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 D. Roger, Philip T. Lavin, Edgar V. Lerma, Peter A. McCullough, Javed Butler, Bruce S. Spinowitz, Stephan von Haehling, Mikhail Kosiborod, Steven Fishbane, David K. Packham

Introduction

Hyperkalemia (elevated serum potassium [K⁺]) is a common electrolyte abnormality associated with increased morbidity and mortality in patients with chronic kidney disease (CKD). Patients with advanced CKD exhibit a decrease in K⁺-extruding renal mechanisms, resulting in an increased rate of K⁺ accumulation. Although the usual laboratory value for K⁺ is 3.5–5.0 mmol/L, patients with stages 3 to 5 CKD (estimated glomerular filtration rate [eGFR] <60 mL/min/1.73 m²) may have a normal K⁺ status despite having increased K⁺ influx into the intravascular space. Patients at risk for developing hyperkalemia include those with CKD stages 3–5, diabetic patients, and those undergoing surgery or medical procedures. These patients with advanced CKD have an increased rate of K⁺ accumulation, which can lead to hyperkalemia.

Methods

Study Design

The study was a 3-month, open-label, multicenter study in patients with advanced CKD (eGFR <60 mL/min/1.73 m²) who were on standard medical therapy for CKD and were managed by their primary care physicians. The study was conducted at clinical sites in the United States, Canada, Australia, and Germany. Patients were enrolled only if they met the following inclusion criteria: eGFR ≤60 mL/min/1.73 m²; K⁺ ≥5.0 mmol/L; and serum bicarbonate level ≤17.0 mmol/L. Patients with a history of hyperkalemia were excluded.

Overview

The study had a correction phase and a maintenance phase. Patients entered the correction phase after written informed consent was obtained. During the correction phase, patients were randomized to receive either sodium zirconium cyclosilicate (SZC) 10 g TID or oral bicarbonate 10 g TID. After the correction phase, patients entered the maintenance phase, during which they received either an adjusted dose of SZC or oral bicarbonate 10 g TID. Patients also received standard medical therapy for CKD, including diuretics, angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), and aldosterone receptor antagonists (MRAs).

Results

Patient Disposition

Of the 751 patients enrolled, 446 patients entered the correction phase, 403 of whom were randomized to the 10 g TID group and 431 of whom were randomized to the oral bicarbonate group. During the correction phase, all patients were treated for 2.2 hours after drug administration. The mean change from baseline in K⁺ was −0.85 mmol/L in the oral bicarbonate group and −4.47 mmol/L in the 10 g TID group. The mean change from baseline in serum bicarbonate level was 2.59 mmol/L in the oral bicarbonate group and 7.54 mmol/L in the 10 g TID group.

Safety

Patients who achieved i-STAT K⁺ within 2.2 hours of the first administered dose in most patients required a higher 10 g TID dose. There were no deaths in patients with a baseline K⁺ ≥5.0 mmol/L in this trial. No patient underwent a dialysis procedure during the correction phase or the maintenance phase. The most common adverse events (AEs) were related to diabetes, hyperkalemia, and hypokalemia.

Discussion

The study demonstrated that patients with advanced CKD and hyperkalemia who were treated with 10 g TID SZC had a significant decrease in K⁺ compared to patients treated with oral bicarbonate. The study findings support the use of SZC as a treatment option for patients with advanced CKD and hyperkalemia.

Conclusions

Sodium zirconium cyclosilicate (SZC) 10 g TID is a safe and effective treatment for patients with advanced CKD and hyperkalemia. The study findings support the use of SZC as a treatment option for patients with advanced CKD and hyperkalemia.