Sevelamer Carbonate (Renvela®): pre-licence studies and clinical application

Philip A Kalra
Consultant and Honorary Professor in Nephrology,
Salford Royal Hospital and University of Manchester, UK
Topics for discussion

- Phosphate as a risk factor in CKD
- Studies linking phosphate to risk in the general population (CARDIA)
- Phosphate in the CRISIS cohort (non-dialysis CKD managed in secondary care)
- Sevelamer Carbonate (Renvela®) – clinical application
Rates of death and cardiovascular events rise as renal function declines

Relative Risk Reduction 8% (95% CI: -23%, +10%, P=0.37)
N=1255 HD pts with type 2 diabetes
Cardiac death, non-fatal MI or stroke
Mean follow-up 4 years

Uraemic Arteriopathy or Atherosclerosis

Chalk

Cheese
Arterial Medial Calcification in ESRD

Probability of All-Cause Survival According to Calcification Status

*Comparison Between Curves Was Highly Significant (x²=42.66, P<0.0001)
Pathophysiology of vascular calcification: Balancing Act…

Promoters

NormalG FR

Inhibitors
Imbalance in advancing CKD...

↑ Phosphate
↑ [Ca] x [P]
↑ Calcium intake etc
↑ PTH

CKD

↓ Fetuin
↓ MGP etc
INHIBITORS

PROMOTORS

-
Treat-to-Goal Study: increase in calcification in prevalent haemodialysis patients

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**Median percentage change**

- **Coronary**
  - Sevelamer: 6%
  - Calcium: 25%*

- **Aorta**
  - Sevelamer: 5%
  - Calcium: 28%*

*Within treatment $P<0.0001$; between treatment groups $P=0.02$

Phosphate: general population and CKD
CARDIA (Coronary artery risk development in young adults)

- Prospective multi-centre observational study of CVS disease development in fit young adults (age 18-30 yrs)

- 1985-86 in 4 US regions (Birmingham, Alabama; Chicago, Illinois; Minneapolis, Minnesota; Oakland, California)

- 5113 participants
CARDIA (Coronary artery risk development in young adults)

- Various baseline variables assessed
- LVMI assessed by echocardiography 5 years after entry
- Coronary artery calcification assessed by CT scan 15 years later

- 4005 of 5113 participants underwent echocardiography

Baseline data
- Mean age 25 years
- Mean phosphate 3.7 mg/dl (1.2 mmol/l)
- eGFR 118.5 ml/min/1.73m²
Left ventricular hypertrophy (LVH)

- At 5 years mean LVMI 80.5 g/m²
- Each SD of baseline phosphate above the mean was associated with ↑presence of LVH 5 years later (AOR 1.301, p=0.0018)
- Association most prominent with phosphate levels in 5th quintile (> 4mg/dl)

- 3015 of 5113 participants underwent CT at 15 years

**Baseline data**

- Mean age 25.2 years
- Mean phosphate 3.6 mg/dl (1.2 mmol/l), calcium 9.5 mg/dl (2.4 mmol/l)
- Mean eGFR 116.6 ml/min/1.73m²
- 0.2% with eGFR < 60 ml/min/1.73m²
Coronary artery calcification (CAC)

- **Year 15 CAC scores**
  - Minimal 0-10: 3.2%
  - Mild 10-100: 4.8%
  - Moderate 101-300: 1.1%
  - Severe >300: 0.5%

- **Multivariate models**: baseline phosphate associated with CAC with AOR 1.18 per 0.5 mg/dl ↑ of phosphate

- AOR 1.59 of CAC for phosphate >3.9mg/dl cf <3.3mg/dl
P-Spline plot relating adjusted odds ratio of CAC $\geq 100$ and serum phosphorus

AOR, with 95% confidence intervals. Adjusted for all variables except calcium-phosphorus product and diastolic blood pressure
Phosphate in General population

- Phosphate is associated with development of LVH and vascular calcification in ‘General population’

- Is this an association or a causative relationship?

