Author’s response to reviews

Title: Treatment of children and adolescents with ulcerative colitis by adsorptive depletion of myeloid lineage leucocytes as monotherapy or in combination with low dose prednisolone after failure of first-line medications

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Author’s response to reviews: see over
The Editor,
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Dear Editor,

Subject, revised MS: 4413307339698979, Treatment of children and adolescents with ulcerative colitis by adsorptive depletion of myeloid lineage leukocytes as monotherapy or in combination with low dose prednisolone after failure of first-line medications.

The authors thank you for your communication of 25 July 2013 in connection with the above manuscript. Likewise, we thank our reviewer colleagues for their time and courtesy in evaluating our manuscript. We have spared no effort to undertake further revisions and factor their suggestions. In the manuscript, our revisions are shown in blue and are itemized below.

Reviewer 1.

We have thoroughly revised the present version of our manuscript to reflect your comments. As stated in the manuscript, we describe treatment outcomes in paediatric/adolescent cases treated in consecutive setting and not in a clinical trial setting. Our findings should best reflect the reality of the clinical situation concerned with the management of very young patients.

Of the 24 cases we report in this manuscript, 17 developed active UC while on first-line medication, and 12 of these 17 patients responded to GMA without adding any pharmacologic. Therefore, the majority of cases in whom first-line salicylates had failed responded to GMA. The manuscript Abstract and text body have been revised to reflect this. Additionally, Table 1 has been reorganized to show the treatment outcomes more clearly.

Regarding the long-term impact of GMA as a non-drug treatment intervention, Yamamoto, et al.[reference 17] have reported that first episode/new onset cases who responded to GMA without receiving corticosteroids had significantly better long-term clinical course by avoiding corticosteroids at an early stage of the disease. This report has been briefly reviewed in the Discussion section.

On the issue of how long GMA non-responders waited before receiving a corticosteroid (prednisolone), the manuscript states “Patients who achieved a decrease of ≥5 in the clinical activity index (CAI) were to continue with GMA, while non-responders were to receive 0.5 to 1.0 mg/kg/day prednisolone plus additional GMA sessions”. Prednisolone was added immediately after week 4.

Regarding the importance of a controlled trial, we have expanded the paragraph before the conclusion section (Discussion) with the following statements. “We believe that the superiority of GMA over corticosteroids warrants to be shown in a future randomized controlled trial in large cohorts of paediatric UC patients, in whom first-line medications have failed”. Patients in one arm should receive GMA, while patients in another arm receive corticosteroid as remission induction therapy.
The misprint “core”, now reads “score”, thank you.

Reviewer 2
1. The precise study timeline is now written (2000 was a misprint), thank you.
2. CE in CE mark has been defined.
3. We have checked the misprint in the section on safety, feasibility. Regarding grammar, we thought there was no error. Nonetheless, we sent that paragraph to a second UK based academic for a double check. The double-checked paragraph is now added to the manuscript. We hope that this does not reflect acrimony by us.
4. Table 1 has been revised. We have shown first-line responders, GMA responders and GMA+corticosteroid responders as separate sub-groups. We felt that this was a very meaningful modification we undertook in this manuscript, thank you. Alternative changes would require omission of other essential demographic variables. We hope that this may be compromised.

Yours sincerely
Tomotaka Tanaka, MD, PhD
(on behalf of all authors)