

We would like to thank the editors and reviewers for their valuable time and patience in reviewing this manuscript and providing their comments. We have taken into consideration all of their comments. We feel that these were very constructive and have improved the quality of the manuscript.

RESPONSE TO REVIEWERS

Reviewer 1

Please unify the scientific notation behind decimal points regarding OR, P value.

Response: We thank the reviewer for the comment. We have confirmed that all ORs and the *Ps* were presented consistently in their numeric values as generated by the statistical model.

Please provide plausible explanation(s) of the key finding (biological or non-biological) for "lack of SVR12 as a predictor of post-transplant HCC recurrence"

Response: We thank the reviewer for the comment; our study showed that patients with HCV and HCC experiencing relapse following DAA therapy had recurrence of HCC after liver transplant. Published data emphasized on the importance of serum cytokines and liver angiopoietin-2 as key players of HCC development after DAA therapy^{1,2} It is possible that the liver allografts in these patients have alteration in signaling pathways that affect the uptake and efficacy of DAA therapy, and also promoting proliferation of HCC. We briefly highlighted this point within the text; page 12 "cross-talk among inflammatory, immune response, and angiogenesis pathways modulates the impact of DAAs on progression of HCC and the risk of its recurrence".

Reviewer 2

Major revisions: Patients with HBV infection should be eliminated because hepatocellular carcinoma is strictly correlated to HBV infection and replication.

Response: We agree with the reviewer comment. We would like to clarify that the study excluded patients with HBV infection. We only included patients with anti-HBc-positive indicating their past HBV exposure or received HBcAb positive allograft. However, no of these patients were positive for HBsAg and/or HBV DNA. We added this in the exclusion criteria in the "patients and methods" section within the text.

Minor revisions 1. Chronic exposure to aflatoxin is highly associated with HCC due to damaging the DNA of hepatic cells and causing mutation of the p53 tumor suppressor gene.

Response: We agree with the reviewer regarding the importance of aflatoxin in HCC. In this study, all participants are USA residents and aflatoxin is uncommon in the United States.³ The United States Department of Agriculture requires mandatory aflatoxin testing for domestic and imported shipments of products that are susceptible for aflatoxin contamination as corn, almonds, peanuts and pistachios.

2. *There is increased risk of developing HCC in several rare inherited disorders: glycogen storage disease, alpha-1-antitrypsin deficiency, metal storage disease.*

Response: Patients listed for transplant undergo extensive investigations to rule out other causes (including metabolic, genetic and viral causes) of cirrhosis and HCC. None of our patients tested positive for any cause of HCC or cirrhosis except HCV. We added this in the exclusion criteria in the “patients and methods” section within the text.

3. *Were all patients HIV negative? Please specify*

Response: We thank the reviewer for the comment; yes, all patients were HIV negative. We added this in the exclusion criteria in the “patients and methods” section within the text.

References:

1. Debes JD, van Tilborg M, Groothuisink ZMA, et al. Levels of Cytokines in Serum Associate With Development of Hepatocellular Carcinoma in Patients With HCV Infection Treated With Direct-Acting Antivirals. *Gastroenterology*. 2018;154(3):515-517.e3. doi:10.1053/j.gastro.2017.10.035
2. Faillaci F, Marzi L, Critelli R, et al. Liver Angiopoietin-2 Is a Key Predictor of De Novo or Recurrent Hepatocellular Cancer After Hepatitis C Virus Direct-Acting Antivirals. *Hepatology*. 2018;68(3):1010-1024. doi:10.1002/hep.29911
3. Mitchell NJ, Bowers E, Hurburgh C, Wu F. Potential economic losses to the US corn industry from aflatoxin contamination. *Food Addit Contam - Part A Chem Anal Control Expo Risk Assess*. 2016;33(3):540-550. doi:10.1080/19440049.2016.1138545