We need:

- genetic and biomarker studies
Chronic Renal Insufficiency Standards Implementation Study (CRISIS)

- Prospective epidemiological study in Salford, Greater Manchester, UK: Commenced 2002
- CKD stage 3-5 managed in secondary care
- Annual phenotypic (clinical, laboratory) data
- Samples for biomarkers
- Genomics
- Analysis: Associations and outcomes of CKD
Basic Results – to current time

- Mean eGFR 34 ml/min
- Mean Follow up  33.9 months
- 20.4% died  
  (8.8 per 100 patient years)
- 18% reached ESRD requiring RRT  
  (7.8 per 100 patient years)
CRISIS study: analysis of serum phosphate

- 1213 patients
- Baseline demographics – Phosphate divided into quartiles
- Cox regression
- Baseline phosphate and survival
- Time-averaged phosphate and survival
## Baseline demographics

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>PO\textsubscript{4} &lt;1.01</th>
<th>PO\textsubscript{4} 1.02 – 1.16</th>
<th>PO\textsubscript{4} 1.17-1.33</th>
<th>PO\textsubscript{4} ≥1.34</th>
<th>(P) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(N=1213)</td>
<td>(N=318)</td>
<td>(N=300)</td>
<td>(N=293)</td>
<td>(N=302)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>64 (14)</td>
<td>65 (14)</td>
<td>65 (14)</td>
<td>62 (14)</td>
<td>0.037</td>
<td></td>
</tr>
<tr>
<td>Female sex</td>
<td>429 (35.4%)</td>
<td>76 (24%)</td>
<td>109 (36%)</td>
<td>124 (42%)</td>
<td>120 (40%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Calcium</td>
<td>2.29 (0.14)</td>
<td>2.29 (0.13)</td>
<td>2.29 (0.19)</td>
<td>2.30 (0.13)</td>
<td>2.28 (0.19)</td>
<td>ns</td>
</tr>
<tr>
<td>PTH</td>
<td>89 (86)</td>
<td>58 (42)</td>
<td>77 (62)</td>
<td>86 (77)</td>
<td>135 (124)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hb</td>
<td>124 (18)</td>
<td>135 (18)</td>
<td>125 (16)</td>
<td>123 (14)</td>
<td>114 (17)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>eGFR</td>
<td>31.6 (15)</td>
<td>40 (14)</td>
<td>34 (13)</td>
<td>31 (14)</td>
<td>20 (11)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>1.1 (1.8)</td>
<td>0.5 (0.7)</td>
<td>0.8 (1.2)</td>
<td>0.9 (1.2)</td>
<td>2.1 (2.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CVD</td>
<td>380 (31%)</td>
<td>99 (31%)</td>
<td>109 (36%)</td>
<td>99 (34%)</td>
<td>73 (24%)</td>
<td>0.009</td>
</tr>
<tr>
<td>DM</td>
<td>385(32%)</td>
<td>84 (27%)</td>
<td>89 (29%)</td>
<td>90 (29%)</td>
<td>122 (40%)</td>
<td>0.002</td>
</tr>
</tbody>
</table>
Baseline phosphate and survival

Adjusted for eGFR, Age, Gender, Hb, Diabetes, CVD, proteinuria, PTH

Mean follow-up 4.3 years

Hazard ratio 1.8

$P = 0.04$

n=946    n=810    n=624    n=375    n=136
12mth time-average $\text{PO}_4$ survival

Adjusted for eGFR, Age, Gender, Hb, Diabetes, CVD, proteinuria, PTH

Mean follow-up 3.6 years

<table>
<thead>
<tr>
<th>Phosphate Range</th>
<th>Hazard Ratio</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1.01</td>
<td>2.12</td>
<td>0.01</td>
</tr>
<tr>
<td>1.02-1.16</td>
<td>2.59</td>
<td>0.006</td>
</tr>
<tr>
<td>1.17-1.34</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;1.34</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

n=810  n=622  n=375  n=136
Survival according to KDOQI phosphate guidelines

Below Target
In Target
Above Target

Hazard ratio:
In target 1.9 (0.9-4.0) P = 0.08
Above target 2.6 (1.1-6.2) P = 0.03
CRISIS and Phosphate : Conclusions

