Reviewer's report

Title: Clinical trial: Probiotic treatment of acute distal ulcerative colitis with rectally administered Escheria coli Nissle 1917 (EcN)

Version: 5 Date: 23 November 2009

Reviewer: Per Farup

Reviewer's report:

The paper reports the results of a randomised controlled trial (RCT) comparing different doses of a probiotic enema with placebo in patients with distal ulcerative colitis. I have several concerns about the paper, these are the major ones:

• A per protocol (PP) analysis is reported as the main result. According to international guidelines, intention to treat (ITT) analyses should always be the primary results when presenting the results of RCTs, and PP-analyses could be reported if of interest. In this study the ITT-analyses showed no effect. The lack of effect is the main result of the trial, which also is very interesting.

• According to the abstract, the conclusion is that the probiotic is as effective as other treatments for distal ulcerative colitis. The conclusion is wrong since the trial does not compare the probiotic with other treatments. The conclusion is that there is no significant effect above placebo in the ITT-analyses, but the probiotic seems to be superior to placebo in the PP-analyses. Comparisons with other treatments could be discussed in the paper but not presented as the conclusion.

• The analyses of the trial are incorrect. Again, according to international guidelines, two-sided tests (not one-sided) should be used. A lot of the results are poorly or not documented. For example, it is reported that time to remission was shorter in the 40 ml and 20ml groups than in placebo. This is presented in one figure but no statistical calculation was performed.

• In the method section it is said to be a randomised controlled trial with four groups. Later it is written that the placebo group was pooled from the three groups.... What does that mean?

• Please describe the DAI, without a description it is impossible to understand the scoring system. The same applies to the histological classification, how was is made and what was significant inflammation? Without a description it is impossible to understand what “disappearance of histological signs of significant inflammation” means.

• Histological abnormalities of the descending colon were observed in 20/88 patients. These patients had left-sided colitis and not UC proctitis /proctosigmoiditis which was the inclusion criterion. Two patients had remission (histological?) on baseline. Were patients in remission included? Inclusion criteria were mild and moderate disease activity.
• The text refers to table 1 which is not included in the version I have received, and the figures are not the most appropriate ones.

• The presentation is mixed-up.

• English is not my native language, but I think the written language deserves improvement.

It is likely that the trial contains interesting findings. The results might be negative, but that is also of interest. The study deserves new and correct analyses and a better scientific presentation.

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

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.