Reviewer’s report

Title: FimAsartaN proTeinuriA SusTaIned reduCtion in comparison with losartan in diabetic chronic kidney disease (FANTASTIC) : study protocol for randomized controlled trial

Version: 0 Date: 09 Sep 2017

Reviewer: Tarek Abdelaziz

Reviewer’s report:

I reviewed the protocol of FANTASTIC study with interest. The authors have endorsed it in clear language. The study is well designed. The multi-centre participation adds strength to the study.

I would like to ask the authors to consider the following comments:

1) The authors use proteinuria and albuminuria as interchangeable terms on certain occasions which could result in confusion. E.g. in section 2.2.1 Inclusion and exclusion criteria:

'overt proteinuria'. Adding 'or macro -albuminuria' helps clarify the meaning.

Thus, the information in this section will mirror the inclusion criteria in the table 1.

The same is seen in the title 'Proteinuria Sustained Reduction', while the primary outcome measure is albuminuria.

2) In the abstract-discussion: 'The FANTASTIC study will try to provides.....'Please revise the grammar. Also the whole paragraph better to be rephrased to render the meaning more clear.

3) In section 2.2.2 Screening 'However, other antihypertensive drugs were administered without changing the regimens or doses' -Do they include the dihydropyridine CCB? As this might affect the level of proteinuria.

4) In the same section 'subjects were instructed to visit the study site.........or onset of any symptoms of suspected hypertension'. It might be more appropriate in this context to write accelerated hypertension symptoms with detailing a few of them for clarity. Meanwhile, it will be useful to detail how often they were instructed to check their blood pressure at home.

5) There is no mention of the limitations of the study.
6) In section 2-6: 'The primary end point was the rate of change in albuminuria in the fimasartan group and losartan group from baseline to week 24.' I noticed that in section 2.7 other secondary endpoints '2) The change in albuminuria in the fimasartan and losartan groups from baseline to weeks, 4,8,12 and 24'.

It occurs to me that, if albuminuria at 24 weeks is a primary outcome then it cannot be a secondary outcome in the meantime.

7) Also in section 2-7 secondary end points '4) The proportion of subjects who developed microalbuminuria (urine ACR<300 mg/g) in the fimasartan and losartan groups at weeks 4,8,12 and 24'. This merits revision as, the inclusion criteria states ACR≥300 mg/g. It therefore becomes logical that micro-albuminuria cannot be measured as a secondary outcome.

8) In table 1, the inclusion criteria 'Baseline visit (visit 3) - eGFR ≥30/min/1.73m2'. It would be appropriate in the meantime to define the upper cut-off for the eGFR to fulfil the KDIGO definition of CKD.

9) In the conclusion 'It was expected to confirm the reno-protective effect of fimasartan'. This might be misunderstood as anticipation of the results. It might be more appropriate to rephrase it to sound more neutral.

10) In table 2 (Exclusion criteria) 'Moderate or malignant retinopathy< 6 months prior to enrolment '. Do the authors mean hypertensive or diabetic retinopathy? I find it helpful to write a few details about the criteria of retinopathy that renders them excluded. e.g moderate non proliferative diabetic retinopathy.

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