

## **ANSWERING REVIEWERS**

**Reviewer's code: 02529007 "...The manuscript topic and contents is matched with the submitted journal. The manuscript is well-written, aim of study, methods, results and discussion sections are clear and the message is properly expressed. I suggest acceptance of the manuscript"**

We would like to thank the reviewer for these kind comments about our manuscript. Our commitment as investigators is to answer unsolved scientific questions and it's nice to see that we are able to send a clear message that receives positive feedback.

**Reviewer's code: 02936306 "The study results are interesting. It seems that the number of cases and the observation period are not sufficient to prove the role of all the parameters. However, considering the difficulty of collecting the LC-HCV patients requiring beta blocker in single center, data might contribute to the development of this field of hepatologic research, an evidence-based approach regarding the withdrawal of beta blocker after the DAA treatment. I have also experienced few LC-HCV cases who had recurrent variceal bleeding but did not any more after the DAA treatment"**

We acknowledge the limitations of our study regarding the number of patients included and we thank the reviewer for pointing this issue. Our study included patients from Madrid's sanitary area number 5, which has a total of 530000 people, and from them we only selected HCV cirrhotic patients who achieved SVR and were also on betablockers as profilaxis of variceal bleeding. It's because of this, that the number of patients that meets these inclusion criteria is only 33. Nevertheless, it would be interesting to perform a multicenter study that increases sample size.

We would also like to address the comment about the observation period. HVPG was measured 67 weeks (56-83) after the end of DAA treatment, what we could consider enough time to observe haemodynamic changes after HCV

elimination. Most of the published studies evaluate haemodynamic changes earlier than us, after achieved SVR (12-24 weeks after the end of DAA). However it seems that the regression of portal hypertension after SVR is a dynamic process and we still don't know when is the correct moment to measure these changes.

Patients with a HVPG < 12mmHG after HCV elimination in which betablockers were stopped were followed during a period of 17 months. We agree with the reviewer that they would probably benefit from a longer observation period, that's why we are currently performing a 3 year follow-up of these patients.

**Reviewer's code: 03210617 ".... Some of the observations in this manuscript are interesting. However, several points require further attention: 1. The number of patients included in the study was small, making the results less convincing. 2. Why was hepatic venous pressure gradient measured five days instead of seven or ten days after stopping betablockers"**

We thank this reviewer for also addressing the total number of patients included in the study. Reasons behind the lack of patients included in our study are due to the specific inclusion criteria: HCV cirrhotic patients betablocked as profilaxis of variceal bleeding who achieved SVR and because it is a unicentric study. For these reasons the total number of patients included was 33.

Regarding betablocker withdrawal: "At least 5 days are needed for Propranolol clearance after chronic oral dosing" (Evans GH. Clinical Pharmacology and Therapeutics 1973; 14: 487-93.). The longer propranolol interruption, the greater the risk of variceal bleeding [Abraczinskas, D. R. et al. Propranolol for the prevention of first esophageal variceal hemorrhage: A lifetime commitment? Hepatology 34, 1096-1102 (2001)]. This 5-day period has been safely used by other authors in haemodynamic studies with no influence of residual Propranolol in measurements. [Mandorfer, M. et al. Sustained virologic

response to interferon-free therapies ameliorates HCV-induced portal hypertension. *Journal of Hepatology* 65, 692–699 (2016).]