

## ESPS Peer-review Report

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

**ESPS Manuscript NO:** 6395

**Title:** Entecavir Versus Lamivudine Therapy for Na<sup>+</sup>ve Patients with Spontaneous Reactivation of Hepatitis B Presenting as Acute-On-Chronic Liver Failure: A Prospective Cohort Study

**Reviewer code:** 00011164

**Science editor:** Cui, Xue-Mei

**Date sent for review:** 2013-10-16 17:42

**Date reviewed:** 2013-10-30 10:37

| CLASSIFICATION                                     | LANGUAGE EVALUATION   | RECOMMENDATION                      | 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"/> Existed    | <input type="checkbox"/> High priority for publication |
| <input type="checkbox"/> Grade C (Good)            | <input type="checkbox"/> Grade C: a great deal of                     | <input type="checkbox"/> No records | <input type="checkbox"/> Rejection                     |
| <input checked="" type="checkbox"/> Grade D (Fair) | language polishing  | BPG Search:                         | <input type="checkbox"/> Minor revision                |
| <input type="checkbox"/> Grade E (Poor)            | <input type="checkbox"/> Grade D: rejected                            | <input type="checkbox"/> Existed    | <input checked="" type="checkbox"/> Major revision     |
|  |   | <input type="checkbox"/> No records |  |

## COMMENTS TO AUTHORS

Acute on chronic liver failure (ACLF) represents an intractable liver disease with a bad prognosis. Proper diagnosis and massive intervention are required to handle these patients. Even then, the prognosis of ACLF is not still satisfactory especially in developing and resource-constrained countries. The study presented here has attempted to assess the utility of two antiviral agents for management of hepatitis B virus (HBV)-related ACLF. Comments 1. The most important fact about ACLF is its diagnosis. ACLF represents a pathological condition in which an acute insult cause rapidly downhill course of liver disease in a patients with chronic liver diseases. The acute insult may arise may several factors. As discussed in the Background/Aim section of Abstract of this manuscript, the authors have highlighted the fact of spontaneous acute exacerbation of chronic HBV infection. Please specifically respond to the following concerns: A. Is the acute insult of these patients was due to exacerbation of HBV? B. How did you confirm that? C. Increased HBV DNA is not a marker of acute insult in ACLF in patients with chronic HBV infection because several patients have attended the clinics with different situations. The HBV DNA may have risen due to disease process, not due to acute insult of HBV exacerbation.. D. Did you measure anti-HBc IgM in all cases and if that was positive in all patients. 2. The primary end point of the study was to evaluate survival at 60 days and 52 weeks. I am not sure if assessment of survival at 52 weeks can be a primary end point of survival of ACLF patients. These patients have been suffering from chronic HBV infection. Thus, survival after 52 weeks of starting of ACLF may be due to variable factors. Is the concept of 52 weeks survival of ACLF makes a proper scientific logic? In addition, patients were released from hospital and how the patients were followed up for 52 weeks and how the patients passed their life after



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initial recovery. Please explain these facts. 3. There was no difference in survival after 60 day but entecavir was superior to lamivudine when survival was assessed after 52 weeks. Both lamivudine and entecavir are antiviral agents for HBV. What additional capacity or property entecavir may have that may provide a better survival at 52 weeks. This point needs more discussion. 4. Paragraph 4 of Discussion section needs careful citations. Pathogenesis of ACLF is not related to high levels of HBV DNA, but possibly cytokine play a major role. It may not be true that lamivudine has week antiviral activity. Please check the HBV DNA load of patients who died and survived and try to show a relation with HBV DNA level and survival. 5. Did you measure host immunity in patients with good and bad prognosis?

