



### PEER-REVIEW REPORT

**Name of journal:** World Journal of Clinical Cases

**Manuscript NO:** 41084

**Title:** Incident hepatocellular carcinoma developed during tenofovir alafenamide treatment as rescue therapy: A case report and review of the literature

**Reviewer's code:** 02941377

**Reviewer's country:** Turkey

**Science editor:** Xue-Jiao Wang

**Date sent for review:** 2018-07-24

**Date reviewed:** 2018-07-25

**Review time:** 22 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good		<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	(General priority)	Peer-reviewer's expertise on the topic of the manuscript:
<input type="checkbox"/> Grade E: Do not publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Minor revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> General
		<input type="checkbox"/> Rejection	<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

#### SPECIFIC COMMENTS TO AUTHORS

Dear Editor, In this case report Tenofovir Alafenamide was evaluated in old patient with multidrug resistance and renal dysfunction. Authors have presented this case well. Sincerely.



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#### INITIAL REVIEW OF THE MANUSCRIPT

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**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Clinical Cases

**Manuscript NO:** 41084

**Title:** Incident hepatocellular carcinoma developed during tenofovir alafenamide treatment as rescue therapy: A case report and review of the literature

**Reviewer’s code:** 02955164

**Reviewer’s country:** Spain

**Science editor:** Xue-Jiao Wang

**Date sent for review:** 2018-08-01

**Date reviewed:** 2018-08-01

**Review time:** 11 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer’s expertise on the
<input checked="" type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input checked="" type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

In this report, Lu et al. provide a succinct account on the development of hepatocellular carcinoma in a Chinese patient infected with hepatitis B virus. The case illustrates a situation where switching antiviral therapies seems to have little effect on disease



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progression despite suppression of viral replication. In my opinion, the manuscript is weak due to several reasons: (1) Authors concentrate on the evolution of kidney function, but there is little information on the evolution of hepatic function (only ALT values are monitored). (2) How sensitive was the viral load test used? What does it mean undetectable? Is it less than 1 log<sub>10</sub>IU/ml? Is there any information of the HBV genotype infecting the patient? Was it a commonly found strain? (3) Authors should define abbreviations when cited for the first time: HCC in the abstract; eGFR in the text. The recommended way to report the estimated glomerular filtration rate is in “mL/min/1.73 m<sup>2</sup>” (<https://www.niddk.nih.gov/health-information/communication-programs/nkdep/laboratory-evaluation/glomerular-filtration-rate-calculators/mdrd-adults-conventional-units>). Are reported values reasonable for the patient? This should be discussed carefully. (4) Please use μmol/L instead of umol/L throughout the text: e.g. at lines 93 & 95 (5) Please separate values and units. It should read 117 U/L instead of 117U/L. Make appropriate changes at lines 84, 104 and in the Figure (CK value and Cr(μmol/L)) (6) Abstract, lines 50-51 should read: “... we describe a clinical case concerning a 60-year-old individual suffering liver cirrhosis and renal dysfunction, and infected multidrug-resistant HBV. When failing treatment with TDF, he received TAF as rescue therapy.” (7) Page 4, line 86: “took valsartan capsule” (please indicate the precise doses and medication received) (8) Page 4, line 94: “Lam was switched...” This sounds incorrect (at some point I thought Lam was the name of the patient. Probably, authors wanted to write: “Then, the patient was treated with LDT and ADV, instead of LAM and ADV, due to the superior nephron-protective effect of LDT.”

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**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Clinical Cases

**Manuscript NO:** 41084

**Title:** Incident hepatocellular carcinoma developed during tenofovir alafenamide treatment as rescue therapy: A case report and review of the literature

**Reviewer’s code:** 03479017

**Reviewer’s country:** France

**Science editor:** Xue-Jiao Wang

**Date sent for review:** 2018-08-01

**Date reviewed:** 2018-08-19

**Review time:** 18 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
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			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

Lu et al. present a case study illustrating that the risk of HCC is not negligible during treatment with TAF (as is the case with other potent NAs TDF and ETV). This case also demonstrates the complexity of treating HBV-infected patients with several previous



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lines of anti-HBV treatment, multi-drug resistance, and residual HBV DNA replication during TDF (with no evidence of TDF resistant mutant variants). The case is for the most part clear, however, there are certain issues that need to be addressed. HCC developed within a span of 5 months after TAF initiation. It could very well be that HCC had already started developing prior to TAF initiation and HBV suppression due to TAF would not really matter. This needs to be explained in the discussion. The term “recue therapy” as a reason for switch to TAF is a bit simplistic (as this most often refers to emerging treatment resistance and since no concrete HBV resistant mutations have been observed with TDF to date, it is oddly placed). It was mostly due to complications from renal dysfunction and residual HBV DNA replication while undergoing TDF. Please rephrase throughout the manuscript. Minor comments: - In 4. Running title should be “Incident HCC during TAF”. - In 46 and 71. Please add “tenofovir” to “disoproxil fumarate”. - In 79. “coexistence of hepatocellular carcinoma” does not apply as a reason for switching to TAF. The authors could reword it to: “HCC monitoring is lacking in patients switching to TAF due to ...” - In 90. It seems that ADV was added on? It needs to be explained why LAM was continued despite the patient harboring resistant strains. - In 94. Why was ADV, with known renal toxicities, continued with evidence of renal dysfunction? - In 107. There is no evidence in the literature to suspect “TDF resistance”. Suggest rewording to “lack of full viral suppression under TDF”. - In 118. Again, the reason for switch was not due to liver cirrhosis (as presented here). Suggest deleting. - In 127. “TDV” should be replaced with “TDF”. - In 133-4. The evidence for lack of renal issues during TAF suggests no need to add LDT. Please delete the sentence “The combination of LDT and TAF...”

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