

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 4173

Title: Risk factors for the development of hepatocellular carcinoma in patients with drug-resistant chronic hepatitis B

Reviewer code: 02462197

Science editor: Wen, Ling-Ling

Date sent for review: 2013-06-20 09:58

Date reviewed: 2013-06-28 03:41

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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 polishing	<input type="checkbox"/> Existed	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

ESPS Manuscript NO: 4173 Title: Risk factors for the development of hepatocellular carcinoma in patients with drug-resistant chronic hepatitis B This is a large (n=432) monocentre study aimed to evaluate the relationship between drug-resistant HBV chronic infection and the development of hepatocellular carcinoma (HCC). **SPECIFIC COMMENTS** (1) Title: the title appears to be appropriated; (2) Abstract: it needs a reevaluation for the English style. Moreover, AFP and CRP must be explained the first time they are reported in the abstract text. (3) Introduction: the meaning of LAM is explained after the first time it is reported in the text. ETV is not explained in the text. (4) Material and methods: - Authors reported that the great majority of the investigated patients was composed by genotype C HBV cases. However, I think it could be more scientifically valid to report the effective percentages of the different genotypes. - AFP is explained in two different parts of the text. - statistical analysis section is not completely clear: for non-parametric data, Student's t-test is not correct to be used, so in these cases (easily detectable using the Kolmogorov-Smirnov test), it is better to use Mann-Whitney test. Please report it in this section and recalculate the p-value when it is opportune. Authors say that they used a logistic regression analysis with the intent to evaluate the development of HCC and other variables (?): I did not found any use of this statistical test in the text. Afterwards, Authors report the use of a multivariate analysis using the Cox proportional hazards model. Probably, Authors need to select one of these tests (possibly the time-dependent Cox regression model), using a stepwise approach with the intent to minimize the variables inserted in the model. Tests for the risk of multicollinearity must be reported. Kaplan-Meier test is correctly used with the intent to analyze survivals, and the log rank test with the intent to compare them. (5) Results:

CRP is not explained the first time it is reported in the text; (6) Discussion: clearly reported; (7) References: the references are relevant; (8) Table 1: - it is better to use the term “gender” respect to “sex”; - the percentage of male and female patients is not reported; - several variables clearly showing a non-parametric distribution (AST, ALT, AFP) are represented as means \pm SD, despite in the statistical analysis section it is reported that in these cases it is better to report the median value + ranges. Please report these values as medians + ranges or IQR, clearly underlying the variables with non-parametric distribution. In these cases, Student’s t-test is not correct to be used, so the Authors need to recalculate the p-value with adequate statistical tests (U Mann-Whitney test). (9) Table 2: - the upper 95%CI of presence of rtM204I mutants is identical to its HR: please recalculate it. (10) Table 3: - it is better to use the term “gender” respect to “sex”; - the percentage of male and female patients is not reported; - the percentage of UICC groups is not reported; - several variables clearly show a non-parametric distribution (AST, ALT, AFP, CRP, duration of ant-virtual tx): please report median value + ranges and recalculate p-values using the U Mann-Whitney test. (11) Table 4: - it must be updated adopting the same statements used for the table 3. (12) the paper needs to be reevaluated by an English native speaker.

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Title: Risk factors for the development of hepatocellular carcinoma in patients with drug-resistant chronic hepatitis B

Reviewer code: 02451447

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
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<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

The authors reported the risk factors for the development of hepatocellular carcinoma (HCC) in patients with drug-resistant chronic hepatitis B and found cirrhosis, age (>50yrs), HBeAg+, virologic-non-responder status and rtM204I mutants are independent risk factors for developing HCC. Comments: 1. There are many English grammar errors, please correct them and I would suggest find a native-English speaker who knows medicine to read through. 2. Many abbreviations showed up in the text for the first time without giving full-names. Several abbreviations in the text never showed full name even not showing in the abbreviation list. 3. This study involves many statistics. I would suggest the authors to find a statistician to help with the statistics and make sure they correctly used. 4. The authors mentioned majority of the patients are genotype C, do the authors see difference between type C and other types? 5. There are different types of mutants which are associated with different anti-viral drugs, such as LMV, ETV or ADV. What kind of anti-viral drug used in this study? 6. The authors found the R group HCCs with lower CRP, lower AFP and lower stage. Do the authors have any explanation why these HCC patients with lower CRP or AFP? How many HCC patients with liver biopsy? Any difference of HCC differentiation (tumor grade) the authors observed? Any difference of background liver histopathology? More inflamed? 7. The authors only briefly mentioned the relationship between CRP and poor prognosis of HCC. Any explanation for that? Who produced CRP? Background hepatocytes versus HCC cells versus inflammatory cells? It is suggested the authors give some explanation in the discussion. 8. I don't see clear evidence to predict HCC arising from drug-resistant group have a poorer survival. Can the authors explain more in detail in the discussion?