

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 13540

Title: Current systemic treatment of hepatocellular carcinoma: A review of the literature

Reviewer's code: 02861019

Reviewer's country: Italy

Science editor: Yue-Li Tian

Date sent for review: 2014-08-27 14:26

Date reviewed: 2014-09-15 21:29

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 checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" 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 checked="" 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

Dear Editor, I have read with great interest the enclosed manuscript entitled "Current systemic treatment of hepatocellular carcinoma: A review of the literature" in which the authors reviewed all available treatment for advanced hepatocellular carcinoma (HCC). The manuscript is well written and completely describes all the fields of HCC treatments in BCLC stage B and C patients. However, I suggest some minor changes in manuscript: - In the abstract, the authors speak about "symptomatic" treatment; I suggest to better describe those strategy or to use the accurate terminology (i.e. "best supportive care") that are not only "symptomatic" treatments; - In the abstract, the sentence "For example, the patients with BCLC stage 0 (very early stage) and stage A (early stage) HCC, the curable treatment modalities including resection, transplantation, radiofrequency ablation are taken into consideration" is not clear. - The introduction comprises some unclear chapters; first, the authors cited the influence of HBV on the incidence of HCC, but they not gave any "conclusion" on the influence of viral factors or alcohol. The authors briefly describe the BCLC algorithm but, if the reader do not know that algorithm, the results is confounding. Treatment strategies have to be described: why systemic therapy are indicated only for stage B patients? - The Chapter "systemic



BAISHIDENG PUBLISHING GROUP INC

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

<http://www.wjgnet.com>

cytotoxic chemotherapy" is clear; - In order to clarify and simplify available and ongoing data, I suggest to include all the trial conducted in this setting in a Table.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 13540

Title: Current systemic treatment of hepatocellular carcinoma: A review of the literature

Reviewer's code: 02860712

Reviewer's country: Italy

Science editor: Yue-Li Tian

Date sent for review: 2014-08-27 14:26

Date reviewed: 2014-09-02 01:58

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 checked="" type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	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

ABSTRACT. The content of the abstract is inappropriate in regard to the declared aim of the review ("to summarize the historical perspectives and the current developments of systemic therapies of advanced HCC")

INTRODUCTION. The first sentence is awkward. I would omit the sentences on epidemiology SYSTEMIC CYTOTOXIC THERAPY . The mechanisms of resistance to conventional chemotherapy are not described. The most significant results (PIAF, modified PIAF, GEMOX) are not properly reported. PAGE 9 ref 29. It should be stressed that the combined treatment of sorafenib and doxorubicin was undertaken before the conclusion of the SHARP study, and was interrupted after the interim analysis, when the results of the SHARP study were published. MECHANISMS OF RESISTANCE TO SORAFENIB represent a major issue in the current clinical research on advanced HCC and deserve a more detailed description. In regard to SUNITINIB, LIFINAFIB AND BRIVANIB it should be discussed why the expectations of phase II studies were not fulfilled in the subsequent phase III. NEW DIRECTIONSThe Authors report several interesting observations. However, it is unclear whether these hypotheses led to new clinical studies. TAMOXIFEN, MEGESTROL,



BAISHIDENG PUBLISHING GROUP INC

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

<http://www.wjgnet.com>

OCTREOTIDE. I would omit this section, which has only a historical value. IMMUNOTHERAPY The Authors did not report the study on CTL4 blockade with tremelimumab (Sangro et al Journal of Hepatology 2013), which, to my knowledge, is the most significant clinical experience in this field. The readability of this work should be improved using tables. In addition, I should distinguish more clearly II phase and III phase trials (which have a weight in decision making), and insights of basic oncology not yet supported by clinical trials. The language is poor. By the end of the day, which therapy would the Authors advise in patients who progress during sorafenib treatment?

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 13540

Title: Current systemic treatment of hepatocellular carcinoma: A review of the literature

Reviewer's code: 00069262

Reviewer's country: Mexico

Science editor: Yue-Li Tian

Date sent for review: 2014-08-27 14:26

Date reviewed: 2014-09-07 12:04

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 checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" 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 checked="" 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 work is of good quality, distributed and updated. I suggest adding tables and figures where information is concentrated.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 13540

Title: Current systemic treatment of hepatocellular carcinoma: A review of the literature

Reviewer's code: 02860797

Reviewer's country: China

Science editor: Yue-Li Tian

Date sent for review: 2014-08-27 14:26

Date reviewed: 2014-08-28 11:57

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"/> 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		[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

This manuscript entitled "Current systemic treatment of hepatocellular carcinoma: A review of the literature" is well written. It contains all systematic treatment of HCC. I suggest the paper be accepted with minor revision. My minor concerns are as follow: 1) Please consider to put the introduction of mechanisms of sorafenib in front of sorafenib clinical trials. 2) The author mentioned PD-1/PD-L1 pathway, although this has not been tested in human HCC patients. Why not mention CTLA-4 or other systematic immune therapy? 3) Some abbreviations such as CLIP-1, should be explained.