

## PEER-REVIEW REPORT

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

**Manuscript NO:** 38881

**Title:** Development of tenofovir disoproxil fumarate resistance after complete viral suppression in a patient with treatment-naïve chronic hepatitis B: A case report and review of the literature

**Reviewer's code:** 02994642

**Reviewer's country:** Turkey

**Science editor:** Xue-Jiao Wang

**Date sent for review:** 2018-03-21

**Date reviewed:** 2018-03-21

**Review time:** 1 Hour

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" 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 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"/> No	<input 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

An important case report in terms of monitoring HBV therapy and drug response. I think it will be useful scientifically.

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**Reviewer's code:** 00004603

**Reviewer's country:** United States

**Science editor:** Xue-Jiao Wang

**Date sent for review:** 2018-03-21

**Date reviewed:** 2018-03-22

**Review time:** 1 Day

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input checked="" type="checkbox"/> Grade A: Excellent	<input checked="" 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 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

This is an excellently written paper, which represents a case report on previously non-identified resistance of CHB patient to Tenofovir. This negative result seemed to be associated to some unusual mutations, which the authors interpreted as the treatment-induced. The only thing, which is not quite clear is when they mentioned that there was no HBe seroconversion, did they mean that the patient did not develop anti-HBe response or that he still had HBe persistence after the treatment with both nucleoside analogues? This is important because HBe persistence indicates that after the treatment, HBV-infection was still active and thus, the mutations existed at the baseline, but were not treatment-induced. However, if there was no development of anti-HBe in the absence of HBe, it may be related to the lack of protection and a kind of

immunodeficiency in this patient, which potentially leads to re-infection (since his mother was also infected and he was in a contact with her). I wonder, whether the patient developed anti-HBs after successful completion of the treatment course? It will be useful to address these issues in the Discussion

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**Reviewer's code:** 00033049

**Reviewer's country:** United States

**Science editor:** Xue-Jiao Wang

**Date sent for review:** 2018-03-21

**Date reviewed:** 2018-03-23

**Review time:** 2 Days

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	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Duplicate publication	publication
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	language polishing	<input 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 type="checkbox"/> No	

## COMMENTS TO AUTHORS

1. How did you confirm that patient is taking his medication? By prescription and refill history? 2. It was stated that "excluded the presence of systemic diseases that might have been able to explain the ineffectiveness of the drug (p.5). What evaluation were performed and what were excluded? 3. Did you do a workup to exclude other cause of a biochemical flare? Did you rule out HDV super-infection? 4. Were patient ever tested for HCV? 5. Since full genome sequencing were done, can simplify the mutation presentation . 6. Was any of the mutation found in this patient associated with ETV resistance? 7. Why was the patient started on ETV 0.5 mg daily? Since he is treatment experienced, should he be on 1mg daily instead?