Reviewer's report

Title: Enteral Nutrition Tolerance And REspiratory Support (ENTARES Study) in preterm infants: study protocol for a randomized controlled trial

Version: 0 Date: 24 Sep 2018

Reviewer: Cynthia Bell

Reviewer's report:

The authors have clearly written up a well designed study on an important topic of respiratory management in newborns and its effects on time to enteral feeding, an important outcome related to the possible development of NEC in these babies. Balancing the risks and benefits of improved respiration with improved nutritional support is difficult and the results of this trials will be of high interest to those the neonatology field. Overall, the manuscript is well written and I have only a few comments/suggestions:

- Patients who die or are transferred out of the hospital will be excluded from the analysis. Please consider adding these as outcomes or as important SAEs to report. Otherwise, the current ITT analysis plan is appropriate.

- Perhaps consider adding a couple limitations to the study in the discussion. (1) The exclusion of more sick babies (neuro/surg, sepsis, major malformation, etc) makes results less generalizable to all NICU patients and (2) inability to double-blind may influence outcome if practitioners already have preconceived ideas for or against types of respiratory support relating to nutritional delivery systems. However, the second limitations seems to be minimized by the standardization of how much to increase feeds and when to interrupt enteral feeds (Table 1 and 2).

- Table 3 shows what data will be records but I recommend adding the timeframe of each of these recordings. For example, ventilation/respiration parameters recorded when there is a change in respiratory support, feeding parameters recorded daily, etc

- The primary outcome will be analyzed by "survival analysis with a not parametric distribution." Please correct the typo from "not" to "non". Also, I am assuming you mean Kaplan-Meier. I would also suggest employing a Cox regression model or other multivariate model where the stratification factors (GA<>28 weeks and site) could be incorporated into the model to ensure no Type 1 or 2 error bias has resulted by not accounting for these factors (see Kahan and Morris BMC Medical Research Methodology 2013, 13:99).
- What is meant by "by proper" on line 41 page 3?

- What is meant by the delta: 5.7 on line 48 page 3? Is this the difference in time to enteral feeds between the JCPAP and HHHFNC from the observation pilot data? If so please state so more clearly.

**Level of interest**
Please indicate how interesting you found the manuscript:

An article whose findings are important to those with closely related research interests

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable

**Quality of figures**

All images and figures within the manuscript should be genuine i.e. without evidence of manipulation. No specific feature within an image may be enhanced, obscured, moved, removed, or introduced. If you have concerns about the veracity of the figures you should choose the first option below.

**Statistical review**

Is it essential that this manuscript is seen by an expert statistician? If so, please give your reasons in your report.
Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal

Were you mentored through this peer review?

No