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Efficacy of cinacalcet administered with the first meal after dialysis: the SENSOR Study

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Key words
cinacalcet – calcimimetic – secondary hyperparathyroidism – dialysis – iPTH – Ca × P

Abstract. Background: Cinacalcet, a novel calcimimetic, simultaneously lowers parathyroid hormone (PTH), phosphorus (P), calcium (Ca) and Ca × P in patients who are on dialysis with secondary hyperparathyroidism (sHPT) associated with CKD. Previous studies have required cinacalcet to be administered during the dialysis session and at the same time on non-dialysis days. The aim of the SENSOR study was to demonstrate that cinacalcet given in a more clinically practical manner with the first major meal after dialysis is noninferior to cinacalcet given with food during the dialysis session. Methods: In this open-label study dialysis patients with poorly controlled sHPT (intact PTH (iPTH) ≥ 300 pg/ml) were randomized to receive cinacalcet either daily with their post-dialysis meal (n = 337) or with food during the dialysis session (n = 336). The primary endpoint was the proportions of patients with mean iPTH ≤ 300 pg/ml (≤ 31.8 pmol/l) at Weeks 11 and 13 of a 21-week treatment period. Secondary endpoints included the proportion of patients with Ca × P < 55 mg^2/dl^2 (< 4.44 $mmol^2/l^2$) at Weeks 11 and 13 and patients who discontinued the study due to nausea or vomiting. Results: Comparable proportions of patients in the cinacalcet "during dialysis" and "post-dialysis meal" groups had a mean iPTH ≤ 300 pg/ml (54 vs. 57%, respectively, 95% confidence interval (CI) difference –4, +10%) and Ca × P < 55 mg^2/dl^2 (78 vs. 73%, respectively, 95% CI difference –11, +2%) at Weeks 11 and 13. The groups were also comparable at Week 21. Cinacalcet was well tolerated, with < 3% of patients in both groups discontinuing due to nausea or vomiting. A combined post-hoc analysis of both groups showed the incidence of nausea and vomiting was lower if cinacalcet was administered during the evening. Conclusions: Administering cinacalcet with the first main meal after dialysis was as effective as administration with food during the dialysis session. Cinacalcet was well tolerated. The incidence of gastrointestinal adverse events appeared to be lower when cinacalcet was administered in the evening.

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Introduction

Secondary hyperparathyroidism (sHPT) is a common disorder that develops early in chronic kidney disease (CKD) and progresses rapidly in end-stage renal disease [Rodriguez et al. 2005]. This condition is characterized by elevated parathyroid hormone (PTH) and parathyroid hyperplasia, and arises from disturbances in the complex interactions between phosphorus (P), calcium (Ca) and vitamin D (calcitriol) [Holick 2007, Rodriguez et al. 2005, Salem 1997]. Abnormalities in serum P and Ca concentrations have been implicated in bone and cardiovascular disease and an increased risk of mortality in patients with CKD [Block et al. 1998, Ganesh et al. 2001, Young et al. 2004, 2005].

Calcimimetics are a novel class of small molecules that bind to the Ca-sensing receptor (CaR) present on the surface of parathyroid cells [Brown et al. 1993]. Cinacalcet (Mimpara®/Sensipar®) is a calcimimetic that acts as an allosteric modulator of the CaR, increasing the sensitivity of the CaR to activation by extracellular calcium and, in turn, suppressing PTH release [Nemeth et al. 2004]. Phase II/III clinical trials in patients with sHPT have demonstrated that cinacalcet is effective in lowering PTH while simulta-

