



January 23, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 7328-review.doc).

Title: Skin lesions induced by anti-TNF- α therapy correlate with IL-17A, IL-23 and IFN- γ in CD patients

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The manuscript has been improved according to the suggestions of the Editor and the Reviewers and "The revision policies of BPG for brief article":

1. The language has been thoroughly revised and corrected where necessary. We believe that the language of our manuscript has reached Grade A and therefore we have chosen not to have it edited by the English language editing companies.

2. Other revisions in the text have been made as follows:

- (1) The title has been revised and shortened, according to Editor's suggestion. Of note, in order to maintain the informative character of the title and to relate to manuscript contents, we were not able to shorten it below 15 words.
- (2) In response to the Reviewer No 00503612, we would like to state that this is a pilot study, which aimed at analyzing clinical issues in CD patients treated with anti-TNF- α . Our manuscript shows potential correlation between skin lesions and plasma level of cytokines. We are aware of a potential bias; therefore the conclusions of this report will be confirmed in a more developed study on larger groups.

As suggested, following information has been added to exclusion criteria: patients with a history of hypersensitivity, psoriasis, atopic dermatitis and other autoimmune skin lesions were excluded the study.

The IL and IFN levels were measured at the time of the appearance of first cutaneous manifestations and in CD patients without skin involvement at the end of the course of biologic therapy. This pilot study indicates a potential mechanism of drug induced skin lesions; additional study, mentioned earlier, will also consider the change of baseline levels of the IL and INF in CD patients.

Each patient was retested twice in the period of 6 months follow-up. All drug induced skin lesions were reversible, subsided after completion of biological course without necessity to use topical or general treatment.

- (3) In response to the Reviewer No 02461935, we would like to state that there is no correlation between the induction of skin lesions, response to treatment and length of course, what is shown in TABLE1. Drug induced skin lesions in patients with CD occurred in the average time of 10.16 ± 3.42 months following the beginning of the anti-TNF- α therapy.
- (4) In response to the Reviewer No 02461935, we would like to state that further studies are planned, including - inter alia - determination of cytokine levels in several time points of biological therapy, starting from the beginning of the treatment. Our study is a pilot project, which aimed at addressing clinical issues in CD patients treated with anti-TNF- α antibodies.

The data were analyzed using the Statistica 10.0 software (StatSoft, Inc., United States). Analysis was conducted in accordance with the principles of this program. The results have been consulted with a statistician.

Linguistic errors have been corrected.

3. References and typesetting (including title page) were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

Dr. Maria Wiśniewska-Jarosińska, PhD

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