A BC Provincial Renal Agency Formulary Review of Cinacalcet Reimbursement: 2008 - 2015

Matthew Lum, B.Sc.(Pharm); Dan Martinusen, PharmD; Kevin Sin, B.Sc.; Alexandra Romann, M.Sc.; Jonathan F. Mailman, PharmD; William Nevers, PharmD; Robin Cho, PharmD; Clifford Lo, PharmD

Background

- Cinacalcet acts as a calcimimetic at the parathyroid gland reducing parathyroid hormone (PTH) release.
- After studies demonstrated significant improvements in biochemical markers - PTH, calcium (Ca) and phosphate (PO_4), cinacalcet was added to the BC Provincial Renal Agency (BCPRA) formulary in 2008 as a last line agent to treat secondary hyperparathyroidism in patients with mineral bone disorder (MBD).
- In 2012, the first RCT (EVOLVE), found no reduction in CV events or mortality with cinacalcet use. However, Chertow et al. reported a reduction in patient centered outcomes (joint pain and bone pain) and therefore cinacalcet continues to be funded in BC.
- In 2014, $587,000 was spent on cinacalcet by the BCPRA.

Objectives

To determine if we are achieving value for money by:

- Characterizing cinacalcet use from November 2008 to March 2015
- Describing the effect of cinacalcet on the use of PO_4 binders and vitamin D analogues.
- Measuring the effect of cinacalcet on PTH, Ca and PO_4.

Primary outcome

- The defined daily dose (DDD) of sevelamer and lanthanum at baseline, compared to the DDD at 6 months, 1 year and 5 years after initiation of cinacalcet.

Methods

- **Design**: Retrospective administrative database study.
- **Population**: ≥ 18 y/o, on dialysis for ≥ 3 months, funded through BCPRA, experiencing symptoms related to 2^0 hyperparathyroidism causing impairment in QoL, PTH ≥ 88 pmol/L and receiving adequate dialysis (PRU > 65% or KT/V > 1.2).
- **Exclusion criteria:** Calciphylaxis, on cinacalcet prior to the study period for > 2 weeks, non-compliant defined as > 2 refills with a duration that exceeds the quantity dispensed (grace period of 14 days) or cinacalcet not dispensed for > 4 months then restarted.
- **Subject identification** Patients dispensed cinacalcet through the BCPRA contracted pharmacy between 2008 and 2015.
- **Data collection**: Dosage, duration, and number of patients on cinacalcet were obtained from dispensing records. Symptoms, bridging data and number of applications were obtained from application forms. PO_4 binder doses, vitamin D analogue doses, PTH, Ca, PO_4 and baseline characteristics gathered from PROMIS.

Table 1. Baseline characteristics

	Cinacalcet patients (N = 228)
Mean age (years ± SD)	61 ± 15
Male sex	123 (54%)
HD	
- Nocturnal HD	13 (6%)
- Intermittent HD	186 (82%)
PD	
- CCPD	23 (10%)
- CAPD	6 (2%)
- Median dialysate Ca conc. in HD/PD (IQR)	1.25 (1.25 -1.5 mmol/L)
- Median albumin (IQR)	37 (34 - 41 g/L)
Receiving lanthanum	35 (15%)
Receiving sevelamer	87 (38%)
Receiving Ca-based PO_4 binder	106 (46%)
- Calcium acetate	59 (26%)
- Calcium carbonate	47 (21%)
Median symptom score*	
- Bone pain (n = 76)	8/10
- Pruritus (n = 64)	7/10
- Myalgia (n = 62)	8/10
- Joint Pain (n = 16)	8/10
- Neuropathy (n = 15)	8/10

*Data taken from patients in 2011-2015 as symptom severity rating scale was only implemented in 2011 (n=123)