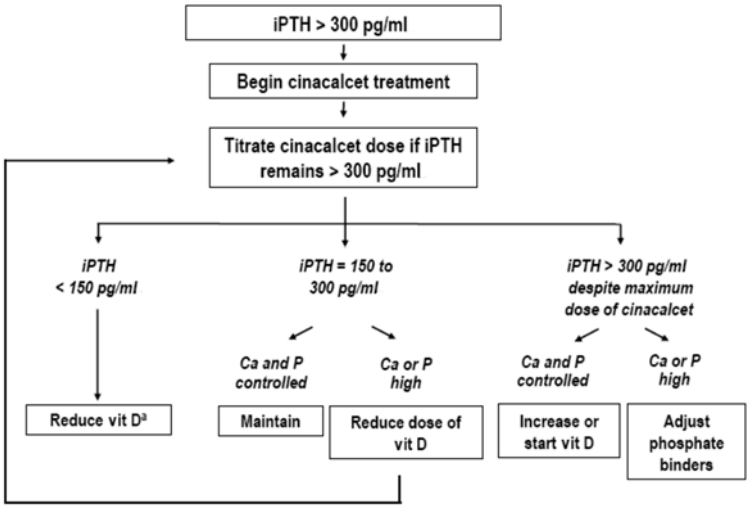

Figure 1. OPTIMA treatment algorithm. Note: When indicated, the dose of a vitamin D sterol can be reduced by approximately 50%, in sequential steps, until a minimum administered dose was reached: intravenous (IV) calcitriol, 0.5 μg TIW; IV alfacalcidol, 1 μg TIW, IV paracalcitol, 2 μg TIW, oral calcitriol, 0.25 μg TIW, oral alfacalcidol, 0.25 μg/day. [a]Reduce dose of cinacalcet if patient is not receiving vitamin D.

neously reducing serum P, Ca and Ca × P [Block et al. 2004, Lindberg et al. 2005, Sterrett et al. 2007] to within the targets recommended by the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (KDOQI) clinical practice guidelines (intact (iPTH) 150 – 300 pg/ml, 15.9 – 31.8 pmol/l, Ca × P < 55 mg^2/dl^2, 4.44 $mmol^2/l^2$) [National Kidney Foundation 2003]. These studies also showed that cinacalcet is well tolerated. The most commonly reported adverse events were nausea and vomiting, of mild to moderate severity [Block et al. 2004, Lindberg et al. 2005].

Because the bioavailability of cinacalcet increases by approximately 50 – 80% with food, it is recommended that cinacalcet is administered with food or shortly after a meal [SmPC 2007]. There is anecdotal evidence that dosing with a large meal can ameliorate cinacalcet-related nausea and vomiting. In the Phase III trials, however, cinacalcet was administered 20 – 24 hours before PTH determination, which has led to the practice of this agent being administered before or during dialysis, making administration with food difficult. Therefore, the SENSOR study was designed to evaluate whether cinacalcet, when administered in a more convenient manner with the first post-dialysis meal, provides comparable (noninferior) efficacy and tolerability to cinacalcet given with food during the dialysis visit. Efficacy was assessed on the basis of the proportions of patients in each dosing group achieving a mean iPTH ≤ 300 pg/ml (≤ 31.8 pmol/l) and Ca × P value < 55 mg^2/dl^2 (< 4.44 $mmol^2/l^2$).

Patients and methods

Patients

Patients aged ≥ 18 years who were on maintenance dialysis for ≥ 1 month prior to enrollment were eligible. Patients had to have a mean baseline iPTH ≥ 300 pg/ml (31.8 pmol/l) or bi-iPTH ≥ 150 pg/ml (15.9 pmol/l) and corrected serum Ca ≥ 8.4 mg/dl (2.1 mmol/l) within 14 days prior to randomization. Patients were allowed prior treatment with conventional therapy, including calcium supplementation, dietary phosphate restriction, oral phosphate binding agents, and active vitamin D sterols. Patients who had previously received cinacalcet were excluded.

The principles of the declaration of Helsinki were adhered to in conducting the study. Independent ethical committees for each study centre approved the study protocol and all patients provided written informed consent before the initiation of study-specific procedures.

Study design

This randomized, open-label trial consisted of two phases: a screening phase and a 21-week treatment period. After the screening phase, patients were stratified at randomization according to their iPTH levels (iPTH ≥ 300 pg/ml (31.8 pmol/l) and ≤ 800 pg/ml or iPTH > 800 pg/ml (84.8 pmol/l)) and vitamin D use. Patients were randomized in a 1 : 1 ratio to receive either daily cinacalcet with the first meal after dialysis ("post-dialysis meal" group) or cinacalcet with food during the dialysis study visit ("during dialysis" group). For all patients, the "OPTIMA" algorithm (Figure 1) was used for adjustments of cinacalcet dose, vitamin D and phosphate binders. This algorithm has been shown to

maximize control of all four KDOQI goals (PTH, P, Ca and Ca × P) [Messa et al. 2007].

