November 5, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 5988-review.doc).

Title: Antiviral treatment of HCV Infection and Factors Affecting its Efficacy.

Author: Yan Zhu, Song Chen

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 5988

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

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

(1) It is an interesting study which focuses on investigating the optimal combination of antiviral therapy to achieve higher efficacy and better medication compliance. This study valuates the efficacy of HCV antiviral therapy but ignores the effects of supplementation therapy such as carnitine, acetyl L carnitine, probiotics, sinbiotics, eritropoyetina. I suggest to create a new paragraph about this theme.

Response: Thanks for the suggestion. A new paragraph about the effects of HCV supplementation therapy was created in Page 15, paragraph 2-3.

(2) Key-words must be “indexed” at MESH

Response: All of the Key-words can be “indexed” at MESH.

(3) ABSTRAC “DAAs in combination with PegIFN-α and RBV therapy is more potent, specific with shorter duration” Therapy duration has not been shortened with the addition of DAAs.

Response: The recommended duration of telaprevir and boceprevir are 48w. Some randomized clinical trials showed that the telaprevir triple therapy for 24 weeks yielded a higher SVR rate than the SOC in naïve HCV genotype 1 patients who achieved RVR. And several other DAAs combination with PegIFN-α and RBV therapy can shorten the duration to 12w in clinic trails. However these views need to be further confirmed. we deleted “shorter duration” and revised ABSTRAC in Page 2, line 11-14.

(4) “The DAAs combinations with IFN-free therapy also showed satisfactory results in clinical studies and appears to be the optimal regimen” This consideration refers to future treatment possibilities. No DAA has been approved for IFN-free therapy yet.

Response: We changed “The DAAs combinations with IFN-free therapy also showed satisfactory results in clinical studies and appears to be the optimal regimen” to “Several DAAs currently in late-stage clinical trials, both with and without peg-IFN and RBV, have several advantages over the previous SOC, including higher specificity and efficacy, fewer side effects, and the ability to be administered orally, and might be optimal regimens in the future” in Page 2, line 11-14.

(5) 1.1.1 Peg-IFN? - last paragraph Please revise the sentence “but lower incidence of skin rash associated with PegIFN-α-2b compared with PegIFN-α-2b[5].”

Response: On Page 5, paragraph 2, line 6，“PegIFN-α-2b” should be “PegIFN-α-2a”

(6) 1.1.3 PegIFN-λ-1a It should be stated which drugs have been studied for each genotype. E.g., PegIFN-λ-1a refers to genotype 2 and 3.

Response: PegIFN-λ-1a plus RBV have been studied in treatment of naive patients with HCV genotypes 2 or 3 compared to the SOC. It was revised in Page 6, line 3-7.

(7) 1.2.1.1 Telaprevir It would be nice to specify that IP treatment is interferon based regimen and that treatment duration is still of 48w. The disadvantage of the need of greasy food intake together with the medication should be mentioned, as it may cause incredible weight increase during treatment. It would be very interesting if clinical applicability and rates of SVR for each treatment for each genotype were mentioned.

Response: The duration, intake together with the need of greasy food were mentioned in

Page 6, Paragraph 3, line 2 and Page 7, line 1.

Telaprevir is not a pan-genotypes medicine and is recommended for the HCV genotype 1 patients.

(8) 1.2.1.6 ABT-450 “in an open”

Response: It is a phase IIa, open-label study.

(9) The title may be rephrased as follows: “Treatment of HCV infection and Factors Affecting its Efficacy

Response: Thanks for the suggestion. The title was rephrased as “Antiviral treatment of HCV infection and Factors Affecting Efficacy”

(10) Abstract –line 2 omit “ and even death.”

Response: On line 2 of Abstract, “ and even death”was omitted.

(11) BACKGROUND Fails to mention extrahepatic complications of HCV infection including metabolic (Bugianesi E, J Hepatol. 2012;56 Suppl 1:S56-65), haematological (Peveling-Oberhag J, J Hepatol. 2013;59:169-77), vascular (Lonardo A. Hot Topics Viral Hep 2012;8:27-35). and rheumatological disease (Buskila D. Rheum Dis Clin North Am. 2009;35:111-23).

Response: We added the above-mentioned content in the BACKGROUND portion of our revised manuscript, according to reviewer’s suggestion (see page 3, line 3-5).

(12) 1.Factors Affecting the Efficacy of HCV Antiviral Therapy - “The main factors influencing the efficacy of HCV antiviral treatments are divided into two categories: viral and host.” ----> rephrase “Host-related”.

Response: “host” was revised to “Host-related” in Page 16, paragraph 2, line 2.

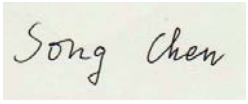
(13) 2.2.2Other Adverse Predictive Factors---> Provide bibliographic references. Expand the role of steatosis. (Adinolfi LE Expert Opin. Pharmacother. 2011;1214:1-19). This submission might benefit from adding some tables and one figure.

Response: Bibliographic references were provided in our revised manuscript. The role of hepatic steatosis was expanded in our revised manuscript, according to reviewer’s suggestion (see page 21, paragraph 1).

3 References and typesetting were corrected

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

Sincerely yours,



Song Chen, MD, PhD
Institute of Infectious Diseases,
Southwest Hospital,
the Third Military Medical University,
Chongqing, China, 400038
Fax: 86-23-68754858
E-mail: cs196@medmail.com.cn