Introduction

- International guidelines recommend renin-angiotensin-aldosterone system inhibitor (RAASi) therapy at the maximal tolerated dose to optimize benefit in chronic kidney disease (CKD) and heart failure (HF). 1-3
- RAASi therapy increases the risk of hyperkalemia (HK), which is perceived as a barrier to achieving guideline-directed dosing of RAASi therapy. 4, 5
- Guidelines recommend novel potassium (K) binders, such as sodium zirconium cyclosilicate (SZC), to manage HK and facilitate continued RAASi therapy. 6-8
- This multi-country, observational cohort study compared the likelihood of maintained or stabilized (or up-titrated) RAASi therapy at 6 months following an HK episode, among patients with CKD and HF treated with SZC for at least 120 days, relative to those receiving no K binder prescription.

Methods

Data sources and study population

- Data were retrospectively collected from hospital records and health claims in the US (Optum’s de-identified Clininformatics® Data Mart database), Japan (Medical Data Vision), and Spain (BIG Data Mart database), July 2019 for the US, May 2020 for Japan, and June 2021 for Spain.
- The observational post-index period became available in the respective country: July 2019 for the US, May 2020 for Japan, and June 2021 for Spain.
- The study included two cohorts of patients who experienced an HK episode:
  - The SZC cohort included patients who were issued or dispensed a prescription for SZC and had at least 120 days of continuous SZC treatment. The index date was the date of the first SZC prescription.
  - The No K binder cohort included patients with a recorded inpatient or outpatient HK episode (ICD-10 code E87.9), without prescription for any K binder during the 180 days before the index date. The index date was the discharge date of an HK inpatient episode or the date of an outpatient HK visit.
- Patients included were adults with CKD (without hemodialysis) and HF, with an outpatient prescription for RAAS therapy within 120 days pre-index.

- Propensity score (PS) matching was applied to balance the SZC cohort to the No K binder cohort on baseline characteristics.
- The proportions of patients in each cohort who up-titrated, stabilized, down-titrated, or discontinued RAASi therapy were meta-analyzed across countries using a random effects model on logit transformed proportions. Logistic regression analysis was performed to compare the odds of maintained (stabilized or up-titrated) RAASi therapy at 6 months in the SZC cohort versus the No K binder cohort; country-level meta-results were generated using a random effects model.

Results

- Baseline patient demographics and characteristics of the PS-matched SZC and No K binder cohorts are shown in Table 1.

Table 1. Patient characteristics of the PS-matched SZC and No K binder cohorts at baseline

<table>
<thead>
<tr>
<th></th>
<th>SZC (n=565)</th>
<th>No K binder (n=600)</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>72 ± 10</td>
<td>72 ± 10</td>
<td>1 (0.99-1.02)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>249 (44)</td>
<td>254 (42)</td>
<td>0.99 (0.88-1.12)</td>
</tr>
<tr>
<td>Female</td>
<td>316 (56)</td>
<td>346 (58)</td>
<td>1 (0.91-1.09)</td>
</tr>
<tr>
<td>CHD</td>
<td>545 (97)</td>
<td>631 (81)</td>
<td>1.26 (1.09-1.46)</td>
</tr>
<tr>
<td>HF</td>
<td>198 (35)</td>
<td>209 (35)</td>
<td>1 (0.93-1.09)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>148 (79)</td>
<td>165 (79)</td>
<td>1.09 (0.93-1.28)</td>
</tr>
<tr>
<td>Recurrent HK episode</td>
<td>522 (93)</td>
<td>628 (81)</td>
<td>1.34 (1.14-1.56)</td>
</tr>
</tbody>
</table>

- At 180 days post-index, 68.9% (US), 79.9% (Japan), and 69.6% (Spain) of patients in the SZC cohorts, and 53.1% (US), 56.0% (Japan), and 48.3% (Spain) of patients in the No K binder cohorts had maintained their RAASi therapy.

RAASi treatment

- Meta-analyzed across countries (Figure 1), the proportions of patients who:
  - Discontinued RAASi were lower in the SZC than in the No K binder cohort.
  - Down-titrated RAASi were similar in the SZC and the No K binder cohort.
  - Stabilized and up-titrated RAASi were higher in the SZC cohort than the No K binder cohort.

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- In the US, Japan, and Spain, respectively, the odds ratios (95% confidence interval [CI]) for maintained RAASi therapy were 2.02 (1.65-2.46), 3.14 (2.58-3.82), and 2.43 (1.46-4.46) for those treated with SZC versus those with no K binder treatment (Figure 2).

- Meta-analyzed across countries, the odds of maintained RAASi therapy at 6 months following a hyperkalemia episode, relative to patients with no K binder treatment.

- Those findings demonstrate the potential of a novel K binder treatment to facilitate maintained and guideline-concordant RAASi therapy following an episode of hyperkalemia to help achieve optimal treatment outcomes in patients with CKD or HF.

Disclosures

- All authors contributed to the manuscript. Medical writing support was provided by Shawn W. Fiskin (BIOinc) and editorial support was provided by Jessica Gallaher, BSc, both of CompleteMedica, London, UK.

References

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Conclusions

- In contemporary routine clinical practice across three countries, patients treated with SZC were substantially more likely to have maintained (stabilized or up-titrated) RAASi therapy at 6 months following a hyperkalemia episode, relative to patients with no K binder treatment.
- Those findings demonstrate the potential of a novel K binder treatment to facilitate maintained and guideline-concordant RAASi therapy following an episode of hyperkalemia to help achieve optimal treatment outcomes in patients with CKD or HF.

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