

Format for ANSWERING REVIEWERS

November 23, 2014



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 14052-review.doc).

Title: Interleukin-28B polymorphisms influence chronic hepatitis C virus genotype 2 treatment outcomes

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The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

Reviewer **02861064**

Thank you for giving comments to our article. We modified it referring to your comments.

(1) IFNL3 (or IFNL4) is the better way to represent the SNP locus that is described.

⇒As the reviewer suggested, *IFNL3* is the better way to represent the SNP locus that is described. We collected all the word "IL28B" to "*IFNL3*".

(2) Page 3, last sentence of abstract should be changed. The association of "IL28B" genotype with SVR in non-RVR patients based on HCV subtype (2a vs 2b) is based on too few patients to make this conclusion, and Figure 3b does not support the suggestion that there is a true difference based on GT2a vs 2b in this regard.

⇒ As the reviewer pointed out, this study scale was too small to make the conclusion that the *IFNL3* genotype was associated with SVR in only HCV subtype G2b patients among non-RVR patients. Therefore, we deleted the sentence "Additionally, in non-RVR patients, the *IL28B* genotype was associated with SVR in only HCV subtype G2b patients", and added the sentence "No significant difference in the SVR rate was found between HCV sub-genotype 2a and 2b" in page 3.

(3) Page 15, sentence starting "Thus, non-RVR patients irrespective of had better discontinue treatment immaturely" is awkward, and provides a clinical suggestion not appropriate for this paper. The decision to terminate therapy already started based on the data in this paper should not be commented upon by the authors.

⇒As the reviewer pointed out, the results of this study could not suggest the decision to terminate therapy. Therefore, the sentence starting "Thus, non-RVR patients irrespective of had better discontinue treatment immaturely" was

deleted, and described the sentences "However, our previous study and the present study revealed that there were no distinct differences in the SVR rates of non-RVR patients who received either 36 or 48 weeks of therapy and that the SVR rate was significantly lower in non-RVR patients (treated with the 36- or 48-week treatment) than in RVR patients (treated with the 24-week treatment). These findings suggested that there are limitations to prolonged treatment duration in non-RVR patients. Specifically, this study highlighted low SVR rates in non-RVR patients with unfavorable *IFNL3* genotypes." in page 15.

Reviewer_02860954

Thank you for giving comments to our article. We modified it referring to your comments.

- (1) **The adherence to both PEG-IFN and RBV is stated to be higher in non-RVR who did not achieve an SVR in Table 2. This needs to be clarified as in the results it is stated that RBV adherence was lower in non-SVR pts.**

⇒ As the reviewer pointed out, we made a mistake in writing the sentence (Page13, in the paragraph : Factors contributing to SVR in non-RVR patients).

Therefore, we collected the sentence to the follows;

"Among on-treatment factors, adherence to RBV was significantly higher in non-SVR patients than in SVR patients ($P = 0.0457$) and adherence to Peg-IFN was numerically higher in non-SVR patients than in SVR patients ($P = 0.0936$), indicating that these adherence factors did not influence SVR."

- (2) **The lack of association between rs8099917 alleles and SVR in non-RVR pts with G2a may be a type 2 error.**

⇒ As suggested by the referee, the lack of association between *IFNL3* SNP genotypes and SVR rates in non-RVR patients with G2a might be a type 2 error. We did not draw definite results and conclusion, because the number of these patients was small. We re-wrote the paragraph (page 13, last para) in the revised Results section.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,



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