

Format for ANSWERING REVIEWERS

January 26, 2015



Dear Editor,

Please find enclosed the edited manuscript in Word format (File name: 15479-review.docx)

Title: **Hepatitis C cirrhosis: New perspectives for diagnosis and treatment**

Authors: Vikas Khullar M.D., Roberto J. Firpi M.D., M.S.

Name of Journal: World Journal of Hepatology

ESPS Manuscript No: 15479

The manuscript has been improved according to the suggestions of the reviewers:

- 1) Format has been fixed. References updated with requested format.
- 2) Conflict of interest statement has been added.
- 3) The following changes have been done to address reviewer comments:

REVIEWER #1

Khullar et al described the new antiviral treatment for HCV infected patients with liver cirrhosis. The authors explained the new Major revisions 1)The tables of simeprevir and ledipasvir are needed for readers to easily understand the efficacy of the new drugs. 2)Why was not VALENCE trail added to Table 5? Minor revisions 1)The figure of 350,000 to 500,000 deaths is per year in the introduction? 2)What is chronically infected patients in the introduction section? HCV? 3)The figure of 3,200 referrals is per year in the epidemiology section? 4)The authors should spell out HIV in the chronic HCV infection section. 5)The authors should spell out peg in the new perspective on treatment section.

Response by Authors:

- 1) Added tables for Ledipasvir and Cosmos trial for sofosbuvir and simeprevir.
- 2) VALENCE trial has been added to revised Table 5
- 3) Fixed “350,000-500,000 deaths per year”
- 4) Explained chronic infection as >6 months in Introduction section.
- 5) HCV = Hepatitis C (added in introduction)
- 6) Reference provided for referral number of 3,200 referral and added “per year”.
- 7) Spelled out HIV in diagnosis and epidemiology section
- 8) Spelled out Peg IFN.

Thank you for your review.

REVIEWER #2

Sofosbuvir showed a rate of response lower in genotype 1b vs 1a (NEUTRINO trial): this point

needs to be reported and discussed In COSMOS trial the role of ribavirin has to be discussed: probably it is not necessary to improve rate of response in association to sofosbuvir +simeprevir... A short description about the mechanism of action of ledispavir is lacking. Patients listed for OLT, treated with sofosbuvir+ribavirin who remain at least one month HCV RNA negative before LT remain HCV RNA negative also post LT: this represents a strong indication to treat patients listed for OLT, even if decompensated. These data should be reported and discussed. The treatment of patients with CTP C cirrhosis remains a controversial topic: it should be cited and discussed.

Response by Authors:

- 1) Added response rates between Genotype 1a and 1b. See NEUTRINO trial section.
- 2) Added table to show different between 2 cohorts to show efficacy of with and without ribavirin. Added sentence in COSMOS trial section.
- 3) Added short mechanism of action of ledispavir.
- 4) Included role of sofosbuvir and ribavirin for treatment of patients pending OLT as per Gastroenterology 2015 paper by Curry et al.
- 5) Addressed treatment advantage and current treatment in patients with decompensated cirrhosis under “Advantages of treatment in HCV cirrhosis patients”.

Thank you for your review.

REVIEWER #3

This manuscript summarized the results of recently completed clinical trials using new drugs in the treatment of patients with HCV-related cirrhosis. Such a review is relevant to the scope of WJH and would provide new information to physicians who are involved in the management of HCV patients. Yet, the current status of this manuscript needs to be refined. 1. Language needs to be revised so as to make this review more concise. 2. Abuse of “patients” was present many times in the text.

Response by Authors:

- 1) Refined language as per request.
- 2) Added additional concise tables for treatment for Sofosbuvir, Simeprevir and Ledipasvir. See tables.

Thank you for your review.

REVIEWER #4

This review is well written, though considering the title not much was done in the area of diagnosis . The authors should update on this

Response by Authors:

- 1) Added additional paragraph in diagnosis section on diagnosis.

Thank you for your review.

Thank you again for publishing our manuscript in the *World Journal of Hepatology*.

Sincerely yours,

Vikas Khullar M.D.