Reviewer's report

Title: Rational and Design of a Double-blind, Placebo-controlled, Randomized Trial to Evaluate the Safety and Efficacy of Nimodipine Preventing Cognitive Impairment in Ischemic Cerebrovascular Events (NICE)

Version: 1 Date: 1 June 2012

Reviewer: Roberto Federico Villa

Reviewer's report:

COMMENTS

Rational and Design of a Double-blind, Placebo-controlled, Randomized Trial to Evaluate the Safety and Efficacy of Nimodipine Preventing Cognitive Impairment in Ischemic Cerebrovascular Events (NICE)

NICE is interesting because this Pathology deals with post-stroke MCI and its pharmacological prevention. In addition, NICE is based on some, albeit insufficient, findings in the literature and, hopefully, should make progress in our knowledge on this problem.

Major Compulsory Revisions - However, a general comment of validity of the experimental plan, needs some important questions and the following points can be raised:

(i) because of the heterogeneity of MCI, the diagnosis should take into account the current clinical classification of the syndrome: amnestic, multiple domain and single, non-memory domain. Thus, a battery of neuropsychological tests (language, attention, executive functions) and tests of activities of daily living should be added to MMSE and ADAS-cog (for example ADDTC). In addition, the evaluation tests to verify the efficacy of pharmacological treatment should be better specified, especially as regards the secondary outcome;

(ii) the two factors that are of basic interest affecting the results are (a) post-stroke hypertension and (b) a history of type 2 diabetes mellitus that should be added to the exclusion criteria;

(iii) the duration should be longer than 6 months. See also later the final comment.

(iv) the time interval selected for ages (30-80 years) is too long lasting, because the effects of all the above mentioned factors are different in the early ages (from 30) respect to those observed in late-life and these are to be expected to interfere when the clinical results will be examined by statistical tests. Thus, the results will be evaluated with great accuracy and precision respect to age (and possibly gender) factor.

However, the main point is that a large trial such as NICE (656 patients enrolled) could have provided many much more important information by tackling the
problem of post-stroke dementia (PSD), even more so because patients with pre-stroke dementia are excluded.

**Level of interest:** An article whose findings are important to those with closely related research interests

**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' below.