhaustion in an ART-experienced African cohort with suboptimal CD4 recovery."
9. Finally the authors need to proof read through the manuscript as there are various adjoining verbs missing.

**Level of interest:** An article whose findings are important to those with closely related research interests

**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 that I have no competing interests'