Etelcalcetide in the Treatment of Secondary Hyperparathyroidism in Patients Uncontrolled with Cinacalcet: Results from a Prospective Study

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Introduction

- Secondary hyperparathyroidism (SHPT) is associated with increased bone turnover, risk of fractures, vascular calcifications and cardiovascular and all-cause mortality.[1]
- Etelcalcetide is a new calcimimetic, recently approved for SHPT treatment, and has a pharmacokinetic profile that allows thrice weekly intravenous (IV) dosing after hemodialysis (HD).
- There is limited clinical experience with this agent with respect to its efficacy in patients with SHPT that is uncontrolled with cinacalcet.

Methods

- We conducted a prospective cohort study in prevalent HD patients treated at 3 DaVita clinics in Portugal who had SHPT that was uncontrolled with cinacalcet treatment for at least 3 months.
  - Inclusion criteria: intact PTH (iPTH) levels > 800 pg/mL and total calcium > 8.3 mg/dL in the previous 3 months.
- After a 1-week cinacalcet washout period, etelcalcetide 5mg IV/HD treatment was initiated. iPTH, serum calcium, and phosphorus were followed over 6 months; FGF-23 and sclerostin levels were analyzed before the start of etelcalcetide treatment and after 6 months.
  - Assays for FGF-23 (C-terminal) and sclerostin were performed by ELISA on the fully automated Gemini Stratec (Diatrom) equipment using Biomedica reagents and following the manufacturer's protocols (Biomedica Medizinprodukte GmbH & Co KG).
  - Both assays were performed on plasma EDTA samples collected using BD Vacutainer K2E. Plasma separation was performed immediately by centrifugation (10 min at 1500*g*). Samples were stored at -25°C.
- Results were considered as means, medians, interquartile ranges and percentages, unless otherwise specified. Wilcoxon and McNemar tests were used for ordinal and dichotomous paired variables, respectively. *P*-values of < 0.05 were considered significant. All statistical analyses were performed using SPSS IBM (v21, SPSS Inc, Chicago, IL, USA).

Results

Figure 1: Serum Calcium, Phosphorus, and Intact PTH Levels at Baseline and After 6 Months of Etelcalcetide Treatment

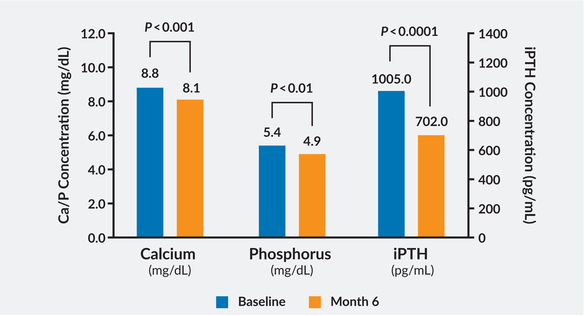
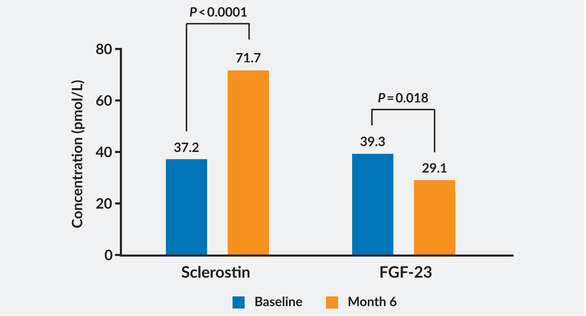


Figure 2: Plasma Sclerostin and FGF-23 Levels at Baseline and After 6 Months of Etelcalcetide Treatment



- Among the 34 patients included in the study:
  - Mean age was 60.7 (SD: 12.3) years
  - Median time on HD was 82.5 (7-296) months
  - Median cinacalcet dose at switch was 180 (90-840) mg/week.
- Median etelcalcetide dose remained at 5mg/HD treatment at 3 and 6 months following switch.
- Serum calcium, phosphorus, and iPTH were all lower at month 6 than at baseline (Figure 1).

- For a subset of patients, serum FGF-23 (n = 13) and sclerostin levels (n = 29) were available. In these patients, over 6 months of etelcalcetide treatment:
  - Serum FGF-23 decreased from 39.3 (23.0-43.3) pmol/L to 29.1 (11.5-115.6) pmol/L (*P* = 0.018).
  - Sclerostin increased from 37.2 (5.8- 200.7) pmol/L to 71.7 (28.2- 185.5) pmol/L (*P* < 0.0001).

Discussion

- Etelcalcetide improved control of severe SHPT in patients undergoing cinacalcet treatment, with reductions in serum calcium and phosphorus levels and also in FGF-23 levels, compared to baseline values.
- The observed increase in the sclerostin levels of patients already under cinacalcet treatment is an original observation and deserves further investigation.
  - This effect is not surprising because PTH down regulates sclerostin expression in osteocytes.[3]
  - It is possible that this effect of etelcalcetide on sclerostin levels may translate into a protective effect on vascular calcification, at the same time reducing osteoblast activity and bone remodeling in the setting of high-turnover bone disease.

Conclusions

- Etelcalcetide was effective in improving SHPT control in this group of patients, previously uncontrolled with cinacalcet treatment.
- Plasma sclerostin concentrations increased following the switch to etelcalcetide: this might be expected considering the inhibitory effect of PTH on sclerostin expression.[3]
  - To our knowledge, this is the first study describing the impact of etelcalcetide treatment on plasma sclerostin levels.

References

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