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Name of Journal: World Journal of Virology
ESPS manuscript N°: 22968 Manuscript Type: MINIREVIEWS
Title: HCV/HTLV-1/2 co-infection: regional burden and virological outcomes in people who inject drugs.

Response Letter to the Reviewers and Editor's suggestions

Dear Reviewers and Editors,

We thank you for your comments and questions. In order to resubmit the manuscript we have taken into account all the changes you provided to the edited file to update the revised version. **The minireview's title has been modified according to the language review of Filipodia.** Also we have updated the references and citations accordingly and added 2 new references related to figure 1. Please note that under your request all 34 PubMed references have been updated with their corresponding PMID and DOI with exception to citation Hlela et al.,^[11] for which no DOI is available.

With regard to authorship order, in the revised version E Roger is second author and E Castro remains corresponding author. This change is in agreement with authors current load of work in the draft's writing, revising and editing.

We have added also to the revised version figure 1 and table 1.

Finally, the abstract and the core tip have been modified and an audio core tip recorded.

Here are our answers to the reviewers:

Reviewer 00189256

No request was formulated by this reviewer.

Reviewer 02447901

Chef de Service : Professeur Jacques Besson
Chef de Département : Professeur Jacques Gasser

AMT037101

Correspondance autre

Q1: Based on information from methods, terms such as HTLV HCV, HCV and HTLV coinfection were set for literature search. Did all retrieved studies include people who inject drugs as analytic population?

R1: No they did not refer only to people who inject drugs.

Q2: What was the estimated prevalence rate of HCV and HTLV-1/2 coinfection in people who inject drugs and general population?

R2: This is an emerging constellation for which prevalence estimates are unknown.

Q3: Different studies showed contradictory findings about the HCV RNA clearance rate in coinfection subjects. Did coinfection produce additional complicated complications and obstacles for treatment?

R3: Current knowledge supports a higher risk of chronic inflammation and liver cancer outcome in patients with hepatitis C and HTLV-1 coinfection.

Q4: Did the infection timing, carrier status, periods, and infection priority impact documented consequences?

R4: The large scale population study from Iki island shows lower response to IFN treatment and sustained virological response in coinfecting patients vs mono-infected HCV subjects.

Q5: Additional figures and Tables would be better for comprehension.

R5: We have added one figure and one table to the article.

Reviewer 00504271

Q1: p. 14, l. 15-7; What are independent host factors and other study parameters?

R1: Thank you for this remark. In fact it should be "~~independent~~ host genetic factors" for instance as HLA genotypes and other genetic factors known to modulate the immune response. The sentence has been corrected accordingly.

Other study parameters, refers to non comparable study populations and/or study criteria issues concerning the Brazilian and the Japanese datasets. Has been also reframed in the revised manuscript.

Q2: Although the authors listed host factors related with HTLV infection below, it is not clear the relationship between the factors and HCV and HTLV-1/2 coinfection. This paragraph should be written precisely rather than listing of host factor names.

R2: What we try to deliver as message is the worsening of HCV infection in the context of HTLV-1 coinfection and the immune mechanism behind it. In order to reinforce this message, the cited paragraph has been updated in the revised manuscript.

Q3: "Mielopathy" should be "myelopathy." p. 3, l. 6 "Kishihara and col." should be "Kishihara et al." p. 4, l. 1 "Sustained virologica response" should be "sustained virological response." p. 4, l. 2 "Trevino and col." Should be "Trevino et al." p. 5, l. 1 "Et col." should be "et al." p. 6, l. 4 "Inhibiteur" should be "inhibitor." P. 6, l. 1

R3: All changes and corrections have been updated in the revised manuscript version.

Reviewer 00504096

Q1: try to summarize the aim of the study, employed methods, main results and findings and conclusions as well as future prospects in the Abstract (Abstract should contain such a summary).

R1: Abstract has been modified in accordingly.

Q2: The main art of a review article is to provide summarizing tables.

R2: One table and one figure have been added.

Q3: try to give a discussion text besides the itemized conclusions and possibly provide a "Future Prospects" section.

R3: Discussion has been improved and includes also future prospects.

Q4: add the date of the publication to the following reference. Leal F. E., Ndhlovu L. C., Hasenkrug A. M., Bruno F. R., Carvalho K. I., Wynn-Williams H., Neto W. K., Sanabani S. S., Segurado A. C., Nixon D. F., Kallas E. G. Expansion in CD39(+) CD4(+) immunoregulatory t cells and rarity of Th17 cells in HTLV-1 infected patients is associated with neurological complications. PLoS Negl Trop Dis.2013; 7:e2028.

R4: I confirm that publication year is 2013 as already present in the peer-review version. Please let me know if this does not answer your request.

Best regards,



CHUV

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