

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 32686

Title: The efficacy of tolvaptan for the patients with advanced hepatocellular carcinoma

Reviewer's code: 03536637

Reviewer's country: Japan

Science editor: Yuan Qi

Date sent for review: 2017-01-19 14:09

Date reviewed: 2017-01-21 21:23

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	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"/> 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 type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input checked="" type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This paper presented about the effect of tolvaptan in liver cirrhosis. This topic could be interesting for readers of World Journal of Hepatology. However, there are some missing information and several problems with this cohort study. 1. Authors concluded that tolvaptan was unable to decrease body weight in liver cirrhosis patients with HCC due to portal vein hypertension. Please show us any data or papers about portal vein hypertension in patients with HCC. In clinical situation, I cannot agree that advanced HCC increases portal pressure so much. 2. Table 1 shows that stepwise multiple regression analysis to predict the decreased BW%. I would like to know the predictive factors for effect of tolvaptan. Could you show us the univariate analysis including patients and HCC characters? Are the portal vein thrombus and HCC staging the predictive factors? 3. Table 2 shows that HCC patients decreased BW smaller than non-HCC patients. The authors need to show the information about baseline data including body weight and approximate volume of ascites. Percentage of body weight decrease does not mean the effect of tolvaptan itself.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 32686

Title: The efficacy of tolvaptan for the patients with advanced hepatocellular carcinoma

Reviewer's code: 03670299

Reviewer's country: Italy

Science editor: Yuan Qi

Date sent for review: 2017-01-19 14:09

Date reviewed: 2017-01-30 22:36

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	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"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
		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

The aim of this manuscript resumed as “an evaluation of the efficacy of tolvaptan treatment in ascites pathology in patients with advanced carcinoma” is very interesting in the conceptual idea. This consideration is further confirmed by scarce literature data regarding analogues treatment in patients with ascites pathology aggravated by advanced carcinoma although, a paper by Suzuki et al. (Hepatology Research 2015; 45: E161-E162), recently published report analogous study objective in only 9 patients. This lack in bibliography is evident in this part of bibliography where more other references have to be reported. This premise is important to clarify that the introduction must be rewrite completely by adding also references and by explaining in a clearly way the purpose of this manuscript. Moreover, some sentences in the paragraph are not completely true. ES. The text reports “The renin-angiotensin-aldosterone (RAA) system, another hormonal regulator of hepatic ascites, is thought to be one of the main causes of hepatic ascites” must be inserted in a more wide concept. In fact, a paper (Hernandez-Guerra M, Garcia-Pagan JC, Bosch J. Increased hepatic resistance: a new target in the pharmacologic therapy of portal hypertension. J Clin Gastroenterol 2005) cited in another very interesting paper (A. KASHANI, C. LANDAVERDE, V. MEDICI and L. ROSSARO,

Fluid retention in cirrhosis: pathophysiology and management, *Q J Med* 2008; 101:71–85) reported a specific concept on ascites pathophysiology by using this interesting sentence “consequence of distortion of hepatic architecture and increased hepatic vascular tone”. A question regarding the dose of 15 mg TLV (probably too high dose). In numerous studies (7 or 15 days treatment) the maximal dose used is 7 mg. In addition, regarding the results, the used figures should be modified a little. Es. Figure 1 could be improved by adding the significative effect of daily treatment with Tolvaptan by using Friedman test with multiple comparison. Furthermore, Figure 2 could be transformed or added in a table with results more significative. In addition, table 2 should be reported first of all other data. Also the conclusion should be modified and rewritten by adding more literature on the field. Here, some papers reported the relation between cirrhosis and hyponatremia as well as predictive treatment effect of tolvaptan. 1. Gaglio P1, Marfo K, Chiodo J 3rd. Hyponatremia in cirrhosis and end-stage liver disease: treatment with the vasopressin V₂-receptor antagonist tolvaptan. *Dig Dis Sci*. 2012 Nov;57(11):2774-85. doi: 10.1007/s10620-012-2276-3. Epub 2012 Jun 26. 2. Yoshitaka Takuma, Hirokazu Miyatake, Shota Iwadou, Shuji Uematsu, Ryouichi Okamoto, Yasuyuki Araki. Predictive factors for the effectiveness of tolvaptan in liver cirrhosis patients with refractory ascites. *Kanzo* Vol. 57 (2016) No. 12 p. 684-687. 3. Ji-Dong Jia , Wen Xie , Hui-Guo Ding , Hua Mao , Yonggang Li , Xiaojin Wang , Jie-Fei Wang , Wei Lu , Cheng-Zhong Li , Yimin Mao , Gui-Qiang Wang , Yue-Qiu Gao , Bangmao Wang , Qin Zhang , Yan Ge , Vincent Wai-Sun Wong. Utility and Safety of Tolvaptan in Cirrhotic Patients With Hyponatremia: A Prospective Cohort Study. *Ann Hepatol* 16 (1), 123-132. 1 2017 2017 Jan-Feb 2017. The manuscript could be accepted only after a major revision

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 32686

Title: The efficacy of tolvaptan for the patients with advanced hepatocellular carcinoma

Reviewer's code: 03647890

Reviewer's country: China

Science editor: Yuan Qi

Date sent for review: 2017-01-19 14:09

Date reviewed: 2017-02-07 11:11

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	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"/> The same title	<input type="checkbox"/> High priority for publication
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<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
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		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

Doctor Miyazaki and his colleagues investigated the efficacy of tolvaptan for the patients with advanced HCC. This study is very important in rational use of and development of a novel therapeutic application. Method of data analysis and writing are good in the manuscript. I think this manuscript is suitable to be published in WJG.