Reviewer's report

Title: Intravenous transplantation of mesenchymal stem cells preconditioned with early phase stroke serum: Current evidences and study protocol of a phase 3 randomized trial

Version: 1 Date: 11 July 2013

Reviewer: Erik Cobo

Reviewer's report:

I read the paper from Suk Jae Kim et al., “Intravenous transplantation of mesenchymal stem cells preconditioned with early phase stroke serum: Current evidences and study protocol of a phase 3 randomized trial”, and I think it is suitable for publication in Trials.

But before recommending publication, I would like authors to address the suggestions indicated below.

Thank you very much for considering our journal and looking forward to your new version,

Looking forward to see a new version of your manuscript,

Erik Cobo

- Major Compulsory Revisions

I’m confused about the confirmatory nature of the trial (abstract: “The results have implications for the development of evidence-based best practices”; and trial characteristics: “phase 3”) and so many unknowns (second section, optimization of treatment: “The appropriate type and dose of cells, the mode of treatment, and the time of application of stem cell therapy remain to be determined.”). Please, define clearly your trial as confirmatory (“pivotal”) or exploratory (“pilot”) and write your report accordingly.

According to your title (“current evidences”), please update table 1 with information about the results of the studies. Ideally, a summary effect size with its imprecision should be provided.

The masked evaluator (if blinding is not broken) can protect against evaluation bias, but open trials also have other risks of bias, such us selection, performance and attrition. Please, provide arguments to prevent such biases.

Some key information is missing from the abstract (i.e., sample size) and the report (i.e., allocation concealment). Please, check with the SPIRIT statement to ensure that you provide all essential features of the trial. [Please, be aware that your future final report should be in accordance with the CONSORT statement and also with its extension for non-pharmacologic interventions.]

The previous STARTING trial, with a sample size of 85 patients, failed to find statistical significance. Please, provide arguments why your new smaller trial (60) will prove to have a beneficial effect (for example, higher expected effect, more
powerful main analysis, more homogeneous population, better reliability in outcome determination, …). Please, specify which will be the main analysis (unadjusted CMH or adjusted ordinal logistic regression).

- Minor Essential Revisions
- Discretionary Revisions

Please note that 'optimal' refers to some criteria. Please, consider either specifying such criteria or removing the term "optimal" from some places.

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

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

**Declaration of competing interests:**

None