

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 14974

**Title:** Clinical outcomes of Autologous bone marrow transplantation in decompensate liver disease: A systemic review and Meta- analysis

**Reviewer's code:** 00012216

**Reviewer's country:** Spain

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2014-11-03 09:19

**Date reviewed:** 2015-02-11 01:49

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

Panjak et al, carry-out a meta-analysis of nine papers about autologous bone marrow transplantation as strategy to improve liver function in decompensated liver disease. They perform a systematic review of different data-bases to select the papers of the study. Only four out of nine selected papers were randomized studies, which could decrease the evidence level. It could be interesting to know if the meta-analysis would be the same including only the randomized studies. The obtained results show a short-term improvement in some variables, such as albumin or transaminases. It could be great to see a table showing the included study features and the clinical features of the experimental and control groups in each study. Statistical methods should be described in more detail since they are essential in a meta-analysis study. In my opinion, the discussion is too general, similar to what would be expected in a review article. I think authors should comment about the statistical and methodological issues of the meta-analysis that could affect the conclusions, such as the heterogeneity and inclusion of non-randomized studies.

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**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 14974

**Title:** Clinical outcomes of Autologous bone marrow transplantation in decompensate liver disease: A systemic review and Meta- analysis

**Reviewer's code:** 00503536

**Reviewer's country:** Japan

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2014-11-03 09:19

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input checked="" type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

The systematic review and meta-analysis written by Pankaj et al. describes the effectiveness of autologous bone marrow transplantation for the treatment of decompensated liver disease. The data show that autologous bone marrow transplantation is an effective treatment to restore liver function in patients with advanced liver cirrhosis, but with limited duration. The data are well-analyzed and well-written. However, there are some concerns that need to be addressed. Major points 1. The effect of autologous bone marrow transplantation is observed for relatively short time. For instance, the preferable effect on serum albumin levels disappeared after 12 months. The authors should discuss on that point with any idea to overcome the problem. Are there any reports in which the treatment was repeatedly performed? 2. The possible cellular or molecular mechanisms for the effectiveness of the treatment should be explained. 2. It is unclear why serum AST or ALT levels were decreased after autologous bone marrow transplantation. The author should discuss on that point. Minor point 1. English editing by native speaker is needed.

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**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 14974

**Title:** Clinical outcomes of Autologous bone marrow transplantation in decompensate liver disease: A systemic review and Meta- analysis

**Reviewer's code:** 00012386

**Reviewer's country:** Japan

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2014-11-03 09:19

**Date reviewed:** 2015-02-27 15:38

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> No	<input type="checkbox"/> Minor revision
		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

## COMMENTS TO AUTHORS

Etiology influences the prognosis of cirrhosis. Authors should describe the etiology of cirrhosis. Invasive methods of autologous bone marrow mononuclear cell or mononuclear stem cell transplantation seems limited to certain patients with decompensated cirrhosis such as better liver function, because they need general anesthesia not but local anesthesia. So, authors should mention these things and revise their manuscript.

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 14974

**Title:** Clinical outcomes of Autologus bone marrow transplantation in decompensate liver disease: A systemic review and Meta- analysis

**Reviewer's code:** 00039518

**Reviewer's country:** Italy

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2014-11-03 09:19

**Date reviewed:** 2015-03-09 03:27

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input checked="" type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

This meta-analysis describes the effectiveness of autologous bone marrow transplantation for the treatment of decompensated liver disease. Although the study shows that autologus bone marrow transplantation is an effective treatment to improve liver function scores and some hematochemical parameters in patients with advanced liver cirrhosis, this effect seems to be of limited duration. Furthermore, the conclusion of the study may be hampered by the heterogeneity of the methods used and by the limited number of patients evaluated in the studies taken into account. The data are appropriately analyzed, the method of the meta-analysis is right and the paper is well-written. No major changes are requested. However, Table 1, summarizing the main features of the 9 studies evaluated, is lacking and the Discussion can be shortened. There are some typographical errors that should be corrected.

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 14974

**Title:** Clinical outcomes of Autologous bone marrow transplantation in decompensate liver disease: A systemic review and Meta- analysis

**Reviewer's code:** 00052899

**Reviewer's country:** China

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2014-11-03 09:19

**Date reviewed:** 2015-03-09 21:08

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> Plagiarism	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		[Y] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

## COMMENTS TO AUTHORS

In this meta-analysis, the author evaluated the efficacy of autologous bone marrow transplantation in the treatment of decompensated liver disease. The author found that autologous bone marrow transplantation could improve liver function and was an effective therapy for decompensated liver disease. Overall, the meta-analysis is carefully prepared and the manuscript is well organized. However, there are still some problems. They are given below. 1. Where is the Table 1? 2. Clarify the exclusion reasons for the 101 articles in Figure 1. 3. In paragraph 2 of "outcome evaluation", "At 6 mo after cell transplantation, patients had a lower level of total bilirubin (MD: -1.32 mg/dL; 95% CI: -3.39 to 0.75; P = 0.04)". The data of total bilirubin in text and Figure 3C were not consistent. 4. In the last paragraph of "outcome evaluation", "P < 0.00001" should be "P=0.05" according to Figure 8B. 5. Heterogeneity was high in several studies.

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**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 14974

**Title:** Clinical outcomes of Autologous bone marrow transplantation in decompensate liver disease: A systemic review and Meta- analysis

**Reviewer's code:** 00011164

**Reviewer's country:** Japan

**Science editor:** Ya-Juan Ma

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

To my understanding the article entitled 'Autologous bone marrow transplantation in decompensated cirrhosis' by Pankaj et al. is a time endeavor as there is lack of appropriate treatment modality for this intractable liver disease. Although some innovative therapeutic regimens have been proposed for this pathological condition, critical analyses of these approaches are still lacking. The present article seems to provide an analysis of bone marrow transplantation in decompensated cirrhosis in this communication that may be worthy in clinics. However, the authors should note the limitation of their article and study design so that it may be a viable one for the readers and clinicians. Comment 1. The systemic review and meta-analysis revealed that autologous bone marrow transplantation improved serum albumin level and down regulated MELD score without any significant impact on prothrombin time in patients with decompensated cirrhosis due to bone marrow transplantation. If we look at the study design, a total of 9 studies were analyzed out of a total of 630 plus 40 studies were preliminary selected. In Fig. 1, the authors have demonstrated why several hundred studies were excluded. Definitely, this has been done due to the impact of inclusion and exclusion criteria.

However, the authors should discuss the logics of exclusion of 101 studies that were excluded at the final state. In fact, a meta-analysis with 9 studies may not be a proper sample size and any meta-analysis may be too early for this subject. 2. The title of the article is 'bone marrow transplantation'. Bone marrow is a mixture of highly heterogeneous population of different cells. In fact, patients receiving translation of bone marrow mononuclear cell (BMMNC) and bone marrow stem cell (BMSC) have been included in this analysis. The outcomes of bone marrow transplantation also show marked heterogeneity, especially regarding prothrombin time. If you show the result of BMMNC transplantation and BMSC transplantation separately, how the overall picture is visualized? Please try to do that, and then the overall outcome may be discussed in Discussion and your comments. 3. Please take cautionary measure to use term like 'appropriate' in conclusion of Abstract. The impact of BMT is far from an appropriate therapeutic measure and a meta-analysis with improvement of some marker for a short duration is not endowed to use the term 'appropriate'. 4. Check the discrepancy of Table 1 versus Fig. 1 in Text and Figure. 5. The future research direction of BMT transplantation should be shown from the experience of this article.