

Comparison of 3x Weekly vs Daily Administration of Oral Cinacalcet for the Control of Secondary Hyperparathyroidism in Patients Receiving Hemodialysis

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Introduction

- Daily oral cinacalcet is effective in lowering parathyroid hormone (PTH) and is commonly used for the treatment of secondary hyperparathyroidism in patients with end-stage kidney disease.
- Published data from a phase I, open-label, multiple dose study and on practice patterns from other countries suggest that 3x weekly administration of cinacalcet at dialysis sessions may offer an effective alternative to daily administration.

Objectives

 We sought to compare control of MBD parameters and clinical outcomes among in-center hemodialysis (ICHD) patients initiating 3x weekly oral cinacalcet vs those initiating daily cinacalcet.

Methods

Data Source and Study Patients

- This was a retrospective observational study. All study data were derived from deidentified patient electronic health records of a large dialysis organization in the US.
- Patients included in the analysis were adults (≥18 years) who were receiving ICHD at the LDO, had Medicare as primary insurance, and who initiated cinacalcet use between 01 Jul 2018 and 31 Jan 2019, with no history of cinacalcet or parsabiv use in the prior 180 days.

Exposure

- 3x weekly cinacalcet patients were those with a physician order for cinacalcet given in center between 01 Jul 2018 and 31 Jan 2019.
- Index date for 3x weekly patients was defined as the date of first treatment with recorded in-center administration of cinacalcet.
- Daily cinacalcet patients were those with a physician order for daily cinacalcet between 01 Jul 2018 and 31 Jan 2019.
- Index date for daily cinacalcet patients was defined as date of the physician order for daily cinacalcet.

Outcomes and Statistical Analysis

- Analyses were performed following intention-to-treat principles: patients were followed forward in time from index date until censoring (for loss to follow-up death, transfer, transplant, withdrawal from dialysis, renal recovery, modality change) or end of study (31 July 2019). Patients were not censored for cinacalcet discontinuation or exposure group crossover.
- Outcome comparisons across exposure groups were made using generalized linear models adjusted for patient characteristics that were imbalanced at baseline.

Results

Table 1. Patient Characteristics at Time of Cinacalcet Initiation

	Daily cinacalcet	3x weekly cinacalcet
	N = 6871	N = 1339
Age, years, mean ± SD	63.0 ± 13.9	61.9 ± 14.1
Female, n (%)	3187 (46.4)	587 (43.8)
Race, n (%)		
White	2149 (31.3)	465 (34.7)
Black	3010 (43.8)	586 (43.8)
Hispanic	1028 (15.0)	163 (12.2)
Asian	247 (3.6)	38 (2.8)
Other/missing	437 (6.4)	87 (6.5)
BMI, kg/m², mean ± SD	30.3 ± 8.6	30.2 ± 8.4
Etiology of ESRD, n (%)		
Diabetes	2542 (37.0)	527 (39.4)
Hypertension	1841 (26.8)	395 (29.5)
Other/missing	2488 (36.2)	417 (31.1)
Dialysis vintage, months, mean ± SD	39.8 ± 38.2	40.3 ± 34.2
Charlson comorbidity index, mean ± SD	5.3 ± 1.8	5.2 ± 1.7
Diabetes, n (%)	4795 (69.8)	980 (73.2)
IV Vitamin D use, n (%)	6285 (91.5)	1176 (87.8)
Parathyroid hormone, pg/mL, mean ± SD	897 ± 462	908 ± 424
median [IQR]	819 [644, 1075]	819 [668, 1039]
Calcium, mg/dL, mean ± SD	9.0 ± 0.7	9.1 ± 0.6
Phosphorus, mg/dL, mean ± SD	6.1 ± 1.7	6.5 ± 1.8
Albumin, g/dL, mean ± SD	3.8 ± 0.4	3.9 ± 0.4
Patient characteristics defined as of index date, or most recent value withi	n prior 30 days	

Patient characteristics defined as of index date, or most recent value within prior 30 days Abbreviations: BMI. body mass index; IQR, interquartile range; IV, intravenous; SD, standard deviation

Table 2. Mortality and Hospitalization among Patients Initiating 3x Weekly vs Daily Oral Cinacalcet

