

ESPS JOURNAL EDITOR-IN-CHIEF'S REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 26423

Title: Supportive therapy for hepatocellular carcinoma: current status and prospects

Journal Editor-in-Chief (Associate Editor): Angelo Sangiovanni

Country: Italy

Editorial Director: Jin-Lei Wang

Date sent for review: 2016-06-20 08:18

Date reviewed: 2016-06-22 20:21

ACADEMIC CONTENT EVALUATION	LANGUAGE QUALITY EVALUATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<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"/> Revision
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor		

JOURNAL EDITOR-IN-CHIEF (ASSOCIATE EDITOR) COMMENTS TO AUTHORS

The paper was revised by two reviewers and modified accordingly to their suggestions. However, before acceptance, I suggest some additional changes. 1) please modify the title, to clarify that the article refers to prevention of "recurrence", and preservation of liver function "after HCC treatment". 2) Overall, the Authors provide data on positive trials supporting the policy adopted to prevent recurrence and liver function deterioration. However, there is no a clear agreement on these policies. I suggest to underline this fact, introducing information on negative trial too, discussing criticisms and limits of the policies adopted, reporting evidence based data. 3) I suggest to add in "HCV-related HCC" paragraph, a few comments on DAA treatment on the risk of HCC recurrence, since it is ongoing a lively scientific debate on this topic.

Answer: We sincerely appreciate Journal Chief Editor for valuable and considerable comments, which are helpful for us to significantly improve our paper. We have addressed the issues, and have revised the manuscript accordingly, as described below. We sincerely hope that our reply will satisfy the concerns expressed by Journal Chief Editor, and that the revision meets your approval.

1, Please modify the title, to clarify that the article refers to prevention of "recurrence", and preservation of liver function "after HCC treatment".

Reply: Thank you very much for your valuable suggestion. We would like to change the title from "Supportive therapies for prevention of hepatocellular carcinoma and preservation of liver function"

to "Supportive therapies for prevention of hepatocellular carcinoma recurrence and preservation of liver function".

2, Overall, the Authors provide data on positive trials supporting the policy adopted to prevent recurrence and liver function deterioration. However, there is no a clear agreement on these policies. I suggest to underline this fact, introducing information on negative trial too, discussing criticisms and limits of the policies adopted, reporting evidence based data.

Reply: Thank you very much for your valuable comment. At first, we collected the paper previously published about the recurrence of hepatocellular carcinoma after BCAA supplementation. We could find 52 papers in PubMed. The list is attached in the below. We did not find negative data about BCAA and HCC. However, we are completely agreed with your suggestion. Therefore, in the section of CONCLUSION, we put new sentence; "We showed results on some positive trials supporting the prevention of HCC-recurrence and the preservation of liver function. Therefore, by generating further data and evidence,~".

3, I suggest to add in "HCV-related HCC" paragraph, a few comments on DAA treatment on the risk of HCC recurrence, since it is ongoing a lively scientific debate on this topic.

Reply: Thank you very much for your valuable comment. We cited new two papers about DAA treatment on the risk of HCC recurrence, and then modified the section of "HCV-related HCC" in page 15 and 16. In the detail, we put these sentences; "Recently, Reig M et al administered DAAs to the patients after curative treatment of HCC and investigated subsequent recurrence rate (ref.88). Although they reported high rate of recurrence after the viral elimination by DAAs, it is a small cohort retrospective study and the reliable opinion is not obtained. In addition, Pol S conducted a multicenter prospective study, and he concluded that there was no evidence that DAAs promote an HCC recurrence (ref.89). It is still needed future analysis." Ref. 88: Reig M, Mariño Z, Perelló C, Iñarrairaegui M, Ribeiro A, Lens S, Díaz A, Vilana R, Darnell A, Varela M, Sangro B, Calleja JL, Forns X, Bruix J. Unexpected early tumor recurrence in patients with hepatitis C virus -related hepatocellular carcinoma undergoing interferon-free therapy: a note of caution. J Hepatol 2016. Ref89: Pol S. Lack of evidence of an effect of Direct Acting Antivirals on the recurrence of hepatocellular carcinoma: The ANRS collaborative study group on hepatocellular carcinoma (ANRS CO22 HEPATHER, CO12 CIRVIR and CO23 CUPILT cohorts). J Hepatol 2016.