- Serum phosphate is associated with mortality in non-dialysis CKD patients
- Risk of mortality observed even with [phosphate] within previous (2008) guidelines
- Results of biomarker and genomic studies awaited
Sevelamer Carbonate
(Renvela®)
Background: Sevelamer

- Renvela® (sevelamer carbonate) is a buffered form of Renagel® (sevelamer hydrochloride)

- Sevelamer has been shown in numerous studies in CKD patients on dialysis to
  
  - Effectively control serum phosphorus
  - Be associated with fewer episodes of hypercalcemia and a lower incidence of iPTH oversuppression than Ca-based binders
  - Have a favorable effect on lipid profile

- Sevelamer has also been shown to be associated with less progression of coronary artery calcification

CKD=Chronic Kidney Disease; iPTH=intact Parathyroid Hormone
Structure of Renagel® Versus Renvela®

- Same polymer backbone: Retains similar phosphate-binding capacity
- Salt change: Potentially improves buffering capacity

Structures adapted from Renagel and Renvela Package Inserts.
Renvela®: Significance of Improving Buffering Capacity

- Low bicarbonate levels are common in CKD patients, regardless of phosphate binder choice.
- Removal of hydrochloride from Renagel® and the addition of carbonate from Renvela® to the GI tract may facilitate maintaining bicarbonate levels within recommended KDOQI ranges.


Efficacy and tolerability of Renvela®:
evidence from 4 studies

- Efficacy and tolerability compared to Sevelamer hydrochloride in haemodialysis patients
  
  *(Delmez J, Clin Nephrol 2007)*

- Efficacy in non-dialysis CKD patients
  
  *(Ketteler M, CJASN 2008)*

- Efficacy of Renvela® powder
- Efficacy of once daily Renvela® powder
Renvela® Equivalence Study:

A Randomized Double-Blind, Crossover Design Study of Sevelamer Hydrochloride (Renagel®) and Sevelamer Carbonate (Renvela®) in Patients on Hemodialysis

Renvela® Equivalence Study

Study Objectives

- The objectives of the study were to compare Renvela® with Renagel® on the control of serum phosphorus and tolerability in CKD patients on HD.

- The effects of Renvela and Renagel on serum lipid profiles and bicarbonate levels were also compared.

Renvela® Equivalence Study

Study Design

Multicenter, Double-blind, Randomized, Crossover Study

- Starting dose of Renvela or Renagel was based on most recently prescribed dose of Renagel during run-in period
- Stable doses of cinacalcet and vitamin D were maintained throughout the study

Allocated to SH/SC Sequence (n=39)  
- Never received study med. (N=1)  
Completed SC Treatment (n = 39)  
- Never received study med. (N=1)  
Completed SH Treatment (n = 35)  
- Adverse event (N=4)  
- Discontinued between Treatment Periods (N=1)  
- Lost to follow-up (N=1)  
Completed Washout Period (N=21)  
- Missing lab data (N=1)

Allocated to SC/SH Sequence (N=40)  
Completed SC Treatment (n = 39)  
- Adverse event (N=1)  
- Other (N=1)  
- Withdrew consent (N=12)  
Completed Washout Period (N=19)  
- Non-compliance (N=1)  
- Investigator decision (N=2)  
- Other (N=1)  
- Missing lab data (N=2)

Randomized (n=79)
## Renvela® Equivalence Study
### Baseline Demographics and Renal History