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**Reviewer code:** 02458762

**Science editor:** Cui, Xue-Mei

**Date sent for review:** 2013-10-16 17:42

**Date reviewed:** 2013-12-01 13:13

| CLASSIFICATION  | LANGUAGE EVALUATION   | RECOMMENDATION                      | 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 checked="" type="checkbox"/> Grade B: minor language polishing | <input type="checkbox"/> Existed    | <input type="checkbox"/> High priority for publication |
| <input type="checkbox"/> Grade C (Good)                 | <input type="checkbox"/> Grade C: a great deal of                     | <input type="checkbox"/> No records | <input type="checkbox"/> Rejection                     |
| <input type="checkbox"/> Grade D (Fair)                 | language polishing  | BPG Search:                         | <input type="checkbox"/> Rejection                     |
| <input type="checkbox"/> Grade E (Poor)                 | <input type="checkbox"/> Grade D: rejected                            | <input type="checkbox"/> Existed    | <input checked="" type="checkbox"/> Minor revision     |
|   |   | <input type="checkbox"/> No records | <input type="checkbox"/> Major revision                |

## COMMENTS TO AUTHORS

In the diagnostic criteria that should be noted: ACLF diagnostic criteria of patient serum total bilirubin should be  $\geq 171$  mol / L, instead of  $\geq 85\mu\text{mol}$  / L. Patients enrolled in the article does not match the current standard clinical diagnostic criteria. In this study, no randomization is a drawback, as the author has mentioned in the discussion section of the article. But as real life data should be allowed in clinical.

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**Title:** Entecavir Versus Lamivudine Therapy for Na<sup>+</sup>ve Patients with Spontaneous Reactivation of Hepatitis B Presenting as Acute-On-Chronic Liver Failure: A Prospective Cohort Study

**Reviewer code:** 00070056

**Science editor:** Cui, Xue-Mei

**Date sent for review:** 2013-10-16 17:42

**Date reviewed:** 2013-12-04 23:10

| CLASSIFICATION                                     | LANGUAGE EVALUATION   | RECOMMENDATION                      | 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"/> Existed    | <input type="checkbox"/> High priority for publication |
| <input checked="" type="checkbox"/> Grade C (Good) | <input type="checkbox"/> Grade C: a great deal of                     | <input type="checkbox"/> No records | <input type="checkbox"/> Rejection                     |
| <input type="checkbox"/> Grade D (Fair)            | language polishing  | BPG Search:                         | <input type="checkbox"/> Rejection                     |
| <input type="checkbox"/> Grade E (Poor)            | <input type="checkbox"/> Grade D: rejected                            | <input type="checkbox"/> Existed    | <input checked="" type="checkbox"/> Minor revision     |
|  |   | <input type="checkbox"/> No records | <input type="checkbox"/> Major revision                |

## COMMENTS TO AUTHORS

In this manuscript, Dr. Zhang and his colleagues described their research on HBV therapy with Entecavir versus Lamivudine. The results in the manuscript may help clinicians to select anti HBV therapy. But the manuscript was poorly written. The manuscript need minor revision before it is accepted for publication in The World Journal of Gastroenterology. The manuscript need to be revised by an native English speaker before it is resubmitted to the journal.

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**Title:** Entecavir Versus Lamivudine Therapy for Na<sup>+</sup>ve Patients with Spontaneous Reactivation of Hepatitis B Presenting as Acute-On-Chronic Liver Failure: A Prospective Cohort Study

**Reviewer code:** 01800545

**Science editor:** Cui, Xue-Mei

**Date sent for review:** 2013-10-16 17:42

**Date reviewed:** 2013-12-07 14:27

| CLASSIFICATION                                     | LANGUAGE EVALUATION   | RECOMMENDATION                      | 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"/> Existed    | <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"/> No records | <input type="checkbox"/> Rejection                     |
| <input type="checkbox"/> Grade D (Fair)            |   | BPG Search:                         | <input type="checkbox"/> Minor revision                |
| <input type="checkbox"/> Grade E (Poor)            | <input type="checkbox"/> Grade D: rejected                            | <input type="checkbox"/> Existed    | <input type="checkbox"/> Major revision                |
|  |   | <input type="checkbox"/> No records |  |

## COMMENTS TO AUTHORS

This study demonstrated that treatment by entecavir could improve the prognosis of spontaneous reactivation of HBV. Major Comments (1) In CTP and MELD scores, the value of T-Bil was used and its value was high in spontaneous reactivation of HBV. Therefore, after the overcome of spontaneous reactivation of HBV, these scores would improve naturally. These scores are useful for chronic liver failure, however, not for acute liver failure. (2) The authors should the criteria which nucleotide analogue, entecavir or lamivudine, was used. Minor Comment Figure 1 is very confusing, which might misunderstand that this study is RCT.