Reviewer's report

Title: Efficacy of Vision Restoration Therapy after Optic Neuritis (VISION-Study): Study Protocol for a Randomized Controlled Trial

Version: 1 Date: 27 April 2012

Reviewer: Erik Cobo

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Major concerns
1) Authors should provide enough details to allow replication of the analysis and to guarantee that analyses will be performed in accordance to protocol. For example, would they analyze the improvement from baseline? Would they adjust for prognostic variables? Which ones? With what method? Without scale transformation? As their variables are numerical, they can read, for example the chapter about “the analysis of change” in “Statistical Issues in Drug Development” from Stephen Senn, Wiley.

2) As the control intervention is not included in the standard of care, please be aware that any positive conclusion will rely on the assumption that this intervention has no negative effects. If feasible, please provide references to justify this.

3) More randomization and concealment details should be provided. Who uses the ‘freeware’ program? Which one? How was the list stored? Does the researcher who recruits patients have access to this list before enrollment? How would authors guarantee (to a quality assurance professional) that the allocation arm was unknown before enrollment? How does the ‘independent’ person tell the patients what treatment to follow? How ‘independent’ is the outcome evaluator from researchers who train patients with allocated treatment? How would authors avoid patients asking questions to the follow-up and evaluator researchers about the intervention?

4) As dropouts and protocol violations would compromise results and interpretation, please, consider methods to boost adherence to the protocol.

5) Please consider if, in your population, having access to a PC at home should be specified as eligibility criteria.

Optional choices
1) Please, consider providing the effect size (difference between groups) with the 95% CI for the results reported on page 5, line 1.

2) Please, consider switching your trial from ‘pilot’ to ‘pivotal’. Although I see your arguments in the discussion, this change would allow proving the effect if its size is moderate. [For a numerical outcome, 80 patients permit testing an effect size close to the SD. See, for example, the Nomogram on “Practical statistics for medical research” from Douglas G. Altman.] Since the intervention has been
tested under other conditions (ref 40), you may derive reasonable values to justify the sample size rationale. If the statistical analysis and the required power result in a reasonable effect size, you will have some reasonable chances (estimated by the power) of demonstrating efficacy. [I’m not completely sure if this change can be made after the trial has started—but, if so, it should be masked to the results. I would appreciate the editor’s point of view. Should you agree on it with your ethical committee?] Please note that this change will imply guaranteeing that the analysis is protected against multiplicity; for example, clearly stating main outcome, analysis, and ITT population.