Author’s response to reviews

Title: Clinical manifestations and anti-TNF alpha therapy of juvenile Behçet’s disease in Taiwan

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Author’s response to reviews:

Dear Ms. Helen Roberton and Mr. Samuel Harris:

Enclosed please find the revised manuscript entitled “Clinical manifestations and anti-TNF alpha therapy of juvenile Behçet’s disease in Taiwan”.

We are grateful for the thoughtful reviews and constructive suggestions from the Reviewers. We have revised the manuscript as the third revised version according to their specifications and all the changes to the manuscript in text was using track changes. The revisions are detailed as follows and highlighted in the revised manuscript:

1. On page 2-3, line 49-53 (in Abstract part), we add the sentence “Due to the limited case numbers, literature reviews of anti-TNF-alpha therapy for refractory JBD were conducted, which had a total 18 JBD patients receiving anti-TNF-alpha therapy, of which fifteen patients had favorable outcomes after treatment with minimal side effects.”

2. On page 9, line 145-147 (in Results, patients’ characteristics and treatments), we remove the sentence “and they were prescribed to 56.4% and 43.6% of the patients, respectively.”
3. On page 11, line 164-165, (in Results, patients’ characteristics and treatments), we shorten the sentence to “Oral prednisolone and colchicine were mostly frequently prescribed as first-line systemic therapy.” At line 167-169, we shorten the sentence to “Azathioprine was the most commonly used immunosuppressive drug (30.9%) and the only immunosuppressant used as first-line treatment.”

4. On page 15-16, line 212-213 & 228-230 (in Results, Anti-tumor necrosis factor-alpha therapy for patients with juvenile Behçet's disease), we change the sentence “Patients #5 and #6 had short statures” to “Two patients had short statures.” We also change another sentence on page 16: “When we tried to reduce the anti-TNF-alpha therapy, disease flares occurred in patients #1 and #2 during the second year of therapy” to “When we tried to reduce the anti-TNF-alpha therapy, disease flares occurred in two patients during the second year of therapy.”

5. On page 17 (Table 4), we delete the column of “the age at diagnosis.”

6. On page 23, line 347 (in Discussion), we remove the sentence: “Two cases had involvement of the central nervous system and two patients presented with Budd-Chiari syndrome, which was a rare presentation of BD.”

7. On page 26, line 383-385 (in Discussion), we change the sentence to “Although further larger prospective studies are needed to determine the efficacy and safety of anti-TNF-alpha therapy in JBD patients, it seems that anti-TNF therapy might play an important role for refractory JBD.”

8. In response to the suggestions of re-editing from the reviewer, we did some revision for the grammatical errors in the text and the locations in text are listed below:

① Background section, line 65-67, page 4
② Methods section, line 106-107 & 109, page 6
③ Discussion section, line 240 & 242-243, page 18
④ Discussion section, line 264, 267, 269-271, 274-276, and 278-280, page 19-20
⑤ Discussion section, line 320 ,322-323, & 325, page 22
⑥ Discussion section, line 337, 338, 343, 351, & 353-354, page 23-24
The point-by-point replies are given in the following pages. We hope that we have addressed satisfactorily all the concerns raised by the Reviewers, and that this manuscript is now acceptable for publication.

Sincerely

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Responses to the Editor:

1. Ethics approval and consent to participate: Please indicate if written informed consent to participate was obtained from parents/legal guardians for the cases described in your study. If the ethics committee specifically waived the need for this, please state this in this section, including the reason why it was waived.

Response: Based on the regulation of National Taiwan University Hospital (NTUH) Research Ethics Committee (REC), the informed consents of participants are not required for studies conducted via retrospective chart review.

2. Consent for publication: We note there is individual patient-level information in Table 4. Please indicate if you have consent to publish this information. If you did not, we ask that exact ages are removed, along with any other information that may identify the individuals.

Response: Thank you. Since there are not required informed consents in the study, we remove the age of the patients in Table 4.
Responses to Reviewer 1

1. The authors could delete the patient numbers in the text (e.g., page 15; instead of patient #5 and #6 had short stature; consider writing "two patients had short stature). The readers could find these data in the tables.

Response: Thank you for the comment to make the text more concise. We remove some patient numbers in the results section, line 212-213 & 228-230, page 15-16.

2. The redundant parts between the main text and tables could be deleted in the text.

Response: Thank you for the suggestion. We delete some repetitive text in the results and discussion sections:

(1) results section, line 145-147, page 9
(2) results section, line 164-165 & 167-169, page 11
(3) results section, line 212-213 & 228-230, page 15-16
(4) discussion section, line 347, page 23

3. The results of the literature review should be mentioned in the abstract (with 1-2 sentences).

Response: Thank you for the suggestion. We add the results of literature review in the result section of abstract. (line 49-53, page 2-3)

4. In the last sentence of the discussion (before conclusion part), the authors stated that the "believe" that anti-TNF may be an effective treatment in refractory juvenile Behçet's disease. Please consider removing the statement "we believe" to keep the conclusions objective.

Response: Thank you for the comment. We change the sentence to “Although further larger prospective studies are needed to determine the efficacy and safety of anti-TNF-alpha therapy in JBD patients, anti-TNF therapy might play an important role for refractory JBD.” (discussion section, line 383-385, page 26)
5. There are minor grammatical errors in the text. Re-editing is advisable.

Response: Thank you for the suggestion. We make some modification.