Biochemical parameters

Blood samples were collected at 2-week intervals throughout the 21-week treatment period for the determination of iPTH and serum P and Ca concentrations. Serum Ca was recorded as an albumin-corrected value. For each 1 g/dl decrease in albumin below 4.0 g/dl, the serum Ca value was increased by 0.8 mg/dl using the following equation: corrected Ca (mg/dl) = total Ca (mg/dl) + 0.8 × (4 – serum albumin g/dl) or corrected Ca mmol/l = total Ca (mmol/l) + 0.2 × (4 – serum albumin g/dl).

Dosing schedule

Cinacalcet was initiated at 30 mg/day and titrated up to a maximum of 180 mg/day. Once daily cinacalcet dosing was used until Week 13, with an increase in dose permitted every 2 weeks if required. From Week 14, patients with a baseline iPTH > 800 pg/ml who did not attain an iPTH ≤ 300 pg/ml (31.8 pmol/l) despite titration to cinacalcet 180 mg/day were able to receive (BID) administration (90, 120, 180 mg BID) twice daily. Dose reductions were possible at any time for reasons related to patient safety. Cinacalcet was given at the same time on dialysis and nondialysis days. The time elapsed between cinacalcet administration and blood sampling was recorded at Weeks 1, 7 and 13.

Study endpoints

The primary endpoint was the proportion of patients in each group with mean iPTH ≤ 300 pg/ml (31.8 pmol/l) at Weeks 11 and 13. Secondary endpoints included the proportions of patients with a mean Ca × P < 55 mg^2/dl^2 (4.4 $mmol^2/l^2$) and iPTH ≤ 300 pg/ml, mean iPTH 150 – 300 pg/ml (15.9 – 31.8 pmol/l), mean Ca × P < 55 mg^2/dl^2, mean P 3.5 – 5.5 mg/dl (1.13 – 1.78 mmol/l), mean Ca 8.4 – 9.5 mg/dl (2.10 – 2.37 mmol/l), and the proportions of patients who did not complete the treatment period (21 weeks) because of nausea or vomiting. Mean values of laboratory results obtained at Weeks 11 and 13 were used to assess the achievement of these efficacy endpoints in the two treatment groups to ensure that they were independent of BID dosing.

Concomitant drugs/medication

Vitamin D and phosphate binder data were collected throughout the study. A short course of anti-emetics or antacids was permitted for patients who experienced intolerable nausea and/or vomiting.

Statistical considerations

The primary efficacy analysis was based on the full analysis set which included all randomized patients with ≥ 1 post-baseline iPTH assessment. The proportion of patients achieving the primary endpoint (adjusted for iPTH and vitamin D use at baseline) was compared between the treatment groups using a noninferiority assessment. The two groups were considered noninferior if the lower limit of the 2-sided 95% confidence interval (CI) for the difference between the two treatment groups was ≤ –15% ("post-dialysis meal group" – "during dialysis" group). For the secondary endpoints, the proportion of patients achieving each endpoint was used together with a 2-sided 95% CI for the difference. The analysis of endpoints at Weeks 11 and 13 was performed using a last value carried forward (LVCF) approach, which is considered a more conservative approach than using observed Week 11 and 13 assessments. Data collected at Week 21 were also analyzed (using observed values rather than LVCF). The safety analysis was based upon patients who were randomized and received ≥ 1 dose of study drug.

Results

A total of 673 patients were enrolled at 85 centres in Germany and 28 centers in Spain. A total of 337 patients were randomized to the cinacalcet "post-dialysis meal" group and 336 patients to the cinacalcet "during dialysis" group. Baseline characteristics and de-

Table 1. Demographics and baseline characteristics.

	Cinacalcet during dialysis (n = 329)	Cinacalcet with post-dialysis meal (n = 332)
Male [%]	57	62
White [%]	98	97
Mean (SD) age [years]	57 (14.5)	57 (14.5)
Vitamin D sterol use [%]	60	60
Phosphate binder use [%] Calcium-based Sevelamer Aluminium	94 57 44 32	90 52 45 34
Mean (SD) iPTH [pg/ml]	781 (510)	840 (766)
Mean (SD) Ca × P [mg^2/dl^2]	58 (20)	58 (22)
Mean (SD) P [mg/dl]	5.9 (1.9)	5.9 (1.9)
Mean (SD) Ca [mg/dl]	9.8 (1.1)	9.8 (1.2)

Table 2. Percentage of patients within KDOQI targets* at baseline.

