

## ESPS Peer-review Report

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

**Ms:** 3235

**Title:** Comparative Effectiveness of Traditional Chemoembolization (TACE) Alone Versus TACE with Sorafenib for the Treatment of Unresectable Hepatocellular Carcinoma

**Reviewer code:** 00038004

**Science editor:** s.x.gou@wjgnet.com

**Date sent for review:** 2013-04-16 10:36

**Date reviewed:** 2013-04-18 18:21

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

## COMMENTS

### COMMENTS TO AUTHORS:

The authors retrospectively compared the overall survival and progression-free survival between patients treated with TACE alone and those with TACE and sorafenib, and they could not demonstrate superiority of combination therapy. They also found that CTP classification and BCLC staging were the significant predictors of survival. There are few studies investigating the impact of TACE plus sorafenib combination for unresectable HCC. In this context, this paper is interesting and informative, although the study including small number of patients was retrospectively performed. The baseline characteristics is significantly different in BCLC staging; all of the 5 patients with BCLC-C belonged to the combination therapy group. BCLC staging was a significant predictor of survival. Inclusion of more advanced patients in the combination therapy group might have affected the outcome, leading to the wrong conclusion. Therefore, the authors should re-analyze data after excluding BCLC-C patients and confirm that their conclusion is the same.

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**Ms:** 3235

**Title:** Comparative Effectiveness of Traditional Chemoembolization (TACE) Alone Versus TACE with Sorafenib for the Treatment of Unresectable Hepatocellular Carcinoma

**Reviewer code:** 00011221

**Science editor:** s.x.gou@wjgnet.com

**Date sent for review:** 2013-04-16 10:36

**Date reviewed:** 2013-04-23 18:31

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 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

### CONFIDENTIAL COMMENTS TO EDITOR:

No conflict

### COMMENTS TO AUTHORS:

Muhammed et al. present a retrospective comparison of outcomes of HCC patients treated either with TACE or TACE + sorafenib. While the manuscript has some merit, the methodological limitations of the study preclude the authors from making some of the interpretations that they make. First, there is no description of what factors led to the assignment of patients to combination therapy versus TACE alone. Since this was not a randomized controlled trial, patient assignment is subject to large potential biases that could explain all of the "trend" towards a mortality benefit seen. Second, there was no "trend" towards a survival benefit from combined therapy despite the authors claim. The differences were not statistically different, and not even close to significant at that, and thus any claims of superiority should be removed. All of the "benefit" occurred early looking at survival curves suggesting patient selection bias more likely explains the differences. Third, at least one (perhaps more) of the TACE only arms had a patient with an AFP > 6000. This suggests understaging of at least one BCLC C patient (AFP > 1000 indicates vascular invasion, possibly not detected by the imaging modality chosen utilized by the authors). If one excludes patients with AFP > 800 or 1000, are there any "trends" differences in survival? The authors can rightfully state that TACE plus sorafenib is safe. A case-control approach in which each case (TACE+sorafenib) is matched to 2 controls (by CTP, TNM, ECOG PS, AFP, age) would be a stronger methodologic approach to deal with biases inherent in this retrospective approach.

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**Ms:** 3235

**Title:** Comparative Effectiveness of Traditional Chemoembolization (TACE) Alone Versus TACE with Sorafenib for the Treatment of Unresectable Hepatocellular Carcinoma

**Reviewer code:** 00071102

**Science editor:** s.x.gou@wjgnet.com

**Date sent for review:** 2013-04-16 10:36

**Date reviewed:** 2013-05-01 10:45

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"/> 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 checked="" type="checkbox"/> Rejection
<input checked="" 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

### CONFIDENTIAL COMMENTS TO EDITOR:

There are some methodological problems in this paper. Title suggests a comparative study of 2 therapies for unresectable HCC, but the groups can not be compared. They are different in terms of tumor burden and author do not explain reasons to add sorafenib in one group. The lack of this information compromises discussion and conclusion of this study. I have doubts about the type of this study (RCT, case-control?? I don't think so. Case series??). I do recommend this paper to WJH.

### COMMENTS TO AUTHORS:

Title suggests a comparative study of 2 therapies for unresectable HCC, but the groups can not be compared. They are different in terms of tumor burden (BCLC). I suggest a better explanation about therapy selection in each group. It also be interesting if the author could include in methods why sorafenib was added to TACE.

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**Ms:** 3235

**Title:** Comparative Effectiveness of Traditional Chemoembolization (TACE) Alone Versus TACE with Sorafenib for the Treatment of Unresectable Hepatocellular Carcinoma

**Reviewer code:** 00160603

**Science editor:** s.x.gou@wjgnet.com

**Date sent for review:** 2013-04-16 10:36

**Date reviewed:** 2013-05-03 23:28

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
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## COMMENTS

### CONFIDENTIAL COMMENTS TO EDITOR:

The sample size was too small. There was a bias possibility since this was not a randomized trial.

### COMMENTS TO AUTHORS:

The sample size was too small. There was still bias possibility since this was not a randomized trial. The severe cases were found more in TACE only group (Hep C and Hep C + Alcohol). The histology also seemed more severe at TACE only group. How do you explain that? There are many incorrect grammar.