

## ANSWERING REVIEWERS

August 29, 2016

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 28114-Revised manuscript.doc).

**Title:** Impact of IL28B and OAS gene family polymorphisms on interferon treatment response in Caucasian children chronically infected with HBV

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**Name of journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 28114

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

### **1 Journal requirements**

Format has been updated.

Our manuscript have been modified in the language professional English language editing company, which was recommend by WJG and could provide the language editing certificate.

### **2 Reviewer's comments**

Reviewer 2860874

1- the definitions of CR (complete response) and PR (partial response) are not clear, seems to be the same definition for CR and for PR.

Answer

In our study, we determined the efficacy of therapy by comparing patients in terms of achieving a defined therapeutic response. We adopted two criteria for the therapeutic response, taking into account achieving HBV DNA level  $< 2,000$  IU/mL and normalization of ALT activity ( $< 40$  IU/L). In order to perform analyses, we compared the patients in terms of achieving partial response and complete response. CR was defined as a suppression of viral replication to HBV DNA level  $< 2,000$  IU/mL and normalization of ALT activity ( $< 40$  IU/L), measured 24 weeks after completing the treatment. PR was defined as HBV DNA level  $< 2,000$  IU/mL or ALT normalization 24 weeks after completing the treatment. Therefore, patients with complete response are required to obtain both established parameters, i.e. HBV DNA level  $< 2,000$  IU/mL and normalization of ALT activity ( $< 40$  IU/L). Patients with partial response must obtain a positive result for at least one of the two parameters. In our study 22 patients (two positive results) achieved the criterion for complete response, and 42 patients (at least one positive result) achieved the criterion for partial response.

Accordingly, a more precise definition of partial response was presented in the manuscript (Page: 9, Line 1-13).

2- I suggest to compare between three groups: PR, CR and non-responders. In their analysis the authors mixed patients and is very confuse, seems that they included non-responders with PR to compare with CR, and then mixed CR with non-responders to compare with PR???? This is very confuse to understand.

Answer

In our study we did not directly compare patients who achieved complete response and partial response (CR vs PR). We compared the patients in terms of achieving defined therapeutic response. One of them was the partial response and the other one was the complete response. The reason behind this form of analysis of the therapeutic response is a limited group of patients. Unfortunately, limited group size is a problem of all studies conducted among pediatric patients. In our retrospective study, we analyzed 52 pediatric patients who met the specific inclusion criteria. The division of this group into three sub-groups, i.e. CR, PR and non-response, consisting of 22, 20 and 10 patients respectively, makes any statistical inference very limited. We realize that if we defined the PR patients as only those who have obtained a half-therapeutic success (without CR), our analyses would not be appropriate. However,

according to our criterion of dividing the patients in terms of PR, in the group of patients who achieved PR criteria – which means at least one positive result - are the patients whom we can define as patients with CR (two positive results). On the other hand, we can define patients who achieved PR as non-responders according to the definition adopted by the Reviewer. To facilitate the understanding of our division groups we presented a more accurate definition of partial response (see question 1). Moreover, we believe that dividing patients into those who achieved CR and those who have not achieved CR, is a more clinically useful criterion in comparison to the division of CR vs NR, because the most important question for a clinician is the chance to obtain a complete response. In this regard, patients with partial response represent also the failure of therapy. On the other hand, the division in relation to the PR criterion allows us to evaluate the chances of the lack of therapeutic response, and to select from the whole group a subgroup of patients with the least chance of success of any therapeutic treatment with interferon.

3- in the statistical analysis the authors made only univariate analysis for each variable, I suggest to make a multivariate analysis including all significant variables in the univariate analysis.

Answer

According to suggestions, factors that were significantly associated with response rates by the univariate analysis were then analyzed by logistic regression analysis.

In the results section, appropriate sentences were added (Page: 9, Line 29-31, Page: 11, Line 10-14 and Page: 12, Line 10-13).

We hope that will find the revised manuscript to be suitable for publication in World Journal of Gastroenterology.

Sincerely yours,

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