	Cinacalcet during dialysis (n = 329) [%]	Cinacalcet with post-dialysis meal (n = 332) [%]
iPTH ≤ 300 pg/ml	< 1	< 1
iPTH 150 – 300 pg/ml*	< 1	< 1
Ca × P < 55 mg^2/dl^2*	46	47
Composite (iPTH ≤ 300 pg/ml + Ca × P < 55 mg^2/dl^2)	0	< 1
P 3.5 – 5.5 mg/dl*	34	33
Ca 8.4 – 9.5 mg/dl*	35	37

iPTH, 1 mmol/l = 1 mg/dl × 0.105; Ca × P, 1 $mmol^2/l^2$ = 1 mg^2/dl^2 × 0.08; P, 1 mmol/l = 1 mg/dl × 0.323; Ca, 1 mmol/l = 1 mg/dl × 0.25.

mographics were similar for the two treatment groups (Table 1). The small proportion of patients in the two groups who were within the KDOQI targets for iPTH, P, Ca and Ca × P at baseline were also comparable (Table 2).

6 patients received study drug before randomization and 8 patients were randomized but did not receive study drug. The 6 patients who received study drug before randomization were excluded from the efficacy analysis but were included in the safety analysis. The efficacy analysis included 329 patients in the cinacalcet "during dialysis" group and 332 patients in the "post-dialysis meal" group and the safety analysis included 334 and 336 patients in these groups, respectively.

A comparable proportion of patients in the cinacalcet "during dialysis" group (n = 78, 23%) and the "post-dialysis meal" group (n = 64, 19%) discontinued treatment during the 21-week treatment period. The reasons for these withdrawals included adverse events (7% of cinacalcet "during dialysis" patients and 6% of "post-dialysis meal" patients), consent withdrawn (3% and 4% of patients in these groups, respectively), kidney transplant (4% and 2%), death (3% and 2%) and other causes (2% and 2%).

iPTH and Ca × P values by study week

Figures 2 and 3 show the patients' mean iPTH and Ca × P values from baseline to Week 21. Baseline iPTH levels were indicative of a population with severe sHPT (781 pg/ml (82.8 pmol/l) in the cinacalcet "during dialysis" group and 840 pg/ml (89.0 pmol/l) in the "post-dialysis meal" group) (Table 1). However, by Weeks 11 and 13, iPTH had decreased by 50% and 51% in these groups, respectively. Similarly, over the same time period, Ca × P values decreased by 21% and 19% in these groups, respectively. Mean iPTH and Ca × P values were comparable in the two groups throughout the 21-week treatment period.

Mean iPTH, Ca × P, P and Ca values

Mean iPTH, Ca × P, P, and Ca levels at Weeks 11 and 13 were similar in the two groups (Figures 2 – 5). For both groups mean iPTH levels at Weeks 11 and 13 were slightly above KDOQI targets, while Ca × P and mean serum P and Ca levels were within KDOQI targets.

Achievement of key endpoints

The proportion of patients in the cinacalcet "during dialysis" group with a mean iPTH ≤ 300 pg/ml (≤ 31.8 pmol/l) at Weeks 11 and 13 was comparable with that in the "post-dialysis meal" group (54 vs. 57%, 95% CI for the

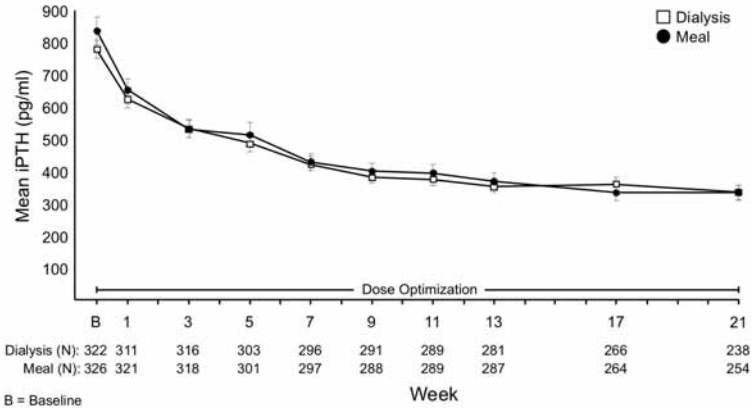

Figure 2. Absolute iPTH levels (SE) by study week for the cinacalcet "during dialysis" and "post-dialysis meal" groups.

