Reviewer's report

Title: Short course daily prednisolone therapy at the time of upper respiratory tract infection in children with relapsing steroid sensitive nephrotic syndrome (PREDNOS 2): protocol for a randomised controlled trial

Version: 3  Date: 4 February 2014

Reviewer: Erik Cobo

Reviewer's report:

I read the PREDNOS trial paper’ from Webb et al., and I think it is suitable for publication in Trials.

I would like to provide some suggestions in order to help authors to improve both this protocol and their future results paper.

- Major Compulsory Revisions

I’m confused about the reference group, the standard of care, the study aims, and the future implications of the PREDNOS trial. From the paper, I understand that the standard of care with those patients (abstract second line and background line 10) is long term prednisolone. So, I was expecting a non-inferior aim of a short regime against the long one (maybe non-inferior efficacy and better safety). But your control group is placebo. If you show differences with placebo, how would you argue that a long regime has to be substituted by your proposed short one? Also, how standard is the long one? How much is it based on evidence? If there are clinical guides for the long regime, is it ethical to randomize to placebo? Please, clarify those points in order to avoid similar doubts for future readers.

I’m also confused by the main variable, sample size rationale, statistical analysis and the length of follow up. SS is based on the comparison of the proportion of patients having a relapse. For this, you only need one episode. After this episode, you may finish the follow up and allow a different open treatment for that patient. It is expected that an analysis with more episodes will have more information and more power. Is this extra power needed? Does it justify extra follow up for the patient which has already had an episode? Will recruitment be easier for a shorter follow-up? [If there is a clear treatment policy after the first episode, do we need to know more information? I.e., is it practically relevant if the treatment (or the outcome) of the first episode affects the outcome of future episodes?] Please, clarify.

Please, in accordance with Trial rules for study protocols, specify that your final report will be published in accordance with the CONSORT statement. Please note that SPIRIT was released last year and it provides you with several chances to improve your design. Of special importance for guaranteeing transparency are items 31a, 31b and 31c, which ask protocol authors to provide details of their dissemination policy. Please, note that the Spirit figure requires your table 1 to
highlight that randomization occurs after recruitment.

- Minor essential Revisions

Please, specify somewhere your efforts to avoid trial attrition. Please, be aware of important advice in http://www.nejm.org/doi/full/10.1056/NEJMr1203730

Please, consider rewording the inclusion criteria to make clear which conditions are required for any patient and which ones are alternative conditions for eligibility.

Please, consider justifying the reasons why a similar effect size is expected for the different subgroups described on page 10.

- Discretionary revisions

Please, consider either deleting the final background sentence (“…important definitive evidence…”) or substituting it with the more technical first sentence in Methods.

Please, consider changing ‘UK’ to ‘developed’ in the last line of the Background section of the Abstract, according to later wording.

My best wishes for the next phases of your meritorious work.

Erik Cobo

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

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests