

ANSWERING REVIEWERS



June 17, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 10960-revise.doc).

Title: Bone marrow-derived mesenchymal stem cell therapy for decompensated liver cirrhosis: A meta-analysis

Author: Xing-Nan Pan, Lian-Qiu Zheng, Xiao-Hua Lai

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 10960

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) **To reviewer NO. 189256**

Thank you for your positive comments, I'm fond of the field of stem cells, especially in the treatment of clinical problems, and I would make further research in this field. Thanks again!

(2) **To reviewer NO. 73425**

1) In the section "Introduction" the Authors missed HCV infection and alcohol as causes of chronic liver diseases; they are more frequent than presented primary biliaris cirrhosis 2) When the term of "liver cirrhosis" was used for the first time the corresponding abbreviation was missed. 3) Term of "cryptogenic cirrhosis" should be changed.

We are so sorry that we have made those mistakes of missing the pathogeny of HCV infection and alcohol. Following the reviewer's suggestion, we have revised them, and deleted the term of cryptogenic cirrhosis. Many thanks for the reviewer's suggestion!

4) The number of cases is not large (80 patients in 5 studies) which may limit validity of conclusions from this study. Discussed study does not present the same assessment of purity and type and volume of infused cells. The causes of chronic liver diseases were different, so they may affect the unambiguous conclusions.

As we known, the clinical studies of BM-MSD were few and the quality is not generally high for the ethical and other issues, so the number of cases is not large, what's more the LC preparations were not the same throughout the trials due to the raw data from each studies included, but the basic of each studies were not significance different. Those actually will affect the stability of the results, but the overall direction should be reliable. According the suggestions of reviewer, we add the sentence of "Assessing these methodologies, it appears possible that the LC preparations were not the same throughout the trials, and it is therefore likely that some variations in the infusions may have affected the results", thank you for your suggestions!

5) It is worth to underline that, in the section "Discussion", that the Authors gave evidence that they are conscious of limitations of this study. However, the limitations require to be discussed in more detail than they are.

According to the suggestion, we have revised some of the discussion. Thank you!

(3) To reviewer NO. 2540460

1) *The population, purity, method of assessment of purity, type of infused cells and volume of cells in the included studies were not all the same so method of comparison is difficult.* 4) *different methods of Stem cells collection and culture.*

Actually, the LC preparations were not the same throughout the trials due to raw data from each studies were not the same (but the basic were not significance) that will affect the stability of the results, but the overall direction should be reliable. According the suggestion of reviewer, we add the sentence of “Assessing these methodologies, it appears possible that the LC preparations were not the same throughout the trials, and it is therefore likely that some variations in the infusions may have affected the results”, thank you for your suggests!

2) *low number of patients in all studies.* 3) *need to add some papers to the data as there are more than 70 papers in same subject.*

Because of the clinical studies of BM-MSK were less for the ethical and others issues, so the number of cases is limit, we will update at any time as the new paper published. Thank you for your comments!

5) *way of analysis of data is not clear.*

ways of analysis of data were revised at statistical analysis. Continuous outcomes were expressed as weighted mean differences and variances by using Review Manager. The data of mean differences before and after treatment were calculated by meta-analyst in one arm. Thank you!

6) *no data about long term side effects and way of treatment.*

We add the long term side effects were report by Peng *et al*^[19], there were no serious side effects and complication during the 192wk follow up. Thank you for your suggestions!

7- *no data about way of filtration of stem cell before injection and way of preservation if done.*

There were no clearly stated in each included studies, we will update at anytime. Many thanks!

(4) To reviewer NO. 01560646

1) *Don't use abbreviation of PT, DLC in the Abstract section.* 2) *Add hepatitis C virus as one of common causes of CLD in the Introduction, line2. Also delete "cryptogenic cirrhosis" in this sentence, because its cause is unknown.*

We are so sorry to make those mistakes for missed the pathogeny of HCV infection and alcohol, and use the PT, DLC at first time without difination. Following the reviewer's suggestion, we have revised them, and deleted the term of cryptogenic cirrhosis. In fact, this is a mistake of us. Many thanks for the reviewer's suggestion.

3 References and typesetting were corrected

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

Sincerely yours,

Xing-Nan Pan



180th Hospital of PLA, MB, Botanic Physician

180th Hospital of People's
Liberation Army QuanZhou,
Fujian province, China.
Fax: +86-21-28919421
E-mail: xnpancn@163.com