Table 2. Biochemical markers

	Baseline Median (IQR)	6 Months Median (IQR)	1 Year Median (IQR)	5 Years Median (IQR)
PTH (pmol/L)	143 (98 - 201)	56 (24 - 106)	38 (11 - 79)	26 (13 - 37)
Ca (mmol/L)	2.4 (2.3 - 2.5)	2.3 (2.1 - 2.4)	2.3 (2.1 - 2.4)	2.4 (2.2 - 2.5)
PO_4 (mmol/L)	1.7 (1.5 - 2.2)	1.5 (1.2-1.9)	1.5 (1.2 - 1.9)	1.3 (1.0 - 1.5)

Figure 1. Estimated annual cinacalcet cost savings

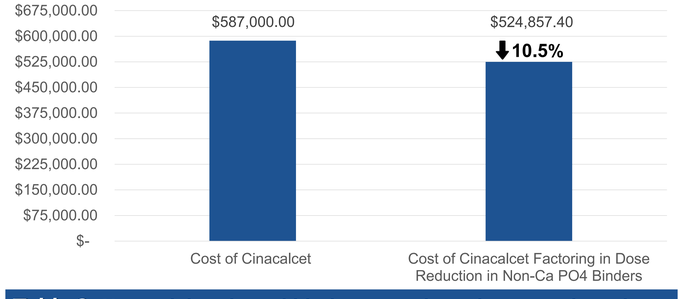

Table 3. Non-calcium-based binder usage in patients on cinacalcet

	Baseline	6 Months	1 Year	5 Years
On cinacalcet at baseline and alive	224	204	190	137
Receiving cinacalcet	224 (100%)	153 (75%)	94 (49%)	9 (7%)
Receiving sevelamer	87 (38%)	57 (37%)	20 (21%)	2 (22%)
Median sevelamer DDD (mg)	4800	4800	2400	6000
Receiving lanthanum	35 (15%)	12 (8%)	6 (6%)	0
Median lanthanum DDD (mg)	2750	3000	3000	n/a

Table 4. Cinacalcet usage

	Results
Median dose of cinacalcet (mg)	
- Baseline	30
- 6 months	60
- 1 year	60
- 5 years	60
Median duration of cinacalcet treatment (years)	0.7 (0.5 - 0.8)
Mean no. of cinacalcet applications annually	63
Cinacalcet application approval rate (%)	81
Mean no. approved for bridging to parathyroidectomy (%)	43
Mean no. of patients on cinacalcet annually	118

Discussion

- After initiating cinacalcet, daily defined doses of lanthanum or sevelamer remain relatively stable during the first year. However, there is a decrease in the number of patients requiring non-calcium based PO_4 binders.
- Overall, the cost savings from reduced non-calcium based PO_4 binder usage did not significantly offset cinacalcet expenditure (~10.5%/year).
- Changes in biochemical markers did not reach statistical significance. However, we hypothesize that the observed reduction in PTH was likely clinically significant.
- 43% of approved cinacalcet cases were for bridging to a parathyroidectomy. In addition, we observed a mortality rate of ~15% during the first year of cinacalcet therapy. Both factors contribute to the relatively short duration of cinacalcet treatment observed in this study (median of ~8 months).

Limitations

- Retrospective review
- Median duration of cinacalcet treatment is ~8 months; therefore the accuracy of data is reduced at each time interval, especially at year 5.
- Assumptions were made to complete the cost analysis (e.g. the proportion of patients on non-calcium based PO_4 binders was extrapolated from cohort data instead of using actual number of patients on a non-calcium based PO_4 binders in 2014).

Conclusions

- This is the first study to report real-world data on cinacalcet usage as well as its influence on related therapies (PO_4 binders and vitamin D analogues). This data will be useful for economic analysis and policy decision-making.
- Initiating cinacalcet does not significantly reduce the cost of non-calcium based PO_4 binders.
- Since cinacalcet failed to demonstrate improvements in CV events and mortality (EVOLVE) and we found no significant reduction in the cost of PO_4 binders used, real-world confirmation of MBD-associated symptom improvement is the next step required to complete our economic evaluation and to determine cinacalcet's place in therapy. This is the next stage of our provincial formulary review.