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To the Editors-in-Chief
Prof. Lian-Sheng Ma, President and Company Editor-in-Chief
Prof. Doctor Damian Garcia-Olmo, MD, PhD
Prof. Saleh A Naser, PhD
Prof. Stephen C Strom, PhD
Prof. Andrzej S Tarnawski, DSc, MD, PhD
World Journal of Gastroenterology

Date: 10th of October 2015
Subject: Answering reviewer

Dear Professor Lian-Sheng Ma, Professor Garcia-Olmo, Professor Naser, Professor Strom, and Professor Tarnawski,

Attached you will find our revised manuscript entitled **'Cytomegalovirus in Inflammatory Bowel Disease: a systematic review'**, which addresses the reviewer's comments and those raised by the science editor. We believe that this has improved the quality of the manuscript. We kindly ask you to consider it for publication in 'World Journal of Gastroenterology'.

Peer-reviewer's comments:

1] What are the definitions used in other immunosuppression associated disease (organ transplant patients)?

We thank you for this comment and have addressed this question in the revised discussion section of our manuscript on page 11: " Already in the nineties consensus meetings were held to formulate the definition for CMV infection in general and for all organ specific involvements in transplant recipients. These definitions were updated again in 2002. CMV infection was defined as isolation of the CMV virus or detection of viral proteins or nucleic acid in any body fluid or tissue specimen. There CMV (gastro)intestinal disease was defined by identification of a combination of a) clinical symptoms, b) findings of macroscopic mucosal lesions on endoscopy, and c) demonstration of CMV infection (by culture, histopathology, IHC, or in situ hybridization) in a (gastro)intestinal tract biopsy specimen. According to this guideline detection of CMV by PCR alone is insufficient for diagnosis of CMV gastrointestinal disease."

2] When possible, quantitative definitions should be presented for antigenemia , PCR and other quantitative tests.

We thank the reviewer for his/her comment. Unfortunately we found that most included studies used qualitative tests to diagnose CMV, as we showed in Table 1a and 1b of the results section. Only few studies used a quantitave PCR value (>10 copies/mg tissue) as a diagnostic tool, shown in the same Tables.

3. The geographic seroprevalence distribution should be interpolated against the prevalence among non-IBD cohorts where available.

This is a valid point which we addressed in the revised discussion section of our manuscript on page 10: “Interestingly, by using the author’s definition, we found the highest prevalence of CMV infection and intestinal disease in East Asia. Population based CMV seroprevalence studies are lacking, but a review on this topic found that seroprevalence tended to be highest in South America, Africa and Asia, and was also higher in parts of Europe and the Middle East. The most likely explanation is the use of different diagnostic methods for CMV infection in different regions of the world.”

We think that our revised manuscript has important implications and provides practical support for clinical practice as well as for the design of future trials.

We affirm that all authors concur with the submission and that none of the data have been previously reported or are under consideration for publication elsewhere. There are no financial disclosures.

Thank you in advance for your reconsideration.

Yours sincerely,

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