	Daily cinacalcet N = 6871	3x weekly cinacalcet N = 1339
At-risk time, years	2790.2	425.7
Hospitalization,		
Number of admissions	4707	710
Crude rate, admits/pt-year	1.69	1.67
Modeled rate (95% CI), admits/pt-year	1.69 (1.64, 1.74)	1.68 (1.56, 1.80)
Adjusted IRR (95% CI) ^a	1 (ref)	0.99 (0.91, 1.08)
Mortality, n (%)		
Number of deaths	315	39
Crude rate, deaths/100 pt-years	11.3	9.2
Modeled rate (95% CI), deaths/100 pt-years	11.4 (10.2, 12.7)	9.5 (6.9, 13.0)
Adjusted IRR (95% CI) ^a	1 (ref)	0.90 (0.57, 1.43)

vvv Adjusted for age, sex, race, and serum phosphorus
Abbreviations: CI, confidence interval; IRR, incidence rate ratio; pt-yr, patient-year

Figure 1. Parathyroid Hormone among Patients Initiating 3x Weekly vs Daily Oral Cinacalcet

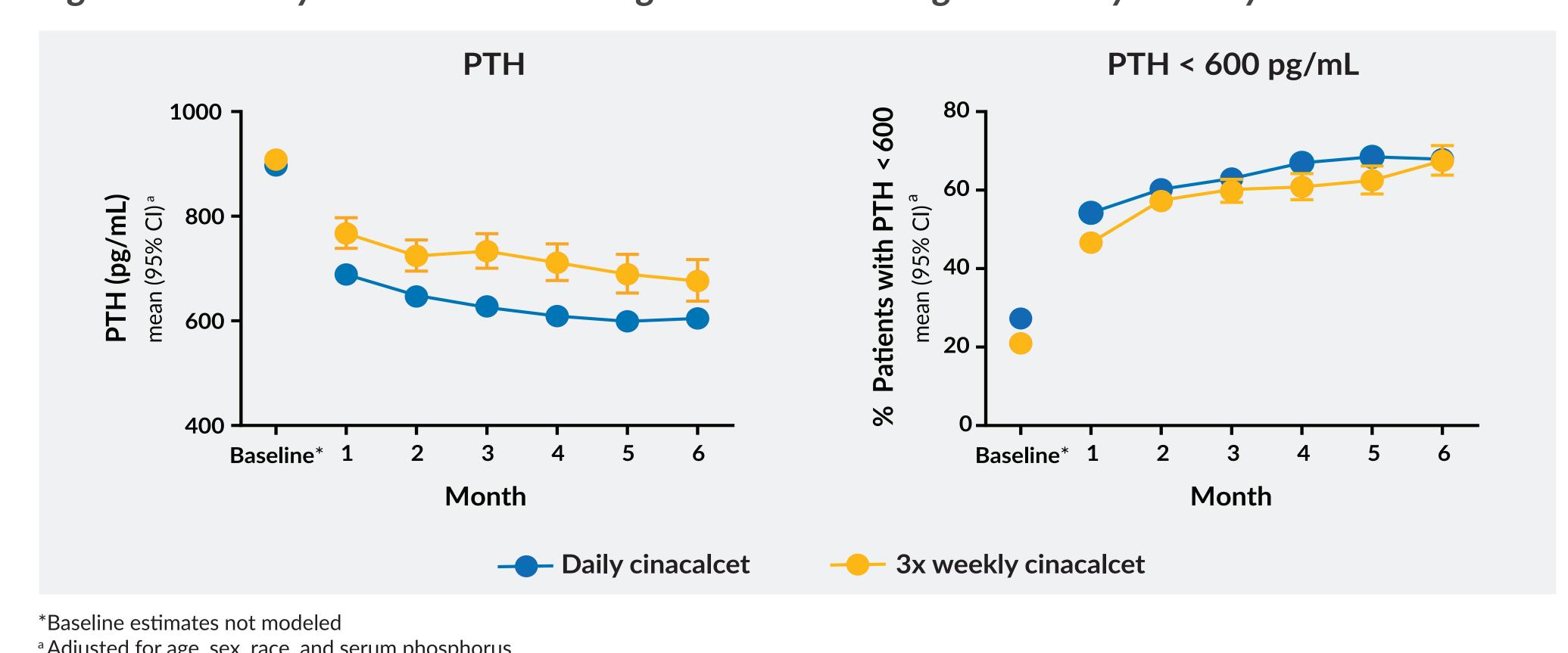


Figure 2. Serum Calcium among Patients Initiating 3x Weekly vs Daily Oral Cinacalcet

