April 6, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 8207 Revised Manuscript.doc).

Title: Pegylated interferon alfa-2b plus ribavirin for treatment of chronic hepatitis C

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Name of Journal: *World Journal of Hepatology*

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

1 Format has been updated

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

	Comments of Reviewer	**Corresponding Author's Response**
Reviewer No: 01560565		
1	In addition to ITT analysis, per protocol analysis should also be done and reported.	In addition to ITT analysis, per protocol analysis is done and the results are incorporated in the revised manuscript.
2	The discussion part can be shortened.	Discussion part is shortened from 1290 to 1080 words.
Reviewer No: 00094071		
1	Does not explain the selection process (consecutive, random...?) of patients.	All patients with chronic hepatitis C, attending the investigational centers, were screened and a total of 100 eligible consecutive patients were enrolled. This has been included under the section, Materials and Methods, and sub section, Patient Selection.
2	Considering that the main rationale for this study is to identify a more cost effective alternative source of peg-IFN, the cost of this generic version should be stated and compared against the cost charged by the original company. It is also unclear if the Virchow product is already registered and in use in India, or in other countries.	Currently, Virchow product is marketed in India at one-third of the cost of innovator product and it is also made available in other emerging countries at a very competitive rate.

Reviewer No: 00012386		
1	Authors should analyze the data of HCV genotypes 1, 3, and 4 separately	Data on baseline characteristics as well as outcome measures for HCV genotypes 1, 3 and 4 are separately analyzed and presented.
2	In Introduction, Authors should delete the following sentence: In view of this, to provide quality healthcare at an affordable cost, Virchow Biotech, an ANVISA Good Manufacturing Practices certified company, developed pegylated interferon alfa-2b from E. coli by using recombinant DNA technology	The sentence is modified.
	Authors should update the references because the references look relatively old. The following references should be added.	The references list is updated and even April 2014 WHO reference is included.
	1) Kanda T, Imazeki F, Azemoto R, Yonemitsu Y, Mikami S, Kita K, Takashi M, Sunaga M, Wu S, Nakamoto S, Tawada A, Arai M, Kato K, Yoshida Y, Koma Y, Fujiwara K, Fukai K, Suzuki N, Yokosuka O. Response to peginterferon-alfa 2b and ribavirin in Japanese patients with chronic hepatitis C genotype 2. Dig Dis Sci. 2011 Nov;56(11):3335-42. doi: 10.1007/s10620-011-1750-7.	This reference is incorporated at appropriate place.
	2) Kanda T, Imazeki F, Yokosuka O. New antiviral therapies for chronic hepatitis C. Hepatol Int. 2010 Aug 19;4(3):548-61. doi: 10.1007/s12072-010-9193-3.	This reference is incorporated at appropriate place.
	3) Kanda T, Nakamoto S, Nishino T, Takada N, Tsubota A, Kato K, Miyamura T, Maruoka D, Wu S, Tanaka T, Arai M, Mikami S, Fujiwara K, Imazeki F, Yokosuka O. Peginterferon Alfa-2a plus ribavirin in Japanese patients infected with hepatitis C virus genotype 2 who failed previous interferon therapy. Int J Med Sci. 2013;10(1):43-9. doi: 10.7150/ijms.5358.	This reference is related to the study conducted on genotype 2 patients who failed previous interferon therapy. Since our study has been conducted on treatment naïve patients with genotypes 1, 3, and 4, except for one patient with genotype 2, this particular reference is not included.

	4. The APASL guideline and AASLD updated guideline for HCV treatment should also be included. 1) APASL Guidelines for HCV (Hepatol Int 2012; 6: 409-435) http://apasl.info/guidelines 2) 5. Ghany, M. G., Nelson, D. R., Strader, D. B., Thomas, D. L. and Seeff, L. B. (2011), An update on treatment of genotype 1 chronic hepatitis C virus infection: 2011 practice guideline by the American Association for the Study of Liver Diseases. Hepatology, 54: 1433–1444. doi: 10.1002/hep.24641	This reference is incorporated at appropriate place. This reference is incorporated at appropriate place.
Reviewer No: 02453015		
1	Sample size. According to pre-study calculation, 100 participants are needed. However, only 82 completed the study. Is this number enough to show significant difference with the pre-designed power?	Sample size was computed based on statistical principles. As per the computation, 100 patients, which included 15% attrition, were enough to determine the endpoints of the study. However, as there was 18% attrition, there were 82 patients completed the study instead of required 85 patients.
2	A stratified statistical analysis is recommended according to the level of HCV copy.	Based on the level of HCV RNA copies, the primary outcome measure SVR was assessed using stratified statistical analysis and it had no impact perhaps due to small number studied. This is stated in the discussion section.
3	No statistical conclusion is made. No p value is shown. Therefore, audience is not sure about the efficacy of the treatment.	Since it is a single arm study, efficacy of treatment was not compared. P values were calculated for baseline characteristics of different genotypes.
4	English needs to be improved.	Necessary changes are made in English.

Thank you again for accepting to publish our manuscript in the *World Journal of Hepatology*

Sincerely yours,

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