Author's response to reviews

Title: Long-term follow-up with leukocytapheresis re-treatment in patients with chronically active inflammatory bowel disease

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Author's response to reviews: see over
Response to Decision Letter version 2, 5 May 2010

Dear Sir/Madame,

Thank you for considering our manuscript entitled “Long-term follow-up with Granulocyte and Monocyte Apheresis re-treatment in patients with chronically active inflammatory bowel disease” for publication as an original paper in BMC Gastroenterology. The originally submitted version of the manuscript has been revised according to the reviewer’s comments as following (the additional information is revised in the manuscript as highlighted):

**Reviewer's report:**
- The fact that 21 out of 25 CD patients had extensive colonic disease, and only 3/25 had small bowel involvement cannot be explained in the Discussion as this "may indicate a higher risk for CD patients with colonic inflammation to become chronic". Maybe, the authors preferred to try apheresis before performing a total proctocolectomy with ileostomy. As the authors state in their comments, "this reflection remains speculative", and many other hypothesis should be taken into account.

Comment to reviewer: added to discussion according to suggestion:

> 3/25 (12%) compared to expected 48% in Stockholm County [49].

An explanation to this recruitment discrepancy might also be a preference to refer patients with chronic inflammation localized to the small bowel or ileo-caecal region to limited surgery while trying GMA treatment on the colitis patients before colectomy

- Table 2: explanations about statistical significance are not clear as far as the authors indicate the variable but not at which time (before tx, 10 weeks after tx, 20 weeks after tx) was the difference significant between groups (responders, non-responders,...).

Comment to reviewer: The text in table 2 has been changed as suggested (according to the statistician’s suggestion):

> Before treatment only white cell count differed significantly (p=0.004) between the three groups (remission/response/non-responders). At 20 weeks after treatment, however, as white cell count still differed significantly between the groups (p=0.038), so did Albumin (p=0.038) and C-reactive Protein (p=0.021).

- Conclusion: I agree with the authors that feasibility and tolerance were excellent. However, can it be stated that GMA did not induce "dependency" when most patients relapsed soon after treatment discontinuation (within the first 6 months as seen in the survival curves) and responded when treatment was re-introduced? Isn't it the definition for steroid-dependency? In my opinion, the main conclusion should be that scheduled maintenance therapy with GMA should be evaluated in CD patients with chronic disease activity who respond to an initial GMA course.
Comment to reviewer: Conclusion has been changed according to suggestion:

**Removed text:**
In addition, by removing pro-inflammatory effector cells from the body rather than administrating drugs, the GMA method does not seem to induce refractoriness or dependency, which is supported by our experience.

**Added text:**
These finding may indicate that scheduled therapy with GMA should be evaluated in IBD patients with chronic disease activity who respond to an initial GMA course.

We feel that this re-revision has added more clarity and quality and hope that the manuscript now can be accepted for publication in BMC Gastroenterology.

Sincerely Yours,

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