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## [Intervention Review]

# Calcimimetics for secondary hyperparathyroidism in chronic kidney disease patients

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**Editorial group:** Cochrane Kidney and Transplant Group. **Publication status and date:** Edited (no change to conclusions), published in Issue 2, 2010.

**Citation:** Strippoli GFM, Tong A, Palmer SC, Elder GJ, Craig JC. Calcimimetics for secondary hyperparathyroidism in chronic kidney disease patients. *Cochrane Database of Systematic Reviews* 2006, Issue 4. Art. No.: CD006254. DOI: 10.1002/14651858.CD006254.

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## ABSTRACT

## Background

Calcimimetic agents have recently been evaluated in the treatment of secondary hyperparathyroidism (SHPT) as add-on therapy to calcitriol and vitamin D analogues and dietary phosphate binders.

## Objectives

To evaluate the benefits and harms of calcimimetics for the prevention of secondary hyperparathyroid bone disease (including osteitis fibrosa cystica and adynamic bone disease) in dialysis patients with chronic kidney disease (CKD).

#### Search methods

MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials and conference proceedings were searched for randomised controlled trials (RCTs) evaluating any calcimimetic against placebo or another agent in pre-dialysis or dialysis patients with CKD.

#### Selection criteria

We included all RCTs of any calcimimetic agent, cinacalcet HCl (AMG-073, Sensipar<sup>®</sup>), NPS R-467 or NPS R-568 administered to patients with CKD for the treatment of SHPT.

## Data collection and analysis

Data were extracted on all relevant patient-centred and surrogate outcomes. Analysis was by a random effects model and results expressed as risk ratio (RR) or mean difference (MD) with 95% confidence intervals.

## **Main results**

Eight studies (1429 patients) were identified, which compared a calcimimetic agent plus standard therapy to placebo plus standard therapy. The end of treatment values of parathyroid hormone (pg/mL) (MD -290.79, 95% CI -360.23 to -221.34), serum calcium (mg/dL) (MD -0.85, 95% CI -1.14 to -0.56), serum phosphorus (mg/dL) (MD -0.29, 95% CI -0.50 to -0.08) and the calcium by phosphorus product (mg<sup>2</sup>/dL<sup>2</sup>)(MD -7.90, 95% CI -10.25 to -5.54) were significantly lower with calcimimetics compared to placebo. No significant effects on patient-based



endpoints were demonstrated except for the risk of hypotension which was significantly reduced with calcimimetics compared to placebo (RR 0.53, 95%CI 0.36 to 0.79).

#### **Authors' conclusions**

Calcimimetic treatment of SHPT leads to significant improvements in biochemical parameters that observational studies have shown to be associated with increased mortality, cardiovascular risk and osteitis fibrosa, but patient-based benefits have not yet been demonstrated in trials. For patients with SHPT, the benefits of calcimimetics over standard therapy remain uncertain until further RCTs become available.

## PLAIN LANGUAGE SUMMARY

#### Calcimimetics for secondary hyperparathyroidism in chronic kidney disease patients

Abnormalities of calcium and phosphorus metabolism are present in all individuals with chronic kidney disease (CKD). These biochemical changes lead to a condition known as secondary hyperparathyroidism (SPTH), resulting in an excessive production of parathyroid hormone which in turn causes bone and metabolic disorders. These disorders are associated with an increased incidence of fracture, bone and muscular pain and abnormalities of bones and joints. Standard management of patients with CKD, particularly those on dialysis, includes treatment to control levels of calcium, phosphorus and parathyroid hormone. This can be achieved initially by dietary restrictions of phosphorus, calcium supplementation, and/or the use of calcitriol. Once patients have commenced dialysis, standard treatment generally includes calcitriol, vitamin D analogues or derivatives, calcium or other phosphate-binding agents and parathyroidectomy. The aim of this review was evaluate the benefits and harms of calcimimetics for the prevention of SHPT in patients with CKD. Eight studies (1429 patients) were identified. After treatment, parathyroid hormone, serum calcium, serum phosphorus and the calcium by phosphorus product were all significantly lower for calcimimetics when compared to placebo. The only patient level outcome which was been found to be reduced with the use of calcimimetics is the risk of hypotension. For patients with SHPT, the benefits of calcimimetics over standard therapy remain uncertain until further RCTs become available.