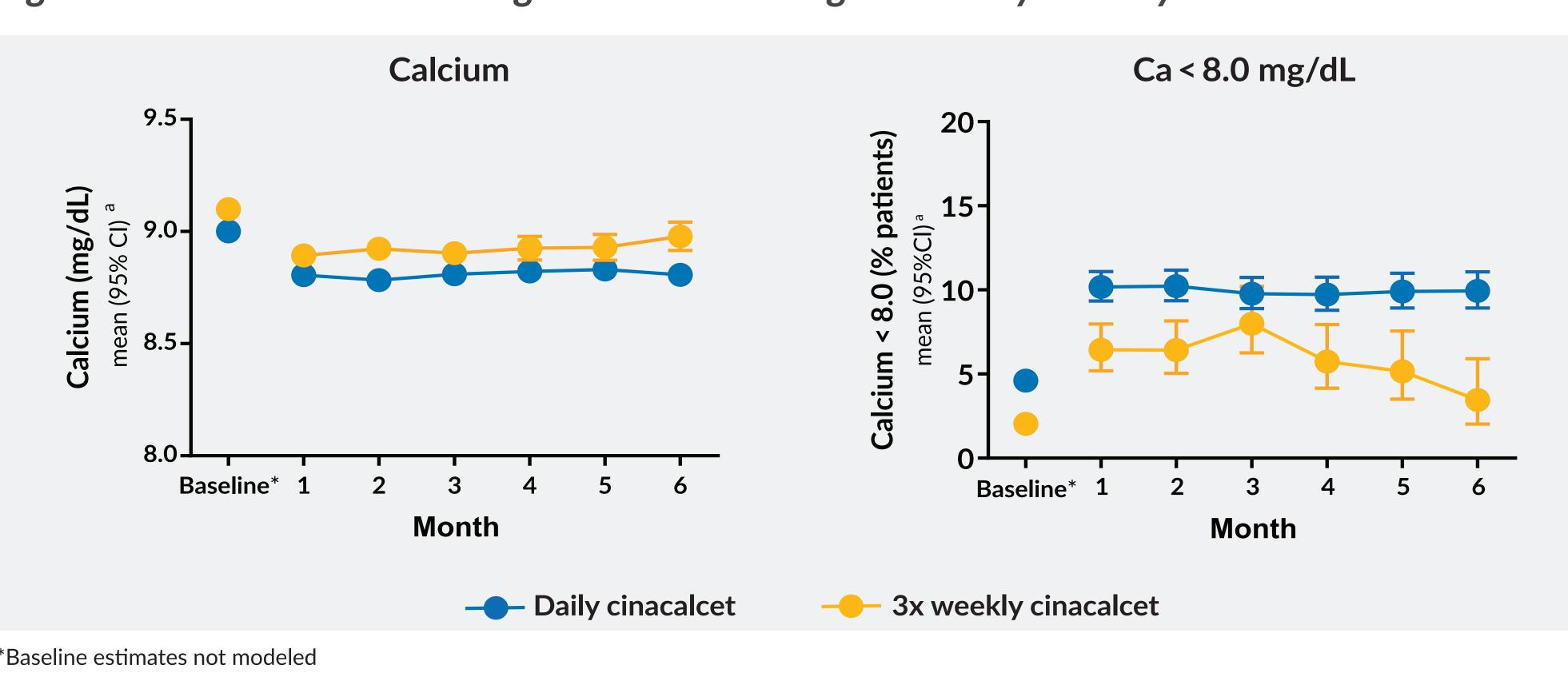
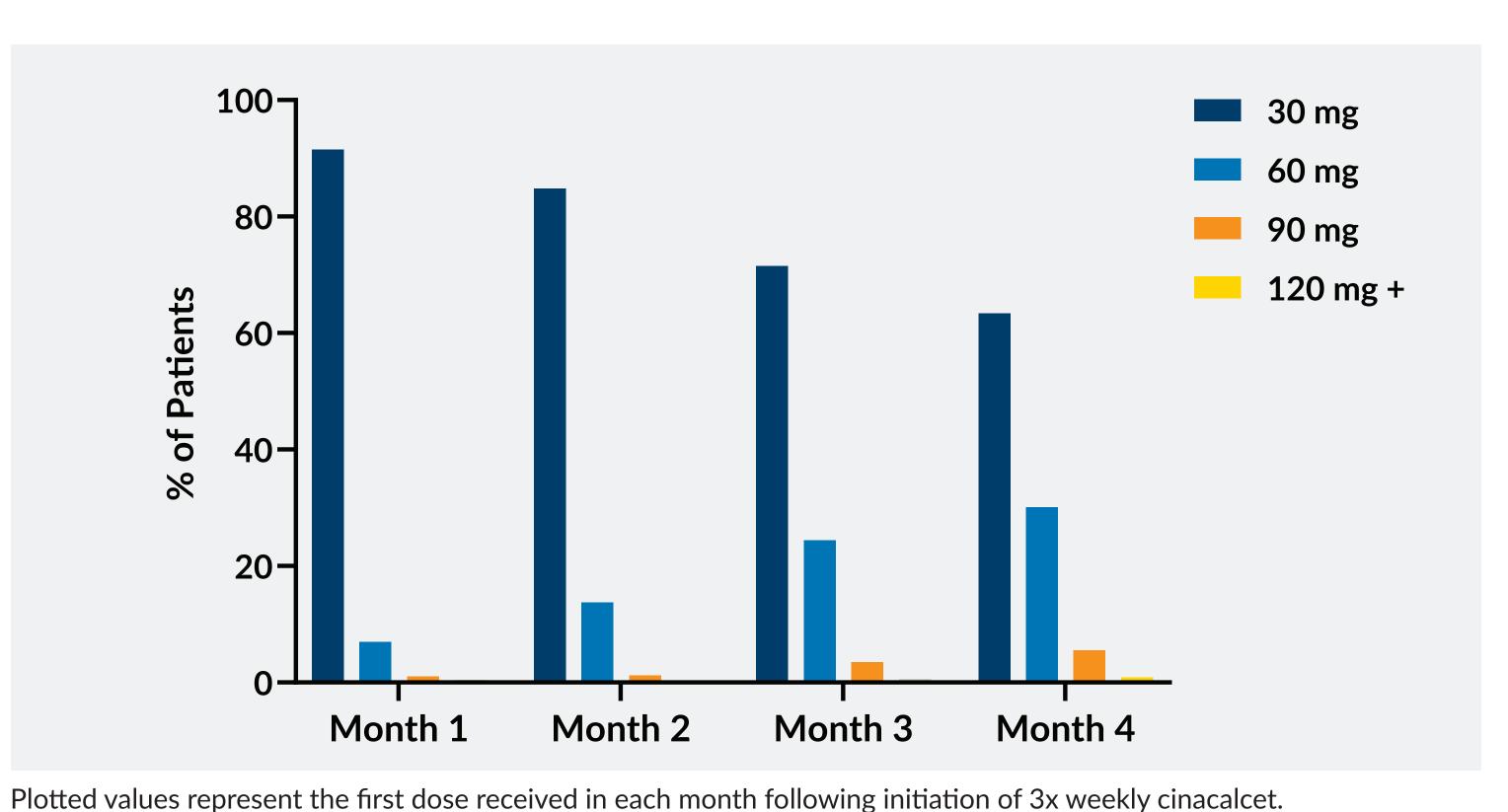


