Reviewer's report

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

Version: 1 Date: 5 May 2010

Reviewer: Prathap Tharyan

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1. Will the study design adequately test the hypothesis?

Yes, it is a well designed trial. The only concern I have is that for study 1, the primary outcome is a difference in mean HDRS ratings of 3 points with an SD of 3. In people with resistant depression starting with scores above 17 on the HDRS, it is doubtful that this difference will be clinically significant. The secondary outcome of remission on the HDRS would be of greater clinical importance but it is unclear if the estimated sample size would permit identification of a significant difference with EPO, should one be demonstrated.

2. Are sufficient details provided to allow replication of the work or comparison with related analyses: if not, what is missing?

Yes

3. Is the planned statistical analysis appropriate?

What is planned appears to be an RMANOVA of HDRS scores. What might prove additionally useful for clinical interpretation would be a dichotomized measure of the proportion reporting significant clinical improvement in Study 1 (defined by a CGI type assessment of global improvement,) and reaching remission , with separate risk ratios and confidence intervals of this measure. A similar attempt to provide dichotomized measures of clinically significant improvement in study 2 would also be useful.

4. Is the writing acceptable?

Yes