

## RESPONSE TO REVIEWERS

April 13, 2013



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 2543-review.doc).

**Title:** "Hepatocellular carcinoma in Hepatitis C Virus/Human Immunodeficiency Virus co-infected patients"

**Author:** Dimitrios Dimitroulis, Serena Valsami, Eleftherios Spartalis, Emmanuel Pikoulis, Gregory Kouraklis

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

**ESPS Manuscript NO:** 2543

Thank you very much for giving us the opportunity to revise our manuscript for possible publication in your distinguished journal. All Editorial and Reviewers' comments and recommendations have been addressed.

In order to facilitate editing, all changes have been highlighted and underlined in red in the revised manuscript. Furthermore, all reviewers' comments have been inserted in italics in our detailed response to reviewers, along with our change. We hope that this revision will satisfy the high standards of your distinguished journal. Please do not hesitate to contact me, should any problems occur. We are looking forward to hearing from you at your earliest possible convenience.

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewers:

### Reviewer #02444981

Thank you very much for the revision of our manuscript.

### Reviewer #02444790

Thank you very much for giving us the opportunity to revise our manuscript. We strongly believe that your comments have added up greatly to the article.

1. Abstract "Short review" should be replaced with "mini review".

**Done. The word has been replaced.**

2. Introduction "So HIV subjects...", "so" should be deleted.

**"So" has been deleted.**

3. "hcc" should be replaced with "HCC"

**You are absolutely right. The change has been highlighted in red in the revised manuscript.**

4. "Bollepali et al reported in 2007 in their epidemiological study", "in their epidemiological study" is not necessary.

**The phrase has been removed.**

5. Clinical impact "...the risk of dying". Do you mean "the risk of death"

**You are right. This change has been done.**

6. "...the pathogenesis of liver injury is believed to be immune mediated". What "immune mediated" mean?

**It means that liver injury is a result of host immune-mediated cytolytic response.**

**The phrase has been changed and highlighted in red in the text.**

7. "...develop liver cirrhosis more quickly than HCV mono-infected individuals as well as a more aggressive course of HCC". Are there data?

**"HIV-HCV coinfectd patients had a mean rate of fibrosis progression of 0.181 fibrosis units per year, which translated into a mean duration from HCV infection to cirrhosis of 26 years. HCV-monoinfected patients had a mean rate of fibrosis progression of 0.135 fibrosis units per year, or a mean duration of 38 years from HCV infection to cirrhosis."**

**(Graham, C.S., et al., Influence of human immunodeficiency virus infection on the course of hepatitis C virus infection: a meta-analysis. Clin Infect Dis, 2001. 33(4): p. 562-9.).**

**Data has been added and highlighted in red in the text.**

8. "Two randomized placebo-controlled...advanced HCC". Are there data?

**Monotherapy with oral sorafenib 400 mg twice daily prolonged median overall survival and delayed the median time to progression in patients with advanced hepatocellular carcinoma, according to the results of a randomized, double-blind, placebo-controlled, multicentre, phase III trial (the Asia-Pacific trial). 271 patients from 23 centres in China, South Korea, and Taiwan were enrolled in the study. Of these, 226 patients were randomly assigned to the experimental group (n=150) or to the placebo group (n=76). Median overall survival was 6.5 months in patients treated with sorafenib, compared with 4.2 months in those who received placebo. Median time to progression was 2.8 months (2.63-3.58) in the sorafenib group compared with 1.4 months (1.35-1.55) in the placebo group.**

**(Cheng AL, Kang YK, Chen Z, et al. Efficacy and safety of sorafenib in patients in the Asia-Pacific region with advanced hepatocellular carcinoma: a phase III randomised, double-blind, placebo-controlled trial. Lancet Oncol. 2009 Jan;10(1):25-34. doi: 10.1016/S1470-2045(08)70285-7).**

**Data has been added and highlighted in red in the text.**

9. "Further epidemiological...HCV". Are there data?

Norris et al reported that at 12 months, 4 of 7 (57.1%) of those coinfecting with HCV were still alive, but by 25 months a further 2 had died. The survival rate of HCV / HIV coinfecting persons was clearly lower than in the HCV monoinfected candidates who received organs during the same period. The latter had actuarial 1- and 2-year survival rates of 87.5 and 83.9%, respectively.

(Norris S, Taylor C, Muiesan P, Portmann BC, et al. Outcomes of liver transplantation in HIV-infected individuals: the impact of HCV and HBV infection. *Liver Transpl.* 2004 Oct;10(10):1271-8.)

Data has been added and highlighted in red in the text.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Hepatology*.

Sincerely yours,

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