

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Initial treatment of steroid-sensitive idiopathic nephrotic syndrome in children with mycophenolate mofetil vs. prednisone: Initial treatment of steroid-sensitive idiopathic nephrotic syndrome in children with mycophenolate mofetil vs. prednisone: Protocol for a randomized, controlled, multicenter trial (INTENT Study)
<b>AUTHORS</b>	Ehren, Rasmus; Benz, Marcus; Doetsch, Jorg; Fichtner, Alexander; Gellermann, Jutta; Haffner, Dieter; Höcker, Britta; Hoyer, Peter; Kästner, Bärbel; Kemper, Markus; Konrad, Martin; Luntz, Steffen; Querfeld, Uwe; Sander, Anja; Toenshoff, Burkhard; Weber, Lutz

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Kazumoto Iijima Department of Pediatrics, Kobe University Graduate School of Medicine, Japan
<b>REVIEW RETURNED</b>	05-Jul-2018

<b>GENERAL COMMENTS</b>	<p>Ehren et al. presented study protocol for a randomized, controlled multicenter trial to examine whether mycophenolate mofetil is not inferior to prednisone regarding sustaiment of remission as initial treatment of steroid-sensitive nephrotic syndrome in children. This study is interesting, significant and well designed. However, I have several concerns.</p> <ol style="list-style-type: none"> <li>1. The regimen for prednisone treatment for relapses during study period should be determined and described in the text (not in Appendix) since secondary endpoints such as number of relapses during follow-up, mean relapse rate per patient and year and number of frequent relapsers may be affected by the regimen.</li> <li>2. P18/106 L427. What is more intense immunosuppressive treatment? The authors should explain it.</li> <li>3. P7/106 L138. "Mycophenolat" should be changed to "Mycophenolate".</li> </ol>
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<b>REVIEWER</b>	Abhijeet Saha Division of Pediatric Nephrology, LHMC, New Delhi, India.
<b>REVIEW RETURNED</b>	15-Jul-2018

<b>GENERAL COMMENTS</b>	The authors have planned this RCT meticulously. We await the results of this eagerly, as results may have major impact on treatment protocols worldwide.
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<b>REVIEWER</b>	Deirdre Hahn Westmead Children's Hospital, Australia
<b>REVIEW RETURNED</b>	07-Aug-2018

<b>GENERAL COMMENTS</b>	<p>Thank you for the opportunity to review the protocol.  This is certainly an interesting study - the notion to trial other therapies besides corticosteroids for the initial presentation of nephrotic syndrome is a novel idea.  It will be interesting to see the outcome to the study.  The investigators have attempted to give some explanation as to why this is an open label study -  One has thought a liquid solution of prednisone could have been sourced.  A blinded trial would have aided in reducing any risk of bias.</p> <p>There are a few grammatical errors - mainly related to sentence structure.  eg  At visit 4, the history since visit 3 is documented, especially, if there occurred one or more relapses since visit 3. - ?should read - especially if one or more relapses occurred since visit 3</p>
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## VERSION 1 – AUTHOR RESPONSE

Dear Professor Iijima (reviewer 1),

Thank you very much for the comprehensive review of our manuscript.

1. The regimen for prednisone treatment for relapses during study period should be determined and described in the text (not in Appendix) since secondary endpoints such as number of relapses during follow-up, mean relapse rate per patient and year and number of frequent relapsers may be affected by the regimen.

Response: Thank you for this remark. We added the regimen on page 16, lines 393 to 395.

2. P18/106 L427. What is more intense immunosuppressive treatment? The authors should explain it.

Response: Thank you for this question, we should have made this point clearer. We therefore added the following lines on page 16 lines 429 to 430 "... more intense immunosuppressive treatment (e.g. CSA, tacrolimus, MMF, cyclophosphamide, rituximab, or levamisole)".

3. P7/106 L138. "Mycophenolat" should be changed to "Mycophenolate".

Response: Thank you. We changed it into "Mycophenolate".

Dear Professor Saha (reviewer 2),

Thank you very much for your positive evaluation of our manuscript.

Dear Dr. Hahn (reviewer 3),

Thank you very much for the comprehensive review of our manuscript.

1. The investigators have attempted to give some explanation as to why this is an open label study -

One has thought a liquid solution of prednisone could have been sourced.

A blinded trial would have aided in reducing any risk of bias.

Response: You raise an important point that we discussed intensely when we were planning the study. Due to the side effects of the steroid treatment that we expect to be visible in the control group, we decided for an open label approach.

1. There are a few grammatical errors - mainly related to sentence structure.

eg At visit 4, the history since visit 3 is documented, especially, if there occurred one or more

relapses since visit 3. - should read - especially if one or more relapses occurred since visit 3.  
 Response: Thank you. As the mentioned sentence is not part of the manuscript, but of the study protocol, we are happy to correct it when the next study amendment becomes necessary.

#### VERSION 2 – REVIEW

<b>REVIEWER</b>	Kazumoto Iijima, MD. PhD. Department of Pediatrics, Kobe University Graduate School of Medicine, Japan
<b>REVIEW RETURNED</b>	03-Sep-2018
<b>GENERAL COMMENTS</b>	The authors addressed my concerns well.