

Reviewer's code: 00159305

COMMENTS TO AUTHORS

To the Authors,

1. There are several grammar/spelling English errors (i.e., page 11, second paragraph, line 2: "CD may be altering.."). Please, makes corrections.

Answer: Thank you for your valuable comment. We checked our manuscript in a detailed manner ("CD may be altering.." was changed to "CD may alter.." in revised manuscript, page 10, lines 21) and it was reviewed by a native speaker of English. Language editing certificate is submitted along with the revised manuscript.

2. Please, re-write and make it clear the last phrase pages 13-14: "We used the CDI...follow-up".

Answer: Thank you for your opinion. The phrase was changed in the revised manuscript more clearly as follows: "In our institution, we routinely check CDAI and perform blood tests, including CRP, in CD patients on IFX maintenance therapy during follow-up. Therefore, we used the CDAI, CRP and the physician's judgement of the duration of the IFX effect to assess the clinical activity of CD in this study." (revised manuscript, page 13, lines 1-4).

3. The core-tip is lacking. Please, write it.

Answer: We're really sorry for missing it. The core-tip was added to the revised manuscript and also recorded as an audio file as well as follows: "Core tip: This study aimed to clarify the clinical implications of infliximab trough levels (IFX-TLs) and antibodies to infliximab (ATI) levels. They were measured using prospectively collected samples in 138 Crohn's disease patients being treated at Asan Medical Center, Korea. Correlations between IFX-TLs/ATIs and the clinical activity ($P < .001$) were verified in the study. Our findings support the usefulness of IFX-TLs/ATI levels in treating CD patients receiving IFX in clinical practices." (revised manuscript, page 4, lines 1-7).

4. Discussion. How can the results of your study be applied in clinical practice; please, make detailed comments in Discussion section.

Answer: Thank you for your valuable comment. As you know, we already discussed the clinical implication of our study results in discussion section as follows: "Among our study patients, we observed 5 patients not following the tendencies of the other patients (3 active patients with high IFX-TLs and low ATI levels and 2 quiescent patients with low IFX-TLs and high ATI levels). For the former 3 patients, there are 2 possible interpretations of this situation: (1) high inflammatory burden of the disease, or (2) factors other than TNF- α that play a major pathologic role in these patients^[33]. In this situation, we should consider dose intensification or switching to another class of drugs such as anti-integrins. For the latter 2 patients, their clinical activity is low despite low IFX-TLs and high ATI levels. In other words, their clinical activity is controlled regardless of anti-TNF- α therapy. In this situation, we should consider stopping the anti-TNF- α therapy if long-term deep remission is achieved^[33]." (revised manuscript, page 12, lines 12-22). Additionally, we added a sentence to the discussion section as follows: "Therefore, we can use IFX-TLs/ATI levels in making decisions in patients with loss of response to IFX therapy." (revised manuscript, page 13, lines 16-17). Finally, we also added sentences regarding the application of this study result

to the Comments Section as follows: “Measuring IFX-TLs and ATI levels could be used in making decisions in patients suffering LOR. If high IFX-TL and low ATI level were shown in the patients, we should consider dose intensification or switching to another class of drugs such as anti-integrins. On the other hand, it can be used in to decide discontinuation of IFX maintenance therapy in patients with quiescent disease. If low IFX-TL and high ATI level were shown in the patients, we should consider stopping the anti-TNF- α therapy if long-term deep remission is achieved.” (revised manuscript, page 14, lines 19-26).

5. References in text: please use brackets.

Answer: Thank you for your comment. According to your recommendation, reference format was modified to superscript with square brackets in the revised manuscript.

6. References: please, write all the references according to the Format for references (PMID and DOI requirements, the name of the first author should be typed in bold-faced letters, the family of all authors should be typed with the initial letter capitalized etc.).

Answer: Reference format was modified according to the PMID and DOI requirements in the revised manuscript.

Reviewer’s code: 00505564

COMMENTS TO AUTHORS

Oh et al. analyzed clinical correlations of infliximab trough levels and antibodies to infliximab in Asian/Korean patients with Crohn’s disease. They enrolled 138 patients with Crohn’s disease (84 with quiescent and 54 with active disease) and observed, indifference in patients with and without concomitant immunomodulator use. However, in patients with quiescent vs. active diseases, the median IFX-TLs were 1.423 $\mu\text{g}/\text{mL}$ and 0.163 $\mu\text{g}/\text{mL}$, respectively ($p < .001$) and the median ATI levels were 8.064 AU/mL and 11.209 AU/mL, respectively ($p < .001$). In the ATI-negative and -positive groups, the median IFX-TLs were 1.415 $\mu\text{g}/\text{mL}$ and 0.141 $\mu\text{g}/\text{mL}$, respectively ($p < .001$). The paper concludes that IFX-TL/ATI levels were well correlated with the clinical activity in Korean Crohn’s disease patients and that the findings support the usefulness of IFX-TLs/ATIs in treating Crohn’s disease patients receiving IFX in clinical practice. The paper is attractive.

There are some grammatical errors that need attention. My suggestion to the authors is that they should have someone with English as first language to help out and should follow the format guidelines stipulated by the journal.

Answer: Thank you for your valuable comment. We checked our manuscript in a detailed manner and it was reviewed by a native speaker of English. Language editing certificate is submitted along with the revised manuscript.