Effect of Patiromer in Patients 75 Years or Older with Diabetic Kidney Disease and Hyperkalemia Receiving a RAAS Inhibitor

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RESULTS

• The prevalence of hyperkalemia (HK) in the general population has been estimated at 2%–3%, and elderly patients are particularly susceptible to this electrolyte disturbance.1

• In older patients, a combination of age-associated reductions in glomerular filtration rate (GFR), diabetes, heart failure, and disturbances in the renin-angiotensin-aldosterone system (RAAS) lead to this predisposition.1,3

• Guideline-recommended RAAS inhibitors (RAASi) are indicated to slow the progression of diabetic kidney disease (DKD) regardless of age; however, patients with DKD are at a higher risk of developing HK, which may prevent the use of these life-saving medicines.4

• Patiromer is a sodium-free, non-absorbed, potassium (K⁺)-binding polymer approved for the treatment of HK in the United States,5 the European Union,5 Switzerland,6 and Australia,7 among others.

• Here we report the results of a subgroup, post hoc analysis of 60 patients aged ≥75 years with chronic kidney disease (CKD) or type 2 diabetes mellitus (T2DM) and HK who were treated with patiromer for ≥8 weeks in the therapeutic phase; 8 weeks of follow-up; and 52 weeks of maintenance therapy.8

Methods

• AMETHYST-ON was a multicenter, open-label trial of 305 randomized patients aged 30–84 years with chronic kidney disease (CKD), type 2 diabetes mellitus (T2DM), and hypertension.

• Patients who were normokalemic (serum K⁺=4.3–5.0 mEq/L) at screening entered a run-in period (up to 4 weeks) and either switched from their current RAASi to maximum labeled dose RAASi/100 mg/day losartan and/or up to 50 mg/day spironolactone (cohort 1) or continued their current RAASi and added spironolactone (cohort 2).

• Patients who developed mild HK (serum K⁺=5.0–5.5 mEq/L) or moderate HK (serum K⁺≥5.5–6.0 mEq/L) during run-in were eligible to be randomized to three separate patiromer starting dose cohorts (Figure 1).

• All patients were on a RAASi during the treatment and maintenance phases.

Figure 1. AMETHYST-ON STUDY DESIGN

| Screening | Assess Baseline | Randomization | Treatment | Long-term therapy | Long-term therapy | Study Visit | FU+28 days | FU+52 weeks | ET
| --- | --- | --- | --- | --- | --- | --- | --- | --- | ---
| Split | Split | Split | Split | Split | Split | Split | Split | Split | Split

Cohort 1

• Mean age of 77 years, 50% male population, mean GFR=42 mL/min/1.73m², and ~40% with NYHA class 3 or 4 heart failure (Table 1).

• 20% of patients in cohort 1 and received an optimal dose of losartan spironolactone for blood pressure control and the remainder were in cohort 3 and continued their current RAASi (Table 1).

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Figure 2. ACHIEVEMENT OF NORMOKALEMIA

<table>
<thead>
<tr>
<th>% of Patients in Normal Range (3.8–5.6 mEq/L)</th>
<th>Cohorts 1–3</th>
<th>Cohort 1</th>
<th>Cohort 2</th>
<th>Cohort 3</th>
<th>Cohort 1</th>
<th>Cohort 2</th>
<th>Cohort 3</th>
</tr>
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<tbody>
<tr>
<td>Week 0</td>
<td>75%</td>
<td>69%</td>
<td>75%</td>
<td>75%</td>
<td>75%</td>
<td>75%</td>
<td>75%</td>
</tr>
<tr>
<td>Week 2</td>
<td>95%</td>
<td>98%</td>
<td>95%</td>
<td>95%</td>
<td>95%</td>
<td>95%</td>
<td>95%</td>
</tr>
<tr>
<td>Week 4</td>
<td>95%</td>
<td>98%</td>
<td>95%</td>
<td>95%</td>
<td>95%</td>
<td>95%</td>
<td>95%</td>
</tr>
<tr>
<td>Week 8</td>
<td>95%</td>
<td>98%</td>
<td>95%</td>
<td>95%</td>
<td>95%</td>
<td>95%</td>
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</table>

CONCLUSIONS

• Patiromer reduced and maintained serum K⁺ to ≤5.0 mEq/L in most (>75%) diabetic CKD patients with HK.

• The majority of patients taking the guideline-recommended dose of losartan (cohort 1) were maintained at that dose through 52 weeks.

• Patiromer was well tolerated with a low rate of adverse events.

• Mean serum calcium and magnesium remained within normal limits through 52 weeks of the study.

LIMITATIONS

• There was a lack of blinding, which may have affected data reporting through observer bias.

• There was a lack of a comparator, which raises the possibility of regression to the mean.

Table 3. SERUM CALCIUM AND MAGNESIUM OVER 52 WEEKS

<table>
<thead>
<tr>
<th>Week</th>
<th>Serum Calcium (mg/dL)</th>
<th>Mean</th>
<th>SD</th>
<th>Mean</th>
<th>SD</th>
<th>Mean</th>
<th>SD</th>
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<tbody>
<tr>
<td>0</td>
<td>9.5±0.3</td>
<td>9.2±0.3</td>
<td>9.3±0.2</td>
<td>9.2±0.2</td>
<td>9.5±0.3</td>
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<td>9.5±0.3</td>
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<tr>
<td>28</td>
<td>9.5±0.3</td>
<td>9.2±0.3</td>
<td>9.3±0.2</td>
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<td>9.2±0.3</td>
<td>9.5±0.3</td>
</tr>
<tr>
<td>52</td>
<td>9.5±0.3</td>
<td>9.2±0.3</td>
<td>9.3±0.2</td>
<td>9.2±0.2</td>
<td>9.5±0.3</td>
<td>9.2±0.3</td>
<td>9.5±0.3</td>
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</table>

Supported by Relypsa, Inc., a Vifor Pharma Group Company.