Reviewer's report

Title: Prevention of hypertension in patients with pre-hypertension: PREVER-prevention trial

Version: 5 Date: 22 December 2010

Reviewer: Stevo Julius

Reviewer's report:

I am delighted that you will undertake a study in prehypertension in which you will compare fixed low dose combination diuretic/amiloride to placebo and that you have obtained support for such a study.

Based on my experience with the TROPHY trial I would strongly recommend that you

a./ Redefine your primary outcome of hypertension. If I understand your design correctly hypertension will be defined as an average of two measurements of >/= 140/90 mmHg. at any single visit throughout the trial. Current JNC 7 and other guidelines stipulate that hypertensive readings ought to be obtained at two successive clinic visits. Thus if you obtain a high clinic reading at one visits this should be followed by another return visit to verify whether the patient developed hypertension. A “three times high BP at any visit in the trial” definition in TROPHY caused a great deal of controversy.

b./ Your graph seems to indicate that you will apply life style modification only at the beginning of the trial. These efforts should continue through the trial and should be re-enforced at each clinic visit.

c. I see no evidence that you will obtain laboratory values at the baseline but you do propose to obtain them at the end of the trial. Consequently, you will not be able to assess changes of laboratory findings through the trial. In as much that chlorthalidone has been associated with new onset diabetes showing whether the treatment altered glucose metabolism would be very important.

Level of interest: An article of outstanding merit and interest 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:

I declare that I have no competing interests in regards to this manuscript.