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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Hepatology
ESPS manuscript NO: 13941
Title: Risk of HBV reactivation in rheumatoid arthritis patients undergoing biologic treatment: extending perspective from old to newer drugs.
Reviewer code: 01868411
Science editor: Xue-Mei Gong
Date sent for review: 2014-09-09 20:51
Date reviewed: 2014-09-20 17:13

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[Y] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] Existing	[ ] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] No records	
[ ] Grade D: Fair		BPG Search:	[ ] Rejection
[ ] Grade E: Poor	[ ] Grade D: Rejected	[ ] Existing	[Y] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS

Comments for authors. This manuscript represents an interesting and exhaustive review on HBV reactivation in patients receiving different treatments used for rheumatic diseases. Overall, the paper reads well and is well presented. There is no major problem with the manuscript, yet, the authors may consider improving it and several comments are made below. Some of these comments should certainly be taken into consideration before acceptance for publication. To be useful to clinicians, such manuscript should propose a very pragmatic final point of view; because many reactivations could be avoided an important educational effort should be promoted. Comments ? Although many drugs have been considered, I was surprised not to read anything on Ofatumumab that has also been associated with HBV reactivation. There is also a warning of several administrations (FDA, EMA…) regarding this issue. Please, make sure that no molecules have been left over in your large review. ? The organization of the manuscript could be improved. Indeed, all the paragraphs on HBV infection generalities are quite long and sometimes unnecessary. The authors should consider shortening the paragraph on natural history. ? I am doubtful regarding the paragraph on HBV vaccination. Is it relevant to the topic in this manuscript? I fully agree that the recommendation should be to vaccine any non-immunized patient before administration of DMARDs but any other aspect on HBV vaccination is certainly out of topic. ? Several inconsistencies were found in the manuscript: 1) I have a real concern regarding OBI! Please make sure that you follow the same entity for OBI

throughout the manuscript. OBI should be clearly defined on the first occurrence (page 2). Then, your definition comes on page 3 (detectable liver HBV-DNA with serum HBV-DNA<200 IU/ml in HBsAg-/anti-HBc+ individuals). First, on a common basis in clinical practice, who looks for HBV-DNA in the liver??? So, OBI cannot be defined by presence of HBV-DNA in the liver because nobody looks for it! Later in your text, you present OBI as detection of circulating DNA without detectable HBsAg; this is clearly contradictory to your definition (page 2). So, on a common basis, I agree that OBI may be defined by presence of circulating DNA without HBsAg (a profile very, very exceptional and usuall without any liver disease). Anyway, it is very important to remain very precise and consistent throughout the manuscript. Since your message should be clear to non-hepatologist, I usually propose to keep very simple clinical entities: "past HBV infection" is defined by presence of anti-HBc without HBsAg, while "OBI" is a past HBV infection with circulating DNA. You may obviously not agree with this concept. Make sure all these entities are defined at their first occurrence in the text. 2) Please try to always use the same abbreviation throughout the manuscript. ALT is sometimes used and should be preferred to "AT"; ALT is commonly and used worldwide. ? The recommendations given do not convey a clear message for non-hepatologist clinicians. I believe the purpose of such manuscript is to educate clinicians and to provide a clear message. I find the recommendations to fuzzy and a clear scheme may be helpful to simplify the message. I would also recommend clearly separating the case of HBsAg positive patients from HBsAg negative patients. In Europe, most (not all) HBsAg positive patients are well identified and care is taken for them. By contrast, anti-HBc positive (HBsAg negative) patients are completely ignored and those are one that are the most at risk. Mixing them together is certainly not a good idea; while HBsAg + patients need to be treated with analogues before bDMARD, HBsAg- patients could just be treated when bDMARD is initiated or even later when the immuno-suppression is maximal. ? Page 10: the threshold of 100 IU/L for anti-HBs is not common and certainly not well defined. Are there any studies showing difference