

To:

Editorial Board of World Journal of Hepatology

RE: Manuscript ID: 21590

Update on Hepatitis C: Direct-acting Antivirals

We would like to express our appreciation to the reviewers and editor for spending time and effort to improve our manuscript. Your suggestions were valuable to help us strengthen our work.

Reviewer(s)' Comments to Author:

Reviewer 1

Seifert et al. reviewed the recent situation of the treatments for chronic hepatitis C. 1. In page 4, line 6 Please make corrections from 9600 kb RNA to 9.6 kb. 2. In page 4, IFN (interferon)-based, RBV (ribavirin), SVR (sustained virologic response) to interferon (IFN), ribavirin (RBV), sustained virologic response (SVR) "treatment of hepatitis c seems": hepatitis C 3. In page 5, line 12, Please make corrections from 9600 kb RNA to 9.6 kb. 4. How was core protein in structural protein?? 5. In page 7, line 11,body weight (≥ 75 kg: 1200 mg/d; < 75 kg: 1000 mg/d).?? 6. In page 11, "These excellent results from clinical trials have recently been approved by several real-life experience studies, such as the TRIO network or the HCV-TARGET consortium. Several other institutions have contributed their experience from real-life treatment of HCV-patients with DAAs in small analysis presented at the conferences of the AASLD or the EASL. The rates of SVR may be inferior to those of the presented phase III clinical trials but still very satisfactory regarding the aggravated circumstances in a real-life setting, notably concerning patient compliance." Authors should add the proper references.

RESPONSE:

1. We appreciate the reviewer's correction of the RNA length. The corresponding sentence now reads: "This single-stranded, positive-sense 9.6 kb RNA-virus is globally prevalent,

showing geographic variation in its genotypic distribution and represents a major cause of end-stage liver disease^[3,4]"

2. We have made sure that hepatitis C is appropriately and consistently capitalized throughout the text.
3. The corresponding sentence now reads: "Its RNA is single-stranded and positive-sensed with a size of approximately 9.6 kb."
4. The "Molecular Structures" section of the manuscript now reads: "The HCV-genome encodes for 9 proteins – 2 are structural (E1 and E2) and 7 non-structural (p7, NS2, NS3, NS4A, NS4B, NS5A, NS5B).^[10,11,13,14]"
5. We corrected the body weight for ribavirin dosing <75 kg to 1000 mg/d.
6. We added references for clinical trials demonstrating real-life experience with direct-acting antivirals.
- 7.

Reviewer 2

The authors provide an extensive review of the current state of treatment for chronic HCV hepatitis. In addition they address the issue of screening and the development of a vaccine in order to both identify undiagnosed cases and also to prevent new cases. There are a few grammatical errors that need addressing. The review of the data is comprehensive- since it was submitted the FDA has approved the use of Daklinza for type 3 HCV and this could be included for the benefit of the US readers. I think a comment regarding drug interactions would be appropriate. Many of the baby boomers have co morbidities and may take medications for this. In addition there is a connection between HCV and diabetes that also results in medication. I have no further substantial comments to make.

RESPONSE:

We appreciate the reviewer's comments. We have performed an English review of the manuscript with correction of grammatical errors.

Reviewer 3

Seifert LL et al have presented an extraordinary state-of-the-art review regarding the new era of direct-acting antivirals for HCV therapy. The authors have concisely written the effect that these new drugs have shown on SVR by genotype compared to peg-INF or RBV and the need for further studies on vaccines to finally combat HVC infection worldwide. It is a very nice integrated paper. I highly recommend publication with a few minor comments: A) The abstract does not reflect the content of the whole work, it falls short compared to the main text. The aim "The analysis of the contribution of the new DAAs to this radical change in the natural history of

hepatitis C and a possible future eradication of the virus" should be placed. I suggest that each section of the paper should be summarized in the abstract. B) May the authors elaborate if possible about the side effects of DDA schemes compared to other antivirals. C) I suggest a diagram or Table to synthesize the therapeutical options given for each genotype. D) Check misspellings on page 4, the hepatitis c; on page 11, grad. Good work and congratulations!

RESPONSE: We have edited the abstract to more closely reflect the content of the whole work. We agree with the reviewer that it is important to include a summary table for the treatment recommendations for different genotypes of HCV. We have added two tables to the manuscript.

Reviewer 4

This is an update review on the treatment of the patients with chronic C hepatitis. Of course, the extensive review can be beneficial to the reader more information on the treatment at the American and European clinics. Two comments to be concerned here: 1. It should be needed to draw a summary table for the different genotypes of hepatitis C virus and its possible response DAA. 2. The writing style of the references needs to follow the author guideline of WJH. In my opinion, it should be accepted for publication after an adequate revision.

RESPONSE: 1. We agree with the reviewer that it is important to include a summary table for the treatment recommendations for different genotypes of HCV. We have added two tables to the manuscript. 2. In addition, we have formatted the references to comply with the World Journal of Hepatology guidelines.

Once again, we appreciate the time that the reviewer and the editor have spent in bringing these points to our attention. We believe that the manuscript is now much improved, and we hope that the response has been adequate. We again appreciate your consideration for publishing this manuscript in *World Journal of Hepatology*.

Sincerely,

Aijaz Ahmed, MD