Clinical benefits of an adherence monitoring program in the management of secondary hyperparathyroidism with cinacalcet:

Results of a prospective randomized controlled study

Forni Valentina¹, Pruijm Menno¹, Isabelle Menetrey¹, Zweiacker Carole¹, Wuerzner Grégoire¹, Tousset Eric², Burnier Michel¹

¹ Service of Nephrology, Department of Medicine, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland

²AARDEX Group Ltd, Visé, Belgium
Background

Adherence and hemodialysis patients

- In Center HD 3 times per week, 4 hours per session, complex medication, multiple dietary restrictions
- Several definitions of non-adherence, cut-off not-well defined
- Prevalence of non-adherence between 2% - 100%
- Increased risk of morbidity/mortality
- Frustrating for medical and nurse team


Background

Pathophysiology of secondary hyperparathyroidism
Treatment of sHPT

- **Vit D derivates**: increase serum Ca level

- **Phosphate- binders**: decrease serum PO$_4$ level
  - Calcium derivates: Ca carbonate or Ca acetate
  - Non-Ca derivates: lanthanum carbonate, sevelamer

- **Cinacalcet**: calcimimetic: immediate effect on PTH level
  - short $\frac{1}{2}$ life (6hours)
  - tablets: 30 - 60 - 90 mg
  - regimen: 1dd, per os 30 - 180 mg / day,
  - duration of treatment: months or years
Background

PTH, bone, cardiovascular risk

**KDIGO target**

12 65 100 200 300 400 500 >600

**Adynamic osteopathy (OPA)**

**Normal, OPA, OF, mixte**

**Osteitis fibrosa (OF)**

**Qunibi W. et al: Target Levels for Serum Phosphorus and Parathyroid Hormone.**


**KDIGO = Kidney Disease: Improving Global Outcomes, 2009**
Background

The pilot study


The new study hypothesis:

Does regular feed-back to patients about monitored cinacalcet adherence data lead to better PTH control as compared to monitoring alone?
Methods

Study description

- **TYPE**: prospective, randomized, controlled multicentric study,

- **POPULATION**: patients $\geq 18$ y, hemodialyzed $\geq 3$ months, Cinacalcet HCl prescription $\geq 1$ months (stable dose) (indication: secondary hyperparathyroidism, sHPT)

- **PRIMARY OBJECTIVE**: $\Delta$ iPTH at 0-6 months
  $\Delta$ Cinacalcet dose at 0-6 months
Methods

Study design

MEMS MONITORING

Ø MEMS MONITORING

Integrated Care

Usual Care

Inclusion

Rand.

Cinacalcet

- x (months)

V0 V1 V2 V3 V4 V5 V6 V7 V8 V9

↓ = iPTH, Ca total, PO4
Methods

Integrated Care approach
Methods

Usual Care approach

Laboratory results
Results

Randomization and follow-up

- Inclusion: 01.2010-03.2011
- 2 linguistic regions
- 9 HD centers

Enrolled and randomized (n=50)

Usual Care (n=26)
- Died (n=1)
- Transplanted (n=1)
- Violation of inclusion criteria (n=1)
- Withdrawn for other reasons (n=1)

Patients analyzed UC (n=22)

Integrated Care (n=24)
- Transplanted (n=1)
- Violation of inclusion criteria (n=2)
- Withdrawn for other reasons (n=2)

Patients analyzed IC (n=19)
## Results

### Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Usual Care</th>
<th>Integrated Care</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>22</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td>Mean (sd)</td>
<td>61.3 (9.8)</td>
<td>59.1 (15.6)</td>
</tr>
<tr>
<td><strong>Time on dialysis (months)</strong></td>
<td>Median (sd)</td>
<td>50 (48)</td>
<td>50 (45)</td>
</tr>
<tr>
<td><strong>Serum calcium (mmol/l)</strong></td>
<td>Mean (sd)</td>
<td>2.10 (0.18)</td>
<td>2.11 (0.13)</td>
</tr>
<tr>
<td><strong>Serum PO4 (mmol/l)</strong></td>
<td>Mean (sd)</td>
<td>1.70 (0.65)</td>
<td>1.67 (0.55)</td>
</tr>
<tr>
<td><strong>iPTH (ng/l)</strong></td>
<td>Median (iqr)</td>
<td>419 (275 - 548)</td>
<td>417 (352 - 622)</td>
</tr>
</tbody>
</table>
Results

iPTH results

* p = 0.05 (Wilcoxon rank-sum test)  
* p = 0.009 (Wilcoxon rank-sum test)

Note: conversion factors for units: iPTH in ng/l to pmol/l, divided by 9.43
Results

Cinacalcet dose change

* p = 0.03 (Wilcoxon rank-sum test)
Results

Δ Adhesion

UC

Δ Adhesion (%)

Months 0–2
Months 4–6

IC

Δ Adhesion (%)

Months 0–2
Months 4–6

UC Δ -5% (mean), -2% (median)

IC Δ +10% (mean), +4% (median)

* p < 0.01

* Wilcoxon matched-pairs signed ranks test
Conclusions

1. The Integrated Care approach, based on drug adherence results, enables to:
   - achieve a better biological control of secondary hyperparathyroidism
   - improve cinacalcet adherence
   - decrease cinacalcet dose without changing the prescription of phosphate binders and Vitamine D derivates.

2. However, the positive effects are vanished 3 months after the interruption of the drug adherence monitoring, suggesting that the intervention should be of long duration.
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