

June 1, 2015

Editors-in-Chief  
World Journal of Gastroenterology

RE: MS#17791

Title: Effect of anti-TNF $\alpha$  antibodies on oxidative stress in patients with Crohn's disease

Authors: Kazunari Yamamoto, Toshimi Chiba, Takayuki Matsumoto

Dear Editors:

Thank you for your e-mail regarding above mentioned manuscript. We also appreciate valuable suggestions of the reviewer.

Based on your kind comment, we made a re-write of the text of the paper, including the title. The modifications of the revision have been indicated in red characters in the text of the paper.

Attached please find a completely revised version of the manuscript and a response to issues raised by the reviewer. Also, please find our responses to the request by your editorial office to upload necessary information regarding the manuscript.

Your kind consideration of this revision for publication in WORLD JOURNAL OF GASTROENTEROLOGY would be greatly appreciated.

Sincerely,

Kazunari Yamamoto  
Division of Gastroenterology  
Department of Internal Medicine  
Iwate Medical University

By way of reply

Responses to the reviewer:

1). I reviewed with interest your paper titled "Effect of anti-TNF $\alpha$  antibodies on oxidative stress in patients with Crohn's disease", my first impression when I read the title was that this paper addresses the impact of anti drug antibodies (ADAs) on oxidative stress, which is why I believe the title is misleading and not appropriate. I suggest you change it to ""Effect of TNF $\alpha$  antagonists on oxidative stress in patients with Crohn's disease".

Based on your suggestion, we changed the title of the manuscript accordingly.

Title page. The title has been changed to "Effect of anti-TNF $\alpha$  antagonists on oxidative stress in patients with Crohn's disease".

2). The abstract is appropriate and summarizes the findings well.

Thank you for your comment.

3). In the second paragraph of your discussion, you eluded briefly to how such findings impacted clinical practice in other specialties, I would suggest you elaborate further to convince the reader that these preliminary findings may have promise.

In accordance with the suggestion, the second paragraph of the discussion has been modified and extended. We added a sentence to state that oxidative stress marker (d-ROM) is a useful biomarker for the risk of cardiovascular diseases.

Page 11, lines 17-20. A sentence has been added.

4). I would however add to the discussion section another obvious limitation of the study: the correlation is not adjusted for certain confounders, namely serum drug concentrations, presence or absence of anti drug antibodies, presence or absence of concomitant immunosuppression (although the percentage of those on AZA concomitantly was low in this study (7%)), baseline CRP, and finally that disease activity was based entirely on clinical symptoms (CDAI), which is known to poorly correlate with endoscopic disease activity in CD.

In accordance with the suggestion, we discussed the limitation of our study further.

Page 13, lines 5-8. Two sentences have been added with a new reference.

Thank you for taking time to review our paper.