

9th of May, 2018

Lian-Sheng Ma,
President and Company Editor-in-Chief
World Journal of Gastroenterology

Dear Editor-in-Chief,

Please find our revision letter on the following manuscript.

Manuscript NO: 39087

Title: "Positioning of old and new biologicals and small molecules in the treatment of inflammatory bowel diseases"

Authors: Jason Reinglas, Lorant Gonczi, Zsuzsanna Kurti, Talat Bessissow and Peter Laszlo Lakatos

Thank you for taking the time to read through the review. We appreciate the positive response and constructive feedback.

Reviewer #1:

- 1. Introduction section is very lengthy. It's better to make it more brief.*
- 2. There is no data on the time of drug cessation in CD or UC which is a debateful area.*
- 3. I recommend adding a table showing different medication based on severity and type of IBD for easier review*

Reply to reviewer 1: Thank you for the comment.

- 1) The introduction has been shortened to less than one page.
 - 2) Although there isn't a significant amount of literature on the topic of cessation of immunosuppressant therapy, there is some data that suggests we can safely trial withdrawing therapy after 6-13 months (see references below).
 - 3) A new table has been added, see Table 3.
- Drobne D, Bossuyt P, Breynaert C, Cattaert T, Vande Castele N, Compennolle G, Jürgens M, Ferrante M, Ballet V, Wollants WJ, Cleynen I, Van Steen K, Gils A, Rutgeerts P, Vermeire S, Van Assche G. Withdrawal of immunomodulators after co-treatment does not reduce trough level of infliximab in patients with Crohn's disease. *Clin Gastroenterol Hepatol.* 2015 Mar;13(3):514-521.e4. doi: 10.1016/j.cgh.2014.07.027.
 - Van Assche G, Magdelaine-Beuzelin C, D'Haens G, Baert F, Noman M, Vermeire S, Ternant D, Watier H, Paintaud G, Rutgeerts P. Withdrawal of immunosuppression

in Crohn's disease treated with scheduled infliximab maintenance: a randomized trial. *Gastroenterology*. 2008 Jun;134(7):1861-8. doi: 10.1053/j.gastro.2008.03.004. Epub 2008 Mar 8.

- Torres J, Boyapati RK, Kennedy NA, Louis E, Colombel JF, Satsangi J. Systematic Review of Effects of Withdrawal of Immunomodulators or Biologic Agents From Patients With Inflammatory Bowel Disease. *Gastroenterology*. 2015 Dec;149(7):1716-30. doi: 10.1053/j.gastro.2015.08.055. Epub 2015 Sep 14. Review

Reviewer #2:

Dr. Peter L Lakatos and colleagues reviewed the existing data on approved biologic and biosimilar agents and provide broader insight on the current positioning of approved therapies of IBD. Patient stratification for selection of specific therapies, therapeutic targets and patient monitoring are discussed. Well-written systematic review. General comments:

i) This is an interesting and informative manuscript.

ii) Greater attention to syntax and grammar (e.g, making sure sentences are complete) would strengthen the manuscript.

iii) For all cited studies (results of review discussed in the text), please include the study design, sample size and demographic where relevant, and key findings to enable readers to understand level of evidence of the observation(s).

Reply to reviewer 2:

i) Thank you for your comment and feedback.

ii) The paper was reviewed and corrections were made.

iii) Cited studies which were lacking this data were supplemented.

Reviewer #3: This manuscript is informative and this reviewer enjoyed reading.

Reply to reviewer #3: Thanks for the positive feedback as well.

We would like to thank you again for the helpful comments and for considering our paper. We believe that the changes have improved the quality of the manuscript and we do hope that the revised manuscript could be of interest to the readers of *World Journal of Gastroenterology*.

Sincerely yours,

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