

February 24, 2017

**To the Editors,**

World Journal of Gastroenterology

8226 Regency Drive, Pleasanton, CA 94588, USA

**RE: Submission of Revised Letter to the Editor per Comments from Reviewers**

Dear Prof. Garcia-Olmo, Prof. Strom, Prof. Tarnawski:

On behalf of my coauthors, I am submitting the letter to the Editor, "Tumor Biopsy and Patient Enrollment in Clinical Trials for Advanced Hepatocellular Carcinoma" revised as per comments from reviewers, for your kind consideration for publication in *World Journal of Gastroenterology*. As per WJG guidelines, all changes in the manuscript are highlighted in the submitted file.

Reviewer #3538668 requested to provide the full name of a gene when first mentioned i.e. AFP, MET, VEGF etc. We have done so and integrated within the re-submitted Letter.

Reviewer #03015689 requested to:

- Explain abbreviations: we have integrated within the Letter.
- Offer a list of instructions / recommendations, hospitals could benefit from including a certain set of more specific guidelines: i.e. bundles with the hospital characteristics required to study these patients, what specific centres are suggested for diverting clinical cases, samples, sample obtention protocols as well as their integral manipulation, etc: we have included in the Letter more specific recommendations regarding hospital characteristics, types of centers suggested for treating second-line HCC patients, tumor sample preparation, that can be of interest to clinicians.

In addition to the changes requested by reviewers, we have updated the information and references to the now completed lenvatinib and tivantinib studies.

I thank you again on behalf of all Authors for considering our letter for publication.

Sincerely,

Lorenza Rimassa, MD

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