

## PEER-REVIEW REPORT

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

**Manuscript NO:** 37331

**Title:** Impact of Direct Acting Antivirals on Occurrence and Recurrence of Hepatocellular Carcinoma: Biologically Plausible or an Epiphenomenon

**Reviewer's code:** 03253532

**Reviewer's country:** Italy

**Science editor:** Na Ma

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**Review time:** 15 Days

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 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 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 adequate and balanced review. I have a few suggestions to improve the paper: 1. In the section DAA and carcinogenesis: Biologically plausible or not?, the authors should include and comment the results of the recent paper from Chu PS et al. published in Plos One (PLoS One 2017; 12: e0179096. doi: 10.1371/journal.pone.0179096). 2. In the section DAA and carcinogenesis: Review of existing evidence/data, the authors should address two important questions: A. Is HCC recurrence accelerated by DAA therapy? B. Do recurrent HCCs present a more aggressive pattern? Regarding these questions, the mean/median time to HCC occurrence/recurrence should be reviewed and the results reported by Renzulli M et al in Eur Radiol 2018; 28: 506-513 should be commented. 3. In the sub-section Geographical variation of incidence of HCC in DAA treated patients, a word of caution should be added regarding the significance of Waziry



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and others' meta-analysis: the extreme heterogeneity of the analysed studies let any conclusion of these meta-analysis without strong support. In addition, similar heterogeneity concerns exist about the significance of the comparisons between DAA treated and IFN-treated patients, due to the baseline differences between the two populations. 4. The final sentence of the paper could be emended with the addition of a word of caution in treating with DAA those patients who received a recent treatment for HCC. Some important Centers in Europe and US have been delaying antiviral treatment for 6 months or more after recent treatment for HCC in these patients.