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ACHIEVEMENT OF RECOMMENDED TREATMENT TARGETS FOR BONE AND MINERAL METABOLISM IN HEMODIALYSIS PATIENTS USING PARICALCITOL -- AN OBSERVATIONAL STUDY

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Short title: Paricalcitol in SHPT patients

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ABSTRACT

Objective

Secondary hyperparathyroidism (SHPT) is a common problem among patients with chronic kidney disease (CKD) on dialysis. This observational multicenter prospective study was conducted to assess the use, effectiveness and safety of intravenous paricalcitol in dialysis patients with various degrees of SHPT.

Material and Methods

The study was conducted in 14 Swedish dialysis centers, from which 92 hemodialysis patients with a mean age of 64 years and with a diagnosis of SHPT associated with CKD were included during May 2007 to June 2008. The decision to initiate treatment with intravenous paricalcitol was made by the treating physician. No treatment algorithms were provided.

Results

Of the 92 patients, 74 patients had an intact PTH of >300 pg/ml at baseline, and 18 patients had an intact PTH ≤300 pg/ml at baseline. Median intact PTH was 589 pg/ml in patients with a baseline PTH of >300 pg/ml. During follow-up there was a decrease in intact PTH to 322 pg/ml at 6 months (-45%, $p < 0.0001$). In parallel, there was a small increase in serum calcium, but serum phosphorous and the calcium-phosphorous product remained unchanged.

Conclusions

This observational multicenter prospective study shows that intravenous paricalcitol substantially and safely decreases intact PTH in hemodialysis patients with a baseline iPTH above the K/DOQI recommended target range (>300 pg/ml) with minimal impact on serum minerals.

INTRODUCTION

Secondary hyperparathyroidism (SHPT) is a common consequence of chronic kidney disease (CKD), presenting in a majority of patients on dialysis (1). As CKD progresses, there is decreased capacity of the kidney to produce 1,25-dihydroxycholecalciferol, the active metabolite of vitamin-D (calcitriol) and to excrete phosphorous, both of which may lead to decreased serum calcium. These three mediators, low serum calcium, elevated serum phosphorous and reduced levels of calcitriol, independently comprise the main causes for increased synthesis and release of parathyroid hormone (PTH) in patients with end-stage renal disease (2). Elevated PTH levels subsequently may result in excessive bone turnover (renal osteodystrophy) often associated with soft tissue and vascular calcifications leading to cardiovascular disease. This is thought to be a key factor in explaining the increased cardiovascular morbidity and mortality among patients with CKD on dialysis (3-5).

Parenteral or oral vitamin-D receptor activators (VDRAs) effectively suppress PTH secretion and are therefore standard therapy for SHPT in patients on dialysis (6). However, such VDRA administration often results in elevated serum calcium and phosphorous levels which may accelerate vascular disease and hasten death (7). In the late 1990s paricalcitol was approved for the treatment of SHPT in the United States. Paricalcitol is considered a selective VDRA that suppresses PTH faster than calcitriol and when appropriately dosed, paricalcitol is associated with smaller changes in serum calcium and phosphorous than is calcitriol (8, 9). Another feature of paricalcitol is that it also suppresses PTH levels in patients with substantially elevated phosphorous levels, a subgroup typically contraindicated for calcitriol (6, 8).

Since morbidity and mortality are high in dialysis patients, the National Kidney Foundation's Kidney Disease Outcome Quality Initiative (NKF-K/DOQI^{TM}) has recommended targets for serum intact PTH

(150--300 pg/ml; 15.9--31.8 pmol/l), serum phosphorous (1.13--1.78 mmol/l), total corrected serum calcium (2.1--2.37 mmol/l), and the calcium-phosphorous product (Ca x P) (<4.44 $mmol^2/l^2$) (10). However, only a small proportion of hemodialysis patients with SHPT achieve these treatment targets, and consistent failure to achieve the recommended targets strongly predict mortality (11-13).

