2019 ANNA NATIONAL SYMPOSIUM
APRIL 14-17 ~ HILTON ANATOLE, DALLAS, TX

Safety and Efficacy of Sodium Zirconium Cyclosilicate for Long-Term Treatment of Hyperkalemia in Patients with Chronic Kidney Disease: Results from an Open-label, Phase 3 Study

Simon Roger, MD, Renal Research, Gosford, Australia
Philip Lavin, PhD, Boston Biostatistics Research Foundation, Framingham, MA
Edgar Lerma, MD, UIC/Advocate Christ, Oak Lawn, IL
Peter A. McCullough, MD, Baylor University Medical Center, Dallas, TX
Javed Butler, MD, University of Mississippi, Jackson, MS
Bruce Spinowitz, MD, New York Hospital Queens, New York, NY
Stephan von Haehling, MD, University of Göttingen Medical School, Göttingen, Germany
Mikhail Kosiborod, MD, Saint Luke's Mid America Heart Institute, Kansas City, MO
Steven Fishbane, MD, Zucker School of Medicine at Hofstra/Northwell, Great Neck, NY
David Packham, MD, Melbourne Renal Research Group, Melbourne, Australia

Sodium zirconium cyclosilicate (SZC) is a potassium (K)-binder for treating hyperkalemia (HK). Patients with chronic kidney disease (CKD) are at high risk for HK. We compared the efficacy and safety of SZC in outpatients with HK (K≥5.1 mEq/L) and baseline (BL) eGFR<30 vs ≥30 ml/min/1.73 m² with data from an open-label, single-arm Phase 3 trial. Patients received 10g SZC TID for 24–72h (correction phase [CP]) until K 3.5–5.0mEq/L (normokalemia; measured by point-of-care device, iSTAT; serum K also measured) then SZC was titrated to K ≤5.0mEq/L for 12mo (maintenance phase [MP]) without restricting diet or RAASi use. A post hoc analysis of patients with baseline (BL) eGFR <30 or ≥30 mL/min/1.73 m² was performed. Patients with eGFR <30 (CP, n=289; MP, n=286) vs ≥30 (CP, n=453; MP, n=451) were male (57% vs 61%), had mean BL eGFR of 21 vs 64 mL/min/1.73 m², more diabetes (70% vs 58%) and used RAASi (73% vs 53%), β-blockers (55% vs 37%), diuretics (55% vs 37%) and calcium channel blockers (CCB; 49% vs 25%). Mean BL iSTAT K was 5.5 mmol/L for both groups. Of patients with eGFR <30, 82%, 84% and 100% achieved iSTAT normokalemia at 24, 48 and 72h, respectively vs 82%, 76% and 95% for eGFR ≥30. Completion rate for MP was 55% (n=158) for patients with eGFR <30 and 67% (n=303) for eGFR ≥30. Mean SZC dose from Day 15 on was higher for eGFR <30 vs ≥30 groups (9.4g vs 7.5g at 12mo). Serum K was decreased from CP baseline at all time points through 12 mo in both eGFR groups. Normokalemia by serum K was maintained through 12mo in both groups. Bicarbonate increased from BL to Day 8 for both groups (1.1 vs 1.0mmol/L; P<0.0001 for both) and the change was sustained in MP. AEs (83% vs 54%), serious AEs (31% vs 16%) and deaths (2% vs 0.7%) were greater in the eGFR <30 group. Common AEs, all more frequent in patients with eGFR <30, were hypertension, peripheral edema, urinary tract infection, nausea and constipation. Overall, oral outpatient SZC treatment normalized K in 72h, sustained normokalemia over 12mo, and had an acceptable safety profile in patients with eGFR <30. Higher AE rates for the eGFR <30 group may reflect more comorbidities, level of renal dysfunction or CCB use. SZC was effective and well-tolerated in outpatients with HK, including CKD patients with eGFR <30.

Abstract selected for presentation at ANNA National Symposium, Dallas, 2019