Author’s response to reviews

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

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To The Editor BMC Infectious Diseases Response to Reviewers comments Ref.: Manuscript INFD-D-16-01689R1 Dear Editor Jean-Claude Desenclos, We have received the editorial letter with the comments of the expert reviewer and we appreciate them. We have checked out the expert reviewer’s questions to improve the manuscript. We appreciate all of reviewer’s suggestions, and based in your comments minor changes were made throughout the text (highlighted in yellow).Reviewer 1: Minor Issues: Line 60: "Worldwide" does not need capitalization. A: This was fixed. “...human immunodeficiency virus (HIV) is common worldwide, it is…” Lines 82-84: Sentence would benefit from listing the DAA medications following a colon. A: We agree, and this was done as suggested. “...NS5A substitutions have been identified in DAA treatment-naïve patients and may reduce the antiviral activity of NS5A inhibitors currently used in the clinic, such as daclatasvir, elbasvir, ledipasvir, ombitasvir and velpatasvir [9-12].” Lines 150-151: The sentence seems to be a fragment as is, and will need minor rewording. A: We agree, and this was done as suggested. “...The NS5A region was successfully sequenced from all 257 samples tested in this study and RASs were found in both treatment-naïve patient groups: HCV monoinfected and HIV/HCV coinfected.” Line 157-158: Can the authors speculate on the significance of the non-RAS mutations that are found within this cohort? A: The non-RAS substitutions could be considered polymorphisms that emerge during virus replication, it is consequence of the lack proofreading activity of viral RNA polymerase, leading to a great diversity in viral population. Lines 216-223: Comparisons to other mutations in different ethnic backgrounds. Is this a normal distribution in comparison to other studies, or are there certain mutations (as discussed in the article) that have higher prevalence and if so how do they compare with other ethnic or geographical populations? The authors hinted at this in the discussion but I think a formal comparison may be helpful to better understand viral mutation distribution and rates within Brazil. A: We agree. This
information was included in the discussion (lines 223-225).“…. The proportion of detectable pre-existing RASs reported in previous studies is 13% of cases in North America and 14% in Europe [35].” Line 236: Change "once" to 'since'. A: We agree, and this was done as suggested. At last, we are willing to send you any further information you may require.

Best regards,
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