

Editorial board of *World Journal of Hepatology*,

We are grateful to reviewers because of their valuable comments on our manuscript (ID: 40193) entitled "**Hepatitis C resistance to NS5A inhibitors: Is it going to be a problem?**". We revised the manuscript according to their comments and hope meets with their approval. Here, you can find our response to reviewers' comments.

Our response to reviewers' comments:

Reviewer: 02942798

- Dear sir, thank you to select me to review an editorial Sharafi H, Alavian MS. Hepatitis C resistance to NS5A inhibitors; is it going to be a problem? Editorial is well written and it could be published unaltered.

**Thank you.**

Reviewer: 02860897

- This editorial state an intriguing comment on recent treatment of chronic hepatitis C based on NS5A inhibitor. In particular, comments on the detection of RAS of NS 5A are quite reasonable. As author mentioned in this report, these tests detecting RAS of NS5A will be destined to fade out.

Thank you.

Reviewer: 00069423

- Authors made an excellent summary of the status of the new problems with HCV resistance to NS5A inhibitors which are included in the majority of the DAAs currently used for HCV treatment. The new knowledge of this resistance appearing after the DAA therapy and the availability of testing for the NS5A RAS would certainly assist the treating physicians in their better management.

Thank you.

Reviewer: 02521807

- The Editorial from Heidar Sharafi and Seyed Moayed Alavian is clear and exposed the author's point of view about a critical topic on hepatitis C infection management specially focussed on NS5A inhibitors and the relevance of their RAMs detection at pre-therapy setting. This reviewer consider that there are two points that need to be more explicative and detailed. These are: 1. On page 5 the authors mention that "The main finding regarding the prevalence of RASs in NS5A inhibitor-naïve patients with HCV genotype-1 (HCV-1) is the higher prevalence of NS5A RASs in patients with HCV-1b than those with HCV-1a". Taking into account the small number of patients analysed, it would be useful for

a stronger support, to specify the number of patients as well as to include a statistical analysis.

Thank you. The data has been added.

- 2. On page the sentence "Considering the costly and time-consuming process of NS5A RASs testing, we don't recommend NS5A RAS testing in NS5A inhibitor-naïve patients prior to treatment with NS5A inhibitor-containing regimens." (page 7) This aseveration may result conflicting considering the cost of the DAA therapy in comparison with Sanger method to detect RAMs. Could the authors offer an estimation of cost that may sustain such aseveration? There are only minor typing errors troughpout the whole text.

The price for HCV resistance testing is variable by the services, the provider and location in the range of 100-500 \$. The cost for testing of every patient figures to be small however, taking into account testing the whole population of patients with HCV to find the patients with RAS>100X (<5% of the population) results in a costly strategy for optimization of HCV antiviral therapy. The data has been added.

Yours Sincerely,

**Dr. Heidar Sharafi, Ph.D.**

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