

Format for ANSWERING REVIEWERS

November 29, 2014



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 13695-review.doc).

Title: Diagnosis and treatment of hepatocellular carcinoma: An update

Author: Javier Tejeda-Maldonado, Ignacio García-Juárez, Jonathan Aguirre-Valadez, Adrián González-Aguirre, Mario Vilatobá-Chapa, Alejandra Armengol-Alonso, Francisco Escobar-Penagos, Aldo Torre, Juan Francisco Sánchez-Ávila, Diego Luis Carrillo-Pérez

Name of Journal: *World Journal of Hepatology*

ESPS Manuscript NO: 13695

We have analyzed the reviewers' comments and suggestions to our paper. We agree with these observations and have made the changes in our manuscript accordingly. Changes appear highlight in the new manuscript version according to the peer- reviewers' comments. We profoundly thank the celerity and appropriateness of the reviewers' comments to our paper. These observations will certainly improve our report.

Reply to the comments made by Reviewer 02860874

According to the title this review pretends to be "an update", but in my opinion this aim was not achieved. Many of the references cited by the authors are over 5 to 10 year-old, or even more old, for example, in the Core Tip authors say "This paper reviews the most recent evidence on hepatocarcinoma including its molecular pathogenesis", the references are so old as 1996 or 1997, all this articles have been cited in other reviews and guidelines, then the present review not achieved the aim to be an update. On the other hand, most of the more recent references cited by the authors 2010 - 2014 are also review articles, one of them even was published in World J Gastroenterology recently. but they did not include original studies related to pathogenesis, diagnosis and new therapeutic options. This review do not provides additional important information different from what is already described in guidelines.

1) Update references

Response: We completely agree. We rewrite de whole section with update information and add information about de specific molecular biology to the development of hepatocellular carcinoma in HCV and HBV. Recent evidence was added on the possibility that despite antiviral therapy for HBV, hepatocarcinoma high risk persists (even though complete response to treatment).

2) Include original articles studies

Response: We completely agree. We included recent original articles, particularly of molecular pathogenesis accordingly with reviewer`s recommendations.

Reply to the comments made by Reviewer 00069262

It's interesting work, I suggest making the following changes: 1. It should be considered mini-review. Of the 54 pages of the article, half are references, figures and images. 2. We can summarize the three images into a single image? 3. The figures are made ??by the authors? or are primary sources? have permissions? Figures can be summarized into one? 4. I ??strongly suggest updating the literature, 50% is more than five years. The review is an update? Very old References

1) It should be considered mini-review

Response: We appreciate the suggestion. References, images and figures have been reduced, keeping the manuscript review length with the intention that it not has the extension of a mini-review.

2) Summarize the three images into a single image

Response: We reduced only to a diagnosis images showing the typical behavior of hepatocarcinoma and treatment related images were removed. These images are from patients of our Institution.

3) Figures are made? by the authors or primary sources? Permissions?

Response: The figures are for primary sources; all of them have been reproduced and modified with permissions of authors and editorials. We believe it is necessary to keep the three figures and should not reduce them to one due to the following reasons:

Show diagnostic algorithms both Eastern and Western International Associations these two approaches are rarely displayed in a single article.

About Figure 3 (BCLC staging system) we have considered relevant keep it because determines the steps to take decisions on the treatment of patients with hepatocellular carcinoma.

4) Updating literature

Response: We completely agree. Whole review was updated with recent references of the latest 3-5 years. We eliminate duplicate references and included recent original studies.

Reply to the comments made by Reviewer 00052707

To editor/authors: It is very interesting work. It is valuable to be published. But English writing and figure legends should be modified. Some errors should be checked and corrected (as: J Hepatol 21012; 56:908-943).

1) Modification of figure legends and English writing

Response: We appreciate the interest to our work. We corrected the figure legends, format of references, and revised English writing with the support of a professional native speaker for grammatical correction. All modifications were written using highlight in yellow.

A handwritten signature in black ink, consisting of a large, stylized 'C' followed by 'Pérez' and 'DL'.

Carrillo-Pérez DL, MD.

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