Author's response to reviews

Title: Effects of Erythropoietin on Depressive Symptoms and Neurocognitive Deficits in Depression and Bipolar Disorder

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Author's response to reviews: see over
Dear Editors-in-Chief: Doug Altman, Curt Furberg, Jeremy Grimshaw and Peter Rothwell

RE: Effects of Erythropoietin on Depressive Symptoms and Neurocognitive Deficits in Depression and Bipolar Disorder

Thank you for considering the above manuscript for publication as an original research paper in Trials and for the valuable comments from the reviewer which are addressed below.

We hope you agree that addressing these points has improved the manuscript and makes it suitable for publication in Trials.

Yours sincerely,

Dr Kamilla Miskowiak
1. We agree with the reviewer that it may be questionable whether a difference in 3 points on the HDRS scale is clinically relevant in patients with moderate to severe treatment-resistant depression. However, this group of patients is particularly difficult to treat, generally showing very low rates of treatment response and little response to placebo. This points to a clinical relevance of even small improvements in depressive symptomatology in this group. Further, it is generally accepted in the literature that a reduction of 2-3 points on the HDRS represents a clinically relevant improvement. We therefore believe that a difference of 3 HDRS scores is clinically relevant in our patient group.

2. OK.

3. The reviewer highlights that it could be useful to include a dichotomized measure of the proportion reporting significant clinical improvement in study 1 as defined by a CGI type assessment of global improvement in addition to remission with separate risk ratios and confidence intervals. CGI has not been included in the study which was initiated a year ago. However, as an alternative measure of global functioning we have included assessment with “Global Assessment of Function (GAF)” before and after treatment. These GAF scores will be reported including confidence intervals. Similarly, confidence intervals will be reported in relation to the proportions in remission. A description of this has now been added to the Methods section under Outcome assessments: “Global Assessment of Function (GAF) scores at week 9 will be reported in addition to the primary outcome.”

4. OK.