



**ESPS PEER REVIEW REPORT**

**Name of journal:** World Journal of Hepatology

**ESPS manuscript NO:** 11345

**Title:** Skin toxicity predicts efficacy to sorafenib in patients with advanced hepatocellular carcinoma

**Reviewer code:** 02861202

**Science editor:** Ling-Ling Wen

**Date sent for review:** 2014-05-18 23:24

**Date reviewed:** 2014-06-06 18:59

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<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	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

**COMMENTS TO AUTHORS**

This paper by Shomura et al. refers to skin toxicity as predictor of efficacy to Sorafenib in patients with advanced HCC. The paper is of interest since it gives important clues for better selection of patients who may benefit at best from treatment with Sorafenib. However it raises few issues that need to be addressed: 1. Aside from HFSR, it would be interesting to know whether patients experienced some other skin reaction that required dose reduction or treatment discontinuation. In our practice, we experience more and more skin reaction different from HFSR, that require dose reduction and almost invariably treatment withdrawal. Since we now routinely advise patients on the use of moisturizers, steroid ointments etc., we see very few cases of HFSR. Were skin reaction other than HFSR included in the analysis as well? If so, there was any difference in terms of predictor of treatment efficacy, according to the type of skin reaction? 2. The authors indicate the occurrence of genetic polymorphisms of VEGF and VEGFR2 as involved in the mechanism of HFSR. How would the authors comment on the possible mechanism of occurrence of skin reactions other than HFSR?



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## ESPS PEER REVIEW REPORT

**Name of journal:** World Journal of Hepatology

**ESPS manuscript NO:** 11345

**Title:** Skin toxicity predicts efficacy to sorafenib in patients with advanced hepatocellular carcinoma

**Reviewer code:** 00181532

**Science editor:** Ling-Ling Wen

**Date sent for review:** 2014-05-18 23:24

**Date reviewed:** 2014-06-20 04:31

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 checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<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 checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

### COMMENTS TO AUTHORS

In this study, the authors reported that significant skin toxicity(>grade 2), younger age (<70 years), and absence of hypoalbuminemia were associated with better overall survival. Significant skin toxicity and nursing intervention were associated with longer treatment duration. The study is limited by its small cohort size and retrospective nature. A few minor comments are provided that need to be addressed.



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## ESPS PEER REVIEW REPORT

**Name of journal:** World Journal of Hepatology

**ESPS manuscript NO:** 11345

**Title:** Skin toxicity predicts efficacy to sorafenib in patients with advanced hepatocellular carcinoma

**Reviewer code:** 02903968

**Science editor:** Ling-Ling Wen

**Date sent for review:** 2014-05-18 23:24

**Date reviewed:** 2014-06-25 23:55

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 checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input checked="" 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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

### COMMENTS TO AUTHORS

I suggest the author review that paper and provide more patients descriptions about whether the nursing treatment model can cope with AEs problem or not. 37 is the small sample data and make this article lack credibility.



**ESPS PEER REVIEW REPORT**

**Name of journal:** World Journal of Hepatology

**ESPS manuscript NO:** 11345

**Title:** Skin toxicity predicts efficacy to sorafenib in patients with advanced hepatocellular carcinoma

**Reviewer code:** 02526284

**Science editor:** Ling-Ling Wen

**Date sent for review:** 2014-05-18 23:24

**Date reviewed:** 2014-06-26 10:19

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 checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<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 checked="" type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

**COMMENTS TO AUTHORS**

This study by Masako Shomura, et al. evaluated study the relationship between adverse events, efficacy, and nursing intervention for sorafenib therapy in patients with hepatocellular carcinoma. Although the authors concluded that skin toxicity was associated with favorable outcomes with sorafenib therapy for advanced HCC and that nursing intervention contributed to better adherence, which may improve the efficacy of sorafenib. However, the sample size of this study seems extremely small to draw any conclusion. In addition, the selection criteria for sorafenib administration seem unclear. What kinds of treatment did other patients with similar HCC stage receive during 3 years? All HCCs had enhancement? If some HCCs did not show enhancement on dynamic imaging, how could be used mRECIST for response evaluation?