Reviewer’s report

**Title:** Effect of eplerenone on parathyroid hormone levels in patients with primary hyperparathyroidism: A randomized, double-blind, placebo-controlled trial

**Version:** 2  **Date:** 8 May 2012

**Reviewer:** Gian Paolo GP Rossi

**Reviewer’s report:**

The Authors espoused the hypothesis of a bidirectional stimulatory link between PTH and aldosterone and proposed this randomized clinical trial to test this hypothesis. However, while in vitro data and in vivo observations support a stimulatory effect of PTH on aldosterone the opposite remains to be shown.

Overt primary hyperparathyroidism was recently described to occur in primary aldosteronism after adrenalectomy and correction of the latter, which would rather suggest an inhibitory effect of aldosterone on PTH.

Moreover, the Authors should acknowledge the fact that Mainiero et al already (Hypertension 2011) showed the presence of type 1 PTH receptors in the human adrenal gland and also mineralocorticoid receptors in the principal cells of the parathyroid gland. The same authors showed the nuclear immunolocalization of the MR receptor thus providing the evidence for this receptor in the parathyroid gland. Agonist binding to the LBD and translocation was also proposed. Hence, it is unclear how the Authors expect eplerenone to be able to reverse a tonic action of aldosterone on the parathyroid gland.

The Authors stated that the study has been approved by the Ethics Committee of the Medical University of Graz.

However, there is, in my view, some concern on the blood pressure lowering effect of eplerenone in normotensive patients, which was not addressed by the Authors.

**Specific comments**

1. The Authors planned to enrolled patients with no consideration to the presence or absence of high blood pressure, but they are planning to administer a BP-lowering drug. Although they did pay attention to the possibility of hyperkalemia no attention was apparently paid to the BP lowering. I wonder what safety precautions were to be taken. They should be declared.

2. No power calculations are given the genetic study but the sample size is clearly underpowered to provide any meaningful information from this standpoint.

3. The reasons for choosing eplerenone instead of spironolactone are not given. The latter is less potent that the former and at equipotent doses does not seem to be more selective for the MR than the much cheaper spironolactone.

**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:

No competing interest.