Reviewer's report

**Title:** immunological predictors of CD4+ T cell decline in antiretroviral treatment interruptions

**Version:** 1  **Date:** 9 October 2007

**Reviewer:** Jonathan Angel

**Reviewer's report:**

General

Dr. Seoane and colleagues present results from a small, prospectively studied cohort of effectively treated HIV infected individuals that interrupt antiretroviral therapy with the focus of this manuscript being the determination of predictors of CD4 T cell decline. As has been demonstrated previously, CD4 nadir is a predictor of this decline. What appears to be a novel observation is that measures of CD4 T cell function similarly predict those individuals with a greater CD4 decline. As CD4 T cell function has been previously demonstrated to be an independent predictor of disease progression, this finding may not be surprising, but it appears that this may be the first report of such an observation.

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

Major Concern:

The one major concern that I have with this manuscript is with the interpretation of the data. The authors state that CD4 positive T cell function is an “independent” predictor of CD4 T cell decline. In fact, this has not been demonstrated. It is, in fact, quite possible (if not likely) that those individuals with lower CD4 nadirs are also those with poor CD4 T cell function and these assays simply identifying the same individuals. Related to this, the authors state that they did not do a multivariate analysis because the numbers were small and therefore a statistical analysis was not done to suggest that there was independence.

Additional Concerns:

1) It is unclear how patients were identified (were they consecutive patients that attended a clinic?), if there were subjects that were offered enrollment but declined participation or why the investigators chose an “n”of 27. All of these issues regarding the study design and conduct should be included.

2) It is stated that three of the 27 subjects re-initiated antiretroviral therapy (1 for acute retroviral syndrome and 2 for thrombocytopenia) but it is not stated how
CD4 counts from these individuals were handled in the data analysis. This needs to be explicitly stated.

3) In the Conclusion it is stated “However, the results are in agreement with previous findings on the safety of treatment interruptions…”. The number of individuals studied here is actually small to suggest safety but more importantly, over 10% of subjects in this study experienced clinical events that prompted re-initiation of therapy. At this rate, I am not so sure that this study confirms the safety of this approach.

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

Discretionary Revisions (which the author can choose to ignore)

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

**Level of interest:** An article of limited interest

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests