Reviewer’s report

Title: Prevalence of naturally occurring NS5A resistance-associated substitutions in patients infected with hepatitis C virus subtype 1a, 1b, and 3a, co-infected or not with HIV in Brazil

Version: 0 Date: 28 Mar 2017

Reviewer: Kevin S Cashman

Reviewer's report:

Overall Assessment: Good quality manuscript in many facets (writing/approach/methodology/analysis). Understanding geographic diversity in antiviral drug resistance is not only needed but crucial in both an epidemiological and patient-centric setting. The overall novelty of the idea is minimal, but the addition of the co-infected cohort and the subtype 3a analysis warrants significant consideration. I would have liked to see a larger study cohort considering some RAV frequencies are low and the statistics only give modest significance, but I think the point of the manuscript is fulfilled. With this being noted, there are a few minor formatting and grammatical issues I would suggest.

Major Issues: None

Minor Issues: 1. I would suggest a little more introduction into the HCV nonstructural proteins and why they are important enough to target in this context. I felt this was lacking in the introduction. 2. Line 124: delete "of" 3. Line 142: "groups" to replace group 4. Lines 228-233: This sentence needs to be structured. As is, it is a run-on. 5. Lines 236-237: The authors speak as though they know that these mutations confer resistance in their current cohort. This patient outcome data was not presented in the manuscript and most resistance discussed in the manuscript is a result of previously published works from other groups. I would suggest rewording this sentence to reflect that this is the theoretical outcome of these mutations. 6. Line 253-256: Need to restructure this sentence. As is, it is a run-on. 7. Abbreviations: PEG-IFNa, AASLD, and RBV are used scarcely throughout the manuscript and do not warrant abbreviation.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?


If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable

**Declaration of competing interests**
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests.

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal