Reviewer’s report

**Title:** Feasibility of a randomized single-blind cross-over trial to assess the effects of the second generation slow-release dopamine agonists pramipexole and ropinirole on cued-recall memory in idiopathic mild or moderate Parkinson's disease without cognitive impairment.

**Version:** 0  **Date:** 10 Jan 2017

**Reviewer:** Martyn Lewis

**Reviewer's report:**

I read with interest this article, and have the following issues for you to consider:

[Page 6]: Requirement to align the article and make reference to the recent CONSORT extension to pilot trials (Eldridge et al., Pilot and Feasibility Studies 2016; 2:64) as opposed to reference 28 (Schulz et al 2010)

[Page 7]: Randomisation is specified as 1:1; I think this was simple randomisation as there was a 12:10 ratio in 1st-order designation between arms; perhaps in a main trial there would be some blocking in the procedure if there is concern that there may be an order effect?

[Page 7]: Washout seems to be classed as 'satisfactory' if 1/16th of the elimination is met - is there any reference to support this?

[Page 9]: 'Outcomes' - It is stated, "The two primary outcomes were efficacy of processes and procedures used to manage symptoms during the washout period … and estimates of cued recall performance". The last of these corresponds with one of the two primary objectives for the pilot trial - as detailed on page 6 and in the abstract; however, it is not too clear that the efficacy of processes and procedures tallies with assessment of safety of switching (though I think this is probably what is being assessed here)?

[Page 13]: Quantitative data - This section is brief, understandably because the focus is not on hypothesis testing. However, a primary aim was to provide estimates for informing a main trial. What I am not clear about is what is the intended main comparison in the main trial - the presentation of data and sample size precursor tend to suggest that the difference (OFF-ON) in cued recall between treatments is what is being targeted, but in the results section (page 16) the clinically important difference seems to be focused on actual cued-recall scores (as opposed to OFF-ON difference) - thus, further clarity around this would be helpful.

[Page 13]: Qualitative - There is limited information in this section (or it is not clear) on selection of the patients for interview. From the results section it is clear that 5 people were interviewed; yet, the pool of potential people would have been far greater (53 declined or didn't respond) - were the 5 interviewed all 5 who declined (48 being non-responders) or was there
some selection around 5 out of xx decliners (and if so how selected)? Also, there is no detail in this section on the other qualitative study which is reported in the results section on selection of 5 from 16 of the study completers in regards to the experience of study participation.

[Page 16]: The authors specify that 10% of the observed range of scores (in this case 0.070) qualifies as a clinically important difference - is there further justification or a reference in support of this, or was it an a priori decision?

[Page 18]: A large part of the discussion section focuses on initial problems with CTU set-up and logistical challenges. This may well have been the case, but identified numbers were quite large - at least relative to the number that actually decided to take part. The problem seemed to lie with eligibility (was this too restrictive?) and uptake of those deemed eligible for the study - two of the mentioned barriers were trial accessibility and fear of the research process - is it that a more developed CTU would have addressed these problems, and moreover contributed to greater recruitment numbers that may have changed the conclusion of the study in relation to its likely feasibility? Some clarity on this is provided in the Conclusion (on page 19) but additional thought and clarification could help clarify the discussion on page 18.

[Page 19]: I am not sure if the interpretation in the Conclusion (of confidence in recruitment now the CTU is fully operational) is completely supported by the findings here - but certainly the required sample size if small for the main trial as indicated is favourable, and any increase in efficiency of logistical processes can only help in making a case towards increased feasibility of conducting a trial.

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Perhaps relating to points 1 and 6 above,

Previously I informed you that I work in the same University as the authors of this manuscript and know some authors well. I reiterate that I have not had any involvement in this work; you confirmed you were happy for me to proceed with the review.

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