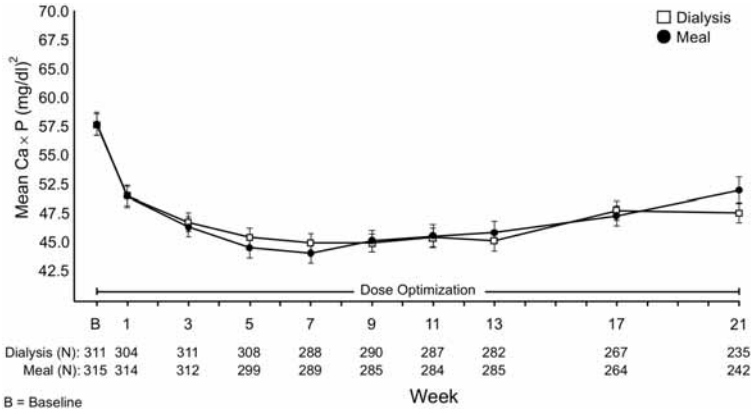

Figure 3. Absolute Ca × P values (SE) by study week for the cinacalcet "during dialysis" and "post-dialysis meal" groups.

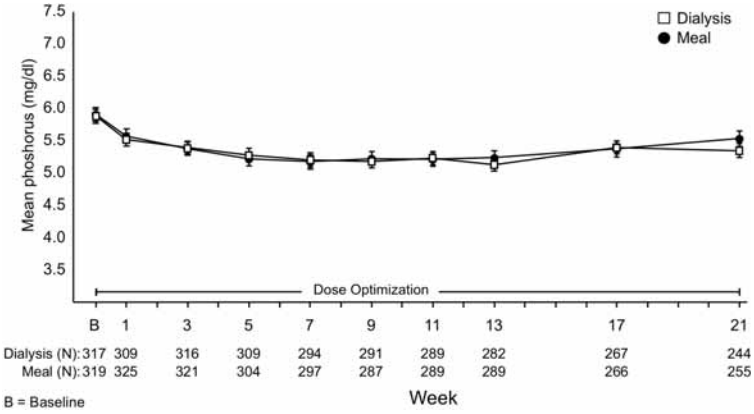

Figure 4. Absolute P values (SE) by study week for the cinacalcet "during dialysis" and "post-dialysis meal" groups.

difference (–4%, 10%)) (Figure 6). Similarly, for Ca × P < 55 mg^2/dl^2 (< 4.44 $mmol^2/l^2$) iPTH ≤ 300 pg/ml + Ca × P < 55 mg^2/dl^2, P 3.5 – 5.5 mg/dl (2.10 – 2.37 mmol/l) and Ca 8.4 – 9.5 mg/dl (1.13 – 1.78 mmol/l) the difference between treatment groups was comparable (78 vs 73%, 46 vs 43%, 49 vs 45%, 44 vs 43%, respectively, CIs for the differences are shown in Figure 6). The proportions of patients in the two treatment groups achieving the KDOQI recommended targets for iPTH and Ca × P remained comparable throughout the study (Figure 7). The mean time elapsed between cinacalcet administration and PTH assessment was similar in the two groups, approximately 19 h in the "post-dialysis meal" group versus 22 h in the "during dialysis group".

Achievement of key endpoints by baseline iPTH or Ca × P

A combined analysis of patients from both cinacalcet treatment groups showed that 70% of patients who had a baseline iPTH ≤ 800 pg/ml (≤ 84.8 pmol/l) achieved the iPTH target of ≤ 300 pg/ml (≤ 31.8 pmol/l) at Weeks 11 and 13, compared with 27% of those who had a baseline iPTH > 800 pg/ml (> 84.8 pmol/l) (Figure 8). The mean reduction in iPTH was approximately 50% in both groups.

Achievement of endpoints was also evaluated by baseline Ca × P (data not shown). Of particular interest was the fact that, most patients (91%) maintained a Ca × P < 55 mg^2/dl^2 (< 4.44 $mmol^2/l^2$) when baseline levels were < 55 mg^2/dl^2 (n = 308) and 61% of patients with a baseline level ≥ 55 mg^2/dl^2 (n = 318) achieved the therapeutic target after the introduction of cinacalcet.

