Reviewer's report

Title: Effectiveness and Safety of Ferric Carboxymaltose Treatment in Children and Adolescents with Inflammatory Bowel Disease

Version: 2 Date: 22 April 2014

Reviewer: Jayson Stoffman

Reviewer's report:

General comments:

An interesting paper, and a good discussion of a common problem in both gastroenterology and hematology. I'm glad that you were able to review your experience with this treatment method to show general efficacy and safety. You have honestly discussed the limitations of the retrospective nature of this study, and the possible impact on your interpretation of the data. Overall, it generates important new questions to asks, and provides data supporting another way of managing IDA.

Major compulsory revisions:

None

Minor essential revisions:

1. Abstract - Background: It should be 'orally given iron'

2. Abstract - Results: You do not need to say 'diagnosed, concomitant iron deficiency anemia'. Saying concomitant is sufficient, since it implies diagnosed.

3. Abstract - Results: The sentence about the improved hemoglobin levels was unclear to me after I read the paper. I thought the improved levels from 9.5 to 11.9 was the range of the final (improved) values, and not the change from baseline to endpoint. This is clear in the paper, but should be clarified in the abstract.

4. Background: In the first three paragraphs, you have used the terms 'iron deficiency' and 'iron deficiency anemia (IDA)' somewhat interchangeably, which they really are not. IDA is one consequence of iron deficiency. The statistics in your first paragraph describe patients who are iron deficient and those who were also anemic. Your focus, and the inclusion criteria for your patient population, is IDA. In the next paragraphs you discuss using hemoglobin to monitor and manage iron deficiency, when I think you really mean IDA, and treating IDA to relieve the acute symptoms of iron deficiency, which is generally asymptomatic until the anemia is manifest. This is a bit of a splitting of hair, but my perspective is as a hematologist, where we do consider iron deficiency without anemia and IDA differently. I would suggest changing the language to IDA to avoid any confusion.
5. Background - Paragraph 2: Good to point out the importance of acute inflammation. I would add one word: '..such as C-reactive protein must 'also' be taken...'. It highlights that this is something else to consider.

6. Methods - Paragraph 6: The definition of baseline is confusing, and it was unclear whether it was a distinct time point from the others. I interpreted it to be either the pre-FCM or the first FCM, which are the two previously defined time points. The graphs don't have a 'baseline', so it isn't a real timepoint. Might be best to define day of first FCM as baseline, with the comment that the pre-FCM measure was used when first FCM was unavailable.

7. Results - Paragraph 1: The last sentence needs some grammar correction - '37/72 (51.3%) patients were younger...'

8. Results - Paragraph 3: Add one word to the second sentence '...from a baseline 'of' 9.5 ...'

9. Results - Paragraph 7: You don't need the parenthesis to explain that oedema is swelling. Just say oedema of the palms and fingers of both hands. Your readers should know what that means.

10. Results - Paragraph 7: You have a confusing double negative in the discussion of the slow rate and high volume administered, which was not in accordance with the instructions not to dilute below 2 mg/mL. It's much clearer in the discussion that dilution went beyond manufacturer's recommendations.

11. Results - Paragraph 7: After changing your dilutions, only one further event (not events) occurred.

12. Discussion - Paragraph 2: The paragraph ends with 'suggest a need for additional iron to avoid repeat deficiency respectively anemia'. I don't know what that is. I think you mean to say 'recurrent IDA', which is what you discuss in Paragraph 4.

13. Discussion - Paragraph 6 - Same comment about oedema that I made in the results section.

Discretionary revisions:

1. Results - Paragraph 2: I would suggest starting with a sentence stating the total number of administrations. You've done this in the abstract, and it would introduce the content of the paragraph well.

2. Results - Table 2: I don't think you need the first row, showing the indication for 100% was IDA. You've stated that clearly in the text, and it doesn't add to the table.

3. Results - Paragraph 4: I wonder if you aren't overinterpreting the changes in the WBC and platelet count. Both of these rise transiently and then fall, and the changes are fairly minor. This may actually represent changes in myelopoeisis
with the management of the IDA. We often see increased platelet counts with IDA because of increased bone marrow activity, which then increases further when iron is provided for hematopoeisis. As the anemia improves, marrow function returns to baseline, which may explain the drop in the counts. I don't know for sure, and that doesn't address the CRP, but it's something to consider.

4. Discussion - Paragraph 5 - Given my previous comments about the falling WBC and platelets, I found your reference to similar findings in other studies interesting. It might be helpful to add one sentence describing their interpretation of that finding.

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

Quality of written English: Needs some language corrections before being published

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

Declaration of competing interests:

I declare that I have no competing interests.