Format for ANSWERING REVIEWERS

May 21, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 17597-edited.doc).

Title: ""Interferon-free regimens for the treatment of hepatitis C virus in liver transplant candidates or recipients"

Authors: Evangelos Cholongitas, Chrysoula Pipili, George Papatheodoridis

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 17597

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

1 Format has been updated. We have performed the appropriate changes after checking our revised manuscript before resubmission using the *CrossCheck* program.

2 Revision has been made according to the suggestions of the reviewers:

a) A well written manuscript which summarizes the litterature for this very interesting subject concerning interferon-free regimens for the treatment of hepatitis C virus in liver transplant candidates or recipients. Thank you for your comments.

b) Interferon-free regimens for the treatment of hepatitis C virus in liver transplant candidates or recipients. Comments to authors: This review gives a summary of the data from clinical trial on DAAs combinaisons for the management of liver transplant candidates and recipients. Although more clinical trials will be required to identify the best suitable treatment for these difficult to treat patients, this review give a clear update on the present situation in this rapidly evolving field. I support its publication in WJG. Thank you for your comments.

Minor comments: -The authors should describe in more detail what is the Child-Pugh score classification (Child Class A, B and C). A=5-6, B… We have added this information in the text (page 6).

-Others recent reviews addressing the same subject are not cited (Ex. Dall'Agata et al., WJG 2014). We have added this excellent review in the Refs of our paper (REF 41).

-Page 9 : No dose adjustment dose of sufosbuvir … We have corrected this typo error (now page 8)

-Table 2: There is no mention of SVR in the table even though SVR is in the legend. We have deleted the abbreviation SVR.

c) Major points: 1. Concerning the triple combination of pegIFN, RBV and boceprevir or telaprevir, the authors should cite another reference where better SVR was observed in naive patients, relapsers and null responders. Example; Kumada H, Suzuki Y, Ikeda K, Toyota J, Karino Y, et al. Daclatasvir plus asunaprevir for chronic HCV genotype 1b infection. Hepatology. 2014 Jun; 59(6): 2083-91. Although the reviewer did not mention which Ref would like to be replaced, we have changed Ref 11 with this paper regarding the efficacy of daclatasvir in CHC patients (page 5).

2. The authors should describe regarding SVR rates of the triple combination of pegIFN, RBV and simeprevir. Example; Hayashi N, Seto C, Kato M, Komada Y, Goto S. Once-daily simeprevir (TMC435) with peginterferon/ribavirin for treatment-na?ve hepatitis C genotype 1-infected patients in Japan: the DRAGON study. J Gastroenterol. 2014 Jan; 49(1): 138-47. Similarly, we have changed Ref 10 with this excellent paper adding information regarding the effectiveness of simeprevir (page 5).

3. Regarding the reference [16], the author should describe the genotype of LT candidate in the first open label phase study. Similarly, the authors should describe the genotype of patients treated with DAAs, cited from the other references, no.25, 29, 39, 40. We have added this information in the text. Thank you.

4. Simeprevir is a low genetic barrier drug, although the authors described “Safe regimens with high potency and high genetic barrier should be preferred to achieve rapid inhibition of HCV replication and eliminate the selection risk of resistant-associated viral strains”. How do the authors think about genetic barrier of simeprevir. We agree with the reviewer that simeprevir is a low genetic barrier agent, but this is the case if it was going to be used as monotherapy which is definitely not recommended. The same is true for daclatasvir, ledipasvir, paritaprevir/ombitasvir and dasabuvir if they were going to be given as monotherapies. In combination with sofosbuvir, however, the combined regimen is of high genetic barrier when it is used in G1 or G4 patients who have not failed to a protease inhibitor containing regimen. We have now made clearer that we meant the combined regimens in our statement.

Miner points: 1. Page 15, Reference 6, you mistook the publication year of the journal "Journal of Viral Hepatitis", 200 → 2004. We have corrected this typo error.

Thank you very much for publishing our manuscript in the World Journal of Gastroenterology.

Sincerely yours,

Evangelos Cholongitas