

To The Editor, World Journal of Gastroenterology

Response to Reviewers' comments

We thank the reviewers for their comments and below provide our responses. Where necessary, changes have been made to the manuscript according to the remarks of the technical editor.

### **Reviewer 1**

In this manuscript, the authors aimed to evaluate the efficacy and safety of additional boceprevir (BOC) to peginterferon/ribavirin (PR) in Russian patients with chronic hepatitis C virus (HCV). Treatment-naïve (TN) and treatment-experienced (TE) patients with chronic HCV genotype 1 infection were enrolled in this placebo-controlled, double-blind study. They found that the sustained virologic response (SVR) was 74.8% in the BOC plus PR arm compared with 46.2% in the control arm with a stratification-adjusted treatment difference of 29.2%, that the SVR rates were higher in the BOC arm in both TN and TE patients, and that anemia was increased in patients receiving BOC plus PR. This study was well designed and conducted. The authors obtained reasonable results. In addition, the manuscript was well prepared. Although the originality is not high, this article may provide useful information to the clinicians in managing patients with chronic HCV infection.

*Authors' response:* Thank you for your comments.

### **Reviewer 2**

These results are very promising for Chinese patients...Good work..

*Authors' response:* Thank you for your comment.

### **Reviewer 3**

#### **GENERAL COMMENTS**

1. The study by Isakov and co-workers, that evaluated boceprevir-based triple therapy in patients with genotype 1 HCV infection, is characterized by a good overall quality. The overall result is remarkable because the success rate (overall result: 74.8% in the boceprevir plus PR arm compared with 46.2% in the control arm; results for the two patient subgroups: 78.4% vs 56.3% and 69.4% vs 30.0% in treatment-naïve and treatment-experienced groups, respectively.) was higher than the values generally reported in the literature for the same regimen. On the basis of this trial, boceprevir has received regulatory approval in Russia.

*Authors' response:* Thank you for your comment.

2. In the Introduction, the authors describe the following regulatory scenario in Russia: "In Western countries, treatment of HCV infection has advanced dramatically over the last 5 years with the introduction of new targeted therapies that substantially shorten treatment duration and improve SVR rates[5,6]. However, in resource-constrained countries, standard treatment protocols are lacking, and PR dual therapy frequently remains the cornerstone of treatment[7,8]. " This sentence is adequate for the Introduction, but –in my view- this important point should be revisited and considerably expanded in the Discussion.(see below)

*Authors' response:* Thank you for your comment. Please see response to comment 3. Additional text regarding access to treatment in resource constrained countries has been added to the discussion on page 17.

3. In the Discussion, the issue of the current regulatory scenario in Russia is not dealt with. This is an important limitation of the present study for the following reasons: a) interferon-free regimens are now considered the current standard of care for these patients because of their undisputed effectiveness (close to 100% of success rates); in this context, the reasons why Russian patients can be treated with boceprevir-based triple therapy rather with the more recent regimens should be explained in much detail.

*Authors' response:* We have added the following statement into the discussion section on page 17: "Despite the world-wide acceptance of interferon-free regimens as a standard of care due to the near 100% efficacy and low adverse events rate, some patients will continue to receive interferon-based treatment. This is due largely to the fact that the approval of interferon-free regimens is not immediately followed by total reimbursement in many countries, or that access to these regimens is dependent on the stage of the liver disease, prioritizing treatment of cirrhotic patients. Easy-to-treat patients can be successfully treated with interferon-based regimens which may be easier to access through reimbursement.."

4. For example, the authors could provide the following information: current regulatory status of interferon-free regimens in Russia; expectations on when (and if) interferon-free regimens will receive regulatory approval in Russia; current cost of boceprevir and sofosbuvir expressed in the local currency and also converted into Euro and US dollars; general information on whether regulatory approval for any new drug implies, in Russia, a consequent reimbursement by the national health system; information on whether the treatments for HCV are already being reimbursed by the national health system or, alternatively, who is expected to pay for these treatments.

*Authors' response:* We added some info into discussion (see above), but due to quite rapid changes at pharmaceutical and financial markets in Russia we think that it will not be useful to provide any additional info about the cost and cost-efficacy calculations as by the time of publication of the paper it will not be actual.

SPEICIFC COMMENTS Table S1 is interesting and could be moved from the Supplementary Material into the main text (at least as regards the information concerning the SVR rate).

*Authors' response:* We agreed with the remark of the reviewer and add Table S1 to the manuscript as the table 5

On behalf of the authors

Prof. Vasily Isakov, MD, PhD