Cinacalcet use

At Weeks 11 and 13 the majority of patients (58%) were receiving a cinacalcet dose of ≤ 60 mg/day (Table 3). The mean dose of cinacalcet administered to patients in the "post-dialysis meal" group at Weeks 11 and 13 (67 mg/day) was similar to that in the "during dialysis" group (70 mg/day). For patients with lower iPTH values and, therefore, less severe disease, lower mean daily doses of cinacalcet were required to control PTH values compared with those with more severe disease (60 mg for baseline iPTH ≤ 800 pg/ml (≤ 84.8 pmol/l) and 109 mg for baseline iPTH

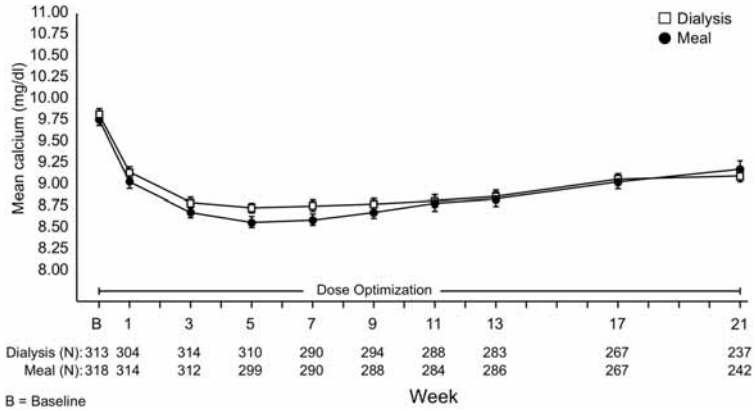

Figure 5. Absolute Ca values (SE) by study week for the cinacalcet "during dialysis" and "post-dialysis meal" groups.

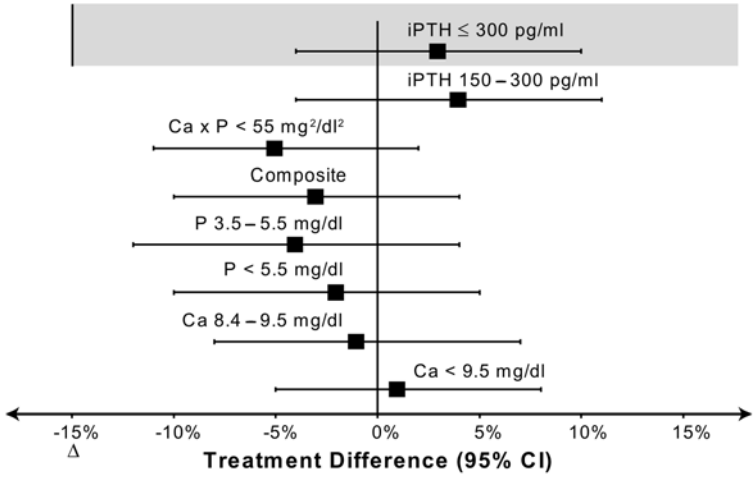

Figure 6. Difference in the percentage of patients achieving key endpoints between the 2 groups (95% CI) at weeks 11/13. For patients where no data were available at weeks 11 and 13, the last observed value was carried forward. Composite, iPTH ≤ 300 pg/ml + Ca × P < 55 mg^2/dl^2. Shading represents primary endpoint.

Table 3. Cinacalcet dose at Weeks 11/13 and Week 21.

Dose [mg/day]	Week 11/13 (n = 592) [%]	Week 21 (n = 509) [%]
≤ 30	37	40
60	21	18
90	15	17
120	11	8
≥ 180	16	17

> 800 pg/ml (> 84.8 pmol/l)). Cinacalcet use overall was comparable at Weeks 11/13 and Weeks 21 (Table 3). Only 22 patients received BID dosing at Week 14. Of the 18 evaluable patients who received BID dosing, 6 patients (33%) achieved iPTH ≤ 300 pg/ml (≤ 31.8 pmol/l) at Week 21.

Vitamin D and phosphate binder use

Vitamin D use was similar for the two cinacalcet treatment groups throughout the study 58% (n = 332) at baseline and 67% (n = 275) at Week 21 in the "post-dialysis meal" group and 57% (n = 329) at baseline and 70% (n = 260) at Week 21 in the "during dialysis" group). The use of phosphate binders remained fairly constant throughout the study: there was an increase of 1% in phosphate binder use (from 94% at baseline) in the cinacalcet "during dialysis" group and an increase of 3% (from 90% at baseline) in the cinacalcet "post-dialysis meal" group. The proportion of patients receiving Ca-containing binders increased by 24% from baseline to Week 21 in the cinacalcet "during dialysis" group and by 29% in the "post-dialysis meal" group, whereas the proportion of patients receiving sevelamer decreased in each of these groups (by 11 and 12%, respectively). A similar decrease was also recorded for the proportion of patients receiving aluminum-containing binders (13% and 15% in the "during dialysis" and "post-dialysis meal" groups, respectively). As observed in previous studies [Block et al. 2004, Lindberg et al. 2005], the median daily dose of phosphate binders did not differ significantly between groups.

