

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 13661

Title: Current and future antiviral drug therapies of hepatitis B chronic infection

Reviewer's code: 02861195

Reviewer's country: Italy

Science editor: Xue-Mei Gong

Date sent for review: 2014-08-31 18:21

Date reviewed: 2014-11-03 23:30

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	PubMed 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"/> Duplicate publication	
<input checked="" type="checkbox"/> Grade D: Fair	<input checked="" type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
		BPG Search:	<input checked="" 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

The manuscript needs considerable English language revision; at some points meaning is compromised. Some examples include: the use of the word "finitive", the phrase "Both antiviral treatments are not capable to eliminate the virus and to efficiently control the infection", "IFN therapy is of finitive duration and associates with low response rates...", amongst others. The abstracts warrants thorough revision, whereas the Core Tip is adequate. The review is very extensive and the sections which, in my opinion, warrant further analysis and mention are actually those less developed within the text, including the new antiviral therapies. The section on "Natural history of chronic HBV infection" does not mention the case of new onset infection during adulthood, which is, unlike Asian countries where most infections are acquired during childhood, the case in the "Western world". The definition of "occult hepatitis B infection" is not adequately explained. The manuscript could be enriched with several tables and/or figures which summarize the information given and are more attractive to readers.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 13661

Title: Current and future antiviral drug therapies of hepatitis B chronic infection

Reviewer's code: 02441405

Reviewer's country: United States

Science editor: Xue-Mei Gong

Date sent for review: 2014-08-31 18:21

Date reviewed: 2014-11-04 04:36

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	PubMed Search:	<input checked="" 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"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
		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 a well written and comprehensive review. To understand the topics better, I will suggest author to add a few summery tables or diagrams illustrating HBV structures, drug targets, and mechanisms of therapeutic effect. For example, a cartoon for cccDNA of HBV will easily give readers a better idea about this structure and how the anti-cccDNA drug works. There is a similar review article published last year by Simon P. Fletcher, William E. Delaney IV (New Therapeutic Targets and Drugs for the Treatment of Chronic Hepatitis B. Semin Liver Dis 2013; 33(02): 130-137). To make this review unique, author may need add more updated information, such as new research on the drug discovery.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 13661

Title: Current and future antiviral drug therapies of hepatitis B chronic infection

Reviewer's code: 02861217

Reviewer's country: Armenia

Science editor: Xue-Mei Gong

Date sent for review: 2014-08-31 18:21

Date reviewed: 2014-10-21 04:45

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	PubMed 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"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor		<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

Dear Dr. Lemonica Koumbi, Your manuscript is excellent overview on HBV-infection. No doubt that it could be published in World Journal of Hepatology. Nevertheless, there are some mechanical mistakes in the text (mentioned with red) and so conceptual inaccuracies: ? Natural history of CHB infection. You mentioned that it is consists four distinct phases: immune-tolerant, immune clearance, inactive residual and re-activation. It is preferable to take as the reliable source as EASL or APASL guideless. According to EASL the natural history of chronic HBV infection can be schematically divided into five phases (1) "immune tolerant phase", (2) "immune reactive HBeAg-positive phase", (3) "inactive HBV carrier state", (4) "HBeAg-negative CHB", (5) "HBsAg-negative phase", which are not necessarily sequential. In APASL the natural course of chronic HBV infection can be divided into (1) "immune tolerant phase", (2) "immune clearance phase", and (3) "residual or inactive phase". ? Eradication of the virus – complete eradication rarely occurs. Over time basic research has shown that even in patients positive for anti-HBs and anti-HBe, HBV DNA may persist lifelong in form of cccDNA (Hepatology – a clinical textbook. Mauss, Berg, Rockstoh, Sarrazin, Wedemeyer – 2014. – p. 40). ? NAs – It is not correct described only Entecavir as guanosine nucleoside analog. It is ought to



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be noticed all other NAs as a synthetic analogs of different nucleoside (f.e. telbivudine is a thymidine analog etc.). Besides, better to put entecavir before tenofovir and after telbivudine. ? Interferon-based therapy - later in future therapies strategies noticed Interferon cccDNA affecting mechanisms, but this information missed in paragraph "Interferon-based therapy". ? Current Antiviral Therapy - more correct title current antiviral drugs, because there is not any information about duration and monitoring of therapy, just a description of medications.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 13661

Title: Current and future antiviral drug therapies of hepatitis B chronic infection

Reviewer's code: 00158184

Reviewer's country: Turkey

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Date sent for review: 2014-08-31 18:21

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	PubMed Search:	<input type="checkbox"/> [Y] 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"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		[Y] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

The manuscript needs to shortened.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 13661

Title: Current and future antiviral drug therapies of hepatitis B chronic infection

Reviewer's code: 01801241

Reviewer's country: Spain

Science editor: Xue-Mei Gong

Date sent for review: 2014-08-31 18:21

Date reviewed: 2014-11-01 01:01

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input checked="" type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	PubMed Search:	<input checked="" 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"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		[Y] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

I think that you have performed a great review.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 13661

Title: Current and future antiviral drug therapies of hepatitis B chronic infection

Reviewer's code: 00092173

Reviewer's country: Germany

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input checked="" type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	PubMed Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" 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"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input checked="" 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 checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This is an excellent and well written review on the subject of current and future therapeutic options of chronic HBV infection. The review is comprehensive, almost well referenced and yet concise in its content. The introduction introduces the subject well and the ensuing sections are informative and interesting to read. Comments: 1) There are some minor typing errors throughout the text. Please correct. 2) Introduction section, 2nd para. The citation for the HBV minichromosome is not correct (Bock et al Virus Genes 1994; 8:215-229; Newbold et al J Virol. 1995; 69:3350-3357; Bock et al J Mol Biol 2001; 307:183-196; 3) The chapter "natural history of CHB" is mainly textbook knowledge and can be shortened accordingly. 4) Also the presented data in the chapter "natural history of CHB" should be updated according current guidelines of CHB (e.g. EASL guidelines) 5) Furthermore, after presenting such a comprehensive review the author may provide a schematic table summarizing in brief the presented therapeutic drug regimens. This would enhance the paper.