



# BAISHIDENG PUBLISHING GROUP INC

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## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 12684

**Title:** Incidence, risk factors and outcome of de novo tumors in liver transplant recipients focusing on alcoholic cirrhosis

**Reviewer's code:** 00504591

**Reviewer's country:** Japan

**Science editor:** Ling-Ling Wen

**Date sent for review:** 2014-07-28 22:04

**Date reviewed:** 2014-07-31 11:44

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 type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" 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

The manuscript entitled, "Incidence, risk factors and outcome of de novo tumors in liver transplant recipients for alcoholic cirrhosis" by Jimenez C et al., performed literature review regarding the de novo malignancies developing in liver transplant recipients with a special reference to alcoholic liver disease as an initial indication for liver transplantation. This review article encompassed the de novo tumors in liver transplant recipients in a constructive fashion. I have some comments. Comments 1. First of all, the text includes many grammatical and spelling errors. Please do English proof-reading before re-submitting the article. 2. The majority of descriptions in the manuscript is associated with the overall de novo tumors after liver transplantation, not specified to those with alcoholic liver disease. I recommend authors to reconsider the title, adding like "focusing on alcoholic cirrhosis". 3. Please make a table summarizing the incidence of each tumor. The table may be preferable to include the incidence of the overall transplant recipients and that of those with alcoholic cirrhosis, separately.



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

**ESPS manuscript NO:** 12684

**Title:** Incidence, risk factors and outcome of de novo tumors in liver transplant recipients focusing on alcoholic cirrhosis

**Reviewer's code:** 00005191

**Reviewer's country:** United States

**Science editor:** Ling-Ling Wen

**Date sent for review:** 2014-07-28 22:04

**Date reviewed:** 2014-08-01 19:48

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 checked="" 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 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 manuscript aims at analyzing the incidence, risk factors, location, and characteristics of de novo tumors in patients with alcoholic cirrhosis (AC) who underwent orthotopic liver transplantation (OLT). The manuscript also aims at evaluating the prognosis and survival after diagnosis of malignancies. The Authors state that liver transplant recipients who develop de novo non-skin tumors have a decreased long-term survival rate, and that this is more evident in patients who develop upper aerodigestive tract or lung tumors. In their conclusions, the Authors list a number of recommendations for AC recipients such as: smoking and alcohol consumption cessation, use of skin protection, avoidance of over-immunosuppression, prevention screenings, etc.. The paper bears an important - though not novel - message for all the clinicians involved in the pre- and post-OLT care of AC recipients. Therefore, it is worth publishing. However, it requires some polishing of the general structure, correction of few mistakes, and further research on some of the issues raised. It is essential for the Authors to insert a "Method" section in the manuscript, following the Abstract. IN such section they should describe how exactly they derived their data. In fact, within their discussion



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they mention several different series of patients, but an opening explanation of the method of observation and of their sources of data is necessary. The final paragraphs of the paper contain few minor mistakes that need correcting. Also, the issue of the risks related to immunosuppression requires further references to the field literature. Once fixed these important matters, the manuscript could be published.



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## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 12684

**Title:** Incidence, risk factors and outcome of de novo tumors in liver transplant recipients focusing on alcoholic cirrhosis

**Reviewer's code:** 00054275

**Reviewer's country:** Italy

**Science editor:** Ling-Ling Wen

**Date sent for review:** 2014-07-28 22:04

**Date reviewed:** 2014-08-09 20:45

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	PubMed Search:	<input 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
<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		<input checked="" 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 is a nice and complete review about the incidence, risk factors and outcome of de novo tumors in liver transplant recipients for alcoholic (but also for non alcoholic) cirrhosis. - As reported by the Authors is very important (but very difficult) to discriminate between the role of smoking and the role of alcohol (very often present together) as risk factors for de novo post LT tumors. Data about the risk of de novo tumors post LT in smokers with NON alcoholic cirrhosis should be reported to help to discriminate the different role of alcohol and smoking. - A table with a summary of different risk for every tumors (with reference) should be reported. - This is only a suggestion: in this review there are many data about incidence of tumors post LT also in non alcoholic cirrhosis: perhaps the title may be changed (instead of "...alcoholic..." "...alcoholic or not alcoholic...").



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

**ESPS manuscript NO:** 12684

**Title:** Incidence, risk factors and outcome of de novo tumors in liver transplant recipients focusing on alcoholic cirrhosis

**Reviewer's code:** 02530754

**Reviewer's country:** Spain

**Science editor:** Ling-Ling Wen

**Date sent for review:** 2014-07-28 22:04

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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
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		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

### COMMENTS TO AUTHORS

In the manuscript by Jiménez-Romero et al, the authors comprehensively reviewed the risk of malignancy in patients with alcoholic cirrhosis undergoing liver transplantation. The manuscript is informative and reads well. I feel that the main evidence is included and successfully discussed. I just have minor comments which can be read below:

- 1- In the section "incidence" the authors said that the overall incidence of de novo tumours after OLT ranges from 2.6% to 15.7%. This information, although relevant, is incomplete. These numbers, which may refer to prevalence rather than incidence, should be compared with the same percentages coming from age matched not transplanted population. I would recommend to add standardized incidence ratios (SIR) which may be found elsewhere, and have been recently summarized in Rodríguez-Perálvarez et al, Curr Opin Organ Transplant, 2014.
- 2- In the section "incidence" the authors wrote: "A significantly higher incidence has been observed in patients who underwent OLT for AC in comparison with other non-AC diseases", and they quoted 8 references. I would be helpful to the reader to have these studies summarized in a table.
- 3- Regarding the section "Immunosuppression", as the authors



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pointed out, the use of immunosuppressive drugs is the key to explain the increased risk of cancer found in the LT population. However the evidence is weak. There are no randomized controlled trials designed to evaluate the influence of different immunosuppression schedules and de novo malignancy after LT. The available evidence comes from observational studies in which there is an increased risk of bias. This should be emphasized in the manuscript. 4- Would the authors propose a pre-LT schedule to rule out pre-malignant conditions in the LT population, particularly for patients with alcoholic cirrhosis? 5- In the section "Survival after diagnosis of de novo tumours", first paragraph, there may be a typo: It should read "turn" instead of "turnor". 6- In the section: "immunosuppression changes..." the role of mTOR inhibitors to replace CNIs should be revised. Several randomized controlled trials have described an increased rejection rates when CNIs are withdrawn within the first year after LT even with the addition of mTOR inhibitors. The role of mTOR inhibitors may be to minimize CNI exposure early after liver transplantation, and only selected patients with a long standing LT without any evidence of rejection (histologically evaluated) should be considered for a true CNI withdrawal.