Observational studies reflect clinician's daily practice and provide important information about the effectiveness of treatment regimes. Since inclusion and exclusion criteria are lacking in observational studies these often better reflect the overall patient population, compared with randomized controlled clinical trials, in which inclusion and exclusion criteria often are stringent. Intravenous paricalcitol (Zemplar) received marketing authorization in Sweden in 2004 for the prevention and treatment of SHPT in patients on dialysis. Accordingly, no information is available on the impact of paricalcitol on markers of SHPT in real life clinical practice in Sweden. To address this, we conducted this observational study to assess the use, effectiveness and safety of paricalcitol in dialysis patients with various degrees of SHPT.

PATIENTS AND METHODS

Clinical data were collected from hemodialysis patients who were more than 18 years of age and who had been prescribed intravenous paricalcitol. Patients previously treated with paricalcitol in any interventional clinical trial were excluded. All patients signed an informed consent form and the study was approved by the Ethics Committee in Stockholm.

STUDY DESIGN

The study is a Swedish observational multicenter prospective study in which dialysis units with an interest in observational research and paricalcitol therapy were approached for inclusion of patients. One aim was to select dialysis centers and patient numbers to ensure that enrollment was broadly representative of the dialysis patients within Sweden at that time. Patients were enrolled during May 2007 to June 2008 from 14 dialysis centers in Sweden. The decision to initiate treatment with intravenous paricalcitol was made by the treating physician. Thus the study observed actual clinical practice in centers and no treatment algorithms were provided.

All patients had already started treatment with paricalcitol when they were asked to participate in this observational study. No clinic visits were acquired beyond those regularly scheduled. No laboratory or diagnostic tests were performed other than those associated with the usual clinical patient care. Medical history, information on co-morbidities, concurrent medication and laboratory data were collected by investigators from patient records: age at enrollment, gender, primary renal disease, time of start of dialysis, number of hours of hemodialysis per week at enrollment, history of kidney transplantation, and parathyroidectomy. In general clinical practice in Sweden, calcium and phosphorous is measured monthly in patients on hemodialysis and PTH is measured quarterly, with additional laboratory tests when treatment is changed, for instance with VDRAs, phosphate binders or cinacalcet.

FOLLOW-UP OF LABORATORY PARAMETERS

In this observational study, the proportion of patients attaining K/DOQI^{TM} targets for intact PTH, phosphorous, calcium and the calcium-phosphorous product was determined at baseline and then every other month up to 6 months of treatment with paricalcitol. We measured absolute values over time and evaluated changes in intact PTH, phosphorous, calcium, and the calcium-phosphorous product.

Furthermore, we assessed the doses of intravenous paricalcitol as well as the use of cinacalcet and phosphate binders (calcium based phosphate binders, sevelamer, lanthanum carbonate and aluminum based phosphate binders).

Safety and tolerability were assessed in terms of incidence of serious adverse events by normal study procedures.

PTH assay information was available from all sites. Most sites used ECLIA (Roche Diagnostics, USA) and others used Centaur or Siemens Medical Solutions and only a few used an automated immunoassay (Abbot Architect, USA). The frequency of PTH measurements was at the discretion of the treating nephrologist, but in general, as pointed out above, PTH is measured quarterly and additionally when medication is instituted or doses changed (VDRA, cinacalcet, phosphate binders).

STATISTICAL ANALYSIS AND CALCULATIONS

This observational study was designed to perform descriptive statistical comparisons. The number of participants was intended to range between 80--150 patients. The analysis population comprised all enrolled hemodialysis patients initiating intravenous paricalcitol therapy. Analysis of observed data and percentages were calculated according to the total number of patients in the full analysis set with no missing data. Patients without reported data on a parameter at a particular time point were excluded from the analysis at that time point. Analyses were descriptive and are presented for all continuous and categorical variables.