Safety

In total, 80% of all cinacalcet-treated patients reported at least one adverse event up to the end of the treatment period, with the incidence comparable between the two treatment groups. For the patients who died, the causes of death were consistent with those commonly seen in this patient population and no deaths were reported to be related to cinacalcet. As in previous studies [Block et al. 2004, Lindberg et al. 2005] nausea and vomiting

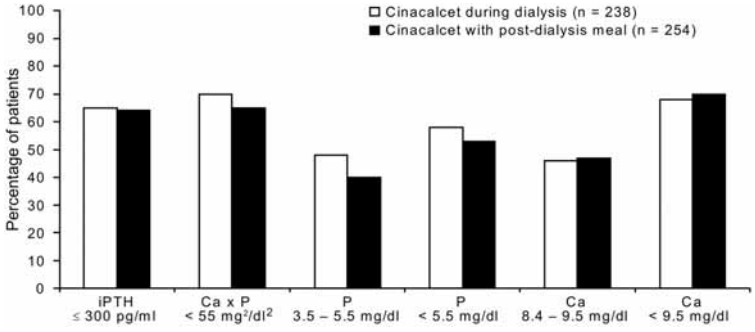

Figure 7. Percentage of patients achieving targets by end of study (Week 21). Observed values; these were predefined exploratory endpoints.

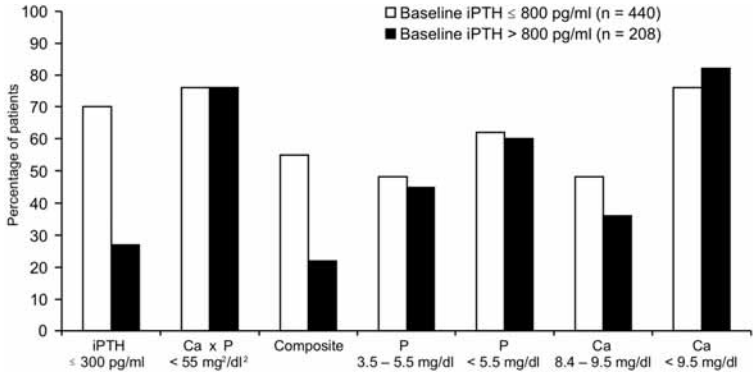

Figure 8. Percentage of patients achieving key endpoints, by baseline iPTH, at weeks 11/13. Both treatment groups combined. Composite, iPTH ≤ 300 pg/ml + Ca × P < 55 mg^2/dl^2.

Table 4. Incidence of nausea and vomiting (21 weeks) based on most frequent time of administration of cinacalcet (n = 620)*.

Time of cinacalcet administration	Nausea [%]	Vomiting [%]
Before noon (n = 185)	37	24
Noon to 6 pm (n = 279)	33	25
After 6 pm (n = 157)	21	15

*Most frequent time of administration not available for 49 patients.

were the most frequently reported adverse events, and these were mostly mild to moderate in severity. The incidence of nausea was numerically higher in the cinacalcet "during dialysis" group compared with the "post-dialysis meal" group (33 vs. 28%, respectively), as was that of vomiting (25 vs. 19%, respectively). The incidence of discontinuation of cinacalcet treatment due to nausea or vomiting was low (2.5% of patients overall), with fewer patients discontinuing in the cinacalcet "post-dialysis meal" group (n = 5; 1%) compared with the "during dialysis" group (n = 12; 4%).

A combined post-hoc analysis of both groups showed that the incidence of nausea and vomiting was reduced if cinacalcet was administered in the evening (Table 4). Cinacalcet treatment was more often stopped due to nausea and vomiting if it was administered during the day: before noon 3.2%, noon to 6 p.m. 3.2%, after 6 p.m. 0.6%. A higher proportion of patients in the "post-dialysis meal" group received cinacalcet in the evening compared with the cinacalcet "during dialysis" group (38 vs. 12%, respectively), which may have led to the observed differences in nausea and vomiting between treatment groups.

