

15<sup>th</sup> January 2015

Dear Editor,

We are very grateful for the review of our manuscript. Please find attached the revised version of our manuscript in the Word format (file name 15325-edited.docx).

Title: **“Relevance of low viral load in hemodialysed patients with chronic hepatitis C virus infection”**

Authors: Jan Sperl, Sona Frankova, Renata Senkerikova, Magdalena Neroldova, Vaclav Hejda, Miroslava Volfova, Dusan Merta, Ondrej Viklicky, Julius Spicak, Milan Jirsa.

Name of Journal: *World Journal of Gastroenterology*

The detailed point by point responses to the reviewer's comments follow. In the revised version of the draft we took into consideration all comments and inspiring suggestions of the reviewer. The revised text was modified in agreement with the reviewer's comments:

- 1) Rapid viral response (RVR) is a well known strong predictor of SVR in HCV patients with normal kidney function undergoing double therapy with PEG-IFN and RBV. In this study RVR was achieved in 52.6% of ESRD patients and 36.1% of control patients. I was surprised that RVR was not included in the regression analysis concerning the independent predictors of SVR in both ESRD and control patients (Figure 2). I can argue that RVR was not significant at univariate analysis. If so, can the Authors comment this result?**

According to reviewer's comment, we mentioned RVR rates and RVR predictive value in the text and we explained the reasons why RVR was not included in our analysis of predictive factors:

Paragraph *Initial viral load, IL28B and IFNL4 genotypes and treatment efficacy*

*ESRD group:* Among 11 patients with high viremia, only one achieved RVR and subsequently SVR (a CC genotype carrier). Among 28 patients with low viremia, 19 (67.9%) achieved RVR and 18/19 then achieved SVR. Altogether, 19/20 patients who had RVR achieved also SVR (95%).

*Control group:* Among 58 patients with high viremia in the control group, 15 patients achieved RVR (25.9%) and all of them subsequently SVR. Among 51 patients with low viremia, 25 (49%) achieved RVR and 25/25 then achieved SVR. In total, 40/40 patients with RVR achieved SVR as well (100%).

Paragraph *Group-specific variables associated with SVR*

In ESRD patients, RVR proved to be a very strong predictor of SVR (OR 171, 95% CI 26 - 490, P <0.001), which reflects the well known fact that RVR and SVR are interdependent because they reflect the same biological phenomenon, i.e. clearance of the virus.

Paragraph Discussion:

....RVR achievement turned out to be a very strong predictor of SVR, but we did not include it into further statistical analysis of our cohort. Our aim was to validate pretreatment factors which allow selecting patients who have a high chance to achieve SVR. RVR, considered as an on-treatment predictive factor, may help to motivate patients to continue in poorly tolerated treatment, but the fact that the patient does not achieve RVR should not represent the reason to stop therapy.

- 2) Page 8, line 25: ESRD patients had lower and not higher baseline ALT activity compared to controls. Please, correct.**

This transcription error has been corrected accordingly: ...had lower baseline ALT activity,...

- 3) Page 9, line 8: the Authors write that 6 (15%) ESRD patients discontinued treatment because of severe adverse events (SAE); however, when detailing the SAE causing discontinuation, 8 patients are reported. I can suppose that 2 patients had two major SAE. Is it right? Please, explain and correct.**

All together, 6 patients discontinued treatment because of a SAE, thrombocytopenia was mentioned twice by mistake. The text was corrected as follows: Six (15%) ESRD patients discontinued the treatment owing to a SAE: non-functional renal allograft rejection (2 patients), thrombocytopenia with bleeding complications (2 patients), interferon-induced autoimmune hepatitis (1 patient) and pneumonia (1 patient).

- 4) Page 11, lines 6-9. The phrase “ Specifically, eleven individuals...” is a repetition of data reported in the previous paragraphs and in my opinion should be deleted.**

According to reviewer’s suggestion, the phrase has been deleted as redundant.

- 5) Page 11, lines 19-22. The phrase “Calculation of odds ratio (OR) showed...” is redundant considering that is written in the following phrase (Age, male gender and IL28B/IFNL4...). I think that this phrase should be deleted.**

According to reviewer’s suggestion, the phrase has been deleted as redundant.

- 6) Table 2 is difficult to read. I think that the addition of continuous lines separating ESRD from control patients and, within groups, SVR from non SVR patients could improve the legibility of the Table.**

The table has been upgraded according to reviewer’s suggestion to be easy to read. Horizontal lines separating different groups were added.

The format of the manuscript has been improved according to comments of the editors including Ethics approval note, Inform consent note, Data sharing note and Comments.

The reference list has also been upgraded and corrected including the DOI numbers.

A few minor transcription errors were corrected (i.e. ml to mL).

We believe that the revised version of our manuscript will be found suitable for publishing in World Journal of Gastroenterology.

Yours sincerely

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