Intact PTH, calcium, phosphorous and the calcium-phosphorous product were based on the median of all values collected within bi-monthly time. Month 2 correspond to day 14--90, month 4 to day 91--150 and month 6 to day 151--227. PTH levels measured by bio-intact assays were converted to intact PTH values by multiplying them by 1.95. Total serum calcium was converted into albumin corrected calcium using the following formulas; If an albumin value was available: Ca-alb (mg/dL) = tot Ca (mg/dL) + 0.8 * (4.5 - alb(g/dL)) (14) and if an albumin value was missing and total calcium was within 2.0--2.8 mmol/L the following calculation was made: (Tot s-Ca (mmol/l) - 0,02 (Tot s-Ca - 4.3 g/L (Ca (mg/dL) = Ca (mmol/L) / 0.25).

SAEs were reported from the first day of paricalcitol treatment throughout the follow-up period

RESULTS

Patients

The study population consists of 92 hemodialysis patients over 18 years of age with a diagnosis of SHPT associated with CKD (Figure 1). Paricalcitol was prescribed according to the Swedish summary of product characteristics (SPC) for paricalcitol (Abbott, Sweden). Patient characteristics are presented in Table 1. Of the 92 patients, 74 patients had an intact PTH of >300 pg/ml at baseline, and 18 patients had an intact PTH ≤300 pg/ml at baseline. Mean age was 64 years, 50% of the patients were male, mean BMI was 26 kg/m^2 and the two most common causes of chronic kidney disease were chronic glomerulonephritis 28%, and diabetic nephropathy 25%. These figures indicate that the study population is representative for the hemodialysis patient population in Sweden (15).

Dose of paricalcitol

The mean total weekly dose of intravenous paricalcitol during the first month of study was 12 µg. After the first month the mean total weekly dose decreased in the group of patients with a baseline intact PTH of ≤300 pg/ml, while the dose of paricalcitol increased in the group of patients with a baseline intact PTH of >300 pg/ml (Table 2). After 6 months of treatment, the mean weekly dose of paricalcitol was 14 µg in the group of patients with an intact PTH of >300 pg/ml at baseline compared to 10 µg in the group of patients with an intact PTH of ≤300 pg/ml at baseline. After 6 months, 72 patients (90%) had ongoing treatment with paricalcitol, 90% in the group of patients with an intact PTH of >300 pg/ml at baseline and 89% in the group of patients with an intact PTH of ≤300 pg/ml at baseline. Reasons for discontinuation at 6 months were: death 4 patients, kidney transplantation 3 patients, hypercalcaemia 2 patients, and other reasons 8 patients. Of the entire patient cohort, 10 patients had a dosing interruption of 14--79 days during the 6 months of follow-up.

PTH, Calcium and Phosphorous during follow-up

Changes in PTH, serum calcium and phosphorous, as well as the calcium-phosphorous product are presented in Table 3. In the entire group of patients, median iPTH was decreased from 503 pg/mL at baseline to 283 pg/mL at 6 months (-44%, p< 0,0001, Table 3). Median intact PTH was 589 pg/ml in patients with a baseline PTH of >300 pg/ml who were prescribed intravenous paricalcitol. During follow-up there was a decrease in intact PTH to 322 pg/ml at 6 months (-45%, p < 0.0001). There was also a decrease in iPTH in the subgroup of patients with an intact PTH ≤300 pg/ml at baseline from 236 pg/mL at baseline and 206 pg/mL at follow-up (-13% p 0,7148).

Median serum phosphorous remained stable from baseline through 6 months, both for patients with a baseline intact PTH of >300 pg/ml as well as for patients with an intact PTH ≤300 pg/ml at baseline, -5,5% , p 0.2398 and - 6,2%, p 0.3877 respectively, Table 3.

Median serum calcium increased slightly both in the group of patients with an intact PTH >300 pg/ml (5%, p 0,0001), as well as in the group of patients with a baseline intact PTH ≤300 pg/ml (5%, p 0.1575, Table 3). At both baseline and 6 months, mean serum calcium was above the K/DOQI target in both groups (Table 3). Median calcium-phosphorous product remained stable from baseline to 6 months both in patients with intact PTH of >300 pg/ml and in patients with a baseline intact PTH ≤300 pg/ml (Table 3).