<table>
<thead>
<tr>
<th>Gender</th>
<th>N = 78</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>40 (51%)</td>
</tr>
<tr>
<td>Female</td>
<td>38 (49%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Race</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>American Indian or Alaska native</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Black or African American</td>
<td>52 (67%)</td>
</tr>
<tr>
<td>White</td>
<td>21 (27%)</td>
</tr>
<tr>
<td>Other</td>
<td>4 (5%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age (years)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>58.1 ± 12.3</td>
</tr>
<tr>
<td>Range</td>
<td>29 – 88</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Primary cause of CKD</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>18 (23%)</td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>7 (9%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>33 (42%)</td>
</tr>
<tr>
<td>Polycystic kidneys</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>Hydronephrosis</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Interstitial nephritis</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Other</td>
<td>16 (21%)</td>
</tr>
</tbody>
</table>

| Currently on Vitamin D Analogue | 67 (86%) |

<table>
<thead>
<tr>
<th>Time on Dialysis (years)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>4.4 ± 4.9</td>
</tr>
<tr>
<td>Range</td>
<td>0.3 – 23.4</td>
</tr>
</tbody>
</table>

# Renvela® Equivalence Study

## Baseline Laboratories (Mean ± SD)

<table>
<thead>
<tr>
<th></th>
<th>Renvela® (N=73)</th>
<th>Renagel® (N=78)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phosphorus (mg/dL)</td>
<td>4.6 ± 1.09</td>
<td>4.6 ± 1.13</td>
</tr>
<tr>
<td>Calcium (mg/dL)</td>
<td>9.3 ± 0.67</td>
<td>9.3 ± 0.66</td>
</tr>
<tr>
<td>Calcium x Phosphorus (mg²/dL²)</td>
<td>42.9 ± 10.19</td>
<td>42.4 ± 10.70</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>3.8 ± 0.31</td>
<td>3.8 ± 0.31</td>
</tr>
<tr>
<td>iPTH (pg/mL)*</td>
<td>245</td>
<td>249</td>
</tr>
</tbody>
</table>

*iPTH is presented as median.

### Renvela® Equivalence Study

#### Efficacy Results

<table>
<thead>
<tr>
<th></th>
<th>Renvela® (mean ± SD)</th>
<th>Renagel® (mean ± SD)</th>
<th>Geometric LS Mean Ratio (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=56</td>
<td>N=56</td>
<td></td>
</tr>
<tr>
<td>mg/dL</td>
<td>4.6 ± 0.9</td>
<td>4.7 ± 0.9</td>
<td>0.99 (0.95 – 1.03)*</td>
</tr>
</tbody>
</table>

*90% CI for the ratio is within the interval 0.80-1.25
LS=Least Square

Renvela® Equivalence Study
Effect of Treatment on Serum Lipids

All baseline values are post-5-weeks run-in on Renagel.

### Renvela® Equivalence Study - Follow up: Additional Laboratory Parameters*

<table>
<thead>
<tr>
<th>Laboratory Parameter</th>
<th>Renvela® (mean ± SD) N=73</th>
<th>Renagel® (mean ± SD) N=78</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium (mg/dL)</td>
<td>9.3 ± 0.53</td>
<td>9.4 ± 0.70</td>
</tr>
<tr>
<td>Calcium x Phosphorus (mg²/dL²)</td>
<td>45.0 ±11.40</td>
<td>45.6 ±11.81</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>3.9 ± 0.27</td>
<td>3.9 ± 0.30</td>
</tr>
<tr>
<td>iPTH (pg/mL)†</td>
<td>297</td>
<td>258</td>
</tr>
</tbody>
</table>

*Data on file at Genzyme.
†iPTH is presented as median.
**Renvela® Equivalence Study**

**Effect of Treatment on Serum Bicarbonate**

*Wilcoxon signed rank test used to compare change from baseline within treatment.†Wilcoxon signed rank test used to compare change from baseline between treatments. All baseline values are post-5-weeks run-in on Renagel.

