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ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 9601

Title: Indicators of the efficacy of sorafenib in patients with advanced hepatocellular carcinoma

Reviewer code: 02860818

Science editor: Qi, Yuan

Date sent for review: 2014-02-20 15:44

Date reviewed: 2014-03-02 18:48

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

COMMENTS TO AUTHORS

A good article, maybe some words about etiology of HCC should be inserted at the appropriate paragraph. Have you checked if etiology has any influence on the outcome (OS and TTP) of the sorafenib treatment?

ESPS Peer-review Report**Name of Journal:** World Journal of Gastroenterology**ESPS Manuscript NO:** 9601**Title:** Indicators of the efficacy of sorafenib in patients with advanced hepatocellular carcinoma**Reviewer code:** 00742216**Science editor:** Qi, Yuan**Date sent for review:** 2014-02-20 15:44**Date reviewed:** 2014-03-08 13:32

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)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

In this paper, the authors examined the relationship between clinical factors and the sorafenib efficacy in HCC patients. Forty-six out of 80 patients in their faculty were enrolled in the study, and evaluated the relationship between clinical parameters and overall survival (OS) and time to progression (TTP). From the data, they proposed that the presence of extracellular tumor lesions and hand-foot syndrome (HFS) might be useful indicators of the favorable outcome. To date, it has been well-known that sorafenib is an only oral agent proven to extend the survival of unresectable HCCs, but its effect for tumor shrinkage is limited. For developing more safe and efficient sorafenib-based therapy, the author's idea to evaluate the clinical parameters predicting the drug efficacy is of interest. Overall, the paper is well-written and well-constructed. However, the clinical parameters shown here is not fully satisfactory and the discussion is still insufficient. To convince the readers of the journal, the authors should add several data such as tumor size & stage. Major point: I. Clinical parameters presented here is still insufficient, and the significance of the tumor size and tumor stage on TTP/OS should be examined. II. From the data, the authors suggest that extra-hepatic major HCC is a "favorable (not poor prognostic)" indicator of the patients. This is significantly interesting, but peculiar to some extents. i) Please indicate a Table, and show the comparative analysis of the clinical parameters (age, tumor size of the intrahepatic tumors, tumor stage, and background liver cirrhosis, sorafenib dosage) in the patient groups with and without extra-hepatic lesion. I am afraid that there are any other reasons for the improved drug efficacy in the group with extra-hepatic lesions. Minor point: i) In their hospital, 80 patients received sorafenib, and 46 were examined in the study. The authors should explain why they only selected around half of the patients for the analysis. ii) The



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definition of "major extra- and intra-hepatic HCC" is vague. iii) Discussion: It has been already reported that the patients with Child-Pugh A group represent favorable outcome after the sorafenib treatment (e.g., PMID 19247201, 22875650, 23715941). The authors should cite these relevant papers and discuss the significance of the stage of liver cirrhosis on the drug efficacy. iv) Discussion: They surmised that extra-hepatic metastasis requires greater angiogenic activity, and might be a main reason for the improved sorafenib efficacy. I am afraid this description is not supported by the evidence. Please show more substantial reasons by citing previous reports. Or, if possible, please cite relevant papers which have already reported that the presence of extra-hepatic HCC is a good prognostic parameter of the sorafenib treatment.