Proportion of patients with intact PTH within K/DOQI target

In the group of patients with a baseline intact PTH >300 pg/ml the proportion of patients within K/DOQI target increased month by month. After 6 months of treatment with paricalcitol 38.9% of patients with a baseline intact PTH of >300 pg/ml had achieved K/DOQI target for PTH (Table 4). Of the remaining patients 4 (7,41 %) had an intact PTH below K/DOQI target (Table 4).
In the group of patients with a baseline intact PTH ≤ 300 pg/ml 42,9 % stayed within the K/DOQI target for PTH. Of the remaining patients 6 (42,9 %) had an intact PTH below K/DOQI target (Table 4).

Proportion of patients with a 30% reduction in PTH

Also shown in Table 4 is the proportion of patients with a 30% reduction or more in PTH during follow-up. At 6 months, 63% of patients with an intact PTH of >300 pg/ml at baseline had a ≥30% reduction in intact PTH. The corresponding figure for patients with an intact PTH ≤300 pg/ml was 21%.

The proportion of hemodialysis patients with an intact PTH >300 pg/ml at baseline who achieved both a 30% reduction in intact PTH and an intact PTH within K/DOQI target was 63% after 6 months of treatment with paricalcitol.

Concomitant medication

The prescription of phosphate binders, cinacalcet and alpha-calcidol at baseline and at 6 months of follow-up is presented in Table 5. Prior to start of treatment with paricalcitol, 93% of the patients had been prescribed oral or intravenous alpha-calcidol (Table 1). At baseline, approximately 45% of patients had a calcium containing phosphate binder and 47% had sevelamer and 24% had lanthanum. At baseline 16 % of patients were receiving cinacalcet (Table 5).

Following 6 months of treatment with paricalcitol, the number of patients on a calcium **containing** phosphate binder decreased from 33 at baseline in patients with an intact PTH >300 pg/ml to 22. In the group of patients with intact PTH ≤300 pg/ml at baseline the use of calcium **containing** phosphate binders was unchanged from 8 to 7 (Table 5). The use of sevelamer was stable, 33 patients at baseline and 32 patients at the 6 month follow-up in patients who had an intact PTH >300 pg/ml at baseline. In the group with intact PTH ≤300 pg/ml at baseline 10 patients used sevelamer at baseline compared with 8 at the 6 month visit (Table 5). The use of lanthanum was also stable, 20 patients at baseline and 17 patients at the 6 month visit used lanthanum in the group who had an intact PTH >300 pg/ml at baseline. In the group with intact PTH ≤300 pg/ml at baseline 2 patients used lanthanum at baseline and 4 at the 6 month visit (Table 5). The use of cinacalcet was also unchanged in the group who had an intact PTH >300 pg/ml at baseline (15 patients at baseline and 16 patients at the end of the 6 month follow-up) and the mean dose did not change between baseline and 6 months (Table 5).

Adverse events

The most common serious adverse event was septicemia which occurred in five patients (five events). Angina pectoris, a cerebrovascular event, chest pain, dyspnoea, impaired wound healing, infection, myocardial infarction, pneumonia, and upper respiratory tract infection were reported in two patients each. No serious adverse events were judged as related to paricalcitol and only two adverse events, one "Confusion" and one "Hypercalcemia", were considered as possibly related to paricalcitol by the investigators. In total, 41 patients (45%) were hospitalized for different reasons during the study.

DISCUSSION

This observational study on the use, effectiveness and safety of intravenous paricalcitol in patients on hemodialysis in Sweden demonstrates that paricalcitol decreases intact PTH substantially in hemodialysis patients with a baseline iPTH above the K/DOQI recommended target range (i.e. >300 pg/ml). Intact PTH was uncontrolled and above the recommended target in 74 of 92 patients who were prescribed paricalcitol, despite that many of these patients had previous treatment for SHPT including phosphate binders , alpha-calcidol, and cinacalcet in some patients. Following the initiation of paricalcitol treatment, beneficial effects were observed for PTH in as soon as 2 months for the group of patients with a baseline intact PTH of >300 pg/ml. After 6 months of treatment, PTH in that subgroup had decreased from 589 pg/ml to 322 pg/ml (-45% , $p<0.0001$). During treatment with paricalcitol, mean serum phosphorous remained stable in both subgroups of patients. There was, however a small increase in mean serum calcium from baseline to 6 months of follow-up in both subgroups (5% , p 0.001 and 5%, p 0.1575 respectively).

