Author's response to reviews

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

Authors:

Martin W Laass (martin.laass@uniklinikum-dresden.de)
Simon Straub (simon.straub@uki.at)
Suki Chainey (suki.chainey@viforpharma.com)
Garth Virgin (garth.virgin@viforpharma.com)
Timothy Cushway (timothy.cushway@viforpharma.com)

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To Dr. Wael El-Matary

Executive Editor

BMC Gastroenterology

RE: MS 6974930291255436

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

Authors: Martin W. Laass, Simon Straub, Suki Chainey, Garth Virgin, Timothy Cushway

Dear Dr. Wael El-Matary,

Thank you very much for your insightful comments.

1. It is surely true, that the correction of iron deficiency anaemia is also related to the treatment of the underlying disease. We included in our study all patients (majority with IBD) treated with intravenous iron in the investigation period. Due to the diversity of our study population (in respect of disease as well as in respect of activity) we did not perform separate analyses of patients with active and inactive disease. For this purpose we should have been calculated disease activity scores: Pediatric Crohn’s Activity Index (PCDAI) and Pediatric Ulcerative Colitis Activity Index (PUCAI). But this is beyond the aim of our study. We write in...
our abstract: “This retrospective study is the first to describe the use of intravenous ferric carboxymaltose (FCM) in the pediatric setting.” Our study is an observational one. The focus of our study was safety and tolerance of intravenous iron in pediatric patients. Our statistic is descriptive. We think that we honestly presented our data. We did not calculate any p-values in order to prove any statistical significance, what would be assuming. In our conclusions we do not over-interprete our data. We use the word “appear” and not “is” or “is proven”: “Overall FCM was well tolerated in this pediatric population and appeared to be effective in correcting iron deficiency anemia.”

The mean CRP in our patients was elevated at day 1 (see figure 4). Nevertheless it seems highly unlikely that the increase in ferritine and other parameters of the iron metabolism will response to the treatment of the underlying disease in week 0-2 as we have seen it. Normal CRP and no use of steroids do not mean that disease is not active and vice versa! To summarize our arguments: we do not think that our data enable subgroup analyses. In order to meet your objections we suggest to add an additional paragraph, which will modify our conclusions: “Due to the observational nature of this study, we cannot confirm if the correction of iron deficiency anaemia is related to the iron supplementation only or also in some part to the treatment of the underlying active disease. This is compounded due to the limitation within our data collection which did not include disease activity at the time of iron treatment and hence we are unable to distinguish clearly between patients with active disease and those in remission. Hence further randomised controlled studies may be required to confirm the true impact of the iron therapy.”

We hope that the re-revised manuscript can be accepted for publication in BMC Gastroenterology.

Yours sincerely,

Martin Laass
(on behalf of all authors)

Martin W. Laass, MD
Department of Pediatric Gastroenterology and Hepatology
Children’s Hospital, Technische Universität Dresden
Fetscherstr. 74, 01307 Dresden, Germany
Tel.:(+) 49-351-458-2267
Fax:(+) 49-351-458-5777
E-mail: martin.laass@uniklinikum-dresden.de
Here we list all changes we made step by step:

1. In the discussion we added the following paragraph:

"Due to the observational nature of this study, we cannot confirm if the correction of iron deficiency anaemia is related to the iron supplementation only or also in some part to the treatment of the underlying active disease. This is compounded due to the limitation within our data collection, which did not include disease activity at the time of iron treatment and hence we are unable to distinguish clearly between patients with active disease and those in remission. Hence further randomised controlled studies may be required to confirm the true impact of the iron therapy."

In the abstract we changed the conclusion into:

Conclusion: "Overall FCM was well tolerated in this pediatric population and appeared to be effective in correcting iron deficiency anemia. We cannot exclude that the correction of iron deficiency anaemia is in some part due to the treatment of the underlying disease and not related to the iron supplementation only."

2. The editor wrote: The title is misleading. Since other "causes" were also included (although a minority of the patients) there are 2 possibilities, either the title should reflect the diversity in the group or authors should report only experience with IBD"

We changed the title into: Effectiveness and Safety of Ferric Carboxymaltose Treatment in Children and Adolescents with Inflammatory Bowel Disease and other gastrointestinal diseases