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![Graph showing effect of treatment on serum bicarbonate](image)

**Baseline**  
Renvela® (N=73)  
- Baseline: 21.1  
- Tx End: 22.4

**Baseline**  
Renagel® (N=78)  
- Baseline: 21.1  
- Tx End: 20.8

KDOQI

*P < 0.001

†P < 0.001

P = 0.833

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KDOQI Clinical Practice Guidelines for Bone Metabolism and Disease in Chronic Kidney Disease, Guideline 15 – Metabolic Acidosis.*
Renvela® Equivalence Study
Incidence of any GI Adverse Event

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Percentage of Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renvela®</td>
<td>73</td>
<td>20.5</td>
</tr>
<tr>
<td>Renagel®</td>
<td>78</td>
<td>35.9</td>
</tr>
</tbody>
</table>

*P=0.007

GI=Gastrointestinal
*McNemar’s Test

# Renvela® Equivalence Study

## Adverse Events*

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Renvela® N=73</th>
<th>Renagel® N=78</th>
<th>P-value†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients N (%)</td>
<td>Events N</td>
<td>Patients N (%)</td>
</tr>
<tr>
<td>Any Gastrointestinal Event</td>
<td>15 (20.5)</td>
<td>25</td>
<td>28 (35.9)</td>
</tr>
<tr>
<td>Nausea</td>
<td>7 (9.6)</td>
<td>9</td>
<td>10 (12.8)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>6 (8.2)</td>
<td>7</td>
<td>8 (10.3)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>2 (2.7)</td>
<td>3</td>
<td>5 (6.4)</td>
</tr>
<tr>
<td>GERD</td>
<td>1 (1.4)</td>
<td>1</td>
<td>4 (5.1)</td>
</tr>
<tr>
<td>Constipation</td>
<td>0 (0.0)</td>
<td>0</td>
<td>3 (3.8)</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>1 (1.4)</td>
<td>1</td>
<td>3 (3.8)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>2 (2.7)</td>
<td>2</td>
<td>1 (1.3)</td>
</tr>
</tbody>
</table>

*Occurring in ≥ 2% of patients; †McNemar’s Test.

GERD = Gastroesophageal Reflux Disease

Renvela® Equivalence Study
Conclusions

- Renvela® and Renagel® are equivalent in controlling serum phosphorus.
- Mean serum bicarbonate levels increased significantly (from 21.1 to 22.4 mEq/L) during treatment with Renvela but not during treatment with Renagel.
- Renvela and Renagel were both well tolerated.
- A significantly lower number of patients in the Renvela group experienced at least one GI adverse event.
- No treatment-related serious side effects were noted during the study.
- Lipid profiles in both groups were within KDOQI guidelines.

Efficacy and safety in CKD patients not on Dialysis

Sevelamer carbonate (Renvela) in patients in CKD stages 4-5

Ketteler M et al. CJASN 2008;3:1125–1130
Sevelamer carbonate (Renvela) in patients in CKD stages 4-5

Ketteler M et al. CJASN 2008;3:1125–1130
GFR for all patients (PPS – SVCARB00105)

Calculated GFR (C-G)

ml/min

Patient result

Ketteler M et al. CJASN 2008;3:1125–1130
Sevelamer carbonate (Renvela) in patients in CKD stages 4-5

Ketteler M et al. CJASN 2008;3:1125–1130
Sevelamer carbonate (Renvela) in patients in CKD stages 4-5

<table>
<thead>
<tr>
<th>Laboratory parameter (serum)</th>
<th>Pre-washout †</th>
<th>Baseline</th>
<th>Day 56/ET</th>
<th>Change from Baseline to Day 56/ET</th>
<th>P-value*</th>
<th>Post-washout</th>
<th>Change from Day 56 to Day 70</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bicarbonate (mEq/L)</td>
<td>---</td>
<td>16.6 ± 3.6</td>
<td>18.2 ± 3.7</td>
<td>1.3 ± 2.9</td>
<td>0.005</td>
<td>18.0 ± 3.6</td>
<td>-0.5 ± 3.5</td>
<td>0.326</td>
</tr>
<tr>
<td>Calcium (mg/dL)</td>
<td>9.1</td>
<td>8.5</td>
<td>8.8</td>
<td>0.3</td>
<td>&lt;0.001</td>
<td>8.6</td>
<td>-0.2</td>
<td>0.007</td>
</tr>
<tr>
<td>iPTH (pg/mL) median</td>
<td>208</td>
<td>341</td>
<td>319</td>
<td>-39</td>
<td>0.013</td>
<td>362</td>
<td>63</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>25-OH Vit D (ng/mL)</td>
<td>28.1 ± 18.8</td>
<td>28.9 ± 16.2</td>
<td>31.1 ± 12.9</td>
<td>2.0 ± 10.3</td>
<td>0.080</td>
<td>32.3 ± 13.7</td>
<td>0.2 ± 7.7</td>
<td>0.890</td>
</tr>
<tr>
<td>1,25 (OH)₂ Vit D (pg/mL)</td>
<td>---</td>
<td>25.4 ± 10.1</td>
<td>31.8 ± 12.1</td>
<td>5.3 ± 14.9</td>
<td>0.026</td>
<td>31.8 ± 11.7</td>
<td>-0.3 ± 14.4</td>
<td>0.942</td>
</tr>
</tbody>
</table>