In the group of patients with iPTH $\leq$ 300 pg/ml at baseline 42.9 % were within the KDOQI guideline 150 -300 pg/ml at 6 months and 42.9 % were treated to a PTH value below the KDOQI target at the six month follow-up. Only one patient had an iPTH value over KDOQI target in this group of patients.

Two epidemiologic studies have shown potentially important systemic effects of vitamin-D receptor activation on the survival of patients on dialysis (16, 17). After adjusting for potential confounders, these studies showed that all cause mortality and cardiovascular mortality were less in hemodialysis patients receiving injectable VDRA, as compared to no treatment with VDRA, and also that the use of paricalcitol was associated with an adjusted 16% survival benefit when compared to the use of calcitriol (16, 17). An important observation in these studies was the fact that a survival benefit of VDRA was apparent across all quintiles of calcium, phosphate and PTH, which suggests that the use of vitamin-D receptor activators may possibly mitigate the deleterious effects of elevated phosphate, calcium and PTH on mortality (16, 17). Both the mortality and morbidity data from these studies suggest that the benefit of paricalcitol was independent of baseline PTH, calcium or phosphorous levels, as a reduction in the risk of both death and the number of hospital admissions was apparent at all levels, when the data was stratified by variables (16-18). In contrast, data from the Dialysis Outcomes Practice Patterns Study (DOPPS) and from a not-for-profit dialysis provider in the United States demonstrated that differences in mortality risk between different vitamin-D receptor activators may be smaller than previously reported and that a prospective randomized controlled clinical trial is both needed and justified (19, 20).

During treatment with intravenous paricalcitol, the use of calcium containing phosphate binders decreased in the group of patients with an intact PTH of >300 pg/ml at baseline while the use of sevelamer increased in parallel in the same group of patients. Cinacalcet was used in comparable doses in 15 patients with an intact PTH >300 pg/ml at baseline and 16 patients at the end of 6 months follow-up. Thus, the positive effect of paricalcitol on PTH was probably not achieved through the use of cinacalcet.

Previous placebo controlled (21) and observational studies (22-24) have shown that cinacalcet alone or in combination with VDRA provide improvements in bone mineral metabolism parameters.

There were no unexpected safety or tolerability concerns during this 6-month study with paricalcitol in hemodialysis patients. The incidence of adverse events was low and serious adverse events were rare. There were relatively few discontinuations and 90% of the patients remained on paricalcitol 6 months after initiation of therapy.

It is important to consider limitations of observational analyses when interpreting the results of this study. The decision to start therapy with paricalcitol was made locally at discretion of the treating physician. The reason for initiation of treatment with paricalcitol in dialysis patients with a baseline PTH >300pg/ml may be that physicians considered preexisting therapies, including different phosphate binders, alpha-calcidol or cinacalcet, as insufficient or associated with side effects. The rationale for starting treatment with paricalcitol in patients with a PTH less than 300 pg/ml may be that patients on previous therapies had hypercalcaemia or hyperphosphatemia or that those patients for other reasons were considered suitable for treatment with paricalcitol. Nephrologists in Sweden participating in this trial may also have been influenced by the knowledge that treatment practices were being observed as part of a prospective study. Dialysis patients and dialysis units were not selected as being representative of Sweden as a whole. The frequency of laboratory testing was based on local clinical practices and variations were apparent across different sites, possibly influencing titration and target achievement. Also, missing data from some time points may have influenced the results. Despite these limitations this study provides new and important information on the use, effectiveness and safety of paricalcitol in clinical practice in hemodialysis patients in Sweden.

