Author’s response to reviews

Title: High efficacy of a dimeticone-based pediculicide following a brief application: in vitro assays and randomized controlled investigator-blinded clinical trial

Authors:
Jorg Heukelbach (heukelbach@web.de)
Doerte Wolf (doerte.wolf@cardiosec.de)
John Clark (jclark@vasci.umass.edu)
Hans Dautel (dautel@insectservices.de)
Kristina Roeschmann (k.roeschmann@Pohl-Boskamp.de)

Version: 3 Date: 18 Sep 2019

Author’s response to reviews:

Dear Editor:

We have now uploaded the manuscript including the requested amendments:

1. Please address the reviewers’ comments at the end of this email.

OK, done – please see our response below.

2. Please clarify the parental consent obtained during your study. If participants were under 16, then parental consent should have been acquired. Please include a statement in your “Ethics approval and consent to participate” section, referring to the parental consent obtained for this study, and clarify whether parental consent was obtained for all participants under 16. Please include whether this consent was written or verbal.

Parental consent was obtained for all minors. We have reworded the statement to make this point clearer. We have also included a statement that the parental consent was written. The statement in the respective section now states the following:

“As children that participated in this study were unable to provide legally binding consent, the legal representative/s of all minor participants had to give informed written consent on his/her behalf prior to enrolment in the trial, and after having been informed about all details concerning the trial (patient information and informed consent from). Furthermore, age appropriate consent forms were used for children aged 7 – 11 year, and adolescents aged 12 – 17 years. All minors
included in this trial provided written or verbal assent, according to age, witnessed by the parent or guardian.”

3. In your 'Availability of Data and Materials' section, please clarify who the data can be requested from.

OK, done.

4. Please remove any duplicates of tables, and move all tables to the end of the manuscript, removing them from the main text.

OK, done.

5. Currently, you have no Figure 2. The second figure's file name is figure 3. Please amend this.

OK, corrected.

6. Please remove the CONSORT document from the end of your manuscript file as this is no longer needed in the publication process.

OK, removed.

7. At this stage, please upload your manuscript as a single, clean version that does not contain any tracked changes, comments, highlights, strikethroughs or text in different colours. All relevant tables/figures/additional files should also be clean versions. Figures (and additional files) should remain uploaded as separate files.

OK, done

Reviewer reports:

Ian Burgess (Reviewer 1): Thank you for your attention to the comments of reviewers. The manuscript now reads much better as a consistent whole and in general has answered nearly all of the questions raised during the previous review process.

There remain a few inconsistencies and points that would make understanding of the value of this study and the methodology clearer for readers.

1. Since you have stated that nit combing was an integral part of the therapy for both clinical interventions, irrespective of whether parent/guardians carried out any additional
combing, it should be made clear to readers that this was a part of your clinical study and was a necessary component of treatment. Without doubt combing contributed to the efficacy of both products, although we cannot determine to what degree this did contribute in the absence of a non-combing arm to the study. Therefore, you need to add in some text to this effect as follows:

a. Title. The title should be changed to read "High efficacy of a dimeticone-based pediculicide with adjunctive nit combing following a brief application: in vitro assays and randomized controlled investigator-blinded clinical trial". Otherwise readers could be misled into thinking that the products achieved this level of efficacy in the absence of combing.

b. Reference to the combing element as part of the therapeutic procedures needs to be added to parts of the text as an important point for clarification of the efficacy, and to avoid misunderstanding, because it could also explain the unexpectedly high efficacy of the comparison product as well as making a contribution towards efficacy of the test product. This should be done at lines 575, 618, 643-644, 691-693, 707.

Response: According to the instructions for use of the reference product and the test product, and in accordance with the current recommendation of the German Robert Koch Institute, patients/caregivers received a comb and combing was recommended, but was not integral part of the therapy. The decision to perform additional combing was in the responsibility of the patients/caregivers and documented for every visit.

In the results and discussion/limitations sections, it is stated that the use of a nit-comb is controversially when assessing the efficacy of pediculicides. Our assessment on treatment failures and their association with the implementation of combing did not find any association.

As presented in the manuscript, 39 patients of the 100 patients included in the trial reported at least at one of the visits no additional combing. A total of 5 patients reported no combing at all throughout the course of the study. None of these 5 patients experienced a treatment failure.

We therefore disagree to implement the change of the title as proposed and also think that the potential effect of combing is adequately displayed and discussed in the manuscript. We have revised some sentences (lines 343, 344, 444, 445, 450, 620 and 621; these line numbers differ from the previous manuscript version and refer to the amended manuscript) to avoid any further misunderstandings and to address the concerns raised by the reviewer.

2. You have made it clear that in the spray test the permethrin comparator could not be sprayed because of viscosity (lines 180-181). However, in lines 422-423 there remains a potential misunderstanding because it is implied that the permethrin product was sprayed.

Response: We have corrected the respective sentence (now lines 377/378).

Best regards,
Jorg Heukelbach