KDOQI™ Target Achievement Is Improved With Cinacalcet (Mimpara®/Sensipar®) in Clinical Practice

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INTRODUCTION

- Cinacalcet (Mimpara®/Sensipar®), a calcimimetic, simultaneously lowers serum parathyroid hormone (PTH), phosphorus (P), calcium (Ca), and Ca x P in dialysis patients with secondary hyperparathyroidism (SHPT)
- Clinical trials have shown that cinacalcet is effective in achieving the bone/mineral metabolism targets recommended by KDOQI™[1,2]
- ECHO is the first pan-European, multicentre, observational study to explore cinacalcet use in daily "real-world" clinical practice

OBJECTIVE

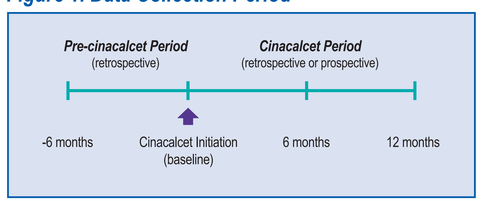
- To explore the effectiveness of cinacalcet in controlling PTH, P, Ca, and Ca x P in clinical practice
- To evaluate the effect of cinacalcet on biochemical parameters by severity of SHPT

METHODS

Study Design

- Pan-European, multicentre observational study
- Patients on dialysis were enrolled 6 months before and ≤ 12 months after initiating cinacalcet (Figure 1)
- Relevant medical history, comorbidities and laboratory data were collected via case report forms

Figure 1. Data Collection Period



Statistical Analysis

- Patients were categorized according to baseline iPTH in 2 separate analyses
  - Median (< 721 pg/mL or ≥ 721 pg/mL)
  - Mild (300–< 500 pg/mL), moderate (500–800 pg/mL) or severe (> 800 pg/mL)
- Final analyses are based on reported data only

RESULTS

- 1865 patients were enrolled between July 2005 and October 2006 from 187 sites in 12 countries
- Patient characteristics at the time of cinacalcet initiation are summarised in Table 1
- KDOQI™ target achievement improved for all 4 parameters after cinacalcet treatment was initiated (Figure 2)
- Changes over time in median serum iPTH, P, and Ca are shown in Figures 3–5
  - Serum iPTH, P, and Ca were insufficiently controlled in the 6-month period prior to cinacalcet initiation
  - Median percent changes from baseline to month 12 were: iPTH, -50%; P, -9%; Ca, -6%; (and Ca x P, -17%)
- ≥ 30% iPTH reduction from baseline was observed in 66% of patients at 12 months
- Most patients (65%) received a cinacalcet dose of ≤ 60 mg/day at month 12 (Figure 6)
- Of 37% of patients receiving ≤ 30 mg/day, 44% of patients were above target for iPTH (mean 580 pg/mL)

Table 1. Patient Characteristics at Initiation of Cinacalcet (N = 1865)*

Mean age [years] (SD)	58.1 (15)
Male/female [%]	57/42
Type of dialysis (HD/PD) [%]	88/12
Received a kidney transplant [%]	20
On transplant waiting list [%]	30
Parathyroidectomy [%]	8
Received vitamin D [%]	62
Received phosphate binders [%] Calcium-based Sevelamer Aluminium Lanthanum carbonate	90 42 66 14 1
Serum iPTH median [pg/mL] (Q1, Q3)	721 (507, 1050)
Serum P median [mg/dL] (Q1, Q3)	5.9 (4.8, 6.8)
Serum Ca median [mg/dL] (Q1, Q3)	9.6 (9.1, 10.4)
Ca x P median [mg^2/dL^2] (Q1, Q3)	56 (46, 67)

iPTH = intact PTH; HD = haemodialysis; PD = peritoneal dialysis
*Some patient characteristics not recorded for small numbers of patients

Figure 2. Patients (%) Achieving KDOQI™ Recommended Targets

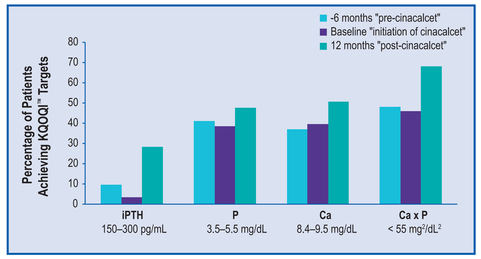
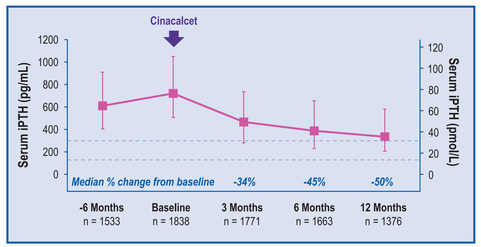
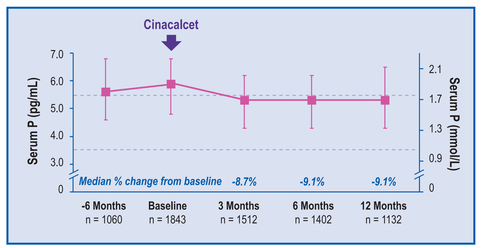


