

Response letter

The manuscript was changed to 12 pt Book Antiqua font and 1.5 line spacing.

All following changes from CrossCheck are shown in yellow. The changes from Review-Check are shown in green and the revise to peer-reviewers' comments are shown in blue. Red is shown what is erased.

A running title was added.

The authors' affiliations were rearranged as wished and the ORCID numbers were added.

The format of the author contributions was changed as wished.

It was filled in a comment that there is no financially support for this manuscript.

The core tipp was added.

The format of the first subtitles were changed to bold and capital.

The format of cited references was changed to [number].

PubMed citation numbers (PMID) and DOI citation are added to the reference list.

In the title of the tables abbreviations were erased as well as signs like * or #.

The ARTICLE HIGHLIGHTS were answered.

The audio core tip was added.

The manuscript was proofreaded by proof-reading-service.com. A certificate is added.

Peer Review:

- 1. Instead oft he term „CD patients“ the preferred term would be „patients with CD“ (multiple instances):**
Changes were made
- 2. The last sentences in part 1 of the INTRODUCTION requires revision to be more clear.**
Sentences were revised.
- 3. The INTRODUCTION is long and should be shortend and focused more.**
Introduction was shortend and focused as wished.
- 4. One assumes that the project was approved as a retrospective case review? And that direct patients consent was not obtained (other than fort he NOD2 analyses)?**
Like in MATERIAL AND METHODS written, is was a retrospective design for the ustekinumab outcome and a written patient consent for participation in our IBD registry which included taking blood samples for further investigations.

5. One further assumes that all the assays (calpro, MRE etc) were conducted on clinical grounds alone?

Because of the retrospective design, the most assays were conducted on clinical grounds, while patients standardized getting lab results and a stool sample for calprotectin at each visit they come.

6. On page 13, it is stated that patients were enrolled. This implies an active recruitment process, but elsewhere it was made clear that this was just retrospective

It is changed now to: the patients were included in the study; to prevent that one assumes an active recruitment process.

7. There are some typographical errors (e.g. heterocytotous) that must be corrected.

This was changed on page 14 to heterozygous

8. The median age (Table 2) is substantially lower than the age range given (61-68). Are these numbers correct??

The numbers are incorrect, instead of 61, 21 was meant. Changes were made in Table 2.

9. Does the use of steroids at baseline reflect disease severity (if so is there not a more direct variable)? Or is an direct effect of steroids upon the acitivity of the drug?

Yes, the use of steroids at baseline reflect disease severity, but also the clinical score HBI shows disease severitiy

10. Some table titles/legens coud be enhanced.

Table titles and tables were enhanced.

11. The spelling f tonsillitis should be corrected.

This is corrected now in Table 6.