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The Authors Reply: We thank Drs Komaba and Fukagawa for their remarks[1] and for giving us the opportunity to add to our review[2] some comments on amino-parathyroid hormone (N-PTH). Determining the exact nature of N-PTH and understanding its regulation and action(s) is an exciting but challenging field for future research. Although a very excessive production of N-PTH can be easily evidenced by the finding of a third/second-generation PTH ratio >1, we would like to underline an important technical point. As several automated third-generation assays will become available soon, it is likely that many studies will focus on the third/second-generation PTH ratio. However, this ratio cannot be calculated from any coupling of PTH assays (one third-generation and one second-generation assay). Indeed, both assays must be calibrated similarly (i.e., must produce the same concentration in a solution of rh1–84 PTH), and the second-generation assay must measure both 7–84 and 1–84 PTH with 100% cross-reactivity, but must not measure N-PTH. To our knowledge, this could currently be achieved only with the Ti-PTH assay (second-generation) and the CA-PTH assay (third-generation) from Scantibodies Laboratories (Santee, CA, USA). Nevertheless, a third/second-generation PTH ratio >1 is a very rare feature,[3] and the best way to improve our knowledge in N-PTH physiology would be to develop a simple and direct N-PTH assay. Indeed, the only published method is complicated and reserved to highly specialized research laboratories.[4] Having said that, the finding by Drs Komaba and Fukagawa of the normalization of a reversed ratio during calcimimetic therapy is striking and deserves further study.[5]

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Statins: do we definitely know whether they are completely inefficacious in ESRD?

To the Editor: We wish to submit a letter concerning the paper by Lam *et al.* in *Kidney International*.[1] Although the data are certainly of interest, we feel that some note of caution will put the argument of the authors into a slightly different perspective.

The paper of Lam *et al.*[1] reports that prescription of statins in dialysis patients continued unchanged despite the negative outcome in hemodialyzed patients of one study (4D; Wanner *et al.*,[2] and in the meantime even in a second one: AURORA[3]).

The observation is certainly of interest, but we wish to raise a note of caution regarding the interpretation of the evidence for the inefficacy of statins.

In the past, it had appeared *a priori* pathogenetically plausible that lipid lowering in uremic patients should reduce cardiac events. That pathophysiological plausibility does not necessarily translate into evidence-based outcomes of adequately powered prospective intervention trials has recently been impressively shown by the TREAT study on erythropoietin treatment.[4]

The issue we wish to raise here is the absolute requirement that studies must be adequately powered before the conclusion is drawn that a given treatment is ineffective. Indeed both the 4D and the AURORA study were underpowered to provide biostatistical proof for the efficacy of statins on myocardial infarction. In both studies the primary outcome was a composite comprising sudden death and death from other cardiac causes, including myocardial infraction and stroke. When planning the studies it was assumed that lipid lowering by statins would reduce such a combined cardiac and cerebrovascular end point. *Post hoc* we noted that statins had definitely no significant effect with respect to sudden death and heart failure. However, as we had pointed out elsewhere,[5] the study was presumably underpowered to exclude efficacy for all types of cardiac death. The *post hoc* analysis even pointed to a suggestive benefit for adjudicated coronary end points that were lower by 19% per 1 mmol lowering of low-density lipoprotein-cholesterol—surprisingly identical with what had been observed previously in studies on nonrenal cardiac patients.[6]

It is also remarkable that both in 4D and the AURORA study, a trend was seen for separation of the survival curves approximately 3 years after start of the study—in stark contrast to the almost immediate effect of statins seen in nonrenal patients with coronary heart disease. It is possible that in hemodialyzed patients statins don't affect inveterate