Patients with chronic kidney disease (CKD) are at an increased risk of hyperkalemia (HK), which is associated with increased risk of cardiovascular events and mortality.1,2 HK (serum K+ >5 mmol/L) results from abnormal HK homeostasis, mainly due to impaired renal excretion.3

Traditional HK binders, such as sodium polystyrene sulphonate or calcium polystyrene sulphonate (SPS/CPS), are unpalatable and poorly tolerated by patients and have been associated with gastrointestinal (GI) side effects.3,4

Adherence to these HK binders is therefore typically low.3

An estimated total of 420 patients will be recruited. A minimum of 60 patients (30 dialysis, 30 non-dialysis) will be recruited from each of seven countries: United States, Canada, Spain, Italy, Germany, France, and Sweden (Figure 3).

Figure 1. APPETIZE study design

All participants will independently taste each product (A, B, and C = SPS/CPS, SPC, and CPSA) in one of six randomized sequences.

Prevalent HK, with K+ >5 mmol/L

Figure 2. Inclusion and key exclusion criteria

Inclusion criteria

- 18 years old
- HK, defined as K+ ≥7.0 mmol/L measured twice ≥90 days apart
- Prevalent HK, with K+ >5 mmol/L
- No change in prescribed HK treatment within 2 weeks of randomization (Figure 4).  

Key exclusion criteria

- Known medical conditions, including K+ values that require urgent medical attention
- Pregnancy
- Unable to hold oral medications

Primary endpoints may be explored per region and over all regions

Figure 3. Participating countries

Objectives

- APPETIZE will evaluate three currently available K+ binders: SPS/CPS, calcium polystyrene-sodium sulfonate (SPS/CPS), and sodium polystyrene sulfonate (SPS/CPS).
- The primary objective is to compare patient-reported overall taste scores (0–10) between SPS/CPS and CPSA, and between SPS/CPS and SPS/CPS.

Study design

- APPETIZE is a non-interventional, exploratory, Phase 4, single-blind, cross-sectional, randomized, cross-over study.
- Patients will be randomized to one of six tasting sequences; all will be blinded to the product being tasted (Figure 1).
- A sip and spit taste-test approach3 will be utilized where patients will be presented with a single dose of each product to taste test. Patients will not ingest the products.
- Doses given are consistent with typical daily recommended maintenance doses:
  - SPS/CPS: 15 g per 60 mL water
  - SPC: 5 g for patients on dialysis and 10 g for patients not on dialysis per 45 mL water
  - CPSA: 8.4 g per 80 mL water.

Rationale for study design

- The cross-over design will increase precision of the effect estimate compared with a parallel design and ensure that eventual carry-over effects are sufficiently mitigated by the selected 6 sequences.
- Patients with CKD and HK were selected for inclusion to replicate as close as possible to the approved label in the real-world scenario as possible, increasing external validity of the study. These medications are indicated for HK and hence the population of interest in this study are those patients who have CKD with prevalent HK.

Patients

- All patients are required to have CKD (either dialysis-dependent and non-dialysis dependent) with HK (Figure 2).
- It is intended that equal proportions of patients ever-treated and never-treated with K+ binders will be included.
- An estimated total of 420 patients will be recruited. A minimum of 60 patients (30 dialysis, 30 non-dialysis) will be recruited from each of seven countries: United States, Canada, Spain, Italy, Germany, France, and Sweden (Figure 3).

Outcomes

- Electronic clinical outcome assessments will be used to compare SPS/CPS and CPSA vs SPS/CPS (Figure 4).
- Patient scoring (taste, texture, smell, and mouthfeel) will be assessed on a 0–10 scale.
- Emotional response will be assessed using the AdSAM tool to evaluate feelings (Appeal, Engagement, and Empowerment) towards patient-centric attributes (taste, texture, smell, and mouthfeel).
- Preferential ranking will be performed after all three products have been tested.

Figure 4. Key study outcomes

Figure 3. Participating countries

Table 1. Study design

<table>
<thead>
<tr>
<th>1. Prevalent HK, defined as K+ ≥7.0 mmol/L measured twice ≥90 days apart</th>
<th>2. Prevalent HK, with K+ &gt;5 mmol/L</th>
<th>3. Known medical conditions, including K+ values that require urgent medical attention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>Overall taste</td>
<td>Scoring preference for taste, texture, smell, and mouthfeel</td>
</tr>
<tr>
<td>Secondary</td>
<td>Emotional response (Appeal, Engagement, and Empowerment) to taste</td>
<td>Preference scoring and emotional response for willingness to take each product</td>
</tr>
<tr>
<td>Exploratory</td>
<td>Overall preference ranking (1, 2, or 3) of the products based on emotional strength index</td>
<td></td>
</tr>
<tr>
<td>Safety</td>
<td>Descriptive safety measures including adverse events and laboratory assessments</td>
<td></td>
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</tbody>
</table>

Conclusions

- Utilizing innovative methodology, APPETIZE will generate evidence intended for patients and physicians regarding patient palatability and patient preference for currently available K+ binders.
- Initial results are anticipated towards the end of quarter 1 of 2021.

References


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