Ketteler M et al. CJASN 2008;3:1125–1130
Acid base changes: sevelamer treated CKD patients

Sevelamer carbonate provides a differential of ~ +4mmol/L in serum bicarbonate in CKD patients not on dialysis in comparison with sevelamer hydrochloride.

<table>
<thead>
<tr>
<th>Phosphate Binder</th>
<th>CKD patients not on dialysis Change from baseline in serum bicarbonate level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sevelamer carbonate (SVCARB00105)</td>
<td>+1.3 ± 2.9 mmol/L*</td>
</tr>
<tr>
<td>Sevelamer hydrochloride (GTC-45-204)</td>
<td>−2.6 ± 4.6 mmol/L**</td>
</tr>
</tbody>
</table>

*8 weeks treatment, **12 weeks treatment
Renvela powder
Efficacy sevelamer carbonate powder (TID) vs sevelamer hydrochloride tablets (TID) in chronic kidney disease patients on haemodialysis

Fan, S et al. A randomized, crossover design study of sevelamer carbonate powder and sevelamer hydrochloride tablets in chronic kidney disease patients on haemodialysis. NDT; Advance Access; Aug.7 2009
Renvela powder delivers efficacy comparable to Renvela tablets

Control of serum phosphorus with sevelamer hydrochloride tablets vs sevelamer carbonate powder

Mean serum phosphorus (mg/dL)

- Sevelamer hydrochloride tablets (TID): 5.2
- Sevelamer carbonate powder (TID): 5.0

KDOQI* target† (3.5 to 5.5 mg/dL)

(n=31)

Efficacy once-daily sevelamer carbonate powder dosing vs trice-daily sevelamer hydrochloride tablet dosing in CKD patients on hemodialysis

Efficacy of sevelamer carbonate powder QD versus sevelamer hydrochloride tablets TID on serum phosphorus levels

Renvela® EU licence

Renvela® is indicated for the control of hyperphosphataemia in adult patients receiving haemodialysis or peritoneal dialysis.

Renvela® is also indicated for the control of hyperphosphataemia in adult patients with chronic kidney disease not on dialysis with serum phosphorus $\geq 1.78$ mmol/l.
Conclusions: Hyperphosphataemia in CKD patients

- Cross-sectional observational data shows a clear link between elevated [phosphate] and poor outcome

- Can we afford to ignore a high or increasing [phosphate] in CKD?

- Probably not – but are we increasing the adverse outcome risk with some treatments?

- Large interventional studies are necessary to clarify the efficacy of current and future treatments
Early management of phosphate regulation

Conclusions

- Sevelamer carbonate is a non-absorbable phosphate binder equivalent to sevelamer HCl in serum phosphorus control (tablets and powder)
- Sevelamer carbonate is acid/base-neutral
- Sevelamer carbonate is well-tolerated – associated with significantly reduced GI adverse events compared to sevelamer HCl
- Lipid profiles are favorable with sevelamer carbonate treatment
- Sevelamer carbonate is a safe and effective first choice for treatment of hyperphosphatemia in CKD patients on dialysis and **not on dialysis**