Reviewer’s report

Title: Randomised placebo-controlled trial on antibiotics for bronchiectasis exacerbations in children: rationale and protocol

Version: 4 Date: 4 July 2012

Reviewer: Erik Cobo

Reviewer’s report:

As the trial is well designed and the paper is well written, from my opinion, it merits acceptance for Trials.

My only major concern requiring compulsory revision is about multiplicity. Greater alpha consumption that the 0.05 specified can come from two ways. The first one is the interim analysis. Authors should specify the way they will take into account the previous formal look. [As they specify 0.001 for the first look, a straightforward procedure can be performing the second test at a 0.049 level.]

The second one is the existence of 2 active treatment arms. If authors are willing to report as positive a result in only one active arm, they should recognize that the alpha levels from both tests 'add in some way' and the chances to declare a treatment as effective are greater than just 5%. If, for example, authors would claim that treatment A is positive unless treatment B is not, they should, for example, adjust individual alpha levels. Please note that first line in page 7 can be interpreted in the sense that the trial would only be positive if both treatment arms were statistically significant. If that is the intention, multiplicity is not a concern, but then, trial power is affected. Please clarify this sentence.

Minor essential revisions

As both active treatments are compared with the same treatment arm, maximum efficiency is achieved if more patients are allocated to the placebo arm -that is employed in both comparisons. Optimal allocation ratio is 1:1:sqrt(2). If, for ethical concerns, authors want to still in a 1:1:1 ratio, this may be highlighted.

As the power for highlighting safety concerns would be different for the non numerable possible outcomes (any expected or unexpected adverse event), please consider deleting the requirement for statistical significance in the DSMC safety revisions.

Discretionary revisions

Please, consider reporting sample size and number of centres in the abstract. Please, consider either deleting first words in line 8, page 6; or addressing the objectives of the second component of BEST.

In order to become fully confirmatory and to avoid ambiguities in predictors selection, please, consider fully specifying them in a prior to unmasking Statistical Analysis Plan. Please consider changing in page 15 lines 11-13 as well as the last one. (Please, see baseline comparisons in the CONSORT
statement).

Please, consider clarifying methods and length of follow up for the secondary outcome "time to next exacerbation".

Please, consider changing "hospitalised" by "previous hospitalised" in page 5, line 12.

Please, consider changing "examine" by "explore" in page 6, point 2. (Should this exploration be performed with a subgroup analysis?)

Please, consider reporting centres in the same order in pages 8 and 9.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

I don't have competing interests for this paper.