

Lian-Sheng Ma

Editor-in-Chief

World Journal of Gastrointestinal Pharmacology and Therapeutics

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Dear Editor;

I, along with my co-authors, would like to ask you to consider our manuscript entitled **“Association of ITPA polymorphism with outcomes of peginterferon- α plus ribavirin combination therapy”** (ESPS Manuscript NO: 2580) for publication in *World Journal of Gastrointestinal Pharmacology and Therapeutics* as an Original Article. All study participants provided informed consent, and the study design was approved by an ethics review board.

We have revised the manuscript according to the comments of reviewers, provided answers to their questions, and included an outline of the revisions made. [See next page: **Answer to the reviewers**]

This manuscript has not been published and is not under consideration for publication elsewhere. All the authors have read the manuscript and have approved this submission. The authors report no conflicts of interest. The manuscript has been carefully reviewed by an experienced medical editor whose first language is English and who is specialized in the editing of papers written by physicians and scientists whose native language is not English.

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We shall look forward to hearing from you at your earliest convenience.

Yours sincerely,

Munehika Enjoji, MD, PhD

Answer to the reviewers

Reviewer 1

1. What is the meaning of full-length treatment ? Should it be full-course treatment regimen? Please identify full-length treatment in the last conclusion paragraph of the text.

[Ans] Full-course means full-length of treatment duration (48 or 72 weeks). The expression is altered. [page 15, line 4]

2. Authors should combine 2 sentences into one and use while not whereas - ‘ The greatest difference in mean hemoglobin reduction was found at week 4. Whereas, platelet reduction was temporally heavier in patients with ITPA CA/AA genotype at weeks 2 and 4 (Fig. 1B).’

[Ans] We have combined the two sentences into one. [page 10, line 6-9]

3. In Tables 2, 3 and 4, please define SVR, RVR, EVR in table footnotes.

[Ans] They are defined in footnotes. [Table 2,3,4]

4. Abbreviation list is missing.

[Ans] Abbreviations are listed. [page 2]

Reviewer 3

1. Much more patients (especially CA/AA genotype) should be included in the study to improve the clinical significance of the presented results, especially to prove (or reject) association between ITPA polymorphism and treatment outcome.

[Ans] We mentioned the problem as a limitation to this study. [page 14, line 11-13]
But a statistician of our hospital has approved this study to be established.

2. Contradictory results concerning association between ITPA polymorphism, hemoglobin decline and outcome of peginterferon- α plus ribavirin combination therapy published so far should be discussed in the Discussion section.

[Ans] Outcomes from some other institutes seem to be inconsistent and contradict our results. The different outcome among the institutes may be due to the difference

of inclusion and/or exclusion criteria. In our study, the relationship between IL28B and ITPA variants were additionally analyzed on treatment outcome. [Discussion, the third paragraph]

3. Why mean concentration of serum AFP in CA/AA was lower than in CC patients (Table 1) and why AFP was not included in Table 4?

[Ans] In CC group, there were a few patients (F4 stage) with AFP >50 ng/mL. AFP was added in Table 4.