

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 69512

Title: Predictive value of infliximab trough level in combination with inflammatory biomarkers on long-term endoscopic outcomes in Crohn's disease with clinical remission during maintenance therapy

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05194519

Position: Peer Reviewer

Academic degree: PhD

Professional title: Academic Research

Reviewer's Country/Territory: Brazil

Author's Country/Territory: China

Manuscript submission date: 2021-10-30

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-11-18 11:39

Reviewer performed review: 2021-11-19 15:15

Review time: 1 Day and 3 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection

Re-review	[<input checked="" type="checkbox"/>] Yes [<input type="checkbox"/>] No
Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No

SPECIFIC COMMENTS TO AUTHORS

The topic is interesting: even if several studies have been performed, there are still space for new data. However, there are some points that need to be better clarified:

Introduction: These sentences need to be referenced, because those affirmations are not clear in the literature:

- 1) High inflammatory load affects the pharmacokinetics of IFX, inducing secondary nonresponse by decreasing blood drug concentration.
- 2) Currently, it is believed that inflammatory biomarkers are good predictors of disease activity. FCP or CRP? In my opinion, the term “phase I study” let someone have a wrong intuition and the word “phase” should be replaced by “part” or “step”

Materials and methods It is not clear how the patients were selected. How many patients had received infliximab? How many of them had done colonoscopy at week 14? How many of them had measured the ITL at week 14? In Study Subjects Design, there are a statement that Clinical, laboratory, endoscopic and imaging evaluation were implemented every two months after IFX induction therapy in all patients. Have they done colonoscopy every 2 months? or that they had done the colonoscopy 8 weeks after the 3rd dose at week 6? Excluding patients who had their therapeutic strategy changed, or who had clinically relapsed of the final analysis, will not bias the results? Let's imagine a patient who have a high ITL at week 14 and had a clinical relapse at weeks 48. Even if you decided to analyze only patients in clinical remission, per protocol, it is important to show the data of those who had clinical relapse during the study with an intention-to-treat analysis where the last observation is carried forward (LOCF). In Data Collection, there are the information that anti-infliximab antibody (ATI) was



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
<https://www.wjgnet.com>

collected, but there is no data about that in the paper. The same happens with the CDAI score (CDAI is a score for activity and not severity of the disease) The therapeutic strategy during maintenance stage was designed as IFX 5mg/kg every 8 weeks combined with AZA 50mg every day. Nevertheless, it is well known that dose below 2mg/kg is ineffective. Why have you chosen this low dose of azathioprine? In Outcome Definition, the colonoscopy was evaluated at week 52 and week 104 after IFX initial therapy, but in other part of the text the time point used was 54 and 108. What exactly means " were evaluated by specialist physicians on IBD under electronic colonoscopy"? Did they review pictures or movie of the original colonoscopy? Results In Characteristics of study subjects, this part is a little confuse. In the 1st part of the study 93 patients were included and in the 2nd part 54 patients, is that correct? What exactly you mean with secondary non-response of IFX? Who had clinical relapse? Why some patients had the course of therapy shorter than two years? Any of them had surgery? Or had changed to another biologic because of disease activity? In Correlation between Infliximab Trough Level, Inflammatory Biomarkers and Endoscopic Outcomes, it is not clear when the infliximabe trough level, CRP and FCP were measured, every 8 weeks or just at week 14?

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 69512

Title: Predictive value of infliximab trough level in combination with inflammatory biomarkers on long-term endoscopic outcomes in Crohn's disease with clinical remission during maintenance therapy

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00036898

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Associate Professor, Doctor

Reviewer's Country/Territory: Spain

Author's Country/Territory: China

Manuscript submission date: 2021-10-30

Reviewer chosen by: Qi-Gu Yao (Online Science Editor)

Reviewer accepted review: 2022-02-20 17:24

Reviewer performed review: 2022-02-26 18:51

Review time: 6 Days and 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection

Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The manuscript presented data from single-center retrospective study that aimed to evaluate the long-term endoscopic outcomes of CD patients receiving IFX treatment by combining blood drug concentration and inflammatory biomarkers. The title reflects the main subject/hypothesis of the manuscript. The abstract summarize and reflect the work described in the manuscript. The key words reflect the focus of the manuscript. The manuscript describe methods in adequate detail. The research objectives are achieved by the experiments used in this study. The manuscript is well, concisely and coherently organized and presented. Conclusions were concise and not speculative. The study reported important information not possible to obtain from the randomized OCTAVE induction and maintenance studies, and its conclusions were clinically relevant. The main limitation of the study was the exclusion of patients who relapse or who were dose escalated. If you want to know the predictive capacity of IFX levels, this should also include patients who have secondary loss of response or complete loss of response, not only those who maintain remission. I suggest making other corrections in the manuscript: Abbreviations such as ITL are not defined in the abstract The discussion is cumbersome, too much data and not very clear concepts, I recommend simplifying it.