In conclusion, paricalcitol was well tolerated by hemodialysis patients with SHPT who had previously been prescribed alphacalcidol, phosphate binders and cinacalcet in different combinations. In the group of patients with an intact PTH of >300 pg/ml there was a substantial decrease in PTH values during 6 months of treatment with paricalcitol. In parallel, there was a small increase in serum calcium, but serum phosphorous and the calcium-phosphorous product remained unchanged. During the study, the use of calcium containing phosphate binders decreased, and the use of cinacalcet and sevelamer was relatively unchanged. Few adverse events occurred and discontinuation of therapy was low. Larger observational and randomized trials of the effects of paricalcitol in patients with CKD are warranted in the future.

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Tables and figures

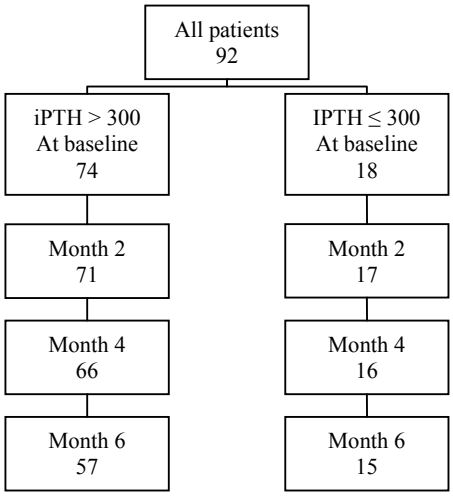

Figure 1. Study outline

Table 1. Baseline characteristics.

	All patients	iPTH > 300 at baseline	iPTH ≤ 300 at baseline
N	92	74	18
Age (years), mean (SD)	64.3 (13.8)	62.8 (14.1)	70.6 (10.6)
Gender Male/female, n	46/46	34/40	12/6
Dry weight (kg), mean (SD)	76.3 (17.7)	76.9(18.5)	73.4(13.9)
BMI (kg/m^2) mean (SD) using dry weight	26.2 (5.4)	26.8 (5.7)	25.6 (3.8)
Reasons for CKD, n (%)			
Chronic glomerulonephritis	26 (28.3)	20 (27.0)	6 (33.3)
Polycystic kidney disease	11 (12.0)	8 (10.8)	3 (16.7)
Nephrosclerosis /Hypertensive nephropathy	13 (14.1)	11 (14.9)	2 (11.1)
Chronic pyelonephritis	2 (2.2)	2 (2.7)	0 (0)
Diabetic nephropathy	23 (25.0)	18 (24.3)	5 (27.8)
Other	17 (18.5)	15 (20.3)	2 (11.1)
Duration of dialysis (months), mean (SD)	39 (33)	39 (34)	41 (31)
Dialysis vintage (years), n (%)			
< 1	19 (21)	16 (22)	3 (17)
1 - 5	53 (58)	43 (59)	10 (56)
> 5	19 (21)	14 (19)	5 (28)
Number of hemodialysis /week mean,(SD)	3.1 (0.5)	3.1 (0.5)	3.2 (0.5)
Hours of hemodialysis /week mean, (SD)	12.7 (2.5)	12.6 (2.6)	12.8 (2.1)
Earlier treatment with Vitamin-D related to SHPT, n (%)	86 (93)	68 (92)	18 (100)
Laboratory Parameters Median (Q1, Q3)			
Serum iPTH, pg/ml	503 (344, 767)	589 (433, 840)	236 (162, 263)
Serum phosphorus, mmol/L	1.8 (1.5, 2.0)	1.8 (1.5, 2.2)	1.6 (1.2, 1.8)
Serum calcium, mmol/L	2.45 (2.31, 2.57)	2.45 (2.31, 2.58)	2.41 (2.31, 2.51)
Calcium x phosphorus	4.25 (3.58, 5.16)	4.36 (3.72, 5.37)	3.70 (3.02, 4.43)

Table 2. Mean paricalcitol dose (μg) /week

	All patients	**PTH>300 at baseline**	**PTH≤300 at baseline**
0	12.35	12.45	12.05
2w	12.60	12.75	11.85
1m	13.20	13.45	12.15
2m	12.95	13.70	9.90
3m	12.00	12.75	9.00
4m	12.60	13.60	8.45
5m	13.15	14.10	9.55
6m	13.15	13.95	9.9

