



BAISHIDENG PUBLISHING GROUP INC

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

http://www.wjgnet.com

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 13385

Title: Long-term antiviral efficacy of entecavir and liver histology improvement in Chinese patients with hepatitis B virus-related cirrhosis

Reviewer's code: 02861007

Reviewer's country: China

Science editor: Jing Yu

Date sent for review: 2014-08-21 14:34

Date reviewed: 2014-09-08 08:18

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"/> 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		[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

It is an important paper, which evaluate the efficacy of ETV in the treatment of HBV-cirrhosis. There are several issues should be addressed before being accepted for publication: 1. The duration of patients recruiting should be reported. How many patients were recruited at the period? How many patients lost follow up? Is there any antiviral regimen change in certain patients? 2. The diagnoses criteria of cirrhosis should be clarified (You may ref. & cite "Type 2 diabetes and hepatocellular carcinoma: A case-control study in patients with chronic hepatitis B. Int. J. Cancer, 131: 1197-1202. doi: 10.1002/ijc.27337"). The ref. 9 in the paper does not show any information on the diagnosis of cirrhosis. So please check all the ref. carefully to ensure the reference were correct.



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 13385

Title: Long-term antiviral efficacy of entecavir and liver histology improvement in Chinese patients with hepatitis B virus-related cirrhosis

Reviewer's code: 00036624

Reviewer's country: Italy

Science editor: Jing Yu

Date sent for review: 2014-08-21 14:34

Date reviewed: 2014-11-10 23:20

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"/> 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"/> No	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input checked="" 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 manuscript cannot be rated in the present form. Apart from some typos, English Language is insufficient. In revising the paper, I also suggest the Authors to pay as much attention as possible to clearly distinguish chronic hepatitis B from cirrhosis due to HBV infection.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 13385

Title: Long-term antiviral efficacy of entecavir and liver histology improvement in Chinese patients with hepatitis B virus-related cirrhosis

Reviewer's code: 02941502

Reviewer's country: Australia

Science editor: Jing Yu

Date sent for review: 2014-08-21 14:34

Date reviewed: 2014-11-11 14:35

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 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 checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		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

? Introduction Page 2 - need to define "CTP" when first used. ? Comment on IL28B polymorphisms - several studies have now shown this is not as important for Hep B as Hep C. need to discuss more. ? In Methods (Efficacy assessment), description of 38 patients undergoing biopsy does not make sense and needs editing. ? Table 1 - baseline data for compensated and decompensated patients should be formally compared, with p values to show which are statistically significant. In the results it is stated that baseline characteristics were "similar", apart from a difference in the proportion of patients with genotype C infection, although no statistics are presented to show that this is a significant difference, and that differences in age etc are not significant. Some other baseline characteristics (eg ALT) look quite different between the two groups. ? Under IL-28 genotypes in results, it is stated that there was no significant association, but p value is not provided. Furthermore, for clarity this should be called the IL-28B polymorphism, and more correctly now IFNL3 ? In Histological Improvement, Fig 1 compares distributions of fibrosis scores at baseline and week 240. In Results, the mean reduction in Knodell score is reported as 3.5 points, and the Ishak fibrosis score 1.3 points, but the mean and



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standard deviation (before and after) for each is not stated, nor whether these are significant changes (with p values). ? For Fig 2, in Results it is stated that baseline viral load was “Significantly correlated with Knodell HAI score and Ishak fibrosis score ($r=0.88$ vs 0.43)”, with similar statement for decrease in viral load at week 240. However there is no comment on the relative correlation. In Fig 2A there is indeed strong correlation with Knodell score ($r=-0.88$), but only weak correlation with Ishak score ($r=0.43$). Similarly in Fig 2B correlation with Knodell score is moderate ($r=0.60$) but weak for Ishak (0.45). Review of the data by a statistician may help to analyse and express this more clearly. ? Clinical Outcome – was the reduction in Child-Pugh class C disease statistically significant, and if so what was the p value? ? In the discussion it is stated that histological improvement was observed in “the majority (89.5%) of patients with paired biopsies”, yet this data should be presented in more detail in the results. ? In Discussion it is stated that “treatment with entecavir was associated with significant improvements in hepatic functional reserve in patients with decompensated cirrhosis”. What is the basis for this statement? Clinical outcomes are presented and not surprisingly the episodes of “clinical progression” occur more commonly in patients who were decompensated at baseline than those who were compensated. However there are no data to show that entecavir altered this rate, as there is no control group of untreated patients to compare to. ? For Entecavir resistance, three different mutations are listed (entecavir requires multiple mutations to become resistant), but it is unclear whether all three patients with viral breakthrough had exactly the same mutations? Please clarify.