

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 15818

Title: Evaluation of antiangiogenic efficacy in advanced hepatocellular carcinoma: Biomarkers and functional imaging

Reviewer's code: 02861134

Reviewer's country: Bulgaria

Science editor: Xue-Mei Gong

Date sent for review: 2014-12-10 16:46

Date reviewed: 2014-12-18 14:34

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" 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 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

The paper is well organized. In my opinion, the paper is publishable with no significant revision.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 15818

Title: Evaluation of antiangiogenic efficacy in advanced hepatocellular carcinoma: Biomarkers and functional imaging

Reviewer's code: 02991769

Reviewer's country: China

Science editor: Xue-Mei Gong

Date sent for review: 2014-12-10 16:46

Date reviewed: 2015-01-26 14:50

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	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"/> 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 type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

MB et al submit an extensive review outlining several prognosis/predictive functionally biological and imaging biomarkers in hepatocellular carcinoma. Potentially these biomarkers could be more successful for monitoring treatment activity, detecting early resistance of treatment and identifying patients who will more likely benefit from treatment ideally before its initiation. The matter is such useful and interesting, however the paper suffers for some limits: 1 The overall quality of the English language remains poor, including some grammatical errors, spelling mistakes and so on. 2 Introduction needs to be rewritten. The general impression is that the introduction section, especially about sorafenib, is unnecessarily lengthy. There is too much unnecessary information, while some important terms and information are left unexplained. 3. P7 line 5-7, "Otherwise, the absence of dermatological adverse effects could not be interpreted as treatment inefficacy since no untreated control arm was evaluated in this study", maybe the authors should provide some evidences to prove this, such as citing some ones that are most relevant and representative. 4 P9 line5-7 "However, in addition to radiological assessment, early reduction of AFP levels following sorafenib treatment

could be helpful to detect patients who could benefit or not from antiangiogenic treatment and to propose better tailor-made strategy management.” The authors need to clearly describe in the text, by providing better visualization of the data. And moving it to the next part “Imaging features and functional imaging” could be better. 5. “Prognosis and predictive value of tissue biomarkers evaluated in hepatocellular carcinoma”. The reviewer thinks this section is unnecessary. One limits is the difficulty to perform in clinical practice, because of its time-consuming and complicated, so the feasibility is very poor. 6 The part about “Which response criteria to apply?” is too long to describe and something should be deleted. This review aims to give a description of biomarkers instead of which criteria is better to evaluate the sorafenib or other antiangiogenic agents for advanced HCC. 7. Description style material about the functional imaging requires structured tables & figures for better presentations, just like clinical biomarkers and circulating biomarkers above.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 15818

Title: Evaluation of antiangiogenic efficacy in advanced hepatocellular carcinoma: Biomarkers and functional imaging

Reviewer's code: 02998194

Reviewer's country: Greece

Science editor: Xue-Mei Gong

Date sent for review: 2014-12-10 16:46

Date reviewed: 2015-02-02 06:34

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" 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 type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input checked="" 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

Dear authors, This is a review in depth from scientists that they know the field very well. There are some issues that need to be managed as follows: **INTRODUCTION** Highlight how common and deadly is HCC (the fifth most common cancer and the second leading cause of cancer-related deaths worldwide, in each year, there are around 750,000 new cases of liver cancer and around 700,000 deaths) Define RECIST criteria Language polishing **BIOMARKERS** Language polishing At the beginning of page 6 repetition of the aims Too long introduction Is it correct to consider imaging as a biomarker? **CLINICAL BIOMARKERS** (cutaneous adverse-events) The ideal biomarker needs also not to be detected in premalignant diseases (eg cirrhosis) Language polishing Explain BCLC staging Too long with no clear conclusions **CIRCULATING BIOMARKERS ALPHA-FETOPROTEIN (AFP)** Highlight that is the only biomarker marker that passed all the five phases of biomarker development It is better to refer to the phases biomarker development and classify the biomarkers accordingly (Pepe M S, Etzioni R, Feng Z, et al. J Natl Cancer Inst, 2001, 93: 1054-1061) Explain the SHARP study as it is mentioned many times in the text **VASCULAR ENDOTHELIAL GROWTH FACTORS (VEGF)**



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Too long TISSUE BIOMARKERS Language polishing IMAGING FEATURES AND FUNCTIONAL IMAGING Language polishing Define mRECIST criteria EPILOGUE (better use conclusion) Which biomarker can be used in clinical practice (clear message) and there is no single ideal biomarker. As a result a combination of efficient biomarkers may be a future solution You can also comment on the following biomarkers: An isoform of AFP, named LENS CULINARIS AGGLUTININ REACTIVE FRACTION OF AFP (AFP-L3) associated with poor survival rate and high chance of tumor recurrence GLYPICAN-3 (GPC3) is a member of the glypican family of cell-surface heparin sulfate proteoglycans. Patients with GPC3 expression in tumors have a lower 5-year survival rate than those with no expression DES-GAMMA CARBOXY-PROTHROMBIN (DCP) is associated with advanced HCC OSTEOPONTIN (OPN) is a highly phosphorylated and glycosylated protein. It relates with metastasis and poor prognosis FIBROBLAST GROWTH FACTORS 3 AND 4 (FGF3/FGF4) can predict response to sorafenib C-MET expression relates to prognosis miRNA relates to prognosis EpCAM-positive circulating tumor cells are associated with advanced HCC CYTOKERATIN 10 AND CYTOKERATIN 19 predict the potential of metastatic HCC.