Reviewer’s report

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

Version: 3 Date: 26 August 2014

Reviewer: mark C gillies

Reviewer’s report:

This is a very interesting study since it tests an entirely new and biologically plausible intervention for diabetic macular oedema. The interventions and outcomes are reasonably well described, the statistics are appropriate

Major Compulsory Revisions

1. "Laser photocoagulation may be performed for non-central clinically significant macular oedema but these cases are often only closely monitored in eye clinics." This statement should be withdrawn since it is controversial, most people would not observe clinically significant macular oedema

2. More rigour is required in formulating the study hypothesis. "This study hypothesised that increased glucose is associated in various ways with a decrease in oxygen supply to the retina, and an increase in oxygen demand." The hypotheses listed should be chosen carefully and limited to what will be tested by the study. This hypothesis will not be tested since measurement of retinal oxygen levels is not an outcome. Similarly, "we hypothesize that wearing light-masks during sleep will prevent dark adaptation and reduce oxygen demand by the rods, which in turn will cause regression and prevent the development and progression of DMO." is not an appropriate hypothesis because they will not test dark adaptation and oxygen demand by the rods when patients are asleep. These may be the rationales for the study. Surely the hypothesis is that using light masks will reduce the thickness of pericentral DMO.

3. I do not believe that there is enough information on how to perform the 5th mechanistic evaluation (something to do with oximetry) for it to be replicated by another group

Minor Essential Revisions

1. The use of control masks should be justified. It seems highly unlikely that patients would wear masks without illumination every night for 2 years. Patients are not masked to treatment allocation anyway.

2. 55 LogMAR letters = 6/24, not 6/18
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: none