Reviewer's report

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

Version: 2 Date: 31 May 2013

Reviewer: Hien Huynh

Reviewer's report:

Tanaka et al. look at the efficacy of therapeutic Granulocyte/Monocyte Adsorption (GMA) in achieving remission in glucocorticosteroid naive children and adolescents with a short duration (\leq 12mo) of active ulcerative colitis (UC) despite first line salicylate medications. Treatment efficacy was assessed by determining UC clinical activity index (CAI) and disease activity index (DAI) before and after treatment. Clinical remission was defined as CAI \leq 4 and endoscopic remission was defined as DAI <3 and absence of stools. They recruited a total of 24 patients into the study with a mean age of 15.3y +/- 2.3y. Seven patients responded to first line medications, so in fact, only 17 patients were treated GMA. 12/17 responded to initial GMA and were continued on GMA monotherapy, while 5/17 did not, and were given prednisolone (PSL) + GMA treatment. All 17 patients achieved clinical remission (CAI \leq 4) following treatment, while 9/17 achieved complete endoscopic remission (DAI<3).

Between the three treatment groups (5-ASA, GMA monotherapy, GMA + PSL), progression to more therapeutics was correlated with disease severity (ie. monotherapy had lower CAI and DAI than dual therapy). GMA therapy was deemed safe with only minor, transient side effects including needle pain, mild headache, nausea, and lightheadedness.

Major revisions:

The use of two different UC indices makes the results more difficult and confusing to interpret. Would it be possible to instead assess these patients using the Pediatric Ulcerative Colitis Activity Index (PUCAI)? If not, I suggest that you use the more common Mayo/DAI UC index, since it assesses both clinical and endoscopic features. This may change how you interpret the success of GMA therapy, since only 9/17 achieved remission based on DAI.

I think the remission maintenance analysis should be presented differently. Since you recruited between 2000 and 2012 - and I suspect they were all treated at different times - total number of patients in remission in 2013 alone does not necessarily reflect rate of remission. Perhaps you can present your data as time to relapse in does that achieve complete remission. You could use the Kaplan-Meier estimator to do this and it would account for the time post-treatment.
What are the demographics of the 17 GMA alone? While you recruited 24 patients, the efficacy of GMA was only tested in 17 of these patients.

Redo demographic table with age, gender, baseline scores, etc. for easier comparison and interpretation.

In addition to your analysis of DAI and CAI subgroup scores, can you analyze whether the location of UC correlates with treatment response?

Minor points
Page 10 Line 21 “[...] and this was did provoke a relapse.”

in discussion: need to mention that While the results showed pre adn post treatment statistical significance, the sample size was small for such a long recruitment period. Even though GMA was successful for your study population, the adult RCT (Sands et al. 2008) demonstrates no difference between GMA and placebo. You could suggest or possibly perform an RCT in pediatric population with mild to moderate UC to assess any placebo effect.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

No to all above