Reviewer's report

Title: Predictors of Serological Failure After Treatment in HIV-infected Patients with Early Syphilis In the Emerging Era of Universal Antiretroviral Therapy Use

Version: 2 Date: 7 November 2013

Reviewer: Arlene Sena

Reviewer's report:

The authors present findings from a large systematic evaluation of HIV-infected patients with early syphilis, in which they assess clinical characteristics and treatment regimens associated with serological response. There have been several other reports in the literature regarding the serological response to treatment of syphilis in HIV-infected patients. Therefore, this study does not provide any new information, but does add consistent findings to the results from other studies. There are some areas in the manuscript that require major revisions or better clarity for improvement.

Major Compulsory Revisions:

1) In Methods, I assume that only patients with early syphilis were included in the study, so please add in the inclusion criteria. It could be inserted in line 127, number 3 as "clear documentation of the patient's stage as primary, secondary or early latent syphilis..."

2) On page 6, inclusion criteria 4 states that those with a history were required to have a> 4 fold increase in titers to indicate re-infection. Was re-infection also defined based on patient history of potential re-exposures?

3) On page 7, please clarify if the CD4 and viral load data that were analyzed were from the time of syphilis diagnosis and/or treatment date.

4) Were medical records also reviewed for other drugs that may have activity against syphilis, such as azithromycin or doxycycline, that were prescribed for these HIV patients, that may have affected their serological response after syphilis therapy?

5) In the Discussion on page 12, the second paragraph is very confusing and is not well written or thought out. Nontrep tests detect lipoidal IgM and IgG antibodies (not provoke). There is no basis for hypothesizing that they slow the response in (?)trep) IgG antibodies, which appear early in syphilis infection. Also, there are no references cited to support the statement that patients with longer infection have slower dividing bacteria.

Minor Essential Revisions

1) Page 12, line 264 - Fourth is misspelled
2) Page 13, line 268 - retrospective is misspelled

Discretionary Revisions

1) On page 9, the authors state that 51% had a prior syphilis history. I was struck with how high this percentage is among HIV-infected patients, and would have liked to see some comment about in the Discussion. It would be interesting to know when the prior syphilis occurred relative to the current infection. It is thought that patients who are re-infected with syphilis tend to have milder presentations than those with initial infections, so I wonder if this may have affected their findings since a serological failure rate of 9.0% seems low for HIV patients with early syphilis (compared to other studies including those among HIV-uninfected patients).

**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 have no competing interests.