Reviewer's report

Title: The association of high-sensitivity c-reactive protein and other biomarkers with Cardiovascular Disease in Patients Treated for HIV: a Nested Case-Control Study

Version: 2 Date: 21 May 2013

Reviewer: Vicente Estrada

Reviewer's report:

This is an interesting study on the association of elevated hs-CRP and CVD in HIV patients. The main research question is well stated and methods used are appropriated for this purpose. In general, the manuscript is well-written and easy to read. Abstract is concise and informative. The main conclusions are also interesting, in part novel, and may pose potential clinical applicability.

I have several comments:

A) Major compulsory revisions:

1. I miss several adjustments for already traditional CVD risk factors in HIV, in particular renal function: the significant association found between elevated hsCRP and CVD is maintained when eFG values are considered?. In the case it was not possible to analyze this, I consider that it is a limitation of the study that has to be mentioned.

2. No mention is made on lipid lowering treatment: how many patients were on statins?. Because of the relevance of the results of the Jupiter study, it seem advisable to mention the effect of statins on hsCRP and CVD. Again, if no data are available, this should be mentioned as a limitation.

3. In abstract, Results, I would suggest change the expression "High hsCRP increase CVD risk" for "are associated with".

4. It is somewhat confusing the terminology used for samples: late samples were collected before the CVD event in cases and the last follow-up in controls; therefore, this is probably the most important sample. Early samples were collected before the late sample in both cases and controls, about 22 months before the CVD event or #24 before the end of follow-up. There is no clear concordance (it should be analyzed) between early and late samples: i.e., no significant difference is found between median hsCRP and % patients with >3 ng/L in early, but significant differences are found only in late samples. Table 1 refers to the clinical characteristics at the time of early, but not late sampling. Perhaps the late sampling time is the most important clinical point time to consider when describing patient population. What is the relevance of describing the early samples?. I would suggest a more clear explanation on this particular aspect.

B) Minor essential revisions
1. I would suggest the inclusion of a figure showing the association between hsCRP and CVD, and also reduce the information provided in tables (early samples, ie) to ease readability.

**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 have no competing interests related to this paper