Author's response to reviews

Title: A phase I study of daily treatment with a ceramide-dominant triple lipid mixture commencing in neonates

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Author's response to reviews: see over
Ms Wella Valenzuela  
BioMed Central Editorial Team  
BMC Dermatology  

Dear Ms Valenzuela,

Thank you for forwarding the reviewers comments regarding our manuscript, titled

"A phase I study of daily treatment with a ceramide-dominant triple lipid mixture commencing in neonates".

We thank the reviewers for their constructive comments on how this work may be improved. We have responded to each comment below. There are a number of comments made by the reviewers’ that we are not certain that we have understood correctly, and if we have misinterpreted any of these comments, we would be happy to provide further information, or justification, as required. In addition, we have transferred the manuscript file into the BMC Dermatology template to ensure that it meets the specified formatting requirements.

We eagerly await your opinion.

Best wishes,

Dr Adrian Lowe, (on behalf of the authors of this manuscript).

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**Reviewer 1**

**Comment 1:** Measurement of skin characteristics were done. Although no results were given, the authors reported "substantially" lower TEWL compared to previously reported. This need to be corrected.

**Response:** Table 2, which summarizes the biophysical properties of the participants’ skin at the six week follow-up, was not included in the original submission. We apologize for this oversight. The mean value of 9.3 (range=7.2-10.5) g/m²/hr for trans-epidermal water loss appears to be lower than that reported in previous studies conducted on infants (mean=26 for infants aged 3-6 months). However, differences in the study protocols and age groups tested, we are unable to draw any strong conclusions concerning these observations.

In response to this comment, we have added table 2, and also modified the sentence in the discussion to read as follows:

“Due to the lack of a control group, no conclusions can be made concerning the effect of the intervention on skin barrier, although the obtained TEWL values appear to be substantially lower than those reported previously in this age group (mean=9.3 g/m²/hr, range=7.2-10.5 for the current study compared with mean = 26 g/m²/hr for infants aged 3-6 months in a prior publication).

**Reviewer 2**

**Comment 1:** Phase 1 study is a clinical study to find out the chance of adverse effects of new drug. Because EpiCream® was approved by FDA, this is a well performed phase 1 study in neonates. As author claims, a number of adverse events occurred which are unlikely to be related to the study treatment. Because it is a phase 1 study, 10 normal infants with a family history of allergic disease were recruited. Then, conclusion is “FDA approved moisturizer did not show adverse event also in neonate”.

**Response:** We have modified the conclusion section to read as follows:

“The treatment used in this study, EpiCeram, has been approved by the Food and Drug authority for the treatment of eczema. This pilot study supports the safety and parental compliance with daily applications of this formulation to the skin of neonates, for the purpose of possible eczema prevention. However, recruitment remains problematic.”

**Comment 2:** More detail information of moisturizer is necessary (especially what kind of ceramide is contained?)

**Response:** A link to the ingredient list for this moisturizer has been added to the text of the manuscript (http://www.epiceram-us.com/prescribing-information). This formulation contains the pseudo ceramide N-(2-hydroxyethyl)-2-pentadecanolyhexadecanamide, which has again been added to the methods section of the manuscript.

**Comment 3:** Are the data sound? No

**Response:** We presume that the reviewers concerns regarding the soundness of the data either relates to the data not being reported on biophysical properties of the skin in the submitted version of the manuscript, or the relatively small sample size. As noted in
response to reviewer 1’s comment, the table of outcome data at six weeks has now been added. Also, we have included a paragraph in response to reviewer 2’s comment 5 below, which more explicitly acknowledge the limitations of this study, including the sample size. We would be happy to address any other specific concerns with the study data if the reviewer could provide further clarification.

**Comment 4:** Does the manuscript adhere to the relevant standards for reporting and data deposition? Questionable

**Response:** Again, we are not entirely sure what the reviewer is referring to with this comment. We have added the table of biophysical outcome data to the manuscript, and we hope that this satisfies the reviewer’s concern.

**Comment 5:** Are limitations of the work clearly stated? No comments

**Response:** Although the limitations of the study are mentioned in various places within the discussion, we agree that a distinct paragraph on this would benefit the manuscript. For this reason, we have added the following:

“This study has two important limitations. Firstly, although we did not observe any adverse skin effects of the study treatment, the relatively sample size means that we can not exclude the possibility that this treatment may cause rarer adverse effects. Secondly, the lack of a control group precludes us from assessing if this treatment may help improve skin barrier function and reduce the risk of eczema. We are currently developing further trials to address these limitations”.

**References**