

Sodium Zirconium Cyclosilicate Corrects Hyperkalaemia Within 72 hours Among Outpatients With Severe Hyperkalaemia (Baseline Serum Potassium ≥ 6 mmol/L) Regardless of Renal Function Level or RAASi Use: Post Hoc Subgroup Analysis of a Phase 3 Trial

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Background and Aims:

Most patients with severe hyperkalaemia are treated in hospital settings and are often receiving renin–angiotensin–aldosterone system inhibitors (RAASi) and/or have chronic kidney disease. Sodium zirconium cyclosilicate (SZC) is an orally-administered, non-absorbable, inorganic, selective potassium (K⁺) binder for the treatment of adults with hyperkalaemia. We report time to achievement of normokalaemia by baseline RAASi use and estimated glomerular filtration (eGFR) level from a 12-month Phase 3 sub-study among outpatients with baseline serum K⁺ ≥ 6 mmol/L undergoing acute treatment up to 72 hours.

Method:

This international, multicentre, open-label, single-arm trial among adults with point-of-care (i-STAT) K⁺ ≥ 5.1 mmol/L included prespecified efficacy analyses by baseline serum K⁺ ≥ 6 mmol/L. During the acute phase (AP), patients received SZC 10 g three times a day from 24 up to 72 hours until normokalaemia (i-STAT K⁺ 3.5–5 mmol/L) was achieved, whereupon they entered maintenance treatment. In this analysis of the AP only, we report time to achievement of normokalemia (serum K⁺ 3.5–5 mmol/L) using the Kaplan-Meier (KM) method, mean change in serum K⁺ from baseline at 24 hours and distribution of change during the entire AP, and adverse events (AEs) by baseline RAASi use and eGFR level (<30 vs ≥ 30 mL/min/1.73m²).

Results:

Of 749 patients in the intention-to-treat AP population of the main study, 126 (16.8%) had baseline serum K⁺ ≥ 6 mmol/L, and the vast majority of these patients had achieved normokalaemia by 72 hours (KM estimated proportions 98.6% and 96.1% in the serum K⁺ <6 and ≥ 6 mmol/L groups, respectively).

Among patients with baseline serum K⁺ ≥ 6 mmol/L not on RAASi with an eGFR ≥ 30 mL/min/1.73m² (no RAASi/eGFR ≥ 30), KM estimated median time to normokalemia was fastest, 22.5 hours (95% Confidence Interval [CI]: 22.0, 68.3), followed by patients on RAASi with an eGFR ≥ 30 mL/min/1.73m² (RAASi/eGFR ≥ 30), 23.5 hours (95% CI: 22.6, 46.1), followed by patients not on RAASi with an eGFR <30 mL/min/1.73m² (no RAASi/eGFR <30), 45.2 hours (95% CI: 22.6, 46.6), and slowest among patients on RAASi with an eGFR <30 mL/min/1.73m² (RAASi/eGFR <30), 46.6 hours (95% CI: 45.7, 47.4). KM estimated proportions achieving normokalaemia at 24, 48 and 72 hours, respectively, were 57.1%, 69.4%, and 89.8% with no RAASi/eGFR

≥30; 54.9%, 73.0%, and 86.5% with RAASi/eGFR ≥30; 41.3%, 80.4%, and 100% with no RAASi/eGFR <30; and 25.4%, 75.8% and 100% with RAASi/eGFR <30.

Median/range/mean change serum K⁺ values at 24 hours were 4.9/4.3-6/-1.22, 5.1/3.8-6.2/-1.26, 5.3/4.7-6/-1.02, and 5.3/4-6.6/-1.00 mmol/L in the no RAASi/eGFR ≥30, RAASi/eGFR ≥30, no RAASi/eGFR <30, and RAASi/eGFR <30 groups, respectively. No patients with baseline serum K⁺ ≥6 mmol/L experienced an increase in serum K⁺ or hypokalaemia.

No AEs occurred in the no RAASi/eGFR ≥30 group. AEs occurred in 10.3% of patients in the RAASi/eGFR ≥30 group (n=1 each of myopia, nausea, urinary incontinence, and hypertension), 23.1% of patients in the no RAASi/eGFR <30 group (n=1 each of diarrhoea, urinary tract infection, and muscle spasms), and 8.7% of patients in the RAASi/eGFR <30 group (n=1 each of constipation, peripheral oedema, sinusitis, urinary tract infection, back pain, and skin ulcer). No AEs were serious or led to discontinuation.

Conclusion: Outpatient treatment with SZC rapidly normalized serum K⁺ among patients with baseline serum K⁺ ≥6 mmol/L with few adverse events. Although patients on RAASi and with an eGFR <30 mL/min/1.73m² normalized at a slower rate, these patients nevertheless achieved normokalaemia by 72 hours. Neither concomitant RAASi therapy nor eGFR level appear to limit achievement of normokalemia with SZC among this population of outpatients with high baseline serum K⁺ ≥6 mmol/L.