Table 3. Change in iPTH and phosphorus, calcium (albumin corrected) and calcium x phosphorus. (median, Q1, Q2)

	iPTH (pg/mL)			**Phosphorous (mmol/L)**			**Calcium (mmol/L)**			**CaxP ($mmol^2/L^2$)**		
	All	**iPTH >300 at baseline**	**iPTH ≤300 at baseline**	**All**	**iPTH >300 at baseline**	**iPTH ≤300 at baseline**	**All**	**iPTH >300 at baseline**	**iPTH ≤300 at baseline**	**All**	**iPTH>300 at baseline**	**iPTH≤300 at baseline**
0	503 (344,767)	589 (433,840)	236 (162,263)	1.8 (1.5,2.0)	1.8 (1.5,2.2)	1.6 (1.2,1.8)	2.45 (2.31,2.57)	2.45 (2.31,2.58)	2.41 (2.31,2.51)	4.25 (3.58,5.16)	4.36 (3.72,5.37)	3.70 (3.02,4.43)
2	344 (217,480)	381 (300,560)	163 (140,216)	1.7 (1.4,2.1)	1.8 (1.4,2.2)	1.6 (1.5,1.8)	2.51 (2.42,2.66)	2.51 (2.43,2.64)	2,58 (2.36,2.72)	4.41 (3.53,5.58)	4.46 (3.62,5.68)	4.31 (3.38,4.97)
4	358 (232,503)	392 (273,577)	215 (177,273)	1.7 (1.5,2.2)	1.7 (1.5,2.2)	1.6 (1.4,2.0)	2.51 (2.35,2.66)	2.53 (2.37,2.67)	2.48 (2.31,2.66)	4.43 (3.53,5.28)	4.44 (3.60,5.36)	3.70 (3.22,5.15)
6	283 (200,435)	322 (210,462)	206 (123,249)	1.7 (1.4,2.1)	1.7 (1.4,2.1)	1.5 (1.3,2.1)	2.56 (2.45,2.68)	2.57 (2.45,2.70)	2.52 (2.36,2.64)	4.27 (3.48,5.38)	4.32 (3.49,5.40)	3.79 (3.20,4.81)
P*	<0.0001	<0.0001	0.07148	0.5649	0.2398	0.3877	<0.0001	0.0001	0.1575	0.2756	0.7569	0.1040

*p baseline vs 6 months

Table 4. Proportion of patients with iPTH within K/DOQI target 150 - 300pg/ml or at least a 30% reduction in iPTH after six months

	All patients (%)	**iPTH>300 at baseline (%)**	**iPTH≤300 at baseline (%)**
Achieved Target (150-300)	**39.7**	**38.9**	**42.9**
Below Target (<150)	**14.7**	**7.4**	**42.9**
Achieved ≥30% reduction in iPTH	**54.4**	**63.0**	**21.4**

% based on number of patients with iPTH for the 6 month window

Table 5. Changes in concomitant medication during follow-up. *Percentage is shown only for baseline.

	All pats n (%*)	iPTH >300 at baseline (n)	Mean dose	iPTH ≤300 at baseline (n)	Mean dose
Baseline medication					
Phosphate binder					
Calcium based	41 (44.6)	33	-	8	-
Aluminium based	2 (2.2)	1	-	1	-
Lanthanum Carbonate	22 (23.9)	20	2224	2	1875
Sevelamer	43 (46.7)	33	4873	10	4480
Cinacalcet	15 (16.3)	15	58	0	-
Alphacalcidol	2 (2.2)	2	0.88	0	-
6 month medication					
Phosphate binder					
Calcium based	29	22	-	7	-
Aluminium based	2	1	-	1	-
Lanthanum Carbonate	21	17	2447	4	2000
Sevelamer	40	32	4117	8	5540
Cinacalcet	16	16	53	0	-
Alphacalcidol	2	1	0.75	1	0.50