Figure 3. Per-Treatment Dose among Patients Initiating 3x Weekly Oral Cinacalcet



- Characteristics of patients initiating 3x weekly and once daily cinacalcet are shown in Table 1.
- PTH levels decreased over follow up for both groups: from 908 to 676 pg/mL in 3x weekly patients and from 897 to 605 pg/mL in daily patients (Figure 1A).
- At 6 months after cinacalcet initiation, the percentage of patients with PTH <600 pg/mL was similar in the two groups (67.5% vs 67.9% for 3x weekly and daily, respectively; Figure 1B).
- Compared to patients initiating daily cinacalcet, patients initiating 3x weekly cinacalcet had higher levels of serum calcium and experienced fewer episodes of hypocalcemia (Figure 2A and B).
- Mortality and hospitalization rates over follow up were equivalent in the two exposure groups (Table 2).
- Dosing patterns among patients initiating 3x weekly cinacalcet are shown in Figure 3: the majority of patients (91.6%) initiated therapy at a per-treatment dose of 30 mg. By month 4, 63.4% of patients remained on a dose of 30 mg/treatment; approximately 6% of patients were receiving a per-treatment dose of ≥ 90 mg.

Study Limitations

- Despite adjustment of analyses to promote fair comparisons, differences between groups may remain.
- Analyses were performed following intention-to-treat principles; persistence on therapy was not considered in these analyses. Information on cinacalcet dosing was not available for patients on daily therapy.

Conclusions

- These results suggest that 3x weekly dosing of oral cinacalcet may be an effective therapeutic strategy for the management of SHPT in patients on HD.
- The majority of patients initiated 3x weekly cinacalcet at a dose of 30 mg per treatment, representing a lower cumulative weekly dose than that typically prescribed for those on daily therapy.

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