Discussion

The results of this study confirm that cinacalcet co-administered with the first meal after dialysis provides comparable (noninferior) efficacy to cinacalcet given with food during the dialysis session. A high proportion of patients in both the "during dialysis" and "post dialysis meal" groups achieved the primary endpoint of iPTH ≤ 300 pg/ml (≤ 31.8 pmol/l, 54 vs. 57%, respectively) as well as Ca × P < 55 mg^2/dl^2 (< 4.44 mmol^2/l^2, 78 vs. 73%), P 3.5 – 5.5 mg/dl (1.13 – 1.78 mmol/l, 49 vs. 45%), serum Ca 8.4 – 9.5 mg/dl (2.10 – 2.37 mmol/l, 44 vs. 43%), and composite iPTH ≤ 300 pg/ml + Ca × P < 55 mg^2/dl^2 (46 vs. 43%). The proportions of patients achieving primary and secondary endpoints were consistent with the results obtained in the cinacalcet Phase III trials [Block et al. 2004, Lindberg et al. 2005]. Importantly, although mean iPTH levels at baseline (781 pg/ml for the "during dialysis" group and 840 pg/ml for the "post-dialysis meal" group) were higher than previously observed (640 and 507 pg/ml, respectively) [Block et al. 2004, Lindberg et al. 2005, Messa et al. 2007], a significant proportion of patients still achieved KDOQI targets.

Overall, the incidence of nausea or vomiting and of discontinuations due to these adverse events was moderately lower in the cinacalcet "post-dialysis meal" group vs. the "during dialysis" group. The findings also

showed that the incidence of nausea or vomiting was lower if cinacalcet was administered in the evening. As more patients in the "post-dialysis meal" group received cinacalcet in the evening compared with the "during dialysis" group, the observed differences in nausea and vomiting between the two treatment groups is likely to be linked to the timing of administration rather than a food effect.

In reporting these findings, we should acknowledge that we did not collect data on meal content although we performed the study in two countries only to limit national differences. However, a recently published manuscript by Padhi et al. [2007] showed that administration of cinacalcet with either high- or low-fat meals resulted in a similar increase in exposure. Therefore, we can presume that in our study the difference in food composition between the two groups had very little effect on exposure. Another potential weakness of the study was that there was a small difference in the time elapsed from cinacalcet administration to the blood sampling period (3 h), however, this difference was unlikely to have impacted PTH levels and was, therefore, not considered clinically relevant.

Cinacalcet is more commonly used in sHPT patients with severely uncontrolled PTH or with Ca × P > 55 mg^2/dl^2. In this study, a smaller proportion of patients with a baseline iPTH > 800 pg/ml achieved the target of iPTH ≤ 300 pg/ml compared with those who had a baseline iPTH ≤ 800 pg/ml, although the mean iPTH value was significantly reduced in this severe patient population. In total, 52% of patients were receiving a cinacalcet dose of ≤ 60 mg/day at Weeks 11 and 13, which suggests that lower doses of this agent can be effective even in patient populations with moderate/severe sHPT. The mean doses of 70 mg/day in the cinacalcet "during dialysis" group and 67 mg/day in the "post-dialysis meal" group were lower than in the Phase III trials, despite this study having a patient population with more severe disease. This could be because the Phase III studies were designed before the advent of the KDOQI guidelines, and cinacalcet was titrated to achieve a more stringent treatment target (100 – 200 pg/ml, 10.6 – 21.2 pmol/l). Taken together, these findings suggest that it could be prudent to administer treatment as early as possible using lower doses of cinacalcet. This would allow more patients to achieve and maintain better control of PTH, Ca × P and PTH + Ca × P.

In summary, this study demonstrated that cinacalcet administered with the first main meal after dialysis was an effective and practical treatment option for patients with sHPT. In addition, cinacalcet was well tolerated with a lower incidence of nausea and vomiting in the evening. These findings, therefore, support the practicality of administering cinacalcet with a post-dialysis meal in the evening.

Conflict of interest declaration

The results presented in this manuscript have not been published previously in whole or part except in abstract form. Roland Schaefer has given lectures supported by Amgen. Jordi Bover has given lectures supported by Amgen, Abbott and Genzyme. He has also participated in advisory boards for Abbott. Peter Michael Jehle received a grant from Amgen to support a clinical study in dialysis patients. He has also participated in advisory boards/meetings supported by Amgen. Valter Zani is an employee of Amgen. Dave Carter is employed as a contractor for Amgen.

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