



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 40524

Title: Ten years of sorafenib in hepatocellular carcinoma: Are there any predictive and/or prognostic markers?

Reviewer's code: 03656580

Reviewer's country: China

Science editor: Ze-Mao Gong

Date sent for review: 2018-07-03

Date reviewed: 2018-07-03

Review time: 3 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good		<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	(General priority)	Peer-reviewer's expertise on the topic of the manuscript:
<input type="checkbox"/> Grade E: Do not publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Minor revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> General
		<input type="checkbox"/> Rejection	<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Although a few markers associated with HCC prognosis have been reviewed, authors should find to more biomarkers to predict its efficacy in patients with advanced HCC.



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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 40524

Title: Ten years of sorafenib in hepatocellular carcinoma: Are there any predictive and/or prognostic markers?

Reviewer's code: 00503849

Reviewer's country: Taiwan

Science editor: Ze-Mao Gong

Date sent for review: 2018-07-03

Date reviewed: 2018-07-06

Review time: 3 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	(General priority)	Peer-reviewer's expertise on the topic of the manuscript:
<input type="checkbox"/> Grade E: Do not publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Minor revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Major revision	<input type="checkbox"/> General
		<input type="checkbox"/> Rejection	<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This manuscript summarized the research results in recent 10 years for the possibility to find the potential factor(s) or marker(s) to predict the treatment response of sorafenib in advanced unresectable hepatocellular carcinoma (HCC). Although the conclusion is still



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no validated prognostic or predictive factor or marker, the contents of the manuscript may provide a whole view of sorafenib in HCC treatment. I recommend publishing this manuscript. Minor comment: 1. All abbreviations should be spelled in full in their first appearances and be applied consistently in whole text. (e.g. PFS should be spelled in full in its first appearance in page 7 rather than in page 8. The hand-foot skin reaction (HFSR) was spelled as HSFR in page 7. It is not necessary to describe “hand-foot skin reaction (HFSR)” again in page 8.) 2. The authors need to make sure the following sentences are correct. a. They showed, in a small series of patients treated with sorafenib, that patients with > grade 2 of HSFR had a significantly higher disease control rate with respect to patients without HSFR or HSFR. (page 7) b. Casadei Gardini et al. evaluated for the first time SII, NLR e platelet-lymphocyte ratio (PLR) in a small case series[40], observing that SII and NLR were independent prognostic factors for OS. (page 13)

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 40524

Title: Ten years of sorafenib in hepatocellular carcinoma: Are there any predictive and/or prognostic markers?

Reviewer’s code: 02445626

Reviewer’s country: China

Science editor: Ze-Mao Gong

Date sent for review: 2018-07-03

Date reviewed: 2018-07-16

Review time: 13 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good		<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
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		<input type="checkbox"/> Rejection	<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
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SPECIFIC COMMENTS TO AUTHORS

The article by Marisi G reviews the recent progress in biomarkers for sorafenib therapy in hepatocellular carcinoma. In general, the manuscript was well written. I have a few minor concerns. 1. FDA approved sorafenib for treating advanced unresectable



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hepatocellular carcinoma in 2007. The article has mentioned a couple of times that sorafenib was used for treating advanced HCC in 2008. Please clarify which year is correct. 2. Regarding adverse events of sorafenib treatment, a recently published meta-analysis review article can be cited (Hand-foot skin reaction is a beneficial indicator of sorafenib therapy for patients with hepatocellular carcinoma: a systemic review and meta-analysis. *Expert Rev Gastroenterol Hepatol.* 2017 Sep 3:1-8.). 3. Please modify Figure 1. It is well-known that sorafenib inhibits the Raf/MEK/ERK signaling pathway and tyrosine kinase receptors including VEGFR, PDGFR, Flt3 and c-Kit. However, from Figure 1, it seems that sorafenib inhibits the Raf/MEK/ERK signaling pathway through its inhibitory effects on VEGFR, PDGFR, Flt3 and c-Kit. 4. The manuscript reviews each biomarker based on single-factor analyses. It would be better by discussing multiple-factor analyses. Please see the reference: Novel biomarker-based model for the prediction of sorafenib response and overall survival in advanced hepatocellular carcinoma: a prospective cohort study. *BMC cancer*, 2018, 18(1): 307. 5. The manuscript could also be improved by including some markers based on medical imaging examinations. Such as: Advanced Hepatocellular Carcinoma: Pretreatment Contrast-enhanced CT Texture Parameters as Predictive Biomarkers of Survival in Patients Treated with Sorafenib. *Radiology*, 2018: 171320.

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