Figure 3. Median (Q1, Q3) Serum iPTH Level Over Time



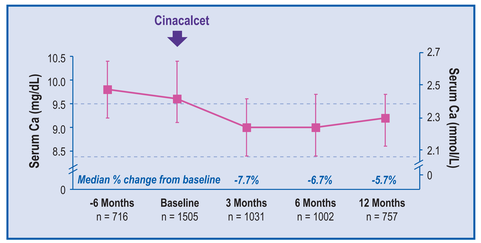
- - - KDOQI™ recommended targets

Figure 4. Median (Q1, Q3) Serum P Level Over Time



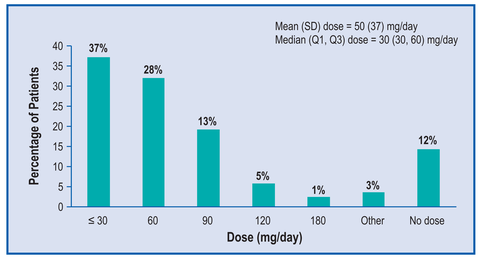
- - - KDOQI™ recommended targets

Figure 5. Median (Q1, Q3) Serum Ca Level Over Time



- - - KDOQI™ recommended targets

Figure 6. Cinacalcet Prescribed Dose at 12 Months (N = 1607)



The percentages do not add up to 100% as missing values have not been included

Vitamin D and Phosphate Binder Use

- Vitamin D sterol use (calcitriol, alfacalcidol, paricalcitol) remained fairly stable throughout the study
- Some changes in phosphate binder use were observed from baseline to Month 12
- Use of sevelamer decreased by 13.1% whereas use of calcium-based binders increased by 5.6%. However, doses of phosphate binders remained stable.

Achievement of KDOQI™ Recommended Targets by Disease Severity

- A higher proportion of patients with less severe disease (< 721 pg/mL) achieved iPTH targets by Month 12 vs patients with more severe disease (≥ 721 pg/mL) (Figure 7)
- Proportions of patients achieving the targets for P, Ca, and Ca x P were comparable for both groups
- Cinacalcet dose (SD) at month 12 was 43 (33) mg/day in patients < 721 pg/mL and 57 (39) mg/day in patients ≥ 721 pg/mL
- The magnitude of iPTH reduction was greater in patients with more severe disease at baseline (Figure 8)
- Table 2 shows the dose of cinacalcet in mild, moderate, and severe patients by target achievement. Patients with baseline iPTH > 800 pg/mL who were not achieving targets were receiving up to only 11 mg additional cinacalcet per day.

Figure 7. Patients (%) Within KDOQI™ Recommended Targets by Disease Severity

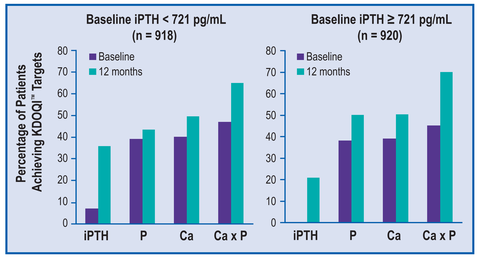
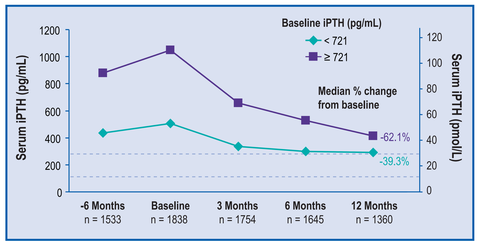


Figure 8. Magnitude of iPTH Reduction Differed According to Baseline iPTH



- - - - - - = KDOQI™ recommended targets

Table 2. Mean Cinacalcet Dose in Patients Achieving/Not Achieving KDOQI™ Targets at 12 months by Baseline iPTH

	Mean Cinacalcet Dose [mg/day] (SD) [No of Patients]	
Baseline iPTH [pg/mL]	150 to 300 pg/mL	> 300 pg/mL
300 to <500	33.5 (25.8) [n = 126]	49.7 (35.1) [n = 134]
500 to 800	48.3 (34.6) [n = 145]	55.1 (38.2) [n = 286]
>800	52.7 (30.9) [n = 146]	63.7 (40.2) [n = 474]

Adverse Events

- Adverse events related to treatment were reported in 11.3% of patients
- The most common adverse events (reported by > 1% of patients) were
  - Nausea (4.6%)
  - Vomiting (3.1%)
- Six patients (0.3%) experienced serious adverse events; there were no treatment-related deaths
- 75.5% of patients remained on cinacalcet at end of study; the main reason for discontinutaion was renal transplantation (5.2% of patients)

CONCLUSIONS

- The effectiveness of cinacalcet in clinical practice is consistent with that reported in similar patients in randomized, controlled trials[1,2]
- Cinacalcet improved attainment of KDOQI™ PTH, P, and Ca targets in a patient population with severe SHPT (median iPTH was 721 pg/mL and 54% of patients had uncontrolled Ca x P at baseline)
- Greatest achievement of iPTH targets occurred in patients with less severe disease (iPTH < 721 pg/mL)
  - Patients with less severe SHPT required lower cinacalcet doses (43 mg/day) to achieve PTH targets
  - Cinacalcet was insufficiently titrated in those patients who did not achieve PTH targets
- Earlier use of cinacalcet might result in better control of SHPT

REFERENCES

1. Block GA, et al. *N Engl J Med.* 2004;350:1516-25.
2. Lindberg JS, et al. *J Am Soc Nephrol.* 2005;16:800-7.

ACKNOWLEDGEMENT

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