Author’s response to reviews

Title: The clinical efficacy and safety of light-masks at preventing dark adaptation in the treatment of early diabetic macular oedema (CLEOPATRA): A Multicentre Phase III Randomised Controlled Single-Masked Clinical trial

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The clinical efficacy and safety of light-masks at preventing dark adaptation in the treatment of early diabetic macular oedema (CLEOPATRA): A Multicentre Phase III Randomised Controlled Single-Masked Clinical trial

Thank you for your useful comments on our manuscript. The authors of this manuscript have given full consideration to the comments and would like to submit a revised manuscript for consideration.

The points raised concerning the submission have been addressed as fully as possible as follows:

Editorial requests:
1. Email addresses are included for all authors on the title page.
2. The Ethics committee that approved the study is now added to the methods section. It is a national committee that gives approval for conduct of the study at all sites.

Reviewer 1 Comments:
Major compulsory revisions
1. The sentence ‘but these cases are often only closely monitored in eye clinics’ have been deleted.
2. The word hypothesis is changed to ‘rationale’.
3. We have now added that Oximetry will be evaluated using Oxymap T1 oximeter.

Minor Essential Reviews:
1. We have added under ‘blinding’ that it is likely that some participants in the control arm may not use the control mask without illumination daily over 2 years.
2. We have changed that 55 logmar letters = 6/24.

We have made further language corrections. We have also added two authors – the trial manager and the trial expert for the mechanistic evaluation.

We have just received REC approval for an amendment and we have taken this opportunity to add these changes to the document.
They include:
1. We have changed that 55 logmar letters = 6/24.
2. The randomisation stratifiers of HbA1C also includes measurement in mmol/litre
3. The statistical analysis is refined to ensure that DMEC will monitor the study power throughout the study and the analysis of primary outcome will include
   ‘The primary outcome will be analysed using a two-sided test from a linear mixed effect model for repeated measures across visits, which will enable a comparison between participants receiving light-masks (active) and control masks, with covariates for each follow-up visit of baseline, randomisation
stratifiers and arm, and with a random participant effect at each visit with unstructured covariance matrix. ’

The authors would like to thank the editor and reviewer for their time in providing such valuable comments. We believe that the revised manuscript is a much stronger piece of work.

Yours sincerely

Miss Sobha Sivaprasad (for the CLEOPATRA study team)
27-09-2014