Reviewer’s report

Title: The DARS (Dopamine Augmented Rehabilitation in Stroke) trial: protocol for a randomised controlled trial Does Co-careldopa treatment in combination with routine NHS occupational and physical therapy, delivered early after stroke within a stroke rehabilitation service, improve functional recovery including walking ability and arm function?

Version: 2 Date: 29 April 2014

Reviewer: Erik Cobo

Reviewer’s report:

I read the DARS trial paper from Dr. Bipin Bhakta et al. about Dopamine Augmented Rehabilitation in Stroke, and I think it is very well designed and written. It deserves publication in Trials.

Nevertheless, I would like to make some comments to the authors in order to help them enhance the impact of DARS.

- Major Compulsory Revisions

Please provide details about your dissemination policy, such as those suggested in SPIRIT item 31.

Decisions about further rehabilitation therapy can be a result of the previous treatments (page 14: “The decision about need for rehabilitation interventions (when to start, finish and type) will be made by the treating clinicians, therapists and nurses in consultation with patients and families as part of the routine management of the patient”). If, for example, patients treated with Do-Careldopa progress clearly better, maybe they will require less rehabilitation therapy. If so, there is some risk of performance bias. Please, consider if some measure of the amount of rehabilitation therapy can be devised to analyze this risk.

- Minor essential Revisions

You specify the outcome: “as measured by a score of 7 or higher and can walk 10 metres”. Please, specify from which item or measure the first criterion originates. If feasible, please consider if a shift/ordinal analysis (a common estimate of the effect through any (or more relevant) cut-points) may provide extra-power —provided it is still possible to change the main outcome measure.

As both groups in comparison have rehabilitation, please consider changing “in combination with” (title, abstract, text) to “in addition to” —since the former may suggest that the reference group has neither D_Careldopa nor Rehabilitation. For example, change the title to something like: “Does the addition of Do-careldopa to routine NHS rehabilitation therapy improve recovery?”

- Discretionary revisions

On page 10 you specify “to receive either Co-careldopa or placebo for six weeks within 5 to 42 days post stroke”. And on page 14 “…sessions for a maximum of
six weeks”. But on page 7, “The study drug will be continued at home if rehabilitation treatment continues after discharge from hospital”. Please, clarify.

Your description of the masking on page 10 agrees with Prisma and Consort. It is so precise that it makes “double-blind” unnecessary. Please consider if ‘double-blind” can be omitted sometimes or changed to blinded.

Please, consider changing “Recruitment and randomisation process” to “Recruitment and randomisation processes” (or just “Recruitment and randomisation”) to avoid the usual misunderstanding that both are just the same process (the first must precede the second: see SPIRIT figure). Please, consider also removing “allocation” in the central box of the figure for the same reason.

My best wishes for the next phases of your meritorious work.

Erik Cobo

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests