Author’s response to reviews

Title: Liver fibrosis and accelerated immune dysfunction (immunosenescence) among HIV-infected Russians with heavy alcohol consumption - An observational cross-sectional study

Authors:

Kaku So-Armah (kaku@bu.edu)
Matthew Freiberg (matthew.s.freiberg@vanderbilt.edu)
Debbie Cheng (dmcheng@bu.edu)
Joseph Lim (joseph.lim@yale.edu)
Natalia Gnatienko (Natalia.Gnatienko@bmc.org)
Gregory Patts (gpatts@bu.edu)
Margaret Doyle (Margaret.Doyle@uvm.edu)
Daniel Fuster (daniel.fuster@bmc.org)
Dmitry Lioznov (dlioznov@ya.ru)
Evgeny Krupitsky (kruenator@gmail.com)
Jeffrey Samet (Jeff.Samet@bmc.edu)

Version: 2 Date: 18 Nov 2019

Author’s response to reviews:

We thank you for the opportunity to revise and resubmit our manuscript. All remaining reviewer comments are addressed point-by-point below.

Reviewer reports:

Xiaogang Xiang (Reviewer 3): The authors have revised the manuscript appropriately.
Response: Thank you for your review.

Zhou Zhou (Reviewer 4): The current version of "Liver fibrosis and accelerated immune dysfunction (immunosenescence) among HIV-infected Russians with heavy alcohol consumption - An observational cross-sectional study" answered the previous major concerns sufficiently. Here are some more minor concerns to be addressed:
1. According to the flow cytometry strategy in the "Method" section, the authors did not use CD3 or any other method to gate T cells before gating out CD4 and CD8 T cells. Nor did the authors use any marker to gate out NKT cells. Given the authors are analyzing the HIV patients, the contaminating cells, including NKT cells and DCs among others, may have an in-negligible impact on the results. Moreover, the authors did not analyze cell concentration, but only cell percentage in the results. Cell concentration itself may have major impact to the outcome of liver fibrosis and the authors may have a different conclusion if cell concentration is analyzed. The authors should describe these method limitations in the manuscript.

Response: While we agree with the reviewer that the measurement of CD4 and CD8 without CD3 in the assay may alter our percentages of CD4 and CD8 due to the other cell types mentioned, we did not use the %CD4+ or %CD8+ in our analysis. We looked at subsets of CD4 and CD8 and, because of the known variability in measuring CD4 and CD8 without CD3, presented our data as a percent of the respective CD4 or CD8 subset. We acknowledge that cell counts or concentrations might yield different results and have added the following to our limitation section (page 24, line 290): Our analysis only examined T-cell phenotypes as percentages of CD4 or CD8, where an absolute count, which was unavailable, might yield different conclusions.

2. The authors should include the explanation of log-transformed and back-transformed results in the manuscript.

Response: We have explained log transformed and back-transformed results (page 11, line 194):

For this and other back transformed T-cell subsets, the ratio of means is interpreted as follows: Mean proportion of T-cell subset in the advanced liver fibrosis/cirrhosis group compared to the group without advanced liver fibrosis/cirrhosis.

3. The authors should point out that the race and ethnicity of the subjects in this study, even though they are possibly all Caucasian, for the convenience of the possible future meta-analysis.

Response: We have specified that all participants were Caucasian (page 8, line 178).