

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Hepatology

**Manuscript NO:** 56366

**Title:** Subclinical proximal tubulopathy in hepatitis B: the roles of nucleot(s)ide analogue treatment and the hepatitis B virus

**Reviewer's code:** 02541859

**Position:** Editor-in-Chief

**Academic degree:** FACG, FACP, FASGE, FRCP, MD, MRCP

**Professional title:** Associate Professor, Doctor

**Reviewer's Country/Territory:** United States

**Author's Country/Territory:** France

**Manuscript submission date:** 2020-06-11

**Reviewer chosen by:** Ya-Juan Ma

**Reviewer accepted review:** 2020-08-24 15:15

**Reviewer performed review:** 2020-08-25 17:47

**Review time:** 1 Day and 2 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input checked="" type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

#### **SPECIFIC COMMENTS TO AUTHORS**

This is a small study. study results are not given in tables. The manuscript is not well-writren.

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**Name of journal:** World Journal of Hepatology

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**Title:** Subclinical proximal tubulopathy in hepatitis B: the roles of nucleot(s)ide analogue treatment and the hepatitis B virus

**Reviewer's code:** 02567669

**Position:** Editorial Board

**Academic degree:** MD

**Professional title:** Emeritus Professor

**Reviewer's Country/Territory:** Germany

**Author's Country/Territory:** France

**Manuscript submission date:** 2020-06-11

**Reviewer chosen by:** Ya-Juan Ma

**Reviewer accepted review:** 2020-08-22 19:21

**Reviewer performed review:** 2020-08-29 17:46

**Review time:** 6 Days and 22 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

#### **SPECIFIC COMMENTS TO AUTHORS**

The authors investigated the prevalence and incidence of proximal tubulopathy in patients with chronic hepatitis B, particularly in patients treated with ETV or TDF. The study is well performed and the statistical evaluations seems to be completely correct.

However, I have some questions. 1. The authors state that there are no data about the prevalence of SPT in the general population. If that is true, where does the cut-off originate to judge one of the markers as indicator of SPT? 2. It is difficult to understand why the authors haven't included a matched study population without HBV infection. This could be done without problems. 3. The main study criterium was the prevalence of SPT at month 24. Why didn't they investigate markers of early tubulotoxicity, this means early after start of therapy? 4. How was the course of SPT during antiviral therapy? Early occurrence and attenuation after one year (or later)? 5. Is there a dose dependency of tubulotoxicity? Cumulative dose of antivirals? Dose-independent tubular damage ("Idiosyncratic renal damage")? 6. Is the choice of the two markers really ideal? The authors should explain, why they have not used more specific markers of tubulotoxicity?

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**Name of journal:** World Journal of Hepatology

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**Title:** Subclinical proximal tubulopathy in hepatitis B: the roles of nucleot(s)ide analogue treatment and the hepatitis B virus

**Reviewer's code:** 02441083

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Associate Professor

**Reviewer's Country/Territory:** Spain

**Author's Country/Territory:** France

**Manuscript submission date:** 2020-06-11

**Reviewer chosen by:** Ya-Juan Ma

**Reviewer accepted review:** 2020-08-30 16:20

**Reviewer performed review:** 2020-08-30 16:41

**Review time:** 1 Hour

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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#### **SPECIFIC COMMENTS TO AUTHORS**

This is a prospective multicentric study to assess subclinical proximal tubular dysfunction in HBV-patients undergoing TDF or ETV or naïve patients. The results are inconclusive, as the trend in favor of ETV did not reach significance, most likely due to underpowered size or relatively short F-U (24 months). I would like the authors further clarify some key aspects: 1. How was the sample size calculated? 2. How were the patients assigned to each one of the three options? 3. There could be a selection bias as the baseline parameters that could influence renal function were not well balanced regarding drug assignation.

## RE-REVIEW REPORT OF REVISED MANUSCRIPT

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**Reviewer's Country/Territory:** Germany

**Author's Country/Territory:** France

**Manuscript submission date:** 2020-06-11

**Reviewer chosen by:** Jia-Ru Fan

**Reviewer accepted review:** 2020-10-08 12:21

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**Review time:** 1 Hour

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
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The manuscript can be accepted



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**Reviewer chosen by:** Jia-Ru Fan

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**Review time:** 1 Hour

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
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I do not understand 'The median survival time without SPT in the tenofovir disoproxil-treated group was 5.9 mo'. Thank you. Otherwise looks good.

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**Review time:** 1 Hour

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
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Thank you for addressing most of my comments