

Response letter Manuscript NO 39055.

We thank the editor and the reviewers for carefully reading our manuscript and for their helpful comments.

Response to editor

We adjusted our manuscript according to the editor's suggestions. All changes are highlighted in the text.

Response to the reviewers

Reviewer 1

Comments: 1. To my knowledge, asunaprevir was not approved by European Medicines Agency (EMA), so it is interesting to hear from the authors why they choose DCV and ASV instead of other DAAs for study since their transplant patients have no chance to access DCV plus ASV regimen in Northern Europe countries. 2. Delete the last word 'by' in the final sentence, 2nd paragraph of Results, Daclatasvir and asunaprevir show a combined antiviral effect with MPA. 3. Give full terms for IRF1, IRF9 etc. for their first appearance in the text and clarify 'IFTIM3' or 'IFITM3' in 3rd paragraph of Results, Daclatasvir and asunaprevir show a combined antiviral effect with MPA.

Reply:

Comment 1: Daclatasvir was approved by the EMA in 2014 and by the FDA in 2015 for treatment of HCV infected individuals. The combination of daclatasvir and asunaprevir is currently approved for treatment of HCV patients in Japan, Korea and China. In these countries 1,3%, 1,5% and 0,8% of the respective populations is infected with HCV, affecting the lives of millions of people. Therefore our results can be relevant for many patients.

Comment 2: We deleted the word 'by' from the text.

Comment 3: We included the full terms for IRF1, IRF9 etc., and corrected the spelling of IFITM3.

Reviewer 2

This study investigated, whether tacrolimus, rapamycin, cyclosporine and MMF affect the antiviral action of DCV or ASV. This question is new and was not investigated before, when searching via pubmed. In two in vitro models for HCV infection the Group investigated the effect of These immunosuppressants. The results encourage to use MMF in combination with the antiviral drugs and emphasize the confirmation of the results in the clinical Setting.

Reply:

Thank you for your comment and your suggestions for further research.

Reviewer 3

The aim of this study were to evaluate the specific effects of immunosuppressants on the antiviral action of DCV and ASV. The antiviral activity of DCV and ASV combined with immunosuppressants was tested using two in vitro models for HCV infection. It is a very well designed study, with a shortage of publications on the subject, therefore, it is a important article, however, some points should be highlighted: - A review in writing must be performed, minor errors in concordance; - In Methods: more details of the statistical analysis are necessary

Reply:

We corrected errors in the text.

We added more information about the statistical analysis.

Reviewer 4

This was a straight-forward study which addresses an important question for transplant physicians treating recurrent hepatitis C. However, I was intrigued why asunaprevir and daclatasvir were chosen as these medications are not the first line choice for treating recurrent HCV in most transplant programs. A brief explanation on this issue would be helpful for readers. As this study was simplistic in design, there were no concerns with study design or statistical analysis. There were very few grammatical errors (such as uncompetitive instead of non-competitive when describing MPA, Because at the beginning of a sentence) but these minor concerns are not significant and may acceptable by other English speakers.

Reply:

The combination of daclatasvir and asunaprevir has been approved for the treatment of HCV in Japan, Korea and China, reaching a large population of infected individuals. In these countries 1,3%, 1,5% and 0,8% of the respective populations is infected with HCV, affecting the lives of millions of people. Therefore our results can be relevant for many patients. We emphasized this now